Modul 4B Anhang 4-G

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Iptacopan (Fabhalta®)

Novartis Pharma GmbH

Modul 4B Anhang 4-G

***Nicht vorbehandelte** erwachsene Patienten mit PNH, die eine hämolytische Anämie aufweisen*

Ergänzende Analysen zu der Studie APPOINT-PNH (CLNP023C12301)

Stand: 26.06.2024

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1 Ergänzende Analysen zur Studie APPOINT-PNH zum primären Datenschnitt am 02.11.2022 (Hauptbehandlungsphase)

1.1 FACIT-Fatigue

1.1.1 Deskriptive Darstellung

Table 1-1: FACIT-Fatigue: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
FACIT-Fatigue	
	N' | Mean (SD)
Baseline	40 | 32.78 (10.17)
Day 7	36 | 35.61 (8.26)
Day 14	36 | 38.67 (8.25)
Day 42	39 | 41.26 (7.81)
Day 84	38 | 42.94 (5.98)
Day 126	35 | 43.03 (8.21)
Day 140	37 | 43.08 (7.47)
Day 154	36 | 43.56 (6.78)
Day 168	37 | 43.89 (6.24)
Day 126 - 168	**40 | 43.35 (6.46)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation

Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 02-Nov-2022

1.1.2 Änderung des FACIT-Fatigue Scores gegenüber Baseline mittels MMRM-Analyse zu verschiedenen Erhebungszeitpunkten

Table 1-2: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
FACIT-Fatigue	
	N' | LS Mean (SE)
Day 7	36 | 3.38 (1.06)
Day 14	36 | 6.13 (1.11)
Day 42	39 | 9.11 (1.19)
Day 84	38 | 10.56 (1.02)
Day 126	35 | 10.17 (1.33)
Day 140	37 | 10.81 (1.21)
Day 154	36 | 11.19 (1.16)
Day 168	37 | 11.94 (1.08)
Day 126 - 168	40 | 10.79 (1.07)

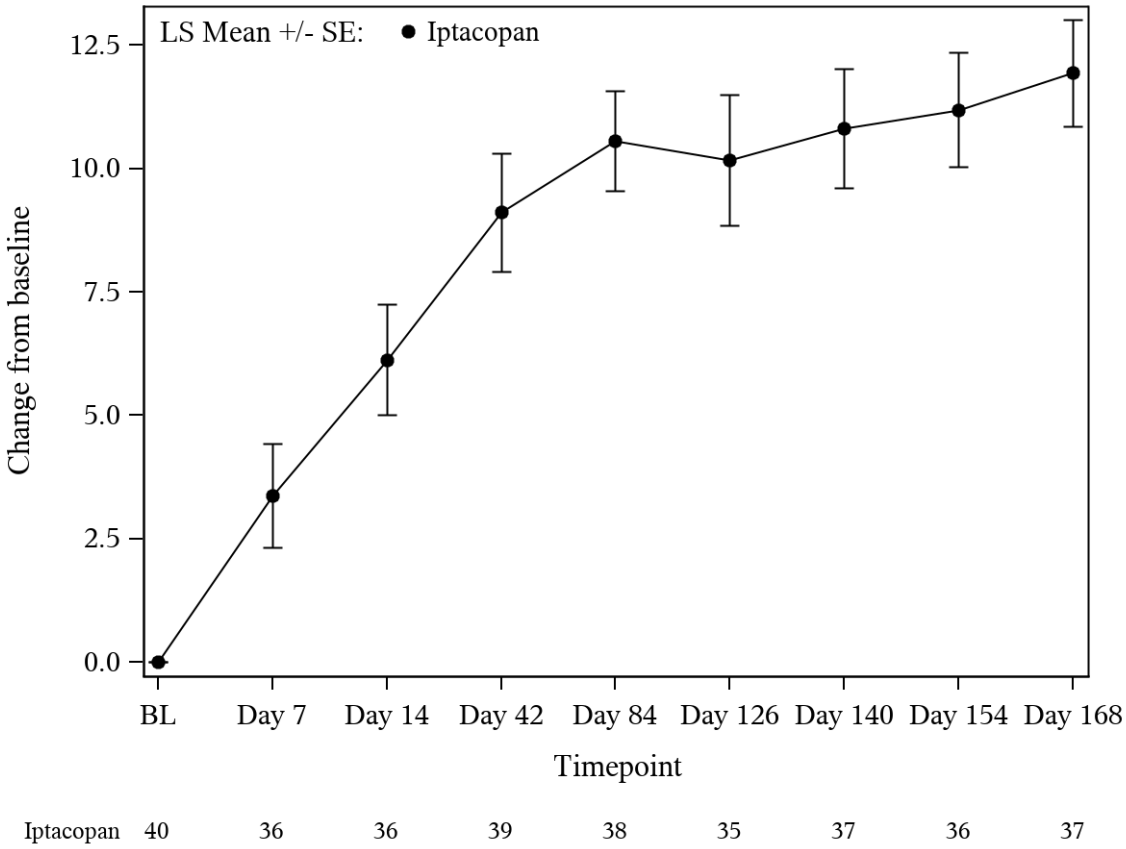
N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
LS Mean: Least square mean
SE: Standard error
MMRM: Mixed model for repeated measures

Analysis methods:
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
LS Means at Day 126 - 168 were calculated as linear function of the parameter estimates.

Patients with an evaluable baseline score and at least one evaluable post-baseline score were included in the analysis.

Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only.

Cut-off date for analysis: 02-Nov-2022



LS Mean: Least square mean; SE: Standard error
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-1: FACIT-Fatigue: line chart of least squares mean change from baseline (Full Analysis Set)

1.2 Symptomskalen des EORTC QLQ-C30

1.2.1 Deskriptive Darstellung

Table 1-3: EORTC QLQ-C30 Symptoms: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Fatigue	
	N' | Mean (SD)
Baseline	40 | 45.00 (24.39)
Day 14	36 | 31.48 (19.25)
Day 42	39 | 26.78 (21.13)
Day 84	38 | 25.44 (19.32)
Day 126	35 | 23.49 (20.13)
Day 140	37 | 24.02 (20.37)
Day 154	36 | 21.60 (16.58)
Day 168	37 | 21.92 (14.93)
Day 126 - 168	**40 | 23.17 (15.25)**
QLQ-C30 - Nausea and vomiting	
	N' | Mean (SD)
Baseline	40 | 8.96 (12.43)
Day 14	36 | 6.48 (10.75)
Day 42	39 | 3.85 (8.08)
Day 84	38 | 2.63 (9.11)
Day 126	35 | 4.29 (9.34)
Day 140	37 | 3.15 (11.68)
Day 154	36 | 2.78 (7.45)
Day 168	37 | 1.80 (6.55)
Day 126 - 168	**40 | 2.95 (5.49)**
QLQ-C30 - Pain	
	N' | Mean (SD)
Baseline	40 | 20.63 (18.49)
Day 14	36 | 13.89 (17.59)
Day 42	39 | 12.39 (20.13)
Day 84	38 | 10.09 (15.76)
Day 126	35 | 8.10 (15.32)
Day 140	37 | 6.31 (12.01)
Day 154	36 | 9.26 (14.61)
Day 168	37 | 10.81 (13.73)
Day 126 - 168	**40 | 8.72 (12.00)**

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Dyspnoea	
	N' | Mean (SD)
Baseline	40 | 29.58 (24.02)
Day 14	36 | 17.59 (18.66)
Day 42	39 | 17.95 (24.00)
Day 84	38 | 9.65 (15.32)
Day 126	35 | 15.24 (18.69)
Day 140	37 | 14.41 (21.57)
Day 154	36 | 11.11 (15.94)
Day 168	37 | 11.71 (17.94)
Day 126 - 168	**40 | 13.61 (16.55)**
QLQ-C30 - Insomnia	
	N' | Mean (SD)
Baseline	40 | 24.17 (25.86)
Day 14	36 | 18.52 (24.49)
Day 42	39 | 18.80 (23.93)
Day 84	38 | 17.54 (22.91)
Day 126	35 | 14.29 (20.27)
Day 140	37 | 20.72 (22.70)
Day 154	36 | 18.52 (23.16)
Day 168	37 | 14.41 (20.09)
Day 126 - 168	**40 | 16.74 (17.85)**
QLQ-C30 - Appetite loss	
	N' | Mean (SD)
Baseline	40 | 22.08 (23.08)
Day 14	36 | 9.26 (15.14)
Day 42	39 | 8.55 (14.75)
Day 84	38 | 5.26 (12.32)
Day 126	35 | 5.71 (12.75)
Day 140	37 | 8.11 (16.49)
Day 154	36 | 4.63 (11.69)
Day 168	37 | 5.41 (12.46)
Day 126 - 168	**40 | 6.25 (10.74)**

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Constipation	
	N' | Mean (SD)
Baseline	40 | 9.17 (13.58)
Day 14	36 | 12.04 (18.09)
Day 42	39 | 13.68 (18.29)
Day 84	38 | 11.40 (17.80)
Day 126	35 | 12.38 (21.52)
Day 140	37 | 7.21 (13.91)
Day 154	36 | 12.04 (16.24)
Day 168	37 | 12.61 (24.03)
Day 126 - 168	**40 | 11.39 (16.33)**
QLQ-C30 - Diarrhoea	
	N' | Mean (SD)
Baseline	40 | 6.67 (15.92)
Day 14	36 | 4.63 (14.15)
Day 42	39 | 7.69 (16.15)
Day 84	38 | 5.26 (12.32)
Day 126	35 | 5.71 (20.59)
Day 140	37 | 1.80 (7.64)
Day 154	36 | 5.56 (12.60)
Day 168	37 | 6.31 (15.39)
Day 126 - 168	**40 | 5.42 (11.93)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation

Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 02-Nov-2022

1.2.2 Änderung der Symptomskalen des EORTC QLQ-C30 gegenüber Baseline mittels MMRM-Analyse zu verschiedenen Erhebungszeitpunkten

Table 1-4: EORTC QLQ-C30 Symptoms: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Fatigue	
	N' | LS Mean (SE)
Day 14	36 | -12.83 (2.65)
Day 42	39 | -17.92 (3.22)
Day 84	38 | -18.96 (2.99)
Day 126	35 | -19.06 (3.33)
Day 140	37 | -20.55 (2.95)
Day 154	36 | -22.96 (2.39)
Day 168	37 | -23.42 (2.69)
Day 126 - 168	40 | -21.30 (2.30)
QLQ-C30 - Nausea and vomiting	
	N' | LS Mean (SE)
Day 14	36 | -2.67 (1.66)
Day 42	39 | -5.15 (1.35)
Day 84	38 | -6.88 (1.56)
Day 126	35 | -4.38 (1.55)
Day 140	37 | -5.68 (1.94)
Day 154	36 | -6.48 (1.36)
Day 168	37 | -6.70 (1.27)
Day 126 - 168	40 | -5.36 (0.99)
QLQ-C30 - Pain	
	N' | LS Mean (SE)
Day 14	36 | -7.45 (2.25)
Day 42	39 | -8.80 (3.27)
Day 84	38 | -10.64 (2.39)
Day 126	35 | -12.57 (2.61)
Day 140	37 | -14.43 (2.14)
Day 154	36 | -11.09 (2.35)
Day 168	37 | -10.65 (2.25)
Day 126 - 168	40 | -11.62 (1.96)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Dyspnoea	
	N' | LS Mean (SE)
Day 14	36 | -9.79 (2.51)
Day 42	39 | -10.13 (3.60)
Day 84	38 | -16.84 (3.00)
Day 126	35 | -11.10 (3.24)
Day 140	37 | -14.26 (3.68)
Day 154	36 | -16.72 (2.77)
Day 168	37 | -16.79 (3.23)
Day 126 - 168	40 | -14.58 (2.74)
QLQ-C30 - Insomnia	
	N' | LS Mean (SE)
Day 14	36 | -4.29 (3.07)
Day 42	39 | -4.87 (3.53)
Day 84	38 | -6.06 (3.42)
Day 126	35 | -6.72 (3.41)
Day 140	37 | -3.98 (3.49)
Day 154	36 | -5.33 (4.00)
Day 168	37 | -9.59 (3.27)
Day 126 - 168	40 | -6.12 (2.83)
QLQ-C30 - Appetite loss	
	N' | LS Mean (SE)
Day 14	36 | -14.71 (2.26)
Day 42	39 | -14.95 (2.36)
Day 84	38 | -17.55 (2.02)
Day 126	35 | -17.02 (2.34)
Day 140	37 | -16.35 (2.71)
Day 154	36 | -18.53 (1.99)
Day 168	37 | -18.75 (2.28)
Day 126 - 168	40 | -16.71 (1.75)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Constipation	
	N' | LS Mean (SE)
Day 14	36 | 1.53 (2.46)
Day 42	39 | 3.51 (2.84)
Day 84	38 | 1.05 (2.97)
Day 126	35 | 1.44 (3.39)
Day 140	37 | -2.67 (2.32)
Day 154	36 | 2.63 (2.47)
Day 168	37 | 1.75 (3.51)
Day 126 - 168	40 | 0.89 (2.13)
QLQ-C30 - Diarrhoea	
	N' | LS Mean (SE)
Day 14	36 | -1.85 (1.74)
Day 42	39 | 0.67 (1.79)
Day 84	38 | -0.95 (2.29)
Day 126	35 | -1.40 (3.44)
Day 140	37 | -4.89 (1.47)
Day 154	36 | -0.69 (2.10)
Day 168	37 | -0.87 (2.59)
Day 126 - 168	40 | -1.87 (1.82)

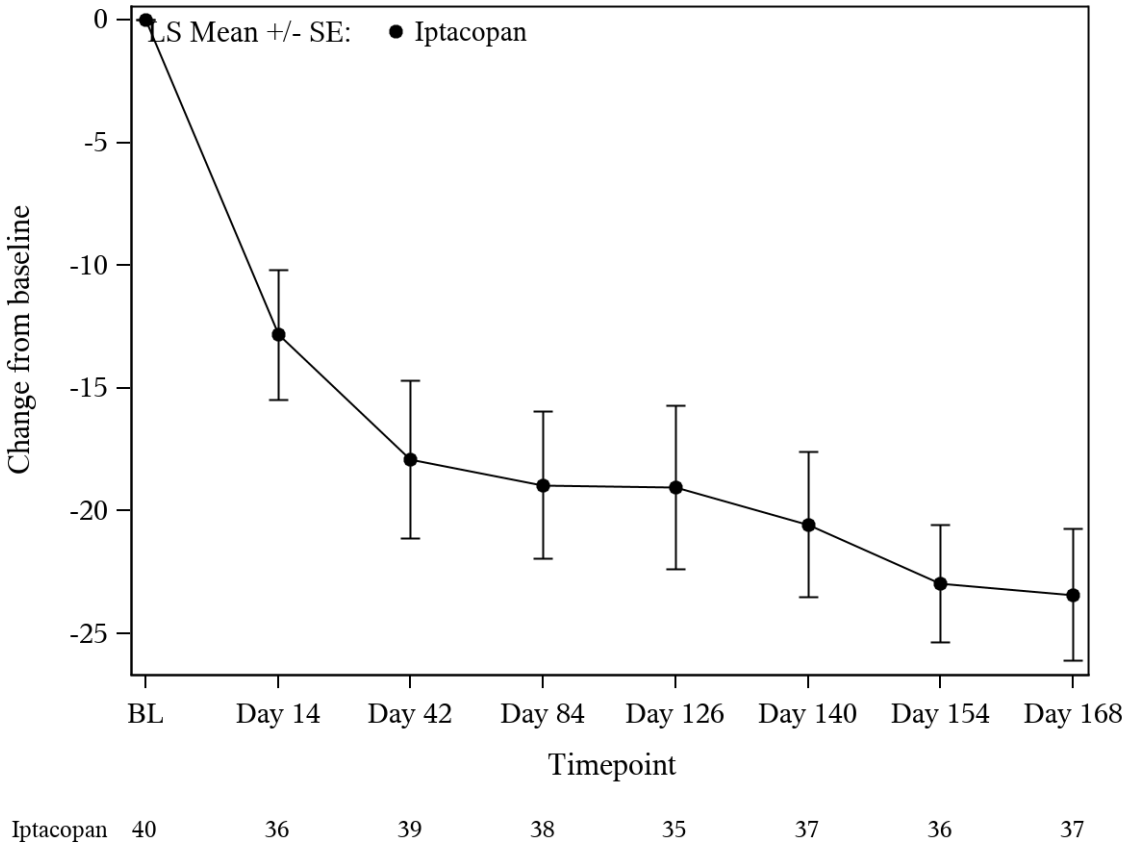
N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
LS Mean: Least square mean
SE: Standard error
MMRM: Mixed model for repeated measures

Analysis methods:
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
LS Means at Day 126 - 168 were calculated as linear function of the parameter estimates.

Patients with an evaluable baseline score and at least one evaluable post-baseline score were included in the analysis.

Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only.

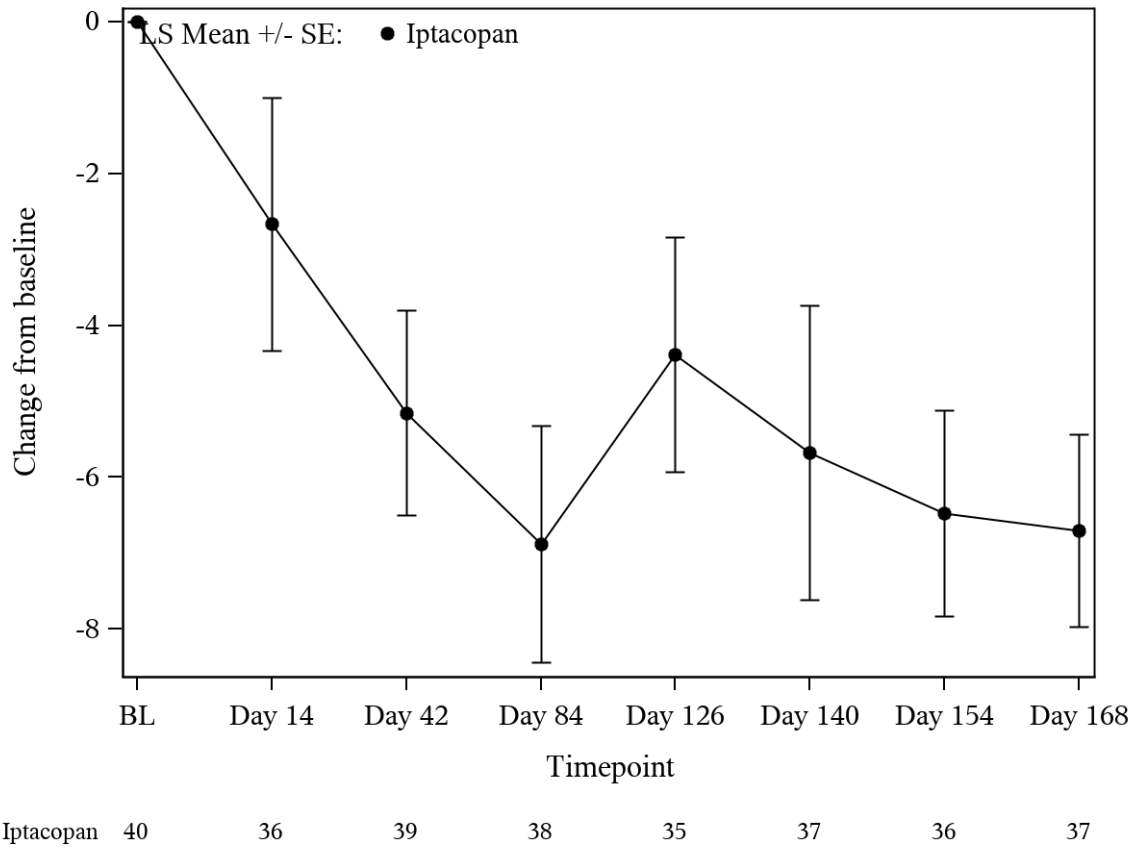
Cut-off date for analysis: 02-Nov-2022



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

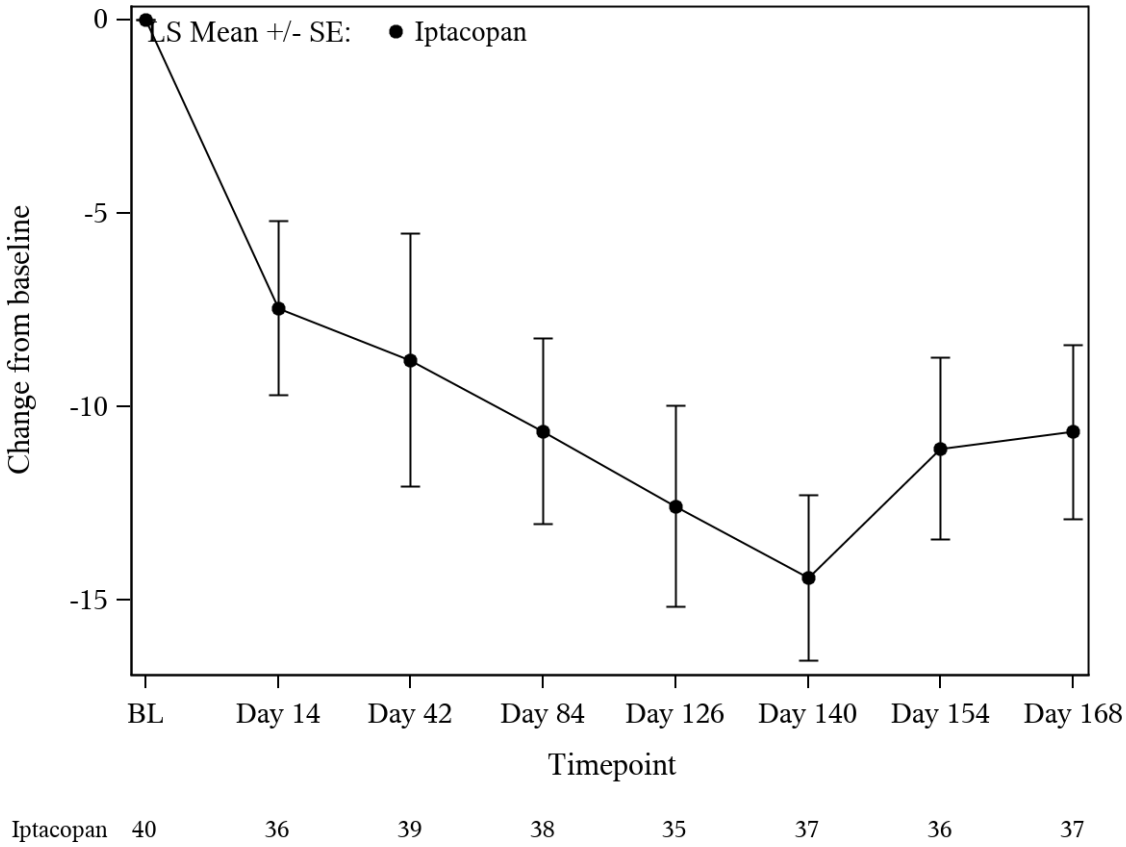
Figure 1-2: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Fatigue



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

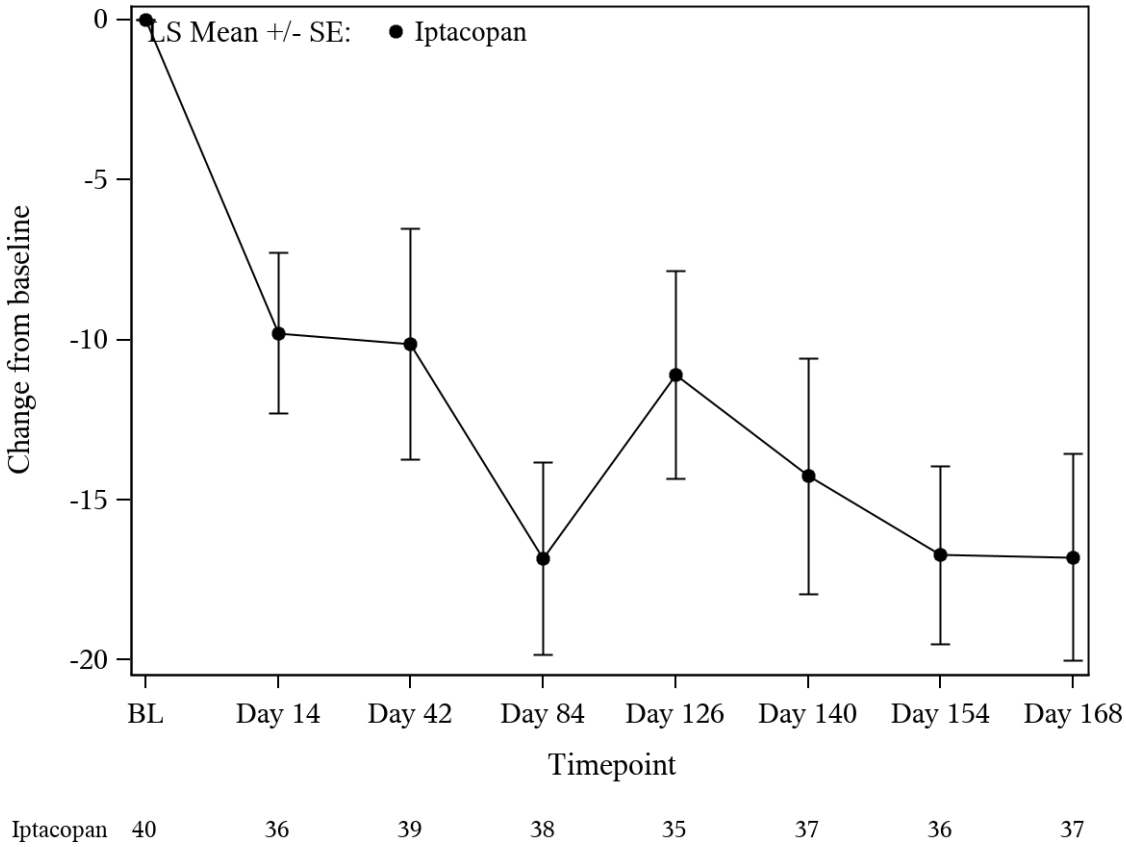
Figure 1-3: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Nausea and vomiting



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

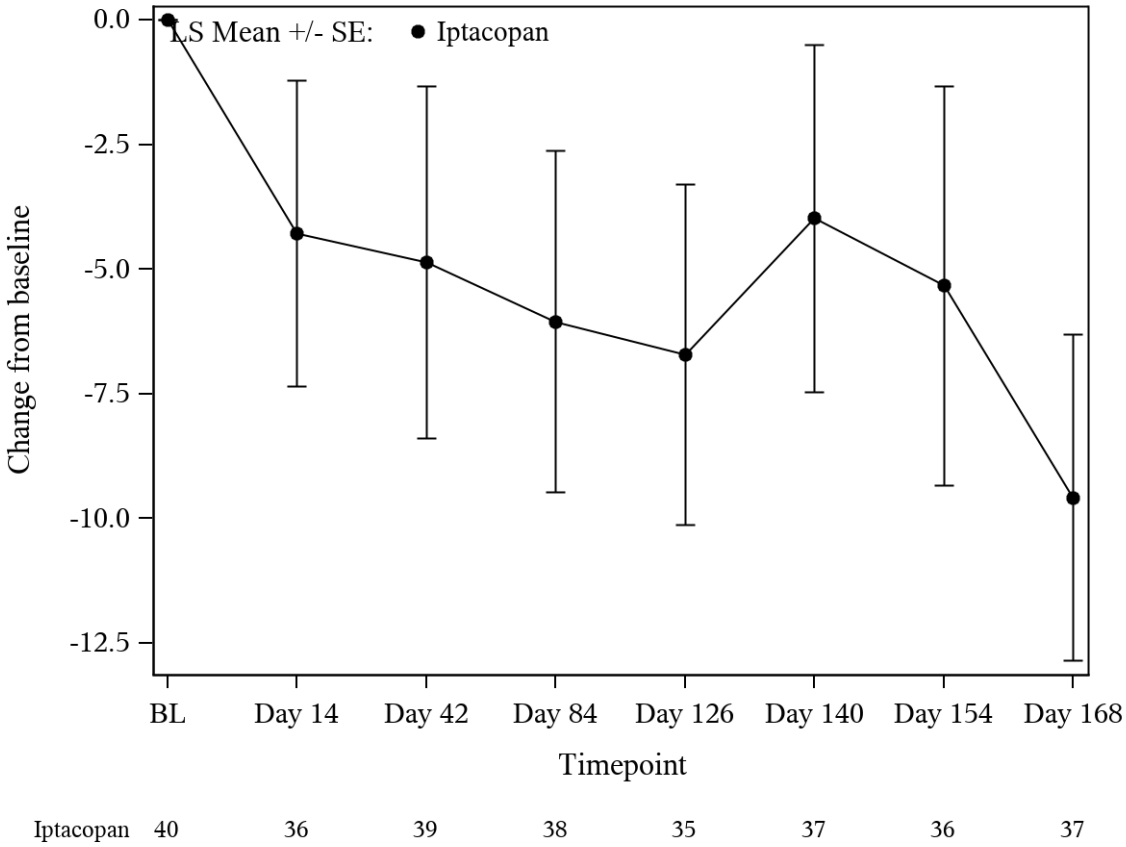
Figure 1-4: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Pain



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

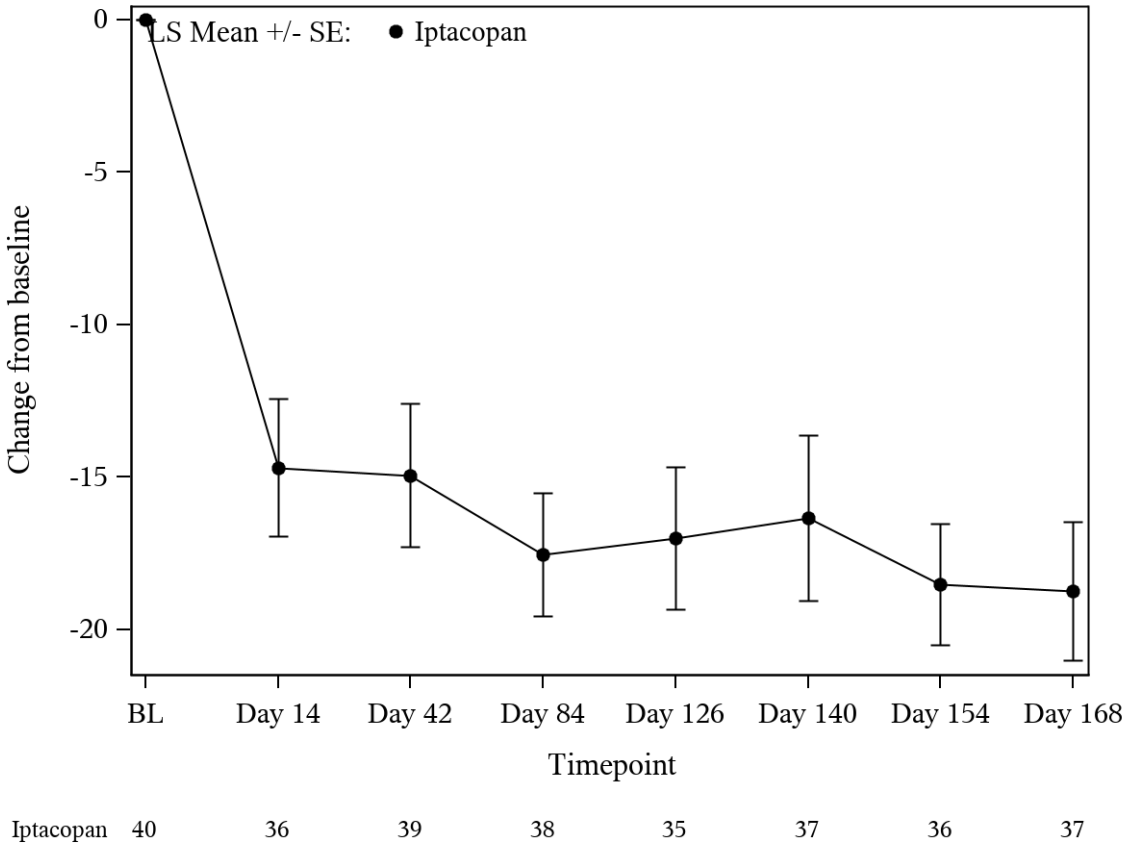
Figure 1-5: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Dyspnoea



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

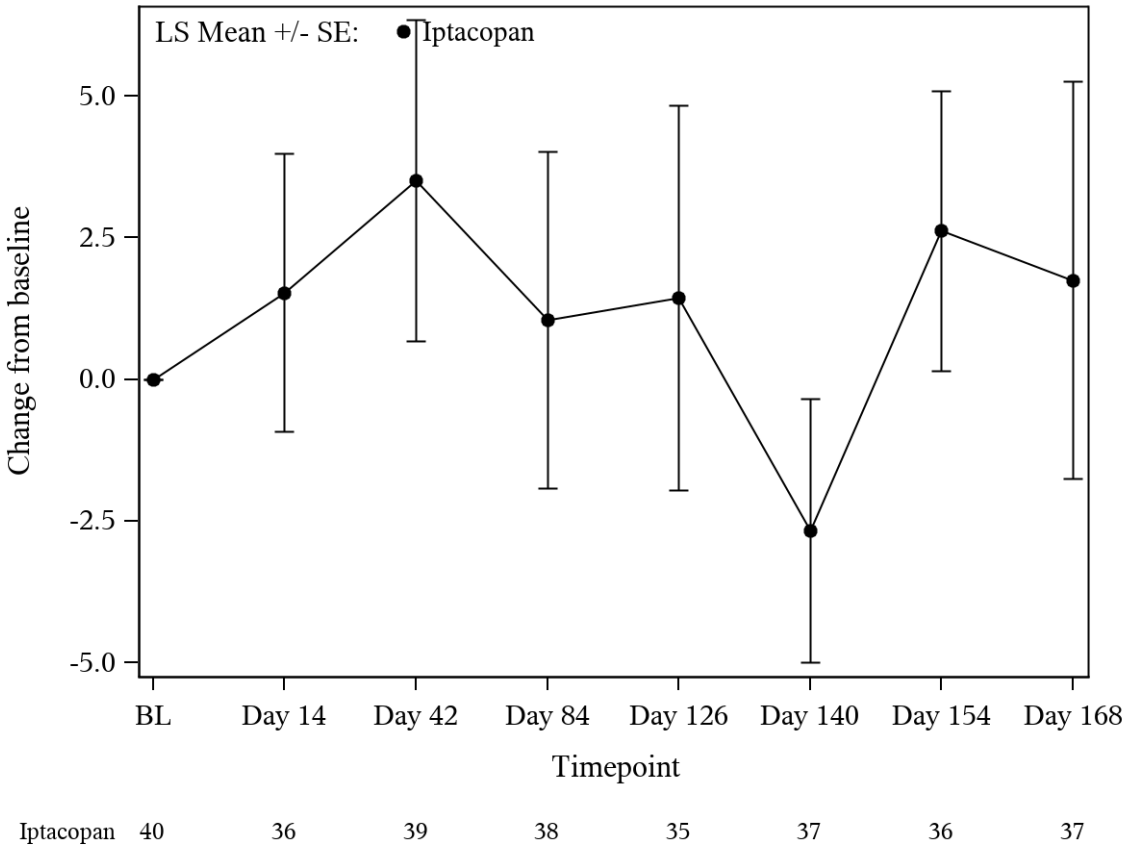
Figure 1-6: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Insomnia



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-7: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Appetite loss



LS Mean: Least square mean; SE: Standard error

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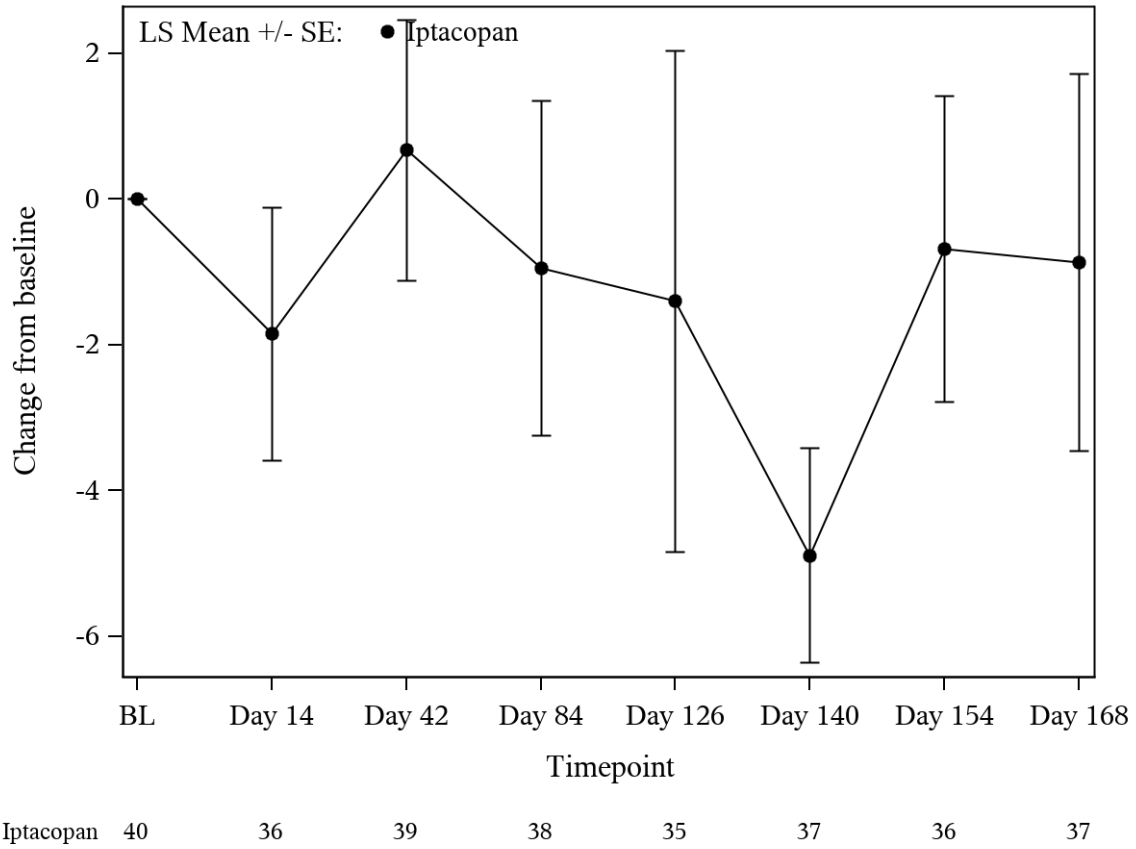
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-8: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Constipation



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-9: EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set) – Diarrhoea

1.3 Fatigue mittels PGIS

1.3.1 Deskriptive Darstellung

Table 1-5: PGIS: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
PGIS	
	N' | Mean (SD)
Baseline	40 | 1.73 (0.85)
Day 7	36 | 1.39 (0.77)
Day 14	36 | 1.11 (0.67)
Day 42	39 | 0.92 (0.77)
Day 84	38 | 0.66 (0.63)
Day 126	35 | 0.80 (0.72)
Day 140	37 | 0.86 (0.75)
Day 154	36 | 0.75 (0.65)
Day 168	37 | 0.76 (0.64)
Day 126 - 168	**40 | 0.80 (0.54)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation

Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

The ordinal scale was used for the nominal categories of the PGIS (No symptoms = 0, mild = 1, moderate = 2, severe = 3, very severe = 4).

Cut-off date for analysis: 02-Nov-2022

1.3.2 Änderung der PGIS gegenüber Baseline mittels MMRM-Analyse zu verschiedenen Erhebungszeitpunkten

Table 1-6: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
PGIS	
	N' | LS Mean (SE)
Day 7	36 | -0.27 (0.14)
Day 14	36 | -0.56 (0.11)
Day 42	39 | -0.78 (0.13)
Day 84	38 | -1.00 (0.11)
Day 126	35 | -0.86 (0.12)
Day 140	37 | -0.84 (0.13)
Day 154	36 | -0.94 (0.11)
Day 168	37 | -0.94 (0.12)
Day 126 - 168	40 | -0.89 (0.09)

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
LS Mean: Least square mean
SE: Standard error
MMRM: Mixed model for repeated measures

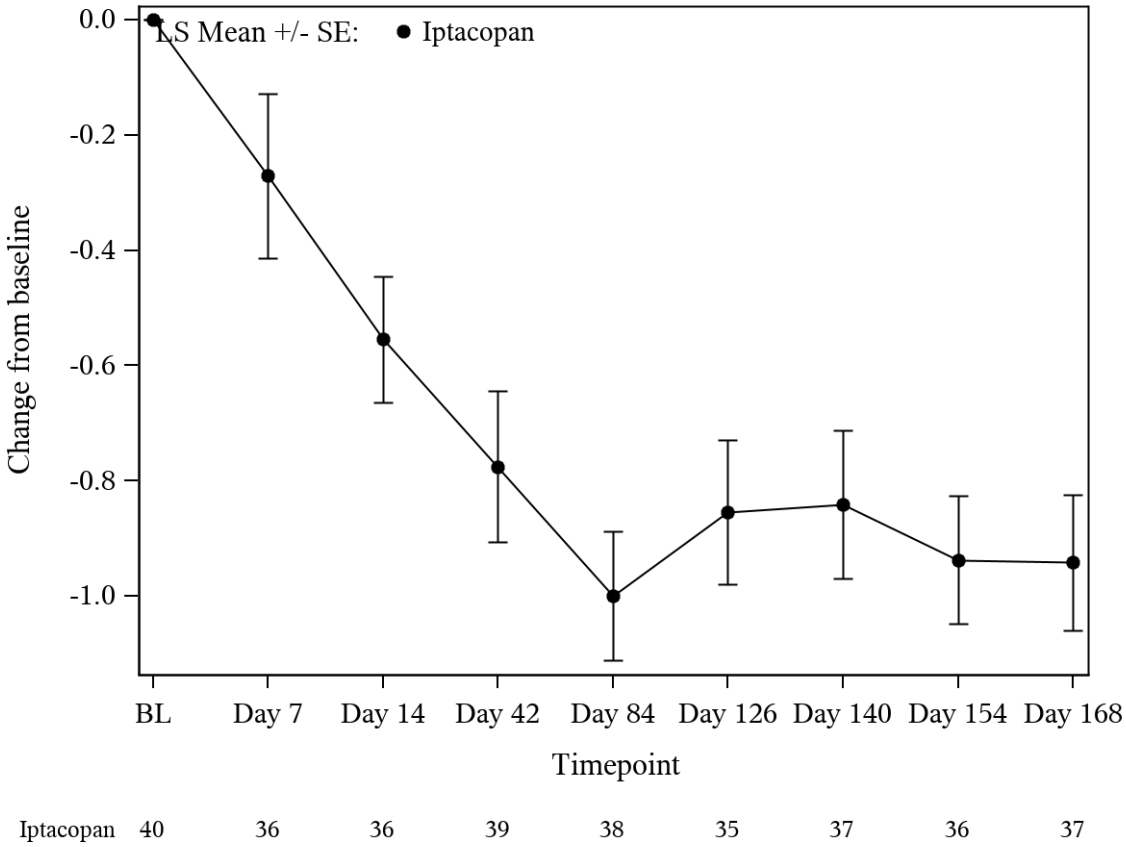
Analysis methods:
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
LS Means at Day 126 - 168 were calculated as linear function of the parameter estimates.

Patients with an evaluable baseline score and at least one evaluable post-baseline score were included in the analysis.

Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only.

The ordinal scale was used for the nominal categories of the PGIS (No symptoms = 0, mild = 1, moderate = 2, severe = 3, very severe = 4).

Cut-off date for analysis: 02-Nov-2022



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only.

The ordinal scale was used for the nominal categories of the PGIS (No symptoms = 0, mild = 1, moderate = 2, severe = 3, very severe = 4).
Cut-off date for analysis: 02-Nov-2022

Figure 1-10: PGIS: line chart of least squares mean change from baseline (Full Analysis Set)

1.4 EQ-5D VAS

1.4.1 Deskriptive Darstellung

Table 1-7: EQ-5D VAS: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
EQ-5D VAS	
	N' | Mean (SD)
Baseline	40 | 61.78 (19.39)
Day 14	35 | 70.83 (16.80)
Day 42	39 | 74.44 (15.68)
Day 84	38 | 79.74 (14.31)
Day 126	35 | 79.77 (16.92)
Day 140	37 | 80.00 (15.41)
Day 154	36 | 81.28 (13.78)
Day 168	37 | 81.16 (13.57)
Day 126 - 168	**40 | 80.68 (13.60)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation

Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 02-Nov-2022

1.4.2 Änderung des EQ-5D VAS Scores gegenüber Baseline mittels MMRM-Analyse zu verschiedenen Erhebungszeitpunkten

Table 1-8: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
EQ-5D VAS	
	N' | LS Mean (SE)
Day 14	35 | 7.98 (1.74)
Day 42	39 | 13.26 (2.38)
Day 84	38 | 18.36 (2.08)
Day 126	35 | 17.84 (2.33)
Day 140	37 | 17.86 (2.25)
Day 154	36 | 20.22 (1.93)
Day 168	37 | 20.97 (2.09)
Day 126 - 168	40 | 19.00 (1.90)

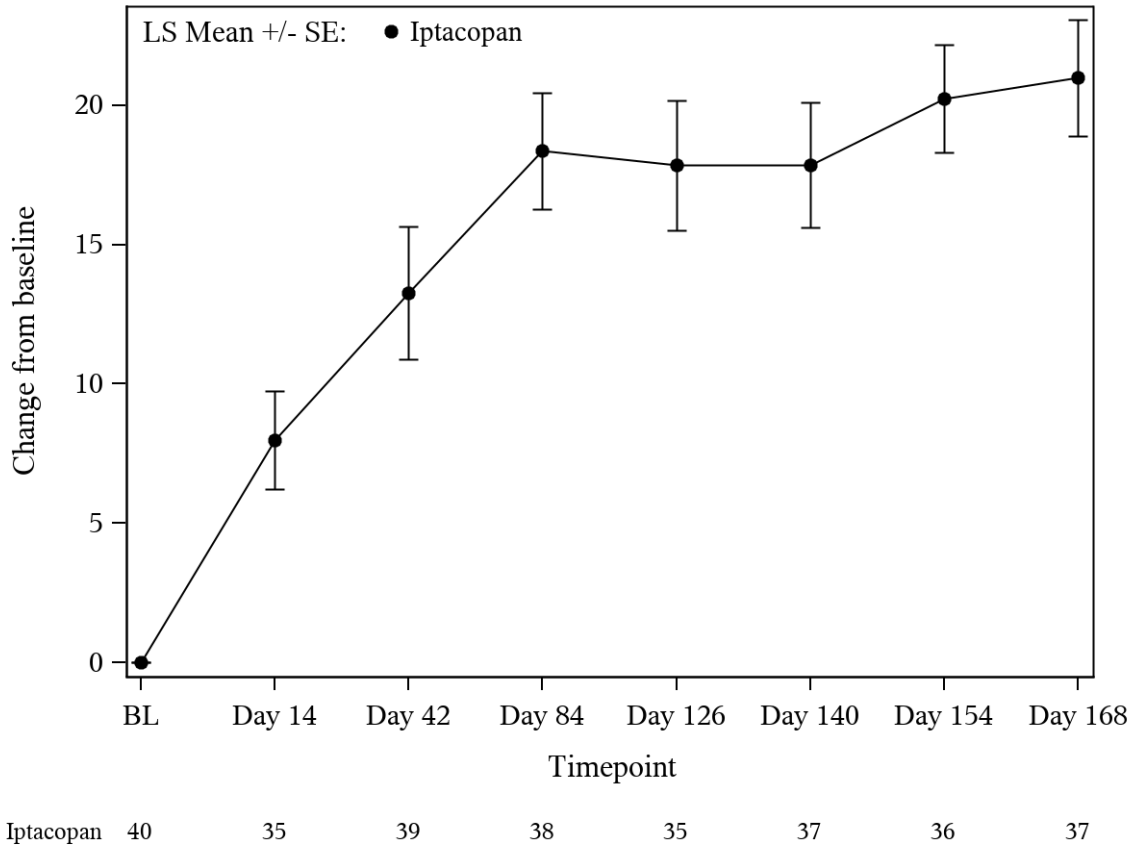
N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
LS Mean: Least square mean
SE: Standard error
MMRM: Mixed model for repeated measures

Analysis methods:
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
LS Means at Day 126 - 168 were calculated as linear function of the parameter estimates.

Patients with an evaluable baseline score and at least one evaluable post-baseline score were included in the analysis.

Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only.

Cut-off date for analysis: 02-Nov-2022



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-11: EQ-5D VAS: line chart of least squares mean change from baseline (Full Analysis Set)

1.5 Funktionsskalen und globale Gesundheits- und Lebensqualitätsskala des EORTC QLQ-C30

1.5.1 Deskriptive Darstellung

Table 1-9: EORTC QLQ-C30 QoL: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Global health status	
	N' | Mean (SD)
Baseline	40 | 52.92 (18.69)
Day 14	36 | 63.43 (17.96)
Day 42	39 | 70.94 (18.02)
Day 84	38 | 77.85 (15.04)
Day 126	35 | 77.86 (17.38)
Day 140	37 | 77.25 (16.97)
Day 154	36 | 75.23 (15.36)
Day 168	37 | 76.13 (14.85)
Day 126 - 168	**40 | 76.72 (14.42)**
QLQ-C30 - Physical functioning	
	N' | Mean (SD)
Baseline	40 | 72.67 (16.98)
Day 14	36 | 80.93 (13.16)
Day 42	39 | 85.64 (10.98)
Day 84	38 | 87.72 (8.42)
Day 126	35 | 87.43 (11.86)
Day 140	37 | 87.03 (11.96)
Day 154	36 | 89.26 (11.96)
Day 168	37 | 88.29 (11.91)
Day 126 - 168	**40 | 88.14 (10.26)**

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Role functioning	
	N' | Mean (SD)
Baseline	40 | 64.79 (24.35)
Day 14	36 | 74.07 (20.10)
Day 42	39 | 80.34 (19.82)
Day 84	38 | 84.21 (17.31)
Day 126	35 | 80.48 (23.04)
Day 140	37 | 84.23 (19.22)
Day 154	36 | 85.65 (19.17)
Day 168	37 | 86.49 (15.13)
Day 126 - 168	**40 | 84.62 (16.28)**
QLQ-C30 - Emotional functioning	
	N' | Mean (SD)
Baseline	40 | 69.38 (18.72)
Day 14	36 | 80.32 (20.62)
Day 42	39 | 80.98 (16.66)
Day 84	38 | 81.80 (20.67)
Day 126	35 | 81.43 (23.14)
Day 140	37 | 83.78 (19.93)
Day 154	36 | 82.41 (22.69)
Day 168	37 | 80.41 (22.33)
Day 126 - 168	**40 | 81.22 (22.10)**
QLQ-C30 - Cognitive functioning	
	N' | Mean (SD)
Baseline	40 | 72.71 (20.41)
Day 14	36 | 77.78 (19.11)
Day 42	39 | 79.06 (19.01)
Day 84	38 | 81.14 (19.05)
Day 126	35 | 78.57 (21.23)
Day 140	37 | 76.58 (21.68)
Day 154	36 | 77.78 (19.11)
Day 168	37 | 78.83 (21.75)
Day 126 - 168	**40 | 77.67 (19.91)**

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Social functioning	
	N' | Mean (SD)
Baseline	40 | 62.08 (24.02)
Day 14	36 | 65.28 (25.93)
Day 42	39 | 72.65 (23.72)
Day 84	38 | 76.75 (23.74)
Day 126	35 | 75.71 (23.69)
Day 140	37 | 77.93 (20.43)
Day 154	36 | 79.17 (21.22)
Day 168	37 | 78.38 (24.80)
Day 126 - 168	**40 | 77.88 (20.46)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation

Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 02-Nov-2022

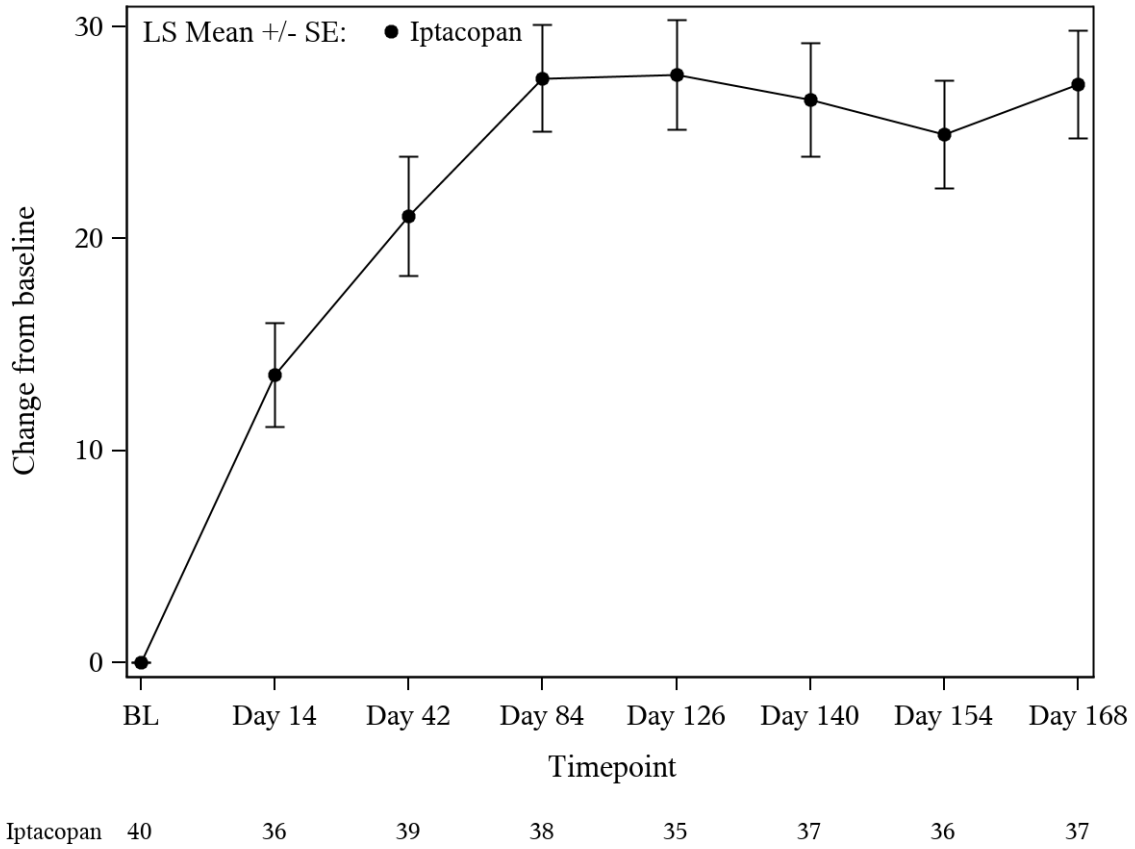
1.5.2 Änderung Funktionsskalen und der globalen Gesundheits- und Lebensqualitätsskala des EORTC QLQ-C30 gegenüber Baseline mittels MMRM-Analyse zu verschiedenen Erhebungszeitpunkten

Table 1-10: EORTC QLQ-C30 QoL: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Global health status	
	N' | LS Mean (SE)
Day 14	36 | 13.59 (2.45)
Day 42	39 | 21.05 (2.81)
Day 84	38 | 27.56 (2.52)
Day 126	35 | 27.74 (2.58)
Day 140	37 | 26.57 (2.67)
Day 154	36 | 24.92 (2.54)
Day 168	37 | 27.28 (2.54)
Day 126 - 168	40 | 26.16 (2.26)
QLQ-C30 - Physical functioning	
	N' | LS Mean (SE)
Day 14	36 | 8.36 (1.86)
Day 42	39 | 13.37 (1.60)
Day 84	38 | 15.39 (1.44)
Day 126	35 | 14.65 (1.72)
Day 140	37 | 15.50 (1.82)
Day 154	36 | 17.51 (1.88)
Day 168	37 | 16.77 (1.92)
Day 126 - 168	40 | 15.62 (1.54)
QLQ-C30 - Role functioning	
	N' | LS Mean (SE)
Day 14	36 | 7.66 (2.82)
Day 42	39 | 16.63 (2.97)
Day 84	38 | 19.75 (2.80)
Day 126	35 | 16.93 (3.28)
Day 140	37 | 20.10 (2.81)
Day 154	36 | 21.22 (2.63)
Day 168	37 | 23.38 (2.52)
Day 126 - 168	40 | 20.11 (2.31)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Emotional functioning	
	N' | LS Mean (SE)
Day 14	36 | 10.60 (2.94)
Day 42	39 | 12.58 (2.91)
Day 84	38 | 11.89 (3.17)
Day 126	35 | 10.87 (3.63)
Day 140	37 | 13.58 (3.36)
Day 154	36 | 12.54 (3.78)
Day 168	37 | 13.03 (3.55)
Day 126 - 168	40 | 12.24 (3.20)
QLQ-C30 - Cognitive functioning	
	N' | LS Mean (SE)
Day 14	36 | 7.35 (2.51)
Day 42	39 | 7.55 (2.64)
Day 84	38 | 10.85 (2.94)
Day 126	35 | 6.61 (3.25)
Day 140	37 | 5.34 (3.01)
Day 154	36 | 5.38 (2.96)
Day 168	37 | 8.05 (2.95)
Day 126 - 168	40 | 6.14 (2.74)
QLQ-C30 - Social functioning	
	N' | LS Mean (SE)
Day 14	36 | 4.41 (3.59)
Day 42	39 | 12.08 (3.47)
Day 84	38 | 16.53 (3.58)
Day 126	35 | 14.58 (3.54)
Day 140	37 | 17.90 (3.31)
Day 154	36 | 17.43 (3.73)
Day 168	37 | 19.19 (3.96)
Day 126 - 168	40 | 16.76 (3.09)

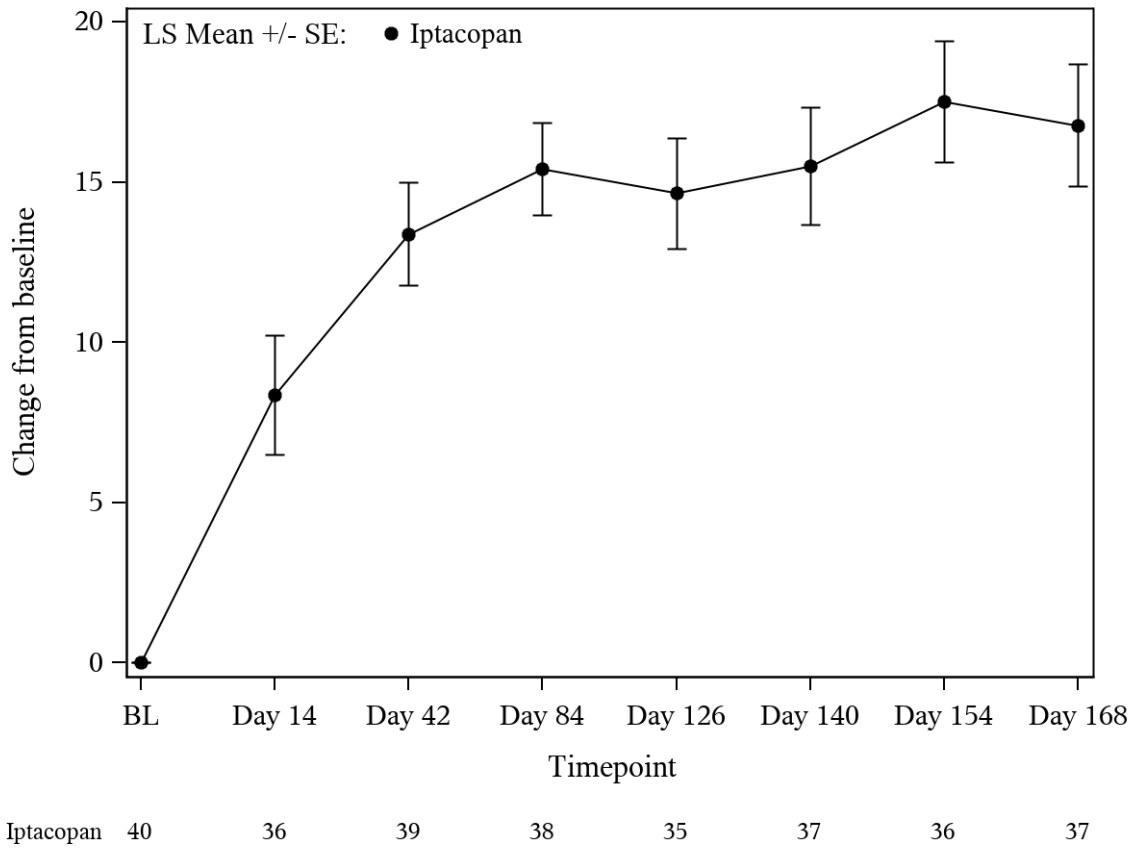
	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures Analysis methods: Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) LS Means at Day 126 - 168 were calculated as linear function of the parameter estimates. Patients with an evaluable baseline score and at least one evaluable post-baseline score were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

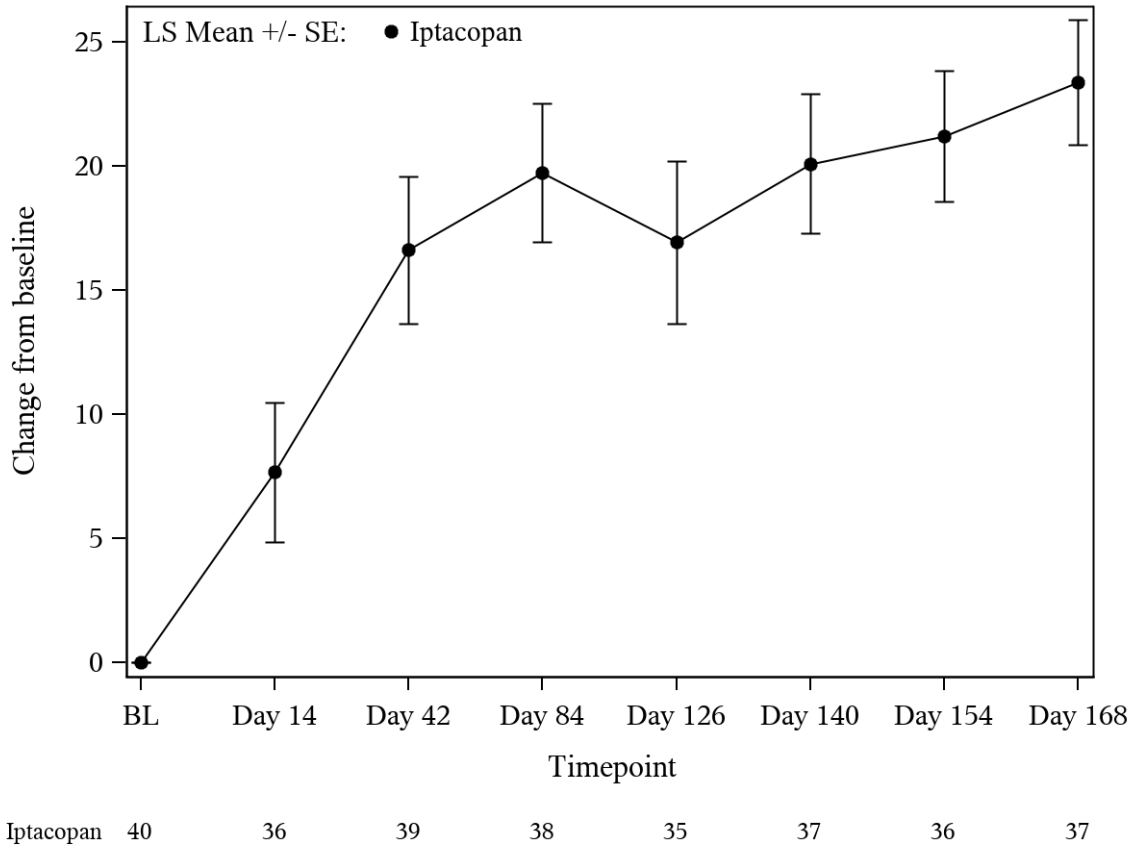
Figure 1-12: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Global health status



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

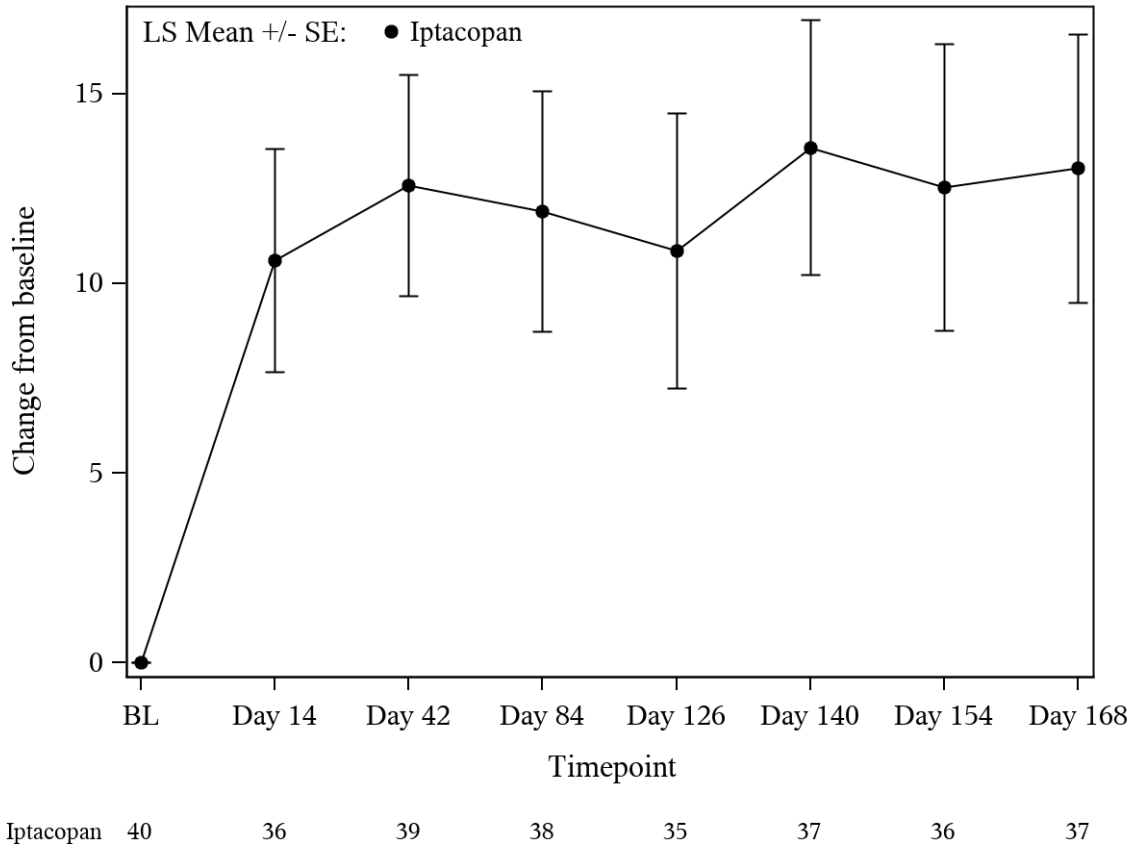
Figure 1-13: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Physical functioning



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

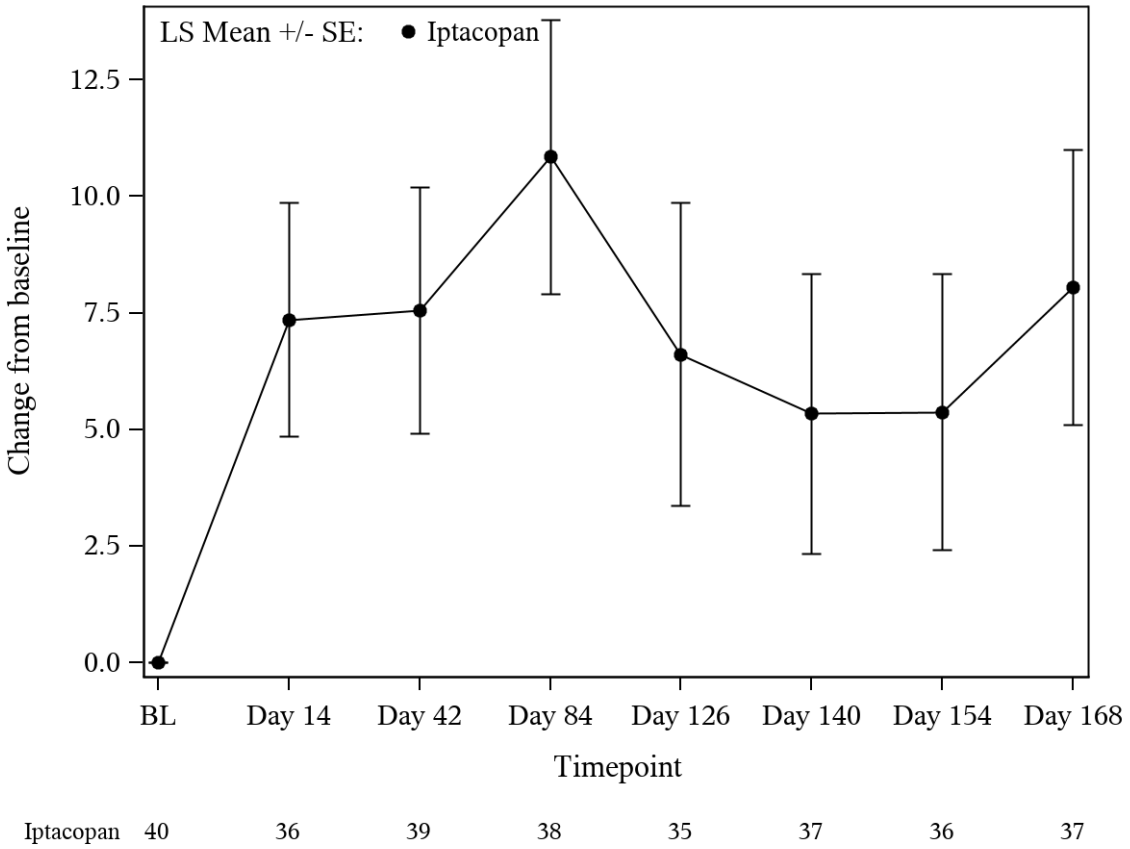
Figure 1-14: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Role functioning



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

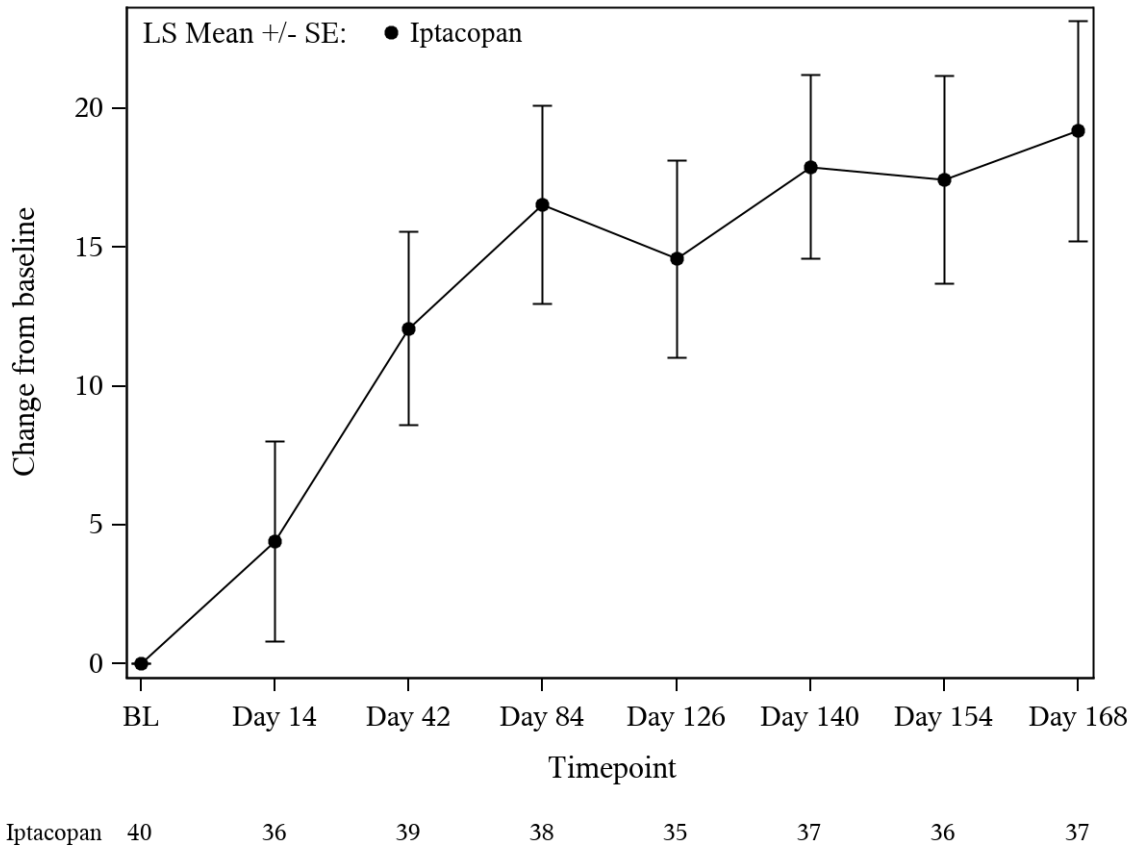
Figure 1-15: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Emotional functioning



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-16: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Cognitive functioning



LS Mean: Least square mean; SE: Standard error

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years)
Intercurrent events stemming from breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022

Figure 1-17: EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set) – QLQ-C30 – Social functioning

1.6 Verträglichkeit

1.6.1 Unerwünschter Ereignisse jeglichen Schweregrads nach SOC und PT

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Table 14.3.1-1.1a (Page 1 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Number of patients with at least one event	37 (92.5)
Blood and lymphatic system disorders	1 (2.5)
Neutropenia	1 (2.5)
Cardiac disorders	2 (5.0)
Sinus bradycardia	1 (2.5)
Tachycardia	1 (2.5)
Eye disorders	3 (7.5)
Cataract	2 (5.0)
Vision blurred	1 (2.5)
Gastrointestinal disorders	11 (27.5)
Diarrhoea	3 (7.5)

	LNP023 200mg b.i.d.
	N=40
Primary system organ class **Preferred term**	**n (%)**

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.

On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 2 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Abdominal pain	2 (5.0)
Constipation	2 (5.0)
Nausea	2 (5.0)
Vomiting	2 (5.0)
Abdominal pain upper	1 (2.5)
Chronic gastritis	1 (2.5)
Dyspepsia	1 (2.5)
Gastritis	1 (2.5)
Gastrooesophageal reflux disease	1 (2.5)
Haemorrhoidal haemorrhage	1 (2.5)
General disorders and administration site conditions	7 (17.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 3 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Pyrexia	2 (5.0)
Asthenia	1 (2.5)
Chest pain	1 (2.5)
Fatigue	1 (2.5)
Influenza like illness	1 (2.5)
Peripheral swelling	1 (2.5)
Hepatobiliary disorders	1 (2.5)
Hepatic function abnormal	1 (2.5)
Infections and infestations	16 (40.0)
COVID-19	6 (15.0)
Upper respiratory tract infection	5 (12.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 4 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Conjunctivitis	2 (5.0)
Gastrointestinal infection	1 (2.5)
Hordeolum	1 (2.5)
Influenza	1 (2.5)
Mucosal infection	1 (2.5)
Pneumonia bacterial	1 (2.5)
Rhinitis	1 (2.5)
Injury, poisoning and procedural complications	3 (7.5)
Contusion	1 (2.5)
Ligament sprain	1 (2.5)
Vaccination complication	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 5 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Investigations	12 (30.0)
Blood glucose increased	2 (5.0)
Amylase increased	1 (2.5)
Blood creatine phosphokinase increased	1 (2.5)
Blood creatinine increased	1 (2.5)
Blood follicle stimulating hormone increased	1 (2.5)
Blood magnesium decreased	1 (2.5)
Blood triglycerides increased	1 (2.5)
Blood uric acid increased	1 (2.5)
C-reactive protein increased	1 (2.5)
Dihydrotestosterone decreased	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 6 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Fibrin D dimer increased	1 (2.5)
Immunosuppressant drug level increased	1 (2.5)
Lipids abnormal	1 (2.5)
Protein urine present	1 (2.5)
Reverse tri-iodothyronine increased	1 (2.5)
Weight increased	1 (2.5)
White blood cell count increased	1 (2.5)
Metabolism and nutrition disorders	7 (17.5)
Iron deficiency	3 (7.5)
Hyperlipidaemia	2 (5.0)
Hyperglycaemia	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 7 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Hypomagnesaemia	1 (2.5)
Type 2 diabetes mellitus	1 (2.5)
Musculoskeletal and connective tissue disorders	4 (10.0)
Periarthritis	2 (5.0)
Osteoporosis	1 (2.5)
Pain in extremity	1 (2.5)
Nervous system disorders	13 (32.5)
Headache	11 (27.5)
Dizziness	1 (2.5)
Memory impairment	1 (2.5)
Psychiatric disorders	2 (5.0)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 8 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Bipolar disorder	1 (2.5)
Insomnia	1 (2.5)
Renal and urinary disorders	5 (12.5)
Renal impairment	2 (5.0)
Proteinuria	1 (2.5)
Renal disorder	1 (2.5)
Renal injury	1 (2.5)
Reproductive system and breast disorders	1 (2.5)
Dysmenorrhoea	1 (2.5)
Heavy menstrual bleeding	1 (2.5)
Menstrual disorder	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 9 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Respiratory, thoracic and mediastinal disorders	6 (15.0)
Epistaxis	2 (5.0)
Nasal congestion	2 (5.0)
Nasal dryness	1 (2.5)
Oropharyngeal pain	1 (2.5)
Sneezing	1 (2.5)
Skin and subcutaneous tissue disorders	7 (17.5)
Dermatitis allergic	2 (5.0)
Acne	1 (2.5)
Erythema multiforme	1 (2.5)
Haemorrhage subcutaneous	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.1a (Page 10 of 10)
Treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Pruritus	1 (2.5)
Rash maculo-papular	1 (2.5)
Skin discolouration	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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1.6.2 Unerwünschte Ereignisse nach SOC, PT und Schweregrad

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Table 14.3.1-1.20a (Page 1 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Number of patients with at least one event	26 (65.0)	10 (25.0)	1 (2.5)
Chest pain	0 (0.0)	0 (0.0)	1 (2.5)
Pneumonia bacterial	0 (0.0)	0 (0.0)	1 (2.5)
Dermatitis allergic	0 (0.0)	2 (5.0)	0 (0.0)
Headache	10 (25.0)	1 (2.5)	0 (0.0)
COVID-19	5 (12.5)	1 (2.5)	0 (0.0)
Upper respiratory tract infection	4 (10.0)	1 (2.5)	0 (0.0)
Diarrhoea	2 (5.0)	1 (2.5)	0 (0.0)
Abdominal pain	1 (2.5)	1 (2.5)	0 (0.0)
Conjunctivitis	1 (2.5)	1 (2.5)	0 (0.0)
Epistaxis	1 (2.5)	1 (2.5)	0 (0.0)
Acne	0 (0.0)	1 (2.5)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 2 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Asthenia	0 (0.0)	1 (2.5)	0 (0.0)
Dyspepsia	0 (0.0)	1 (2.5)	0 (0.0)
Erythema multiforme	0 (0.0)	1 (2.5)	0 (0.0)
Gastritis	0 (0.0)	1 (2.5)	0 (0.0)
Mucosal infection	0 (0.0)	1 (2.5)	0 (0.0)
Nasal dryness	0 (0.0)	1 (2.5)	0 (0.0)
Proteinuria	0 (0.0)	1 (2.5)	0 (0.0)
Rhinitis	0 (0.0)	1 (2.5)	0 (0.0)
Type 2 diabetes mellitus	0 (0.0)	1 (2.5)	0 (0.0)
Weight increased	0 (0.0)	1 (2.5)	0 (0.0)
Iron deficiency	3 (7.5)	0 (0.0)	0 (0.0)
Blood glucose increased	2 (5.0)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 3 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Cataract	2 (5.0)	0 (0.0)	0 (0.0)
Constipation	2 (5.0)	0 (0.0)	0 (0.0)
Hyperlipidaemia	2 (5.0)	0 (0.0)	0 (0.0)
Nasal congestion	2 (5.0)	0 (0.0)	0 (0.0)
Nausea	2 (5.0)	0 (0.0)	0 (0.0)
Periarthritis	2 (5.0)	0 (0.0)	0 (0.0)
Pyrexia	2 (5.0)	0 (0.0)	0 (0.0)
Renal impairment	2 (5.0)	0 (0.0)	0 (0.0)
Vomiting	2 (5.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	1 (2.5)	0 (0.0)	0 (0.0)
Amylase increased	1 (2.5)	0 (0.0)	0 (0.0)
Bipolar disorder	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 4 of 8)

Treatment-emergent adverse events in the core treatment period by preferred term and severity

Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Blood creatine phosphokinase increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood creatinine increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood follicle stimulating hormone increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood magnesium decreased	1 (2.5)	0 (0.0)	0 (0.0)
Blood triglycerides increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood uric acid increased	1 (2.5)	0 (0.0)	0 (0.0)
C-reactive protein increased	1 (2.5)	0 (0.0)	0 (0.0)
Chronic gastritis	1 (2.5)	0 (0.0)	0 (0.0)
Contusion	1 (2.5)	0 (0.0)	0 (0.0)
Dihydrotestosterone decreased	1 (2.5)	0 (0.0)	0 (0.0)
Dizziness	1 (2.5)	0 (0.0)	0 (0.0)
Dysmenorrhoea	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 5 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Fatigue	1 (2.5)	0 (0.0)	0 (0.0)
Fibrin D dimer increased	1 (2.5)	0 (0.0)	0 (0.0)
Gastrointestinal infection	1 (2.5)	0 (0.0)	0 (0.0)
Gastrooesophageal reflux disease	1 (2.5)	0 (0.0)	0 (0.0)
Haemorrhage subcutaneous	1 (2.5)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	1 (2.5)	0 (0.0)	0 (0.0)
Heavy menstrual bleeding	1 (2.5)	0 (0.0)	0 (0.0)
Hepatic function abnormal	1 (2.5)	0 (0.0)	0 (0.0)
Hordeolum	1 (2.5)	0 (0.0)	0 (0.0)
Hyperglycaemia	1 (2.5)	0 (0.0)	0 (0.0)
Hypomagnesaemia	1 (2.5)	0 (0.0)	0 (0.0)
Immunosuppressant drug level increased	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 6 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Influenza	1 (2.5)	0 (0.0)	0 (0.0)
Influenza like illness	1 (2.5)	0 (0.0)	0 (0.0)
Insomnia	1 (2.5)	0 (0.0)	0 (0.0)
Ligament sprain	1 (2.5)	0 (0.0)	0 (0.0)
Lipids abnormal	1 (2.5)	0 (0.0)	0 (0.0)
Memory impairment	1 (2.5)	0 (0.0)	0 (0.0)
Menstrual disorder	1 (2.5)	0 (0.0)	0 (0.0)
Neutropenia	1 (2.5)	0 (0.0)	0 (0.0)
Oropharyngeal pain	1 (2.5)	0 (0.0)	0 (0.0)
Osteoporosis	1 (2.5)	0 (0.0)	0 (0.0)
Pain in extremity	1 (2.5)	0 (0.0)	0 (0.0)
Peripheral swelling	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 7 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Protein urine present	1 (2.5)	0 (0.0)	0 (0.0)
Pruritus	1 (2.5)	0 (0.0)	0 (0.0)
Rash maculo-papular	1 (2.5)	0 (0.0)	0 (0.0)
Renal disorder	1 (2.5)	0 (0.0)	0 (0.0)
Renal injury	1 (2.5)	0 (0.0)	0 (0.0)
Reverse tri-iodothyronine increased	1 (2.5)	0 (0.0)	0 (0.0)
Sinus bradycardia	1 (2.5)	0 (0.0)	0 (0.0)
Skin discolouration	1 (2.5)	0 (0.0)	0 (0.0)
Sneezing	1 (2.5)	0 (0.0)	0 (0.0)
Tachycardia	1 (2.5)	0 (0.0)	0 (0.0)
Vaccination complication	1 (2.5)	0 (0.0)	0 (0.0)
Vision blurred	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.20a (Page 8 of 8)
Treatment-emergent adverse events in the core treatment period by preferred term and severity
Safety Analysis Set

Preferred term	LNP023 200mg b.i.d. N=40 Mild n(%)	Moderate n(%)	Severe n(%)
White blood cell count increased	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a preferred term is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- Preferred terms are sorted in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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1.6.3 Schwerwiegende unerwünschte Ereignisse nach SOC und PT

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Table 14.3.1-1.2a (Page 1 of 1)
Serious treatment-emergent adverse events in the core treatment period
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class **Preferred term**	**LNP023 200mg b.i.d.** **N=40** **n (%)**
Number of patients with at least one event	4 (10.0)
Eye disorders	1 (2.5)
Cataract	1 (2.5)
Infections and infestations	2 (5.0)
COVID-19	1 (2.5)
Pneumonia bacterial	1 (2.5)
Metabolism and nutrition disorders	1 (2.5)
Type 2 diabetes mellitus	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period.
On-treatment period is from first dose date until 7 days after the date of last dose administered.

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1.6.4 Unerwünschte Ereignisse von besonderem Interesse (AESI)

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Table 14.3.1-2.1a (Page 1 of 1)
Treatment-emergent adverse events of special interest in the core treatment period
by risk level terms and preferred term
Safety Analysis Set

Risk name Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Number of patients with at least one event	5 (12.5)
Infections capsular bacteria	1 (2.5)
Pneumonia bacterial	1 (2.5)
PNH Haemolysis and Thrombosis	1 (2.5)
Blood creatinine increased	1 (2.5)
Serious or severe infections	2 (5.0)
COVID-19	1 (2.5)
Pneumonia bacterial	1 (2.5)
Testicular effects	1 (2.5)
Blood follicle stimulating hormone increased	1 (2.5)
Dihydrotestosterone decreased	1 (2.5)
Thyroid changes	1 (2.5)
Reverse tri-iodothyronine increased	1 (2.5)

		LNP023 200mg b.i.d.
		N=40
Risk **Preferred term**	**name**	**n (%)**

- A patient with multiple adverse events within risk is counted only once in the total row.
- A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment.
- Risks are presented in alphabetical order; preferred terms are sorted within risk in descending frequency of AEs in the LNP023 column.
- MedDRA version 25.1 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period for LNP023 is from first dose date until 7 days after the date of last dose administered.
- A patient with multiple occurrences of a risk under one treatment is counted only once for the same risk for that treatment.
- Compound Case Retrieval Strategy Sheet as of 20-Dec-2022.

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2 Subgruppenanalysen zur Studie APPOINT-PNH zum primären Datenschnitt am 02.11.2022 (Hauptbehandlungsphase)

Table 2-1: Subgroups (Full Analysis Set)

	Treatment Group
	Iptacopan (N = 40)
Length of time since diagnosis, n (%)	
< 3 years	18 (45.0)
≥ 3 years	22 (55.0)
Age categories, n (%)	
< 45 years	24 (60.0)
≥ 45 years	16 (40.0)
Sex, n (%)	
Male	23 (57.5)
Female	17 (42.5)
Baseline hemoglobin, n (%)	
< 8 g/dL	15 (37.5)
≥ 8 g/dL	25 (62.5)
History of MAVE prior to screening, n (%)	
No	35 (87.5)
Yes	5 (12.5)
Transfusion in the last 6 months prior to start of study treatment, n (%)	
No	12 (30.0)
Yes	28 (70.0)
Number of transfusions in the last 6 months prior to start of study treatment, n (%)	
< 2	19 (47.5)
≥ 2	21 (52.5)
China vs. countries other than China, n (%)	
China	20 (50.0)
Other	20 (50.0)
Region, n (%)	
Europe	14 (35.0)
Other	26 (65.0)

N: Number of patients in the analysis set
MAVE: Major Adverse Vascular Event

N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 02-Nov-2022

2.1 Hb-Erhöhung bei gleichzeitiger Transfusionsvermeidung

Table 2-2: Increase in hemoglobin levels ≥2g/dL from baseline without requiring pRBC transfusions: frequency – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
Increase in hemoglobin levels ≥ 2 g/dL from baseline[a] without requiring pRBC transfusions[b]	
	n / N' (%) [95% CI]
Length of time since diagnosis	
< 3 years	14 / 18 (93.3) [68.1; 99.8]
≥ 3 years	17 / 22 (94.4) [72.7; 99.9]
Age categories	
< 45 years	18 / 24 (90.0) [68.3; 98.8]
≥ 45 years	13 / 16 (100.0) [75.3; 100.0]
Sex	
Male	18 / 23 (100.0) [81.5; 100.0]
Female	13 / 17 (86.7) [59.5; 98.3]
Baseline hemoglobin	
< 8 g/dL	14 / 15 (100.0) [76.8; 100.0]
≥ 8 g/dL	17 / 25 (89.5) [66.9; 98.7]
History of MAVE prior to screening	
No	28 / 35 (93.3) [77.9; 99.2]
Yes	3 / 5 (100.0) [29.2; 100.0]
Transfusion in the last 6 months prior to start of study treatment	
No	9 / 12 (100.0) [66.4; 100.0]
Yes	22 / 28 (91.7) [73.0; 99.0]
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	15 / 19 (100.0) [78.2; 100.0]
≥ 2	16 / 21 (88.9) [65.3; 98.6]
China vs. countries other than China	
China	14 / 20 (93.3) [68.1; 99.8]
Other	17 / 20 (94.4) [72.7; 99.9]
Region	
Europe	11 / 14 (91.7) [61.5; 99.8]
Other	20 / 26 (95.2) [76.2; 99.9]

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients included in the analysis n: Number of patients with response CI: Confidence interval Analysis methods for within-subgroup analysis: Simple proportion with Clopper-Pearson 95% CI a: between day 126 and day 168 (at least 3 out of 4 scheduled assessments) b: between day 14 and day 168 Cut-off date for analysis: 02-Nov-2022	

Table 2-3: Hemoglobin levels ≥12 g/dL without requiring pRBC transfusions: frequency – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
Hemoglobin levels ≥ 12 g/dL[a] without requiring pRBC transfusions[b]	
	n / N' (%) [95% CI]
Length of time since diagnosis	
< 3 years	10 / 18 (66.7) [38.4; 88.2]
≥ 3 years	9 / 22 (50.0) [26.0; 74.0]
Age categories	
< 45 years	11 / 24 (55.0) [31.5; 76.9]
≥ 45 years	8 / 16 (61.5) [31.6; 86.1]
Sex	
Male	13 / 23 (76.5) [50.1; 93.2]
Female	6 / 17 (37.5) [15.2; 64.6]
Baseline hemoglobin	
< 8 g/dL	5 / 15 (38.5) [13.9; 68.4]
≥ 8 g/dL	14 / 25 (70.0) [45.7; 88.1]
History of MAVE prior to screening	
No	18 / 35 (60.0) [40.6; 77.3]
Yes	1 / 5 (33.3) [0.8; 90.6]
Transfusion in the last 6 months prior to start of study treatment	
No	7 / 12 (87.5) [47.3; 99.7]
Yes	12 / 28 (48.0) [27.8; 68.7]
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	11 / 19 (73.3) [44.9; 92.2]
≥ 2	8 / 21 (44.4) [21.5; 69.2]
China vs. countries other than China	
China	7 / 20 (50.0) [23.0; 77.0]
Other	12 / 20 (63.2) [38.4; 83.7]
Region	
Europe	8 / 14 (61.5) [31.6; 86.1]
Other	11 / 26 (55.0) [31.5; 76.9]

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients included in the analysis n: Number of patients with response CI: Confidence interval Analysis methods for within-subgroup analysis: Simple proportion with Clopper-Pearson 95% CI a: between day 126 and day 168 (at least 3 out of 4 scheduled assessments) b: between day 14 and day 168 Cut-off date for analysis: 02-Nov-2022	

2.2 Änderung des FACIT-Fatigue Scores gegenüber Baseline mittels MMRM-Analyse

Table 2-4: FACIT-Fatigue: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
FACIT-Fatigue	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 9.93 (1.71)
≥ 3 years	22 | 10.35 (1.26)
Age categories	
< 45 years	24 | 10.82 (1.24)
≥ 45 years	16 | 10.30 (1.36)
Sex	
Male	23 | 9.37 (1.34)
Female	17 | 11.59 (1.28)
Baseline hemoglobin	
< 8 g/dL	15 | 11.94 (1.57)
≥ 8 g/dL	25 | 9.37 (1.16)
History of MAVE prior to screening	
No	35 | 10.59 (0.96)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 9.66 (1.73)
Yes	28 | 10.68 (1.05)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 9.91 (1.29)
≥ 2	21 | 11.09 (1.16)
China vs. countries other than China	
China	20 | 11.18 (1.87)
Other	20 | 9.81 (1.32)
Region	
Europe	14 | 9.08 (1.42)
Other	26 | 12.45 (1.63)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

2.3 Änderung der Symptomskalen des EORTC QLQ-C30 gegenüber Baseline mittels MMRM-Analyse

Table 2-5: QLQ-C30 - Fatigue: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Fatigue	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -19.41 (3.56)
≥ 3 years	22 | -22.11 (3.39)
Age categories	
< 45 years	24 | -20.14 (2.97)
≥ 45 years	16 | -20.01 (3.28)
Sex	
Male	23 | -17.60 (2.99)
Female	17 | -24.78 (3.38)
Baseline hemoglobin	
< 8 g/dL	15 | -29.46 (4.38)
≥ 8 g/dL	25 | -17.98 (2.58)
History of MAVE prior to screening	
No	35 | -20.99 (2.36)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -21.73 (4.75)
Yes	28 | -23.34 (2.36)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -21.70 (3.68)
≥ 2	21 | -24.63 (2.51)
China vs. countries other than China	
China	20 | -21.71 (4.66)
Other	20 | -19.21 (3.38)
Region	
Europe	14 | -17.42 (3.93)
Other	26 | -24.20 (3.75)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-6: QLQ-C30 - Nausea and vomiting: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Nausea and vomiting	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -4.13 (1.51)
≥ 3 years	22 | -6.80 (0.99)
Age categories	
< 45 years	24 | -4.37 (1.32)
≥ 45 years	16 | -7.10 (1.23)
Sex	
Male	23 | -5.72 (1.22)
Female	17 | -5.03 (1.33)
Baseline hemoglobin	
< 8 g/dL	15 | -6.29 (2.35)
≥ 8 g/dL	25 | -5.99 (1.04)
History of MAVE prior to screening	
No	35 | -5.70 (0.98)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -5.60 (1.64)
Yes	28 | -6.60 (1.02)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -5.47 (1.27)
≥ 2	21 | -6.46 (1.16)
China vs. countries other than China	
China	20 | -9.10 (1.77)
Other	20 | -5.59 (1.17)
Region	
Europe	14 | -7.84 (1.99)
Other	26 | -7.99 (1.55)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-7: QLQ-C30 - Pain: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Pain	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -12.91 (3.01)
≥ 3 years	22 | -10.18 (2.23)
Age categories	
< 45 years	24 | -12.55 (2.57)
≥ 45 years	16 | -9.23 (2.79)
Sex	
Male	23 | -9.42 (2.67)
Female	17 | -10.45 (2.77)
Baseline hemoglobin	
< 8 g/dL	15 | -13.03 (2.18)
≥ 8 g/dL	25 | -11.57 (2.57)
History of MAVE prior to screening	
No	35 | -12.51 (1.80)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -11.38 (5.13)
Yes	28 | -11.96 (1.81)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -13.15 (1.51)
≥ 2	21 | -10.21 (2.41)
China vs. countries other than China	
China	20 | -10.71 (3.08)
Other	20 | -12.15 (2.77)
Region	
Europe	14 | -14.56 (3.40)
Other	26 | -14.28 (2.55)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-8: QLQ-C30 - Dyspnoea: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Dyspnoea	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -13.00 (3.60)
≥ 3 years	22 | -16.31 (3.71)
Age categories	
< 45 years	24 | -12.01 (3.61)
≥ 45 years	16 | -20.11 (3.33)
Sex	
Male	23 | -12.59 (3.24)
Female	17 | -20.52 (3.87)
Baseline hemoglobin	
< 8 g/dL	15 | -20.40 (4.26)
≥ 8 g/dL	25 | -13.20 (3.18)
History of MAVE prior to screening	
No	35 | -15.99 (2.62)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -18.34 (5.55)
Yes	28 | -15.59 (2.39)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -16.81 (4.03)
≥ 2	21 | -16.91 (2.77)
China vs. countries other than China	
China	20 | -12.46 (5.56)
Other	20 | -15.73 (3.27)
Region	
Europe	14 | -11.70 (4.28)
Other	26 | -15.64 (3.96)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-9: QLQ-C30 - Insomnia: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Insomnia	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -8.79 (3.21)
≥ 3 years	22 | -1.95 (3.62)
Age categories	
< 45 years	24 | -9.41 (2.88)
≥ 45 years	16 | -3.76 (4.10)
Sex	
Male	23 | -4.71 (2.95)
Female	17 | -2.63 (4.12)
Baseline hemoglobin	
< 8 g/dL	15 | -10.34 (4.11)
≥ 8 g/dL	25 | -4.43 (3.21)
History of MAVE prior to screening	
No	35 | -4.78 (2.61)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -4.40 (3.88)
Yes	28 | -8.22 (2.67)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -4.77 (3.37)
≥ 2	21 | -8.52 (3.01)
China vs. countries other than China	
China	20 | -9.58 (5.17)
Other	20 | -6.14 (3.25)
Region	
Europe	14 | -5.76 (4.33)
Other	26 | -7.27 (3.88)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-10: QLQ-C30 - Appetite loss: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Appetite loss	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -15.71 (2.21)
≥ 3 years	22 | -13.92 (2.10)
Age categories	
< 45 years	24 | -11.82 (2.45)
≥ 45 years	16 | -19.54 (1.58)
Sex	
Male	23 | -13.40 (2.02)
Female	17 | -18.36 (2.58)
Baseline hemoglobin	
< 8 g/dL	15 | -16.70 (3.65)
≥ 8 g/dL	25 | -16.11 (1.70)
History of MAVE prior to screening	
No	35 | -15.40 (1.83)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -16.24 (5.08)
Yes	28 | -17.44 (1.74)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -16.99 (2.61)
≥ 2	21 | -17.55 (2.14)
China vs. countries other than China	
China	20 | -14.11 (4.06)
Other	20 | -18.84 (1.44)
Region	
Europe	14 | -20.58 (1.89)
Other	26 | -14.69 (3.00)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-11: QLQ-C30 - Constipation: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Constipation	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | -0.68 (2.14)
≥ 3 years	22 | 4.50 (3.48)
Age categories	
< 45 years	24 | 3.37 (2.59)
≥ 45 years	16 | 0.10 (3.22)
Sex	
Male	23 | -0.80 (1.96)
Female	17 | 5.04 (4.16)
Baseline hemoglobin	
< 8 g/dL	15 | -2.90 (3.14)
≥ 8 g/dL	25 | 2.82 (2.56)
History of MAVE prior to screening	
No	35 | 2.87 (2.22)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 4.81 (4.06)
Yes	28 | 0.84 (2.25)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 4.21 (3.22)
≥ 2	21 | 1.03 (2.65)
China vs. countries other than China	
China	20 | -0.84 (4.29)
Other	20 | 2.17 (2.03)
Region	
Europe	14 | 4.27 (2.94)
Other	26 | 1.63 (3.33)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-12: QLQ-C30 - Diarrhoea: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Diarrhoea	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 5.09 (2.03)
≥ 3 years	22 | -2.62 (2.27)
Age categories	
< 45 years	24 | -0.32 (2.40)
≥ 45 years	16 | -5.49 (1.44)
Sex	
Male	23 | -1.20 (1.40)
Female	17 | -1.86 (3.40)
Baseline hemoglobin	
< 8 g/dL	15 | 9.05 (3.86)
≥ 8 g/dL	25 | -4.15 (1.41)
History of MAVE prior to screening	
No	35 | -2.41 (1.67)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | -5.39 (2.02)
Yes	28 | -1.00 (1.91)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | -1.06 (2.15)
≥ 2	21 | -2.28 (2.12)
China vs. countries other than China	
China	20 | -3.16 (3.26)
Other	20 | -1.50 (1.87)
Region	
Europe	14 | -0.44 (2.59)
Other	26 | -2.91 (2.43)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

2.4 Änderung des EQ-5D VAS Scores gegenüber Baseline mittels MMRM-Analyse

Table 2-13: EQ-5D VAS: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
EQ-5D VAS	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 17.06 (2.69)
≥ 3 years	22 | 19.56 (2.18)
Age categories	
< 45 years	24 | 17.98 (2.05)
≥ 45 years	16 | 18.16 (2.42)
Sex	
Male	23 | 15.62 (2.12)
Female	17 | 20.51 (2.40)
Baseline hemoglobin	
< 8 g/dL	15 | 27.63 (2.22)
≥ 8 g/dL	25 | 15.03 (1.83)
History of MAVE prior to screening	
No	35 | 18.34 (1.75)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 14.97 (2.53)
Yes	28 | 20.49 (1.92)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 15.68 (2.28)
≥ 2	21 | 20.79 (1.89)
China vs. countries other than China	
China	20 | 24.48 (2.35)
Other	20 | 15.84 (2.48)
Region	
Europe	14 | 13.67 (2.25)
Other	26 | 24.50 (2.51)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

2.5 Änderung der Funktionsskalen und der globalen Gesundheits- und Lebensqualitätsskala des EORTC QLQ-C30 gegenüber Baseline mittels MMRM-Analyse

Table 2-14: QLQ-C30 - Global health status: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Global health status	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 26.15 (4.59)
≥ 3 years	22 | 23.18 (2.29)
Age categories	
< 45 years	24 | 21.90 (2.66)
≥ 45 years	16 | 25.49 (2.80)
Sex	
Male	23 | 21.22 (2.60)
Female	17 | 26.56 (2.81)
Baseline hemoglobin	
< 8 g/dL	15 | 33.25 (3.12)
≥ 8 g/dL	25 | 20.57 (2.50)
History of MAVE prior to screening	
No	35 | 24.97 (2.31)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 23.67 (4.99)
Yes	28 | 23.91 (2.00)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 22.39 (3.25)
≥ 2	21 | 24.53 (2.11)
China vs. countries other than China	
China	20 | 31.27 (3.66)
Other	20 | 19.78 (3.02)
Region	
Europe	14 | 17.57 (3.27)
Other	26 | 30.28 (3.20)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-15: QLQ-C30 - Physical functioning: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Physical functioning	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 13.36 (2.05)
≥ 3 years	22 | 14.40 (2.17)
Age categories	
< 45 years	24 | 14.67 (1.91)
≥ 45 years	16 | 16.67 (2.30)
Sex	
Male	23 | 11.96 (2.01)
Female	17 | 18.85 (2.01)
Baseline hemoglobin	
< 8 g/dL	15 | 18.27 (2.91)
≥ 8 g/dL	25 | 14.45 (1.65)
History of MAVE prior to screening	
No	35 | 15.61 (1.42)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 14.91 (2.99)
Yes	28 | 15.91 (1.55)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 15.30 (2.03)
≥ 2	21 | 15.45 (1.80)
China vs. countries other than China	
China	20 | 15.00 (3.18)
Other	20 | 16.47 (1.56)
Region	
Europe	14 | 15.43 (2.38)
Other	26 | 15.75 (2.36)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-16: QLQ-C30 - Role functioning: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Role functioning	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 17.23 (3.53)
≥ 3 years	22 | 21.42 (2.86)
Age categories	
< 45 years	24 | 20.40 (2.55)
≥ 45 years	16 | 18.42 (3.27)
Sex	
Male	23 | 18.15 (2.79)
Female	17 | 21.62 (3.00)
Baseline hemoglobin	
< 8 g/dL	15 | 22.20 (3.78)
≥ 8 g/dL	25 | 18.17 (2.51)
History of MAVE prior to screening	
No	35 | 19.83 (2.04)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 19.65 (3.92)
Yes	28 | 19.82 (2.26)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 19.95 (2.49)
≥ 2	21 | 20.12 (2.69)
China vs. countries other than China	
China	20 | 20.55 (2.99)
Other	20 | 19.66 (3.31)
Region	
Europe	14 | 19.19 (3.00)
Other	26 | 21.64 (3.45)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-17: QLQ-C30 - Emotional functioning: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Emotional functioning	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 12.86 (3.68)
≥ 3 years	22 | 13.58 (4.61)
Age categories	
< 45 years	24 | 7.28 (4.08)
≥ 45 years	16 | 17.64 (3.46)
Sex	
Male	23 | 5.48 (3.93)
Female	17 | 21.02 (3.81)
Baseline hemoglobin	
< 8 g/dL	15 | 19.53 (3.99)
≥ 8 g/dL	25 | 9.12 (3.35)
History of MAVE prior to screening	
No	35 | 12.36 (2.96)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 11.54 (7.27)
Yes	28 | 15.93 (2.59)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 9.73 (4.60)
≥ 2	21 | 18.07 (2.38)
China vs. countries other than China	
China	20 | 11.26 (6.74)
Other	20 | 11.89 (3.22)
Region	
Europe	14 | 8.18 (3.60)
Other	26 | 12.64 (5.02)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-18: QLQ-C30 - Cognitive functioning: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Cognitive functioning	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 3.94 (3.06)
≥ 3 years	22 | 5.50 (4.22)
Age categories	
< 45 years	24 | 3.38 (3.39)
≥ 45 years	16 | 8.69 (2.66)
Sex	
Male	23 | 1.88 (2.64)
Female	17 | 11.67 (4.20)
Baseline hemoglobin	
< 8 g/dL	15 | 6.28 (4.14)
≥ 8 g/dL	25 | 5.02 (2.78)
History of MAVE prior to screening	
No	35 | 6.15 (2.49)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 8.71 (4.54)
Yes	28 | 4.99 (2.46)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 5.71 (2.85)
≥ 2	21 | 7.13 (3.05)
China vs. countries other than China	
China	20 | 0.64 (5.69)
Other	20 | 8.65 (2.33)
Region	
Europe	14 | 6.04 (2.38)
Other	26 | 2.56 (4.29)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

Table 2-19: QLQ-C30 - Social functioning: MMRM analysis of change from baseline – subgroup analysis (Full Analysis Set)

	Treatment Groups
	Iptacopan (N = 40)
QLQ-C30 - Social functioning	
	N' | LS Mean (SE)
Length of time since diagnosis	
< 3 years	18 | 13.30 (4.34)
≥ 3 years	22 | 14.19 (4.53)
Age categories	
< 45 years	24 | 13.21 (3.98)
≥ 45 years	16 | 18.71 (3.72)
Sex	
Male	23 | 7.81 (3.51)
Female	17 | 25.43 (4.47)
Baseline hemoglobin	
< 8 g/dL	15 | 15.93 (7.64)
≥ 8 g/dL	25 | 16.99 (2.69)
History of MAVE prior to screening	
No	35 | 16.37 (2.99)
Yes	N.E.
Transfusion in the last 6 months prior to start of study treatment	
No	12 | 15.45 (4.92)
Yes	28 | 17.15 (3.12)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 | 16.21 (3.60)
≥ 2	21 | 18.84 (3.46)
China vs. countries other than China	
China	20 | 9.14 (6.41)
Other	20 | 22.89 (2.92)
Region	
Europe	14 | 20.97 (3.04)
Other	26 | 9.56 (5.30)

	Treatment Groups
	Iptacopan (N = 40)
N: Number of patients in the analysis set N': Number of patients with evaluable baseline and post-baseline score at visit LS Mean: Least square mean SE: Standard error MMRM: Mixed model for repeated measures N.E.: Not estimable Analysis methods for within-subgroup analysis: Adjusted mean (LS Mean) change from baseline obtained from MMRM with first-order autoregressive covariance matrix: Change from baseline = visit + baseline value + baseline value * visit + transfusion history + sex + age (indicator of age ≥ 45 years) Covariates transfusion history, sex and age were excluded from the model equation if they were connected to the subgroup factor. LS Means are calculated at Day 126 - 168 as linear function of the parameter estimates. Patients with an evaluable baseline value and at least one evaluable post-baseline value were included in the analysis. Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values. Missing values were not imputed, i.e. the analysis was based on observed data only. Cut-off date for analysis: 02-Nov-2022	

2.6 Verträglichkeit

Table 2-20: Adverse events overview: binary analysis – subgroup analysis (Safety Set)

	Treatment Group
	Iptacopan (N = 40)
Any adverse event	
	n / N (%)
Length of time since diagnosis	
< 3 years	17 / 18 (94.4)
≥ 3 years	20 / 22 (90.9)
Age categories	
< 45 years	22 / 24 (91.7)
≥ 45 years	15 / 16 (93.8)
Sex	
Male	22 / 23 (95.7)
Female	15 / 17 (88.2)
Baseline hemoglobin	
< 8 g/dL	15 / 15 (100.0)
≥ 8 g/dL	22 / 25 (88.0)
History of MAVE prior to screening	
No	33 / 35 (94.3)
Yes	4 / 5 (80.0)
Transfusion in the last 6 months prior to start of study treatment	
No	12 / 12 (100.0)
Yes	25 / 28 (89.3)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	19 / 19 (100.0)
≥ 2	18 / 21 (85.7)
China vs. countries other than China	
China	19 / 20 (95.0)
Other	18 / 20 (90.0)
Region	
Europe	13 / 14 (92.9)
Other	24 / 26 (92.3)
Any severe adverse event	
	n / N (%)
Length of time since diagnosis	
< 3 years	1 / 18 (5.6)

	Treatment Group
	Iptacopan (N = 40)
≥ 3 years	0 / 22 (0.0)
Age categories	
< 45 years	1 / 24 (4.2)
≥ 45 years	0 / 16 (0.0)
Sex	
Male	1 / 23 (4.3)
Female	0 / 17 (0.0)
Baseline hemoglobin	
< 8 g/dL	0 / 15 (0.0)
≥ 8 g/dL	1 / 25 (4.0)
History of MAVE prior to screening	
No	1 / 35 (2.9)
Yes	0 / 5 (0.0)
Transfusion in the last 6 months prior to start of study treatment	
No	1 / 12 (8.3)
Yes	0 / 28 (0.0)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	1 / 19 (5.3)
≥ 2	0 / 21 (0.0)
China vs. countries other than China	
China	0 / 20 (0.0)
Other	1 / 20 (5.0)
Region	
Europe	1 / 14 (7.1)
Other	0 / 26 (0.0)
Any serious adverse event	
	n / N (%)
Length of time since diagnosis	
< 3 years	2 / 18 (11.1)
≥ 3 years	2 / 22 (9.1)
Age categories	
< 45 years	1 / 24 (4.2)
≥ 45 years	3 / 16 (18.8)
Sex	
Male	4 / 23 (17.4)
Female	0 / 17 (0.0)

	Treatment Group
	Iptacopan (N = 40)
Baseline hemoglobin	
< 8 g/dL	1 / 15 (6.7)
≥ 8 g/dL	3 / 25 (12.0)
History of MAVE prior to screening	
No	3 / 35 (8.6)
Yes	1 / 5 (20.0)
Transfusion in the last 6 months prior to start of study treatment	
No	2 / 12 (16.7)
Yes	2 / 28 (7.1)
Number of transfusions in the last 6 months prior to start of study treatment	
< 2	2 / 19 (10.5)
≥ 2	2 / 21 (9.5)
China vs. countries other than China	
China	2 / 20 (10.0)
Other	2 / 20 (10.0)
Region	
Europe	2 / 14 (14.3)
Other	2 / 26 (7.7)

N: Number of patients in the analysis set
n: Number of patients with event

Cut-off date for analysis: 02-Nov-2022

3 Analysen zur Studie APPOINT-PNH zum finalen Datenschnitt am 18.04.2023 (Extensionsphase)

3.1 Mortalität

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Table 14.3.1-1.12 (Page 1 of 1)
On-treatment and post-treatment deaths by system organ class and preferred term
Safety Analysis Set

Timepoint: Not Applicable

There were no observations which met the report criteria

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3.2 Hb-Erhöhung um ≥ 2 g/dl und auf ≥ 12 g/dl bei gleichzeitiger Transfusionsvermeidung

CLNP023C12301

Listing 14.2-2.1 (Page 1 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
Baseline	Non-missing HGB value	40 (100)
Day 7	Non-missing HGB value	39 (97.5)
	HGB increase >=2 g/dL[a]	7 (17.9)
	HGB >=12 g/dL[a]	1 (2.6)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	1 (2.6)
Day 14	Non-missing HGB value	39 (97.5)
	HGB increase >=2 g/dL[a]	11 (28.2)
	HGB >=12 g/dL[a]	4 (10.3)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	4 (10.3)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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Listing 14.2-2.1 (Page 2 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
Day 28	Non-missing HGB value	36 (90.0)
	HGB increase >=2 g/dL[a]	19 (52.8)
	HGB >=12 g/dL[a]	6 (16.7)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	6 (16.7)
Day 42	Non-missing HGB value	35 (87.5)
	HGB increase >=2 g/dL[a]	23 (65.7)
	HGB >=12 g/dL[a]	4 (11.4)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	4 (11.4)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

Listing 14.2-2.1 (Page 3 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
Day 56	Non-missing HGB value	37 (92.5)
	HGB increase >=2 g/dL[a]	29 (78.4)
	HGB >=12 g/dL[a]	11 (29.7)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	11 (29.7)
Day 84	Non-missing HGB value	36 (90.0)
	HGB increase >=2 g/dL[a]	29 (80.6)
	HGB >=12 g/dL[a]	15 (41.7)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	15 (41.7)
Day 112	Non-missing HGB value	32 (80.0)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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Listing 14.2-2.1 (Page 4 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
	HGB increase >=2 g/dL[a]	30 (93.8)
	HGB >=12 g/dL[a]	13 (40.6)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	13 (40.6)
Day 126	Non-missing HGB value	30 (75.0)
	HGB increase >=2 g/dL[a]	27 (90.0)
	HGB >=12 g/dL[a]	14 (46.7)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	14 (46.7)
Day 140	Non-missing HGB value	34 (85.0)
	HGB increase >=2 g/dL[a]	32 (94.1)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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Listing 14.2-2.1 (Page 5 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
	HGB >=12 g/dL[a]	21 (61.8)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	21 (61.8)
Day 154	Non-missing HGB value	32 (80.0)
	HGB increase >=2 g/dL[a]	30 (93.8)
	HGB >=12 g/dL[a]	20 (62.5)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	20 (62.5)
Day 168	Non-missing HGB value	39 (97.5)
	HGB increase >=2 g/dL[a]	37 (94.9)
	HGB >=12 g/dL[a]	26 (66.7)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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Listing 14.2-2.1 (Page 6 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	26 (66.7)
Day 196	Non-missing HGB value	37 (92.5)
	HGB increase >=2 g/dL[a]	35 (94.6)
	HGB >=12 g/dL[a]	26 (70.3)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	26 (70.3)
Day 224	Non-missing HGB value	36 (90.0)
	HGB increase >=2 g/dL[a]	35 (97.2)
	HGB >=12 g/dL[a]	26 (72.2)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	26 (72.2)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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Listing 14.2-2.1 (Page 7 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
Day 252	Non-missing HGB value	38 (95.0)
	HGB increase >=2 g/dL[a]	35 (92.1)
	HGB >=12 g/dL[a]	27 (71.1)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	27 (71.1)
Day 280	Non-missing HGB value	37 (92.5)
	HGB increase >=2 g/dL[a]	36 (97.3)
	HGB >=12 g/dL[a]	30 (81.1)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	30 (81.1)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

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CLNP023C12301

Listing 14.2-2.1 (Page 8 of 8)
Number (%) of patients meeting the specified criterion by timepoint
Full Analysis Set

Visit	Criterion	LNP023 200mg b.i.d. N=40 n(%)
Day 308	Non-missing HGB value	33 (82.5)
	HGB increase >=2 g/dL[a]	30 (90.9)
	HGB >=12 g/dL[a]	24 (72.7)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	24 (72.7)
Day 336	Non-missing HGB value	39 (97.5)
	HGB increase >=2 g/dL[a]	38 (97.4)
	HGB >=12 g/dL[a]	31 (79.5)
	HGB increase >=2 g/dL & HGB >=12 g/dL[a]	31 (79.5)

HGB refers to Hemoglobin. Central lab assessments are included.
n = Number of patients meeting the specified criterion
N = The total number of patients
The baseline value of Hemoglobin is defined to be the mean of the two confirmatory measurements (planned) taken during screening that confirm the hemoglobin entry criterion in patients who do not receive a transfusion between the first and second confirmatory measurement. In patients who receive a transfusion after the first confirmatory measurement, the baseline will be the first measurement.
a: Percentage is calculated based on number of patients with non-missing HGB value at this visit.

/csr_3/pgm/eff/t_hgbnum_02.sas@@/main/5-26JUN2023:14:15 Final Version

Table 14.2-1.8 (Page 1 of 1)
Proportion of patients not receiving and not requiring pRBC transfusions between Day 14 and Day 336
Full Analysis Set

Responder Criterion	Treatment	n/M	Marginal proportion (95% CI)[1]
Patients not receiving and not requiring pRBC transfusions (#)	LNP023 200mg b.i.d. N=40	39/40	97.5 (92.5, 100.0)

N: Total number of patients included in the model (without missing covariates).
n: The number of patients who responded based on non-missing data.
M: The number of patients with response variable defined based on non-missing data (evaluable patients)
1 The 95% confidence intervals for the proportion of responders is computed using bootstrap from logistic regression model with covariates sex, age category, baseline hemoglobin category, history of transfusion (yes, no) 6 months prior to treatment start. If the logistic regression fails to convergence in at least one of the datasets or the bootstrap samples, then the estimates will be obtained using simple proportion.
between Day 14 and Day 336. Requiring pRBC refers to any patient receiving transfusions or meeting protocol defined criteria.

/csr_3/pgm/eff/t_eff_hgb_eval.sas@@/main/1-26JUN2023:14:11 Final Version

3.3 Änderung des FACIT-Fatigue Scores gegenüber Baseline zu verschiedenen Erhebungszeitpunkten

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Table 14.2-3.1 (Page 1 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline[a]	n	40		
	Mean (SD)	32.8 (10.17)		
	Median	34.3		
	Q1 - Q3	24.5 - 40.0		
	Min - Max	13 - 51		
Day 7	n	36	36	36
	Mean (SD)	32.7 (9.84)	35.8 (8.49)	3.1 (6.56)
	Median	34.3	35.5	2.0
	Q1 - Q3	24.5 - 39.5	30.5 - 42.5	-0.3 - 6.5
	Min - Max	13 - 51	18 - 50	-20 - 18
Day 14	n	36	36	36
	Mean (SD)	32.5 (10.50)	38.7 (8.25)	6.2 (7.73)
	Median	34.3	38.5	4.3

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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Table 14.2-3.1 (Page 2 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Q1 - Q3	24.3 - 40.0	33.5 - 45.0	0.3 - 12.0
	Min - Max	13 - 51	21 - 52	-6 - 24
Day 42	n	39	39	39
	Mean (SD)	32.6 (10.25)	41.3 (7.81)	8.6 (10.02)
	Median	33.5	43.0	9.0
	Q1 - Q3	24.5 - 40.5	36.0 - 47.0	2.0 - 16.5
	Min - Max	13 - 51	23 - 52	-17 - 28
Day 84	n	38	38	38
	Mean (SD)	32.4 (10.29)	42.9 (5.98)	10.6 (9.44)
	Median	33.3	45.0	9.3
	Q1 - Q3	24.5 - 39.5	37.0 - 48.0	3.0 - 15.5
	Min - Max	13 - 51	31 - 51	-5 - 30
Day 126	n	35	35	35

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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Table 14.2-3.1 (Page 3 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Mean (SD)	32.3 (10.00)	43.0 (8.21)	10.8 (10.00)
	Median	33.0	46.0	11.5
	Q1 - Q3	24.5 - 39.5	38.0 - 50.0	2.5 - 16.5
	Min - Max	13 - 51	16 - 52	-11 - 30
Day 140	n	37	37	37
	Mean (SD)	33.0 (9.92)	43.1 (7.47)	10.1 (10.51)
	Median	35.0	45.0	9.0
	Q1 - Q3	25.5 - 39.5	39.0 - 49.0	3.0 - 17.0
	Min - Max	13 - 51	24 - 52	-11 - 30
Day 154	n	36	36	36
	Mean (SD)	32.5 (10.06)	43.6 (6.78)	11.1 (9.77)
	Median	34.3	46.5	9.3
	Q1 - Q3	24.3 - 39.5	39.0 - 48.0	3.8 - 16.3

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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Table 14.2-3.1 (Page 4 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Min - Max	13 - 48	27 - 52	-5 - 34
Day 168	n	37	37	37
	Mean (SD)	31.8 (9.89)	43.9 (6.24)	12.1 (9.93)
	Median	33.0	46.0	11.5
	Q1 - Q3	24.5 - 39.5	39.0 - 49.0	5.0 - 21.0
	Min - Max	13 - 48	29 - 52	-9 - 31
Day 196	n	40	40	40
	Mean (SD)	32.8 (10.17)	44.1 (5.91)	11.4 (9.75)
	Median	34.3	45.5	10.3
	Q1 - Q3	24.5 - 40.0	41.0 - 48.5	3.5 - 18.3
	Min - Max	13 - 51	24 - 52	-4 - 32
Day 224	n	37	37	37
	Mean (SD)	33.0 (10.38)	43.2 (6.95)	10.2 (11.40)

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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Table 14.2-3.1 (Page 5 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Median	35.0	45.0	9.0
	Q1 - Q3	24.5 - 40.5	40.0 - 48.0	1.5 - 16.5
	Min - Max	13 - 51	23 - 52	-11 - 32
Day 252	n	38	38	38
	Mean (SD)	32.6 (10.07)	43.2 (7.20)	10.6 (10.92)
	Median	34.3	45.0	9.8
	Q1 - Q3	24.5 - 39.5	39.0 - 48.0	2.5 - 20.5
	Min - Max	13 - 51	22 - 52	-18 - 31
Day 280	n	37	37	37
	Mean (SD)	32.4 (10.35)	43.5 (5.72)	11.1 (9.76)
	Median	33.5	45.0	11.0
	Q1 - Q3	24.5 - 39.5	41.0 - 47.0	3.0 - 18.0
	Min - Max	13 - 51	29 - 51	-6 - 31

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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Table 14.2-3.1 (Page 6 of 6)
Summary statistics of FACIT-Fatigue scores by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	32.8 (10.17)	44.1 (6.26)	11.3 (9.89)
	Median	34.3	46.5	10.8
	Q1 - Q3	24.5 - 40.0	41.0 - 49.0	3.0 - 17.0
	Min - Max	13 - 51	26 - 52	-7 - 34
Day 336	n	39	39	39
	Mean (SD)	32.6 (10.21)	42.9 (7.21)	10.4 (10.14)
	Median	33.5	45.0	12.5
	Q1 - Q3	24.5 - 39.5	39.0 - 49.0	1.5 - 16.5
	Min - Max	13 - 51	21 - 52	-12 - 32

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline score of fatigue using the FACIT-Fatigue questionnaire will be defined as the mean of first assessment prior to Day 1 and the Day 1 value.

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3.4 Änderung der Symptomskalen des EORTC QLQ-C30 gegenüber Baseline zu verschiedenen Erhebungszeitpunkten

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Table 14.2-10.1 (Page 43 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	45.0 (24.39)		
	Median	41.7		
	Q1 - Q3	33.3 - 58.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	45.5 (25.09)	31.5 (19.25)	-14.0 (18.52)
	Median	41.7	33.3	-11.1
	Q1 - Q3	33.3 - 63.9	22.2 - 33.3	-22.2 - 0.0
	Min - Max	0 - 100	0 - 78	-78 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 44 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	45.2 (24.69)	26.8 (21.13)	-18.4 (25.50)
	Median	44.4	22.2	-16.7
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-44.4 - 0.0
	Min - Max	0 - 100	0 - 89	-61 - 33
Day 84	n	38	38	38
	Mean (SD)	44.4 (24.91)	25.4 (19.32)	-19.0 (23.09)
	Median	38.9	33.3	-16.7
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-38.9 - 0.0
	Min - Max	0 - 100	0 - 67	-61 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 45 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	45.1 (23.91)	23.5 (20.13)	-21.6 (24.58)
	Median	44.4	22.2	-22.2
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-38.9 - 0.0
	Min - Max	0 - 100	0 - 89	-67 - 33
Day 140	n	37	37	37
	Mean (SD)	44.1 (23.46)	24.0 (20.37)	-20.1 (21.45)
	Median	38.9	22.2	-16.7
	Q1 - Q3	33.3 - 55.6	11.1 - 33.3	-33.3 - -5.6
	Min - Max	0 - 100	0 - 89	-67 - 28

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 46 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	45.8 (24.07)	21.6 (16.58)	-24.2 (19.75)
	Median	41.7	22.2	-25.0
	Q1 - Q3	33.3 - 58.3	5.6 - 33.3	-33.3 - -8.3
	Min - Max	0 - 100	0 - 67	-67 - 17
Day 168	n	37	37	37
	Mean (SD)	47.0 (23.84)	21.9 (14.93)	-25.1 (24.38)
	Median	44.4	22.2	-27.8
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-50.0 - 0.0
	Min - Max	0 - 100	0 - 56	-67 - 22

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 47 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	45.0 (24.39)	22.8 (16.30)	-22.2 (25.35)
	Median	41.7	22.2	-25.0
	Q1 - Q3	33.3 - 58.3	11.1 - 33.3	-38.9 - 0.0
	Min - Max	0 - 100	0 - 56	-78 - 22
Day 224	n	37	37	37
	Mean (SD)	44.4 (24.88)	27.9 (20.72)	-16.5 (27.20)
	Median	38.9	33.3	-11.1
	Q1 - Q3	33.3 - 55.6	11.1 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 78	-89 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 48 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	45.8 (24.39)	26.3 (19.74)	-19.4 (25.47)
	Median	41.7	22.2	-19.4
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 89	-67 - 33
Day 280	n	37	37	37
	Mean (SD)	45.3 (25.07)	22.5 (13.48)	-22.8 (24.87)
	Median	38.9	22.2	-22.2
	Q1 - Q3	33.3 - 61.1	11.1 - 33.3	-44.4 - 0.0
	Min - Max	0 - 100	0 - 44	-67 - 28

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 49 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Fatigue

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	45.0 (24.39)	23.6 (17.65)	-21.4 (23.72)
	Median	41.7	22.2	-19.4
	Q1 - Q3	33.3 - 58.3	11.1 - 33.3	-36.1 - 0.0
	Min - Max	0 - 100	0 - 67	-78 - 33
Day 336	n	39	39	39
	Mean (SD)	44.7 (24.65)	22.5 (22.15)	-22.2 (24.98)
	Median	38.9	22.2	-22.2
	Q1 - Q3	33.3 - 61.1	0.0 - 33.3	-38.9 - -5.6
	Min - Max	0 - 100	0 - 89	-67 - 56

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 50 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	9.0 (12.43)		
	Median	0.0		
	Q1 - Q3	0.0 - 16.7		
	Min - Max	0 - 42		
Day 14	n	36	36	36
	Mean (SD)	9.5 (12.78)	6.5 (10.75)	-3.0 (12.62)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 16.7	-8.3 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 51 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	9.2 (12.51)	3.8 (8.08)	-5.3 (12.75)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 33
Day 84	n	38	38	38
	Mean (SD)	9.4 (12.58)	2.6 (9.11)	-6.8 (14.22)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 50	-42 - 42

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 52 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	9.8 (12.86)	4.3 (9.34)	-5.5 (13.24)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 25
Day 140	n	37	37	37
	Mean (SD)	9.2 (12.85)	3.2 (11.68)	-6.1 (18.18)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 67	-42 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 53 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	9.7 (12.83)	2.8 (7.45)	-6.9 (14.02)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 33
Day 168	n	37	37	37
	Mean (SD)	9.5 (12.75)	1.8 (6.55)	-7.7 (12.17)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-8.3 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 0

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	9.0 (12.43)	3.3 (7.73)	-5.6 (15.02)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-8.3 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 33
Day 224	n	37	37	37
	Mean (SD)	9.5 (12.75)	4.1 (10.69)	-5.4 (16.22)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 50	-42 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	9.2 (12.67)	3.9 (8.16)	-5.3 (14.29)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 33
Day 280	n	37	37	37
	Mean (SD)	8.6 (12.19)	3.6 (9.73)	-5.0 (13.81)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-8.3 - 0.0
	Min - Max	0 - 42	0 - 50	-42 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Nausea and vomiting

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	9.0 (12.43)	2.5 (7.11)	-6.5 (12.87)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-8.3 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 17
Day 336	n	39	39	39
	Mean (SD)	9.2 (12.51)	3.8 (8.94)	-5.3 (12.75)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 42	0 - 33	-42 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	20.6 (18.49)		
	Median	25.0		
	Q1 - Q3	0.0 - 33.3		
	Min - Max	0 - 58		
Day 14	n	36	36	36
	Mean (SD)	22.0 (18.70)	13.9 (17.59)	-8.1 (14.15)
	Median	25.0	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 58	0 - 50	-42 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	21.2 (18.42)	12.4 (20.13)	-8.8 (24.55)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 100	-58 - 100
Day 84	n	38	38	38
	Mean (SD)	21.7 (18.33)	10.1 (15.76)	-11.6 (15.44)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 67	-50 - 25

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	21.9 (18.64)	8.1 (15.32)	-13.8 (20.61)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 50	-58 - 25
Day 140	n	37	37	37
	Mean (SD)	20.7 (17.53)	6.3 (12.01)	-14.4 (18.28)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-25.0 - 0.0
	Min - Max	0 - 58	0 - 33	-50 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	21.5 (18.83)	9.3 (14.61)	-12.3 (17.19)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 50	-58 - 25
Day 168	n	37	37	37
	Mean (SD)	21.2 (18.28)	10.8 (13.73)	-10.4 (18.78)
	Median	25.0	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 50	-58 - 25

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	20.6 (18.49)	10.4 (15.87)	-10.2 (18.54)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 50	-58 - 25
Day 224	n	37	37	37
	Mean (SD)	22.1 (18.45)	11.3 (15.24)	-10.8 (23.31)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 50	-50 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	20.8 (18.56)	12.3 (19.25)	-8.6 (23.45)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 67	-50 - 42
Day 280	n	37	37	37
	Mean (SD)	20.5 (18.59)	12.2 (16.96)	-8.3 (20.88)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-25.0 - 0.0
	Min - Max	0 - 58	0 - 67	-50 - 42

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Pain

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	20.6 (18.49)	10.0 (18.80)	-10.6 (22.49)
	Median	25.0	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 16.7	-25.0 - 0.0
	Min - Max	0 - 58	0 - 67	-50 - 42
Day 336	n	39	39	39
	Mean (SD)	21.2 (18.42)	13.2 (18.80)	-7.9 (20.50)
	Median	25.0	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-25.0 - 0.0
	Min - Max	0 - 58	0 - 67	-50 - 42

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	29.6 (24.02)		
	Median	33.3		
	Q1 - Q3	8.3 - 33.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	29.2 (24.36)	17.6 (18.66)	-11.6 (17.74)
	Median	33.3	16.7	0.0
	Q1 - Q3	8.3 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	29.5 (24.32)	17.9 (24.00)	-11.5 (25.98)
	Median	33.3	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 50
Day 84	n	38	38	38
	Mean (SD)	28.9 (24.41)	9.6 (15.32)	-19.3 (24.36)
	Median	33.3	0.0	-8.3
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-100 - 0

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	29.5 (24.95)	15.2 (18.69)	-14.3 (22.19)
	Median	33.3	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 33
Day 140	n	37	37	37
	Mean (SD)	29.7 (22.27)	14.4 (21.57)	-15.3 (27.04)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	31.0 (24.28)	11.1 (15.94)	-19.9 (21.01)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 41.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-67 - 33
Day 168	n	37	37	37
	Mean (SD)	30.6 (24.38)	11.7 (17.94)	-18.9 (28.64)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	29.6 (24.02)	14.2 (16.69)	-15.4 (23.38)
	Median	33.3	0.0	-8.3
	Q1 - Q3	8.3 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-67 - 33
Day 224	n	37	37	37
	Mean (SD)	29.7 (24.26)	12.6 (16.39)	-17.1 (22.04)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 0

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	30.3 (24.15)	13.2 (19.82)	-17.1 (26.70)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-100 - 33
Day 280	n	37	37	37
	Mean (SD)	30.6 (24.38)	9.0 (15.01)	-21.6 (25.42)
	Median	33.3	0.0	-16.7
	Q1 - Q3	16.7 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Dyspnoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	29.6 (24.02)	12.5 (19.52)	-17.1 (26.82)
	Median	33.3	0.0	-16.7
	Q1 - Q3	8.3 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 33
Day 336	n	39	39	39
	Mean (SD)	29.5 (24.32)	12.0 (17.91)	-17.5 (28.60)
	Median	33.3	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	24.2 (25.86)		
	Median	16.7		
	Q1 - Q3	0.0 - 33.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	24.1 (26.86)	18.5 (24.49)	-5.6 (19.11)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	24.8 (25.90)	18.8 (23.93)	-6.0 (24.92)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 67
Day 84	n	38	38	38
	Mean (SD)	24.6 (26.21)	17.5 (22.91)	-7.0 (23.77)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	22.9 (23.60)	14.3 (20.27)	-8.6 (25.04)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 83	0 - 67	-67 - 33
Day 140	n	37	37	37
	Mean (SD)	25.2 (26.53)	20.7 (22.70)	-4.5 (25.05)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	25.5 (26.57)	18.5 (23.16)	-6.9 (29.65)
	Median	25.0	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-25.0 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 50
Day 168	n	37	37	37
	Mean (SD)	25.2 (26.24)	14.4 (20.09)	-10.8 (24.60)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	24.2 (25.86)	18.3 (22.58)	-5.8 (27.36)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 0.0
	Min - Max	0 - 100	0 - 67	-67 - 50
Day 224	n	37	37	37
	Mean (SD)	25.7 (26.23)	18.9 (28.91)	-6.8 (36.32)
	Median	33.3	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 83

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	24.1 (25.91)	19.3 (25.27)	-4.8 (30.73)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-16.7 - 16.7
	Min - Max	0 - 100	0 - 100	-67 - 67
Day 280	n	37	37	37
	Mean (SD)	25.2 (26.24)	17.1 (26.78)	-8.1 (31.09)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Insomnia

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	24.2 (25.86)	17.5 (29.22)	-6.7 (31.53)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 67
Day 336	n	39	39	39
	Mean (SD)	24.8 (25.90)	20.5 (27.16)	-4.3 (31.93)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 83

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	22.1 (23.08)		
	Median	16.7		
	Q1 - Q3	0.0 - 33.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	23.6 (23.70)	9.3 (15.14)	-14.4 (19.58)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-67 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	22.6 (23.10)	8.5 (14.75)	-14.1 (23.74)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 33
Day 84	n	38	38	38
	Mean (SD)	23.2 (23.10)	5.3 (12.32)	-18.0 (21.36)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	24.8 (23.35)	5.7 (12.75)	-19.0 (23.27)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 33
Day 140	n	37	37	37
	Mean (SD)	22.1 (23.59)	8.1 (16.49)	-14.0 (30.31)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-100 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	22.7 (23.96)	4.6 (11.69)	-18.1 (21.22)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 0
Day 168	n	37	37	37
	Mean (SD)	23.0 (23.36)	5.4 (12.46)	-17.6 (26.04)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	22.1 (23.08)	2.5 (8.89)	-19.6 (22.92)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-100 - 0
Day 224	n	37	37	37
	Mean (SD)	22.1 (23.59)	6.3 (15.39)	-15.8 (26.63)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-83 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	22.4 (23.34)	7.9 (18.07)	-14.5 (29.55)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-83 - 67
Day 280	n	37	37	37
	Mean (SD)	21.6 (23.20)	6.3 (13.24)	-15.3 (22.35)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Appetite loss

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	22.1 (23.08)	7.5 (17.68)	-14.6 (24.80)
	Median	16.7	0.0	-16.7
	Q1 - Q3	0.0 - 33.3	0.0 - 0.0	-33.3 - 0.0
	Min - Max	0 - 100	0 - 67	-83 - 50
Day 336	n	39	39	39
	Mean (SD)	22.6 (23.10)	10.3 (15.59)	-12.4 (25.28)
	Median	16.7	0.0	0.0
	Q1 - Q3	0.0 - 33.3	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 33	-83 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	9.2 (13.58)		
	Median	0.0		
	Q1 - Q3	0.0 - 16.7		
	Min - Max	0 - 50		
Day 14	n	36	36	36
	Mean (SD)	9.3 (14.05)	12.0 (18.09)	2.8 (13.51)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-17 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	9.4 (13.68)	13.7 (18.29)	4.3 (16.98)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 16.7
	Min - Max	0 - 50	0 - 67	-33 - 33
Day 84	n	38	38	38
	Mean (SD)	9.6 (13.77)	11.4 (17.80)	1.8 (20.06)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-50 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	10.0 (14.12)	12.4 (21.52)	2.4 (20.67)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 100	-33 - 83
Day 140	n	37	37	37
	Mean (SD)	8.6 (13.39)	7.2 (13.91)	-1.4 (14.90)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 50	0 - 33	-33 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	9.7 (14.02)	12.0 (16.24)	2.3 (13.89)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 33	-33 - 33
Day 168	n	37	37	37
	Mean (SD)	9.9 (13.87)	12.6 (24.03)	2.7 (20.23)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 100	-33 - 83

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	9.2 (13.58)	10.0 (17.21)	0.8 (15.54)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-33 - 50
Day 224	n	37	37	37
	Mean (SD)	9.5 (13.91)	11.7 (21.11)	2.3 (18.49)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-33 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	8.3 (13.28)	7.9 (16.32)	-0.4 (13.69)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-33 - 33
Day 280	n	37	37	37
	Mean (SD)	9.9 (13.87)	7.2 (15.98)	-2.7 (10.03)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-33 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 91 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Constipation

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	9.2 (13.58)	12.5 (20.93)	3.3 (15.19)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-17 - 50
Day 336	n	39	39	39
	Mean (SD)	9.4 (13.68)	11.1 (20.71)	1.7 (13.68)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 33.3	0.0 - 0.0
	Min - Max	0 - 50	0 - 67	-17 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	6.7 (15.92)		
	Median	0.0		
	Q1 - Q3	0.0 - 8.3		
	Min - Max	0 - 83		
Day 14	n	36	36	36
	Mean (SD)	6.9 (16.61)	4.6 (14.15)	-2.3 (11.38)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 8.3	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 67	-50 - 17

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	6.8 (16.09)	7.7 (16.15)	0.9 (11.44)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 67	-17 - 33
Day 84	n	38	38	38
	Mean (SD)	7.0 (16.27)	5.3 (12.32)	-1.8 (19.29)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 33	-83 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	7.6 (16.83)	5.7 (20.59)	-1.9 (23.14)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	-16.7 - 0.0
	Min - Max	0 - 83	0 - 100	-50 - 83
Day 140	n	37	37	37
	Mean (SD)	4.5 (10.13)	1.8 (7.64)	-2.7 (12.12)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 50	0 - 33	-50 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	7.4 (16.64)	5.6 (12.60)	-1.9 (16.32)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 33	-50 - 33
Day 168	n	37	37	37
	Mean (SD)	7.2 (16.45)	6.3 (15.39)	-0.9 (21.85)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 67	-83 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	6.7 (15.92)	6.7 (18.80)	0.0 (24.17)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 8.3	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 100	-83 - 83
Day 224	n	37	37	37
	Mean (SD)	7.2 (16.45)	8.1 (21.38)	0.9 (17.10)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 100	-50 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	6.1 (16.17)	6.1 (15.22)	0.0 (17.33)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 0.0	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 67	-50 - 50
Day 280	n	37	37	37
	Mean (SD)	7.2 (16.45)	9.0 (21.73)	1.8 (16.09)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 100	-50 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Diarrhoea

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	6.7 (15.92)	8.3 (18.10)	1.7 (22.90)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 8.3	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 67	-50 - 67
Day 336	n	39	39	39
	Mean (SD)	6.8 (16.09)	8.5 (19.82)	1.7 (16.58)
	Median	0.0	0.0	0.0
	Q1 - Q3	0.0 - 16.7	0.0 - 0.0	0.0 - 0.0
	Min - Max	0 - 83	0 - 100	-50 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	41.3 (36.59)		
	Median	33.3		
	Q1 - Q3	0.0 - 66.7		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	45.4 (36.21)	38.0 (39.16)	-7.4 (19.70)
	Median	50.0	33.3	0.0
	Q1 - Q3	0.0 - 75.0	0.0 - 66.7	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-83 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 100 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	42.3 (36.44)	33.3 (35.04)	-9.0 (24.44)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 66.7	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33
Day 84	n	38	38	38
	Mean (SD)	43.4 (36.25)	28.9 (35.66)	-14.5 (27.99)
	Median	41.7	16.7	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-100 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	44.8 (35.65)	34.3 (32.83)	-10.5 (30.00)
	Median	50.0	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 66.7	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 83
Day 140	n	37	37	37
	Mean (SD)	42.8 (36.54)	29.7 (32.19)	-13.1 (25.20)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 102 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	41.7 (36.41)	29.6 (31.65)	-12.0 (26.01)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33
Day 168	n	37	37	37
	Mean (SD)	44.6 (36.02)	28.8 (32.55)	-15.8 (27.76)
	Median	50.0	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-83 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	41.3 (36.59)	28.3 (31.62)	-12.9 (25.17)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33
Day 224	n	37	37	37
	Mean (SD)	39.6 (35.43)	27.0 (30.26)	-12.6 (25.88)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 104 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	39.9 (37.07)	29.8 (34.48)	-10.1 (23.10)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 66.7	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33
Day 280	n	37	37	37
	Mean (SD)	41.0 (36.13)	30.6 (32.75)	-10.4 (24.01)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 66.7	-16.7 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 105 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Financial difficulties

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	41.3 (36.59)	32.5 (34.17)	-8.8 (23.57)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 66.7	-25.0 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33
Day 336	n	39	39	39
	Mean (SD)	42.3 (36.44)	31.6 (33.29)	-10.7 (25.50)
	Median	33.3	33.3	0.0
	Q1 - Q3	0.0 - 66.7	0.0 - 33.3	-33.3 - 0.0
	Min - Max	0 - 100	0 - 100	-67 - 33

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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3.5 Deskriptive Darstellung der PGIS zu verschiedenen Erhebungszeitpunkten

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Table 14.2-11.1 (Page 1 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
Baseline	No symptoms	2/40 (5.0)
	Mild	14/40 (35.0)
	Moderate	18/40 (45.0)
	Severe	5/40 (12.5)
	Very severe	1/40 (2.5)
Day 7	No symptoms	4/36 (11.1)
	Mild	16/36 (44.4)
	Moderate	14/36 (38.9)
	Severe	2/36 (5.6)
	Very severe	0/36 (0.0)
Day 14	No symptoms	5/36 (13.9)
	Mild	23/36 (63.9)
	Moderate	7/36 (19.4)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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Table 14.2-11.1 (Page 2 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
	Severe	1/36 (2.8)
	Very severe	0/36 (0.0)
Day 42	No symptoms	12/39 (30.8)
	Mild	19/39 (48.7)
	Moderate	7/39 (17.9)
	Severe	1/39 (2.6)
	Very severe	0/39 (0.0)
Day 84	No symptoms	16/38 (42.1)
	Mild	19/38 (50.0)
	Moderate	3/38 (7.9)
	Severe	0/38 (0.0)
	Very severe	0/38 (0.0)
Day 126	No symptoms	12/35 (34.3)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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Table 14.2-11.1 (Page 3 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
	Mild	19/35 (54.3)
	Moderate	3/35 (8.6)
	Severe	1/35 (2.9)
	Very severe	0/35 (0.0)
Day 140	No symptoms	12/37 (32.4)
	Mild	19/37 (51.4)
	Moderate	5/37 (13.5)
	Severe	1/37 (2.7)
	Very severe	0/37 (0.0)
Day 154	No symptoms	12/36 (33.3)
	Mild	22/36 (61.1)
	Moderate	1/36 (2.8)
	Severe	1/36 (2.8)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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Table 14.2-11.1 (Page 4 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
	Very severe	0/36 (0.0)
Day 168	No symptoms	13/37 (35.1)
	Mild	20/37 (54.1)
	Moderate	4/37 (10.8)
	Severe	0/37 (0.0)
	Very severe	0/37 (0.0)
Day 196	No symptoms	15/40 (37.5)
	Mild	20/40 (50.0)
	Moderate	5/40 (12.5)
	Severe	0/40 (0.0)
	Very severe	0/40 (0.0)
Day 224	No symptoms	16/37 (43.2)
	Mild	17/37 (45.9)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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Table 14.2-11.1 (Page 5 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
	Moderate	3/37 (8.1)
	Severe	1/37 (2.7)
	Very severe	0/37 (0.0)
Day 252	No symptoms	14/38 (36.8)
	Mild	20/38 (52.6)
	Moderate	3/38 (7.9)
	Severe	1/38 (2.6)
	Very severe	0/38 (0.0)
Day 280	No symptoms	13/37 (35.1)
	Mild	19/37 (51.4)
	Moderate	5/37 (13.5)
	Severe	0/37 (0.0)
	Very severe	0/37 (0.0)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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Table 14.2-11.1 (Page 6 of 6)
Summary of Patient Global Impression of Severity (PGI-S) by visit
Full Analysis Set

Visit	Score	LNP023 200mg b.i.d. N=40 n/m (%)
Day 308	No symptoms	17/40 (42.5)
	Mild	18/40 (45.0)
	Moderate	5/40 (12.5)
	Severe	0/40 (0.0)
	Very severe	0/40 (0.0)
Day 336	No symptoms	16/39 (41.0)
	Mild	19/39 (48.7)
	Moderate	3/39 (7.7)
	Severe	1/39 (2.6)
	Very severe	0/39 (0.0)

Baseline was defined as assessments at Day 1 or the last value before start of study treatment.
Percentage based on number of patients with baseline and value at a corresponding time point.
N: number of patients in the analysis set.
m = number of patients with assessment at the specified visit .
n: number of patients who are at the corresponding category.

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3.6 Durchbruchhämolyserate

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Table 14.2-6.4 (Page 1 of 1)
Number of breakthrough hemolysis events after the start of LNP023 treatment
Full Analysis Set

Breakthrough hemolysis event	LNP023 200mg b.i.d. N=40	Adjusted annual BTH rate (95% CI)
Number of events	2 (5.0)	0.05 (0.01, 0.17)

N = number of all patients included in the analysis.
n = number of events.
Adjusted annual rate is carried out using the Wilson method.

/csr_3/pgm/eff/t_bio_rate.sas@@/main/3-26JUN2023:14:03 Final Version

3.7 Rate an MAVE

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Table 14.2-7.2 (Page 1 of 1)
Number of major adverse vascular events after the start of LNP023 treatment
Full Analysis Set

Major adverse vascular events	LNP023 200mg b.i.d. N=40	Adjusted annual MAVE rate (95% CI)
Number of events	0 (0.0)	0.00 (0.00, 0.09)

N = number of all patients included in the analysis.
n = number of events.
Adjusted annual rate is carried out using the Wilson method.

/csr_3/pgm/eff/t_bio_rate.sas@@/main/3-26JUN2023:14:04 Final Version

3.8 Änderung der Retikulozytenzahl gegenüber Baseline zu verschiedenen Erhebungszeitpunkten

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Table 14.2-4.1 (Page 1 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline[a]	n	40		
	Mean (SD)	154.33 (63.666)		
	Median	139.20		
	Q1 - Q3	105.00 - 204.90		
	Min - Max	59.4 - 324.8		
Day 7	n	39	39	39
	Mean (SD)	155.59 (63.987)	67.88 (22.191)	-87.71 (60.156)
	Median	144.00	66.70	-80.80
	Q1 - Q3	105.00 - 205.80	52.20 - 84.00	-127.40 - -40.80
	Min - Max	59.4 - 324.8	28.8 - 113.1	-219.4 - 12.3
Day 14	n	39	39	39
	Mean (SD)	154.14 (64.487)	61.79 (20.614)	-92.34 (53.625)
	Median	134.40	58.90	-76.20

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 2 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Q1 - Q3	105.00 - 205.80	46.40 - 68.40	-142.80 - -47.10
	Min - Max	59.4 - 324.8	20.0 - 112.5	-218.4 - -23.1
Day 28	n	36	36	36
	Mean (SD)	155.17 (65.484)	59.59 (22.956)	-95.58 (58.841)
	Median	139.20	55.95	-66.55
	Q1 - Q3	103.65 - 204.90	45.55 - 76.90	-150.50 - -49.50
	Min - Max	59.4 - 324.8	17.6 - 105.6	-235.1 - -16.8
Day 42	n	35	35	35
	Mean (SD)	151.56 (64.894)	64.81 (24.674)	-86.74 (56.954)
	Median	125.40	57.60	-70.80
	Q1 - Q3	105.00 - 204.00	49.00 - 86.40	-144.20 - -45.00
	Min - Max	59.4 - 324.8	14.1 - 114.8	-223.6 - -7.0
Day 56	n	37	37	37

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 3 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Mean (SD)	154.21 (65.106)	73.69 (30.717)	-80.52 (59.454)
	Median	134.40	70.40	-61.20
	Q1 - Q3	105.00 - 204.00	53.30 - 96.20	-123.70 - -35.60
	Min - Max	59.4 - 324.8	16.0 - 139.5	-227.3 - 15.2
Day 84	n	36	36	36
	Mean (SD)	156.63 (63.909)	75.53 (29.113)	-81.11 (56.725)
	Median	144.45	69.05	-71.55
	Q1 - Q3	105.00 - 204.90	54.50 - 92.30	-114.30 - -38.25
	Min - Max	59.4 - 324.8	24.6 - 149.6	-230.5 - 41.6
Day 112	n	32	32	32
	Mean (SD)	146.53 (65.526)	69.71 (23.046)	-76.82 (60.340)
	Median	113.75	65.75	-56.50
	Q1 - Q3	101.85 - 193.80	52.50 - 82.95	-118.80 - -37.95

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 4 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Min - Max	59.4 - 324.8	28.8 - 121.9	-248.3 - -0.2
Day 126	n	30	30	30
	Mean (SD)	154.85 (66.620)	72.43 (32.590)	-82.42 (69.983)
	Median	129.90	68.85	-64.35
	Q1 - Q3	105.00 - 204.00	53.20 - 79.20	-126.40 - -37.80
	Min - Max	59.4 - 324.8	32.9 - 211.2	-254.3 - 103.2
Day 140	n	34	34	34
	Mean (SD)	156.21 (64.339)	72.23 (23.304)	-83.98 (64.137)
	Median	139.20	71.00	-61.80
	Q1 - Q3	105.00 - 204.00	57.60 - 80.00	-129.20 - -36.90
	Min - Max	59.4 - 324.8	28.7 - 132.6	-258.8 - -2.2
Day 154	n	32	32	32
	Mean (SD)	158.14 (65.627)	66.56 (20.185)	-91.58 (60.272)

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 5 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Median	139.20	67.00	-68.75
	Q1 - Q3	105.40 - 208.05	52.05 - 76.40	-134.10 - -48.20
	Min - Max	59.4 - 324.8	30.8 - 130.0	-249.6 - -6.6
Day 168	n	39	39	39
	Mean (SD)	156.05 (63.543)	69.05 (22.137)	-87.00 (65.161)
	Median	144.00	67.20	-63.20
	Q1 - Q3	105.00 - 205.80	55.50 - 83.60	-133.80 - -43.50
	Min - Max	59.4 - 324.8	31.5 - 135.3	-267.6 - 57.6
Day 196	n	37	37	37
	Mean (SD)	157.14 (64.979)	66.10 (20.405)	-91.04 (62.042)
	Median	144.00	64.00	-74.00
	Q1 - Q3	105.00 - 205.80	49.40 - 84.60	-139.20 - -47.90
	Min - Max	59.4 - 324.8	32.4 - 108.1	-263.2 - 8.1

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 6 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 224	n	35	35	35
	Mean (SD)	153.39 (62.871)	68.61 (20.382)	-84.78 (57.973)
	Median	144.00	64.60	-75.20
	Q1 - Q3	105.00 - 205.80	55.50 - 83.20	-123.90 - -40.20
	Min - Max	59.4 - 324.8	27.2 - 115.0	-261.8 - -4.0
Day 252	n	38	38	38
	Mean (SD)	158.11 (63.060)	75.50 (41.399)	-82.62 (56.678)
	Median	144.45	64.55	-73.80
	Q1 - Q3	105.80 - 205.80	55.00 - 85.80	-128.80 - -42.60
	Min - Max	59.4 - 324.8	30.4 - 280.8	-251.2 - 6.4
Day 280	n	37	37	37
	Mean (SD)	157.20 (64.682)	73.13 (30.348)	-84.07 (56.915)
	Median	144.00	72.00	-60.30

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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Table 14.2-4.1 (Page 7 of 7)
Summary statistics of reticulocyte counts (10^9/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
	Q1 - Q3	105.00 - 205.80	49.20 - 91.20	-122.00 - -36.00
	Min - Max	59.4 - 324.8	9.6 - 141.0	-240.2 - -6.0
Day 308	n	32	32	32
	Mean (SD)	149.99 (66.403)	72.93 (45.158)	-77.06 (59.639)
	Median	121.45	65.35	-54.45
	Q1 - Q3	103.65 - 198.60	53.90 - 82.20	-124.90 - -32.55
	Min - Max	59.4 - 324.8	27.3 - 296.7	-243.8 - 16.1
Day 336	n	39	39	39
	Mean (SD)	156.05 (63.543)	79.51 (42.603)	-76.55 (50.149)
	Median	144.00	74.10	-70.30
	Q1 - Q3	105.00 - 205.80	49.20 - 96.90	-120.00 - -49.40
	Min - Max	59.4 - 324.8	14.8 - 218.7	-209.8 - 22.3

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline value of reticulocyte counts is defined to be the last result obtained at or prior to start of study treatment (Day 1).

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3.9 Änderung des LDH-Wertes zu verschiedenen Erhebungszeitpunkten

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Table 14.2-5.1 (Page 1 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline[a]	n	40		
	Mean (SD)	1698.8 (683.33)		
	Geometric Mean	1569.1		
	Median	1581.5		
	Q1 - Q3	1144.5 - 2054.5		
	Min - Max	522 - 3244		
Day 7	n	40	40	40
	Mean (SD)	1698.8 (683.33)	484.1 (177.27)	-1214.7 (531.94)
	Geometric Mean	1569.1	449.8	
	Median	1581.5	460.5	-1113.0
	Q1 - Q3	1144.5 - 2054.5	375.0 - 557.0	-1537.5 - -796.0
	Min - Max	522 - 3244	76 - 935	-2555 - -432

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 2 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 14	n	39	39	39
	Mean (SD)	1712.8 (686.36)	253.1 (73.34)	-1459.8 (634.92)
	Geometric Mean	1581.7	242.3	
	Median	1639.0	245.0	-1367.0
	Q1 - Q3	1139.0 - 2071.0	215.0 - 273.0	-1853.0 - -966.0
	Min - Max	522 - 3244	81 - 446	-2993 - -441
Day 28	n	39	39	39
	Mean (SD)	1712.8 (686.36)	195.8 (52.10)	-1517.0 (662.00)
	Geometric Mean	1581.7	188.8	
	Median	1639.0	191.0	-1461.0
	Q1 - Q3	1139.0 - 2071.0	166.0 - 218.0	-1885.0 - -994.0
	Min - Max	522 - 3244	79 - 343	-2978 - -443

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 3 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	36	36	36
	Mean (SD)	1730.0 (710.70)	192.0 (53.28)	-1538.0 (684.83)
	Geometric Mean	1588.9	185.1	
	Median	1656.5	179.5	-1482.0
	Q1 - Q3	1135.5 - 2117.0	160.0 - 227.5	-1920.0 - -964.0
	Min - Max	522 - 3244	82 - 367	-3017 - -440
Day 56	n	37	37	37
	Mean (SD)	1709.0 (698.16)	205.5 (54.01)	-1503.4 (674.94)
	Geometric Mean	1573.7	198.9	
	Median	1639.0	201.0	-1468.0
	Q1 - Q3	1139.0 - 2038.0	173.0 - 222.0	-1845.0 - -934.0
	Min - Max	522 - 3244	86 - 370	-3033 - -436

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

/csr_3/pgm/eff/t_lb_eff_sum.sas@@/main/1-26JUN2023:14:16 Final Version

Table 14.2-5.1 (Page 4 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 84	n	37	37	37
	Mean (SD)	1661.5 (662.33)	240.1 (55.34)	-1421.4 (645.51)
	Geometric Mean	1536.1	233.3	
	Median	1511.0	245.0	-1278.0
	Q1 - Q3	1139.0 - 2038.0	206.0 - 283.0	-1813.0 - -911.0
	Min - Max	522 - 3244	111 - 339	-2974 - -411
Day 112	n	31	31	31
	Mean (SD)	1724.4 (754.15)	258.7 (65.43)	-1465.7 (730.10)
	Geometric Mean	1568.5	250.6	
	Median	1511.0	268.0	-1261.0
	Q1 - Q3	1132.0 - 2163.0	209.0 - 296.0	-1879.0 - -889.0
	Min - Max	522 - 3244	138 - 393	-2976 - -360

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 5 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	31	31	31
	Mean (SD)	1713.0 (686.26)	254.7 (75.09)	-1458.3 (658.76)
	Geometric Mean	1578.7	244.2	
	Median	1639.0	254.0	-1402.0
	Q1 - Q3	1139.0 - 2071.0	208.0 - 297.0	-1834.0 - -904.0
	Min - Max	522 - 3244	129 - 485	-2946 - -393
Day 140	n	35	35	35
	Mean (SD)	1700.5 (634.55)	255.7 (60.62)	-1444.8 (616.04)
	Geometric Mean	1594.0	249.2	
	Median	1639.0	247.0	-1376.0
	Q1 - Q3	1150.0 - 2038.0	218.0 - 285.0	-1799.0 - -913.0
	Min - Max	700 - 3244	149 - 444	-2946 - -530

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 6 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	33	33	33
	Mean (SD)	1683.9 (679.94)	244.2 (60.67)	-1439.7 (653.23)
	Geometric Mean	1552.0	236.2	
	Median	1639.0	243.0	-1367.0
	Q1 - Q3	1139.0 - 2038.0	203.0 - 280.0	-1831.0 - -914.0
	Min - Max	522 - 3244	101 - 392	-2961 - -421
Day 168	n	39	39	39
	Mean (SD)	1685.7 (687.18)	261.3 (89.16)	-1424.4 (646.56)
	Geometric Mean	1555.5	249.3	
	Median	1524.0	255.0	-1271.0
	Q1 - Q3	1139.0 - 2038.0	210.0 - 291.0	-1830.0 - -920.0
	Min - Max	522 - 3244	122 - 666	-2955 - -400

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	38	38	38
	Mean (SD)	1721.8 (691.01)	266.7 (90.97)	-1455.2 (655.58)
	Geometric Mean	1589.2	253.5	
	Median	1656.5	256.5	-1302.0
	Q1 - Q3	1150.0 - 2071.0	210.0 - 298.0	-1822.0 - -929.0
	Min - Max	522 - 3244	105 - 557	-2946 - -417
Day 224	n	38	38	38
	Mean (SD)	1704.0 (700.93)	300.9 (266.08)	-1403.2 (661.05)
	Geometric Mean	1567.7	260.1	
	Median	1575.0	264.5	-1234.5
	Q1 - Q3	1139.0 - 2071.0	201.0 - 303.0	-1830.0 - -917.0
	Min - Max	522 - 3244	95 - 1818	-2941 - -427

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 8 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	39	39	39
	Mean (SD)	1659.6 (645.13)	281.8 (173.54)	-1377.8 (612.43)
	Geometric Mean	1540.4	256.0	
	Median	1524.0	255.0	-1262.0
	Q1 - Q3	1139.0 - 2038.0	202.0 - 312.0	-1764.0 - -925.0
	Min - Max	522 - 3244	98 - 1239	-2964 - -424
Day 280	n	38	38	38
	Mean (SD)	1663.2 (653.39)	294.5 (203.04)	-1368.7 (633.30)
	Geometric Mean	1540.8	261.8	
	Median	1575.0	263.5	-1201.5
	Q1 - Q3	1139.0 - 2038.0	201.0 - 317.0	-1777.0 - -902.0
	Min - Max	522 - 3244	102 - 1376	-2955 - -418

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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Table 14.2-5.1 (Page 9 of 9)
Summary statistics of LDH levels (U/L) by visit
Full Analysis Set

			LNP023 200mg b.i.d. N=40	
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	32	32	32
	Mean (SD)	1727.8 (744.94)	296.9 (249.78)	-1430.9 (699.74)
	Geometric Mean	1574.7	259.0	
	Median	1575.0	251.5	-1226.5
	Q1 - Q3	1135.5 - 2117.0	207.5 - 298.5	-1830.0 - -901.5
	Min - Max	522 - 3244	98 - 1608	-2951 - -424
Day 336	n	40	40	40
	Mean (SD)	1698.8 (683.33)	305.5 (247.50)	-1393.3 (652.15)
	Geometric Mean	1569.1	268.2	
	Median	1581.5	261.5	-1241.5
	Q1 - Q3	1144.5 - 2054.5	206.0 - 334.0	-1795.0 - -925.0
	Min - Max	522 - 3244	99 - 1739	-2928 - -423

Base = Baseline, Change = Post baseline - baseline.
At each visit, only patients with a value at both baseline and that visit are included.
a. The baseline LDH will be defined as the value on Day 1 (prior to starting treatment). If Day 1 value is not available, then the mean of two screening/LDH confirmatory values will be used. If screening value is not available, the baseline LDH will be defined as single confirmatory LDH value.

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3.10 Änderung der Funktionsskalen und der globalen Gesundheits- und Lebensqualitätsskala des EORTC QLQ-C30 gegenüber Baseline zu verschiedenen Erhebungszeitpunkten

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	52.9 (18.69)		
	Median	52.1		
	Q1 - Q3	39.6 - 66.7		
	Min - Max	21 - 88		
Day 14	n	36	36	36
	Mean (SD)	52.5 (19.53)	63.4 (17.96)	10.9 (15.82)
	Median	50.0	62.5	8.3
	Q1 - Q3	37.5 - 66.7	50.0 - 83.3	0.0 - 16.7
	Min - Max	21 - 88	33 - 100	-21 - 63

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 2 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	52.6 (18.80)	70.9 (18.02)	18.4 (19.28)
	Median	50.0	75.0	16.7
	Q1 - Q3	37.5 - 66.7	58.3 - 83.3	8.3 - 29.2
	Min - Max	21 - 88	25 - 100	-21 - 67
Day 84	n	38	38	38
	Mean (SD)	52.7 (19.01)	77.9 (15.04)	25.1 (18.11)
	Median	52.1	83.3	25.0
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	12.5 - 41.7
	Min - Max	21 - 88	33 - 100	-4 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 3 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	51.5 (19.04)	77.9 (17.38)	26.3 (18.52)
	Median	50.0	83.3	29.2
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	12.5 - 41.7
	Min - Max	21 - 88	33 - 100	-13 - 67
Day 140	n	37	37	37
	Mean (SD)	52.5 (18.67)	77.3 (16.97)	24.8 (18.37)
	Median	54.2	83.3	25.0
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	12.5 - 41.7
	Min - Max	21 - 88	25 - 100	-8 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 4 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	52.3 (18.91)	75.2 (15.36)	22.9 (18.62)
	Median	52.1	83.3	25.0
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	10.4 - 37.5
	Min - Max	21 - 88	25 - 100	-8 - 58
Day 168	n	37	37	37
	Mean (SD)	51.0 (18.01)	76.1 (14.85)	25.1 (18.72)
	Median	50.0	83.3	25.0
	Q1 - Q3	37.5 - 58.3	66.7 - 83.3	8.3 - 41.7
	Min - Max	21 - 88	25 - 100	-8 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 5 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	52.9 (18.69)	79.4 (13.61)	26.5 (19.51)
	Median	52.1	83.3	25.0
	Q1 - Q3	39.6 - 66.7	75.0 - 83.3	12.5 - 41.7
	Min - Max	21 - 88	25 - 100	-4 - 71
Day 224	n	37	37	37
	Mean (SD)	52.6 (19.30)	75.2 (18.05)	22.6 (21.64)
	Median	50.0	83.3	25.0
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	0.0 - 37.5
	Min - Max	21 - 88	25 - 100	-17 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 6 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	52.2 (18.50)	75.0 (17.86)	22.8 (19.15)
	Median	52.1	83.3	25.0
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	8.3 - 41.7
	Min - Max	21 - 88	17 - 100	-8 - 58
Day 280	n	37	37	37
	Mean (SD)	52.7 (18.67)	74.3 (15.39)	21.6 (19.47)
	Median	50.0	83.3	25.0
	Q1 - Q3	41.7 - 66.7	66.7 - 83.3	8.3 - 33.3
	Min - Max	21 - 88	25 - 100	-33 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 7 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Global health status

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	52.9 (18.69)	75.8 (16.32)	22.9 (17.27)
	Median	52.1	83.3	25.0
	Q1 - Q3	39.6 - 66.7	66.7 - 83.3	8.3 - 33.3
	Min - Max	21 - 88	25 - 100	-4 - 58
Day 336	n	39	39	39
	Mean (SD)	52.6 (18.80)	74.6 (16.88)	22.0 (21.29)
	Median	50.0	83.3	20.8
	Q1 - Q3	37.5 - 66.7	66.7 - 83.3	8.3 - 41.7
	Min - Max	21 - 88	25 - 100	-17 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 8 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	72.7 (16.98)		
	Median	73.3		
	Q1 - Q3	58.3 - 86.7		
	Min - Max	43 - 100		
Day 14	n	36	36	36
	Mean (SD)	72.0 (17.44)	80.9 (13.16)	8.9 (13.57)
	Median	73.3	80.0	6.7
	Q1 - Q3	55.0 - 86.7	70.0 - 93.3	0.0 - 18.3
	Min - Max	43 - 100	53 - 100	-17 - 47

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 9 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	72.5 (17.16)	85.6 (10.98)	13.2 (15.00)
	Median	73.3	86.7	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 93.3	3.3 - 26.7
	Min - Max	43 - 100	53 - 100	-20 - 40
Day 84	n	38	38	38
	Mean (SD)	72.1 (17.09)	87.7 (8.42)	15.6 (14.87)
	Median	73.3	86.7	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 93.3	3.3 - 26.7
	Min - Max	43 - 100	67 - 100	-7 - 47

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 10 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	71.9 (16.71)	87.4 (11.86)	15.5 (13.88)
	Median	73.3	86.7	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 100.0	3.3 - 26.7
	Min - Max	43 - 100	67 - 100	-3 - 47
Day 140	n	37	37	37
	Mean (SD)	72.6 (17.39)	87.0 (11.96)	14.4 (16.61)
	Median	73.3	86.7	10.0
	Q1 - Q3	56.7 - 86.7	80.0 - 93.3	0.0 - 26.7
	Min - Max	43 - 100	60 - 100	-13 - 47

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 11 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	71.2 (16.89)	89.3 (11.96)	18.1 (15.78)
	Median	71.7	93.3	16.7
	Q1 - Q3	55.0 - 86.7	83.3 - 100.0	3.3 - 26.7
	Min - Max	43 - 100	60 - 100	-7 - 57
Day 168	n	37	37	37
	Mean (SD)	71.1 (16.48)	88.3 (11.91)	17.2 (16.51)
	Median	73.3	93.3	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 100.0	6.7 - 26.7
	Min - Max	43 - 100	60 - 100	-27 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	72.7 (16.98)	90.5 (9.65)	17.8 (15.52)
	Median	73.3	93.3	13.3
	Q1 - Q3	58.3 - 86.7	86.7 - 100.0	5.0 - 26.7
	Min - Max	43 - 100	60 - 100	-7 - 50
Day 224	n	37	37	37
	Mean (SD)	72.3 (17.62)	88.1 (10.56)	15.8 (18.03)
	Median	73.3	86.7	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 93.3	3.3 - 26.7
	Min - Max	43 - 100	60 - 100	-17 - 47

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	72.7 (17.08)	89.8 (11.98)	17.1 (17.40)
	Median	73.3	93.3	13.3
	Q1 - Q3	60.0 - 86.7	86.7 - 100.0	3.3 - 26.7
	Min - Max	43 - 100	53 - 100	-20 - 57
Day 280	n	37	37	37
	Mean (SD)	72.4 (16.90)	87.9 (9.54)	15.5 (16.85)
	Median	73.3	86.7	10.0
	Q1 - Q3	60.0 - 86.7	86.7 - 93.3	3.3 - 26.7
	Min - Max	43 - 100	60 - 100	-13 - 57

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 14 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Physical functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	72.7 (16.98)	89.3 (10.76)	16.7 (17.65)
	Median	73.3	93.3	13.3
	Q1 - Q3	58.3 - 86.7	80.0 - 100.0	3.3 - 26.7
	Min - Max	43 - 100	67 - 100	-27 - 57
Day 336	n	39	39	39
	Mean (SD)	72.1 (16.87)	88.4 (12.02)	16.2 (17.47)
	Median	73.3	93.3	13.3
	Q1 - Q3	56.7 - 86.7	80.0 - 100.0	3.3 - 26.7
	Min - Max	43 - 100	40 - 100	-13 - 57

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	64.8 (24.35)		
	Median	66.7		
	Q1 - Q3	50.0 - 83.3		
	Min - Max	8 - 100		
Day 14	n	36	36	36
	Mean (SD)	65.0 (24.30)	74.1 (20.10)	9.0 (17.41)
	Median	66.7	66.7	8.3
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 16.7
	Min - Max	8 - 100	33 - 100	-42 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	64.5 (24.61)	80.3 (19.82)	15.8 (24.24)
	Median	66.7	83.3	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	33 - 100	-25 - 75
Day 84	n	38	38	38
	Mean (SD)	64.7 (24.69)	84.2 (17.31)	19.5 (23.51)
	Median	66.7	83.3	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 41.7
	Min - Max	8 - 100	33 - 100	-42 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	64.0 (24.65)	80.5 (23.04)	16.4 (22.73)
	Median	66.7	83.3	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	0 - 100	-42 - 50
Day 140	n	37	37	37
	Mean (SD)	65.3 (24.02)	84.2 (19.22)	18.9 (21.21)
	Median	66.7	83.3	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	17 - 100	-25 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	63.7 (24.73)	85.6 (19.17)	22.0 (19.02)
	Median	66.7	100.0	20.8
	Q1 - Q3	45.8 - 83.3	66.7 - 100.0	4.2 - 33.3
	Min - Max	8 - 100	17 - 100	-8 - 58
Day 168	n	37	37	37
	Mean (SD)	62.6 (23.78)	86.5 (15.13)	23.9 (23.34)
	Median	58.3	83.3	25.0
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	8.3 - 41.7
	Min - Max	8 - 100	50 - 100	-17 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	64.8 (24.35)	86.7 (14.71)	21.9 (25.30)
	Median	66.7	91.7	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	67 - 100	-17 - 92
Day 224	n	37	37	37
	Mean (SD)	64.6 (25.26)	82.9 (18.21)	18.2 (26.34)
	Median	66.7	83.3	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	33 - 100	-33 - 92

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	64.9 (24.06)	84.2 (21.56)	19.3 (22.85)
	Median	66.7	91.7	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	0 - 100	-17 - 75
Day 280	n	37	37	37
	Mean (SD)	64.0 (24.46)	86.9 (14.77)	23.0 (23.27)
	Median	66.7	100.0	25.0
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 41.7
	Min - Max	8 - 100	67 - 100	-17 - 75

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Role functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	64.8 (24.35)	84.2 (19.59)	19.4 (24.27)
	Median	66.7	100.0	16.7
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	17 - 100	-33 - 75
Day 336	n	39	39	39
	Mean (SD)	64.3 (24.48)	81.2 (20.30)	16.9 (22.90)
	Median	66.7	83.3	8.3
	Q1 - Q3	50.0 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	8 - 100	0 - 100	-33 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	69.4 (18.72)		
	Median	66.7		
	Q1 - Q3	62.5 - 81.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	68.1 (18.77)	80.3 (20.62)	12.3 (16.15)
	Median	66.7	83.3	12.5
	Q1 - Q3	62.5 - 75.0	66.7 - 95.8	0.0 - 20.8
	Min - Max	0 - 100	0 - 100	-29 - 42

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	68.9 (18.73)	81.0 (16.66)	12.1 (21.67)
	Median	66.7	83.3	4.2
	Q1 - Q3	62.5 - 79.2	66.7 - 100.0	-8.3 - 29.2
	Min - Max	0 - 100	50 - 100	-29 - 75
Day 84	n	38	38	38
	Mean (SD)	69.4 (19.06)	81.8 (20.67)	12.4 (16.93)
	Median	66.7	83.3	12.5
	Q1 - Q3	62.5 - 83.3	66.7 - 100.0	0.0 - 29.2
	Min - Max	0 - 100	0 - 100	-17 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	68.1 (19.28)	81.4 (23.14)	13.3 (20.08)
	Median	66.7	83.3	16.7
	Q1 - Q3	62.5 - 75.0	75.0 - 100.0	0.0 - 29.2
	Min - Max	0 - 100	0 - 100	-33 - 46
Day 140	n	37	37	37
	Mean (SD)	70.7 (15.32)	83.8 (19.93)	13.1 (22.76)
	Median	66.7	91.7	8.3
	Q1 - Q3	62.5 - 79.2	75.0 - 100.0	0.0 - 29.2
	Min - Max	38 - 100	17 - 100	-54 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	68.8 (19.20)	82.4 (22.69)	13.7 (21.97)
	Median	66.7	87.5	10.4
	Q1 - Q3	62.5 - 81.3	70.8 - 100.0	0.0 - 35.4
	Min - Max	0 - 100	0 - 100	-46 - 50
Day 168	n	37	37	37
	Mean (SD)	67.5 (18.10)	80.4 (22.33)	13.0 (23.69)
	Median	66.7	83.3	12.5
	Q1 - Q3	62.5 - 75.0	66.7 - 100.0	0.0 - 29.2
	Min - Max	0 - 100	0 - 100	-71 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	69.4 (18.72)	82.9 (20.23)	13.5 (21.20)
	Median	66.7	87.5	8.3
	Q1 - Q3	62.5 - 81.3	66.7 - 100.0	0.0 - 29.2
	Min - Max	0 - 100	8 - 100	-63 - 50
Day 224	n	37	37	37
	Mean (SD)	69.0 (18.80)	78.2 (22.77)	9.1 (22.94)
	Median	66.7	75.0	4.2
	Q1 - Q3	62.5 - 79.2	66.7 - 100.0	-4.2 - 25.0
	Min - Max	0 - 100	0 - 100	-71 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	69.1 (18.95)	77.9 (26.66)	8.8 (29.49)
	Median	66.7	87.5	6.3
	Q1 - Q3	62.5 - 79.2	66.7 - 100.0	0.0 - 29.2
	Min - Max	0 - 100	0 - 100	-71 - 50
Day 280	n	37	37	37
	Mean (SD)	69.6 (18.53)	79.1 (23.54)	9.5 (19.83)
	Median	66.7	83.3	8.3
	Q1 - Q3	62.5 - 79.2	66.7 - 100.0	0.0 - 25.0
	Min - Max	0 - 100	0 - 100	-54 - 42

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Emotional functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	69.4 (18.72)	79.2 (25.39)	9.8 (22.72)
	Median	66.7	91.7	8.3
	Q1 - Q3	62.5 - 81.3	70.8 - 100.0	-4.2 - 29.2
	Min - Max	0 - 100	0 - 100	-71 - 50
Day 336	n	39	39	39
	Mean (SD)	69.7 (18.88)	78.0 (23.76)	8.3 (23.38)
	Median	66.7	83.3	4.2
	Q1 - Q3	62.5 - 83.3	66.7 - 100.0	0.0 - 25.0
	Min - Max	0 - 100	0 - 100	-71 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	72.7 (20.41)		
	Median	75.0		
	Q1 - Q3	58.3 - 91.7		
	Min - Max	33 - 100		
Day 14	n	36	36	36
	Mean (SD)	70.8 (20.36)	77.8 (19.11)	6.9 (16.24)
	Median	66.7	83.3	4.2
	Q1 - Q3	58.3 - 87.5	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	73.1 (20.54)	79.1 (19.01)	6.0 (17.20)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 50
Day 84	n	38	38	38
	Mean (SD)	71.3 (19.92)	81.1 (19.05)	9.9 (18.87)
	Median	70.8	83.3	8.3
	Q1 - Q3	58.3 - 83.3	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	17 - 100	-50 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	73.1 (19.81)	78.6 (21.23)	5.5 (18.63)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 50
Day 140	n	37	37	37
	Mean (SD)	72.5 (20.59)	76.6 (21.68)	4.1 (19.51)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 8.3
	Min - Max	33 - 100	17 - 100	-50 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	72.2 (21.18)	77.8 (19.11)	5.6 (17.93)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 20.8
	Min - Max	33 - 100	33 - 100	-25 - 50
Day 168	n	37	37	37
	Mean (SD)	71.8 (20.35)	78.8 (21.75)	7.0 (18.16)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 83.3	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	72.7 (20.41)	81.3 (19.31)	8.5 (17.55)
	Median	75.0	83.3	4.2
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 50
Day 224	n	37	37	37
	Mean (SD)	72.1 (21.08)	78.4 (20.36)	6.3 (22.26)
	Median	66.7	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	17 - 100	-50 - 58

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	72.4 (20.70)	77.2 (25.24)	4.8 (21.97)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	17 - 100	-58 - 50
Day 280	n	37	37	37
	Mean (SD)	72.3 (20.61)	78.8 (20.66)	6.5 (19.56)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	0.0 - 16.7
	Min - Max	33 - 100	33 - 100	-33 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 35 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Cognitive functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	72.7 (20.41)	76.7 (22.90)	4.0 (20.59)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	66.7 - 100.0	-4.2 - 16.7
	Min - Max	33 - 100	33 - 100	-42 - 50
Day 336	n	39	39	39
	Mean (SD)	72.0 (20.19)	74.4 (26.72)	2.4 (22.78)
	Median	75.0	83.3	0.0
	Q1 - Q3	58.3 - 91.7	50.0 - 100.0	-16.7 - 16.7
	Min - Max	33 - 100	0 - 100	-67 - 50

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 36 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Baseline	n	40		
	Mean (SD)	62.1 (24.02)		
	Median	66.7		
	Q1 - Q3	41.7 - 83.3		
	Min - Max	0 - 100		
Day 14	n	36	36	36
	Mean (SD)	60.4 (24.18)	65.3 (25.93)	4.9 (23.18)
	Median	66.7	66.7	0.0
	Q1 - Q3	41.7 - 79.2	50.0 - 83.3	-4.2 - 12.5
	Min - Max	0 - 100	0 - 100	-42 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 37 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 42	n	39	39	39
	Mean (SD)	61.5 (24.08)	72.6 (23.72)	11.1 (23.83)
	Median	66.7	66.7	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 25.0
	Min - Max	0 - 100	17 - 100	-33 - 67
Day 84	n	38	38	38
	Mean (SD)	61.4 (24.39)	76.8 (23.74)	15.4 (24.47)
	Median	66.7	83.3	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-33 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 38 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 126	n	35	35	35
	Mean (SD)	61.2 (23.57)	75.7 (23.69)	14.5 (24.28)
	Median	66.7	66.7	8.3
	Q1 - Q3	41.7 - 75.0	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	17 - 100	-42 - 67
Day 140	n	37	37	37
	Mean (SD)	61.7 (24.65)	77.9 (20.43)	16.2 (24.21)
	Median	66.7	66.7	16.7
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	33 - 100	-25 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 39 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 154	n	36	36	36
	Mean (SD)	62.5 (24.11)	79.2 (21.22)	16.7 (26.50)
	Median	66.7	83.3	8.3
	Q1 - Q3	45.8 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	33 - 100	-33 - 100
Day 168	n	37	37	37
	Mean (SD)	59.7 (23.28)	78.4 (24.80)	18.7 (27.67)
	Median	66.7	83.3	16.7
	Q1 - Q3	41.7 - 66.7	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-33 - 100

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 40 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 196	n	40	40	40
	Mean (SD)	62.1 (24.02)	75.0 (26.15)	12.9 (29.35)
	Median	66.7	75.0	12.5
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-50 - 67
Day 224	n	37	37	37
	Mean (SD)	61.7 (24.88)	75.2 (28.22)	13.5 (29.42)
	Median	66.7	83.3	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-50 - 83

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 41 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 252	n	38	38	38
	Mean (SD)	62.1 (24.18)	76.8 (24.67)	14.7 (26.60)
	Median	66.7	83.3	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-33 - 83
Day 280	n	37	37	37
	Mean (SD)	61.5 (23.60)	74.8 (25.95)	13.3 (22.78)
	Median	66.7	83.3	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 25.0
	Min - Max	0 - 100	0 - 100	-33 - 67

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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Table 14.2-10.1 (Page 42 of 105)
Summary statistics of EORTC-QLQ-C30 by visit
Full Analysis Set

Scale: QLQC03-Social functioning

		LNP023 200mg b.i.d. N=40		
Visit	**Statistics**	**Base**	**Post**	**Change**
Day 308	n	40	40	40
	Mean (SD)	62.1 (24.02)	78.3 (25.37)	16.3 (27.47)
	Median	66.7	83.3	16.7
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-33 - 100
Day 336	n	39	39	39
	Mean (SD)	62.0 (24.32)	75.2 (26.46)	13.2 (28.14)
	Median	66.7	83.3	8.3
	Q1 - Q3	41.7 - 83.3	66.7 - 100.0	0.0 - 33.3
	Min - Max	0 - 100	0 - 100	-50 - 83

Base = Baseline, Change = Post baseline – baseline.
Baseline was defined as the mean of first assessment prior to Day 1 and the Day 1 value, and if one of the assessments is missing, the other available assessment of Screening or Day 1 will be used.
At each time point, only patients with a value at both baseline and that time point are included.
N: number of patients in the analysis set.

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3.11 Verträglichkeit

3.11.1 Gesamtraten von unerwünschten Ereignissen

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Table 14.3.1-1 (Page 1 of 2)
Overview of treatment-emergent adverse events
Safety Analysis Set

Category	LNP023 200mg b.i.d. N=40 n (%)
Adverse events	37 (92.5)
Treatment-related	17 (42.5)
Severe AEs	4 (10.0)
Treatment-related	1 (2.5)
SAEs	8 (20.0)
Treatment-related	2 (5.0)
Fatal SAEs	0
Treatment-related	0
AEs leading to treatment discontinuation	0
Treatment-related	0

- A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment.
- Data collected on AE CRF pages is summarized.
- Serious events are those marked Yes for SAE.
- AEs causing study drug discontinuations refer to those with 'Action taken with study treatment' answered as 'Drug withdrawn'.
- AEs causing study drug interruptions refer to those with 'Action taken with study treatment' answered as 'Drug interrupted'.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period for LNP023 is from first dose date until 7 days after the date of last dose administered.

Source: table 14.3.1-1.1, 14.3.1-1.2, 14.3.1-1.3, 14.3.1-1.5, 14.3.1-1.7, 14.3.1-1.8, 14.3.1-1.12

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Table 14.3.1-1 (Page 2 of 2)
Overview of treatment-emergent adverse events
Safety Analysis Set

Category	LNP023 200mg b.i.d. N=40 n (%)
AEs leading to dose interruption	0
AEs requiring additional therapy	33 (82.5)

- A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment.
- Data collected on AE CRF pages is summarized.
- Serious events are those marked Yes for SAE.
- AEs causing study drug discontinuations refer to those with 'Action taken with study treatment' answered as 'Drug withdrawn'.
- AEs causing study drug interruptions refer to those with 'Action taken with study treatment' answered as 'Drug interrupted'.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period for LNP023 is from first dose date until 7 days after the date of last dose administered.

Source: table 14.3.1-1.1, 14.3.1-1.2, 14.3.1-1.3, 14.3.1-1.5, 14.3.1-1.7, 14.3.1-1.8, 14.3.1-1.12

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3.11.2 Unerwünschte Ereignisse nach SOC, PT und Schweregrad

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Table 14.3.1-1.3 (Page 1 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Number of patients with at least one event	22 (55.0)	11 (27.5)	4 (10.0)
Blood and lymphatic system disorders	0 (0.0)	1 (2.5)	1 (2.5)
Breakthrough haemolysis	0 (0.0)	1 (2.5)	1 (2.5)
Cardiac disorders	2 (5.0)	0 (0.0)	0 (0.0)
Sinus bradycardia	1 (2.5)	0 (0.0)	0 (0.0)
Tachycardia	1 (2.5)	0 (0.0)	0 (0.0)
Eye disorders	4 (10.0)	0 (0.0)	0 (0.0)
Cataract	2 (5.0)	0 (0.0)	0 (0.0)
Vision blurred	2 (5.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	13 (32.5)	4 (10.0)	0 (0.0)
Diarrhoea	5 (12.5)	1 (2.5)	0 (0.0)
Abdominal pain	2 (5.0)	1 (2.5)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.3 (Page 2 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Dyspepsia	0 (0.0)	1 (2.5)	0 (0.0)
Gastritis	0 (0.0)	1 (2.5)	0 (0.0)
Toothache	0 (0.0)	1 (2.5)	0 (0.0)
Constipation	3 (7.5)	0 (0.0)	0 (0.0)
Vomiting	3 (7.5)	0 (0.0)	0 (0.0)
Nausea	2 (5.0)	0 (0.0)	0 (0.0)
Abdominal distension	1 (2.5)	0 (0.0)	0 (0.0)
Chronic gastritis	1 (2.5)	0 (0.0)	0 (0.0)
Gastric dilatation	1 (2.5)	0 (0.0)	0 (0.0)
Gastrooesophageal reflux disease	1 (2.5)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	1 (2.5)	0 (0.0)	0 (0.0)
Pancreatitis	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.3 (Page 3 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
General disorders and administration site conditions	9 (22.5)	1 (2.5)	1 (2.5)
Chest pain	1 (2.5)	0 (0.0)	1 (2.5)
Asthenia	1 (2.5)	1 (2.5)	0 (0.0)
Pyrexia	3 (7.5)	0 (0.0)	0 (0.0)
Fatigue	2 (5.0)	0 (0.0)	0 (0.0)
Influenza like illness	1 (2.5)	0 (0.0)	0 (0.0)
Peripheral swelling	1 (2.5)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	1 (2.5)	0 (0.0)	0 (0.0)
Hepatic function abnormal	1 (2.5)	0 (0.0)	0 (0.0)
Infections and infestations	14 (35.0)	5 (12.5)	2 (5.0)
Pneumonia	0 (0.0)	0 (0.0)	1 (2.5)
Pneumonia bacterial	0 (0.0)	0 (0.0)	1 (2.5)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.3 (Page 4 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 Mild n(%)	 Moderate n(%)	 Severe n(%)
COVID-19	8 (20.0)	1 (2.5)	0 (0.0)
Upper respiratory tract infection	6 (15.0)	1 (2.5)	0 (0.0)
Conjunctivitis	1 (2.5)	1 (2.5)	0 (0.0)
Influenza	1 (2.5)	1 (2.5)	0 (0.0)
Infection	0 (0.0)	1 (2.5)	0 (0.0)
Mucosal infection	0 (0.0)	1 (2.5)	0 (0.0)
Rhinitis	0 (0.0)	1 (2.5)	0 (0.0)
Staphylococcal skin infection	0 (0.0)	1 (2.5)	0 (0.0)
Ear infection	1 (2.5)	0 (0.0)	0 (0.0)
Gastrointestinal infection	1 (2.5)	0 (0.0)	0 (0.0)
Hordeolum	1 (2.5)	0 (0.0)	0 (0.0)
Urinary tract infection	1 (2.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.3 (Page 5 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Injury, poisoning and procedural complications	6 (15.0)	1 (2.5)	0 (0.0)
Joint injury	0 (0.0)	1 (2.5)	0 (0.0)
Contusion	2 (5.0)	0 (0.0)	0 (0.0)
Heat stroke	1 (2.5)	0 (0.0)	0 (0.0)
Ligament rupture	1 (2.5)	0 (0.0)	0 (0.0)
Ligament sprain	1 (2.5)	0 (0.0)	0 (0.0)
Vaccination complication	1 (2.5)	0 (0.0)	0 (0.0)
Wound	1 (2.5)	0 (0.0)	0 (0.0)
Investigations	12 (30.0)	4 (10.0)	0 (0.0)
Blood pressure abnormal	0 (0.0)	1 (2.5)	0 (0.0)
Carbohydrate antigen 125 increased	0 (0.0)	1 (2.5)	0 (0.0)
Carbohydrate antigen 15-3 increased	0 (0.0)	1 (2.5)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Table 14.3.1-1.3 (Page 6 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 Mild n(%)	 Moderate n(%)	 Severe n(%)
Cold agglutinins positive	0 (0.0)	1 (2.5)	0 (0.0)
Weight increased	0 (0.0)	1 (2.5)	0 (0.0)
Amylase increased	2 (5.0)	0 (0.0)	0 (0.0)
C-reactive protein increased	2 (5.0)	0 (0.0)	0 (0.0)
Lipids abnormal	2 (5.0)	0 (0.0)	0 (0.0)
Alanine aminotransferase increased	1 (2.5)	0 (0.0)	0 (0.0)
Aspartate aminotransferase increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood creatine phosphokinase increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood creatinine increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood follicle stimulating hormone increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood glucose increased	1 (2.5)	0 (0.0)	0 (0.0)

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- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period is from first dose date until 7 days after the date of last dose administered.

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Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 Mild n(%)	 Moderate n(%)	 Severe n(%)
Blood magnesium decreased	1 (2.5)	0 (0.0)	0 (0.0)
Blood phosphorus decreased	1 (2.5)	0 (0.0)	0 (0.0)
Blood potassium decreased	1 (2.5)	0 (0.0)	0 (0.0)
Blood triglycerides increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood uric acid increased	1 (2.5)	0 (0.0)	0 (0.0)
Blood urine present	1 (2.5)	0 (0.0)	0 (0.0)
Dihydrotestosterone decreased	1 (2.5)	0 (0.0)	0 (0.0)
Fibrin D dimer increased	1 (2.5)	0 (0.0)	0 (0.0)
Immunosuppressant drug level increased	1 (2.5)	0 (0.0)	0 (0.0)
Lipase increased	1 (2.5)	0 (0.0)	0 (0.0)
Protein urine present	1 (2.5)	0 (0.0)	0 (0.0)
Reverse tri-iodothyronine increased	1 (2.5)	0 (0.0)	0 (0.0)

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Table 14.3.1-1.3 (Page 8 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
White blood cell count increased	1 (2.5)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	9 (22.5)	1 (2.5)	0 (0.0)
Type 2 diabetes mellitus	0 (0.0)	1 (2.5)	0 (0.0)
Iron deficiency	3 (7.5)	0 (0.0)	0 (0.0)
Hyperlipidaemia	2 (5.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	1 (2.5)	0 (0.0)	0 (0.0)
Hypomagnesaemia	1 (2.5)	0 (0.0)	0 (0.0)
Hyponatraemia	1 (2.5)	0 (0.0)	0 (0.0)
Hypophosphataemia	1 (2.5)	0 (0.0)	0 (0.0)
Iron overload	1 (2.5)	0 (0.0)	0 (0.0)
Vitamin D deficiency	1 (2.5)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	5 (12.5)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
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Table 14.3.1-1.3 (Page 9 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Pain in extremity	2 (5.0)	0 (0.0)	0 (0.0)
Periarthritis	2 (5.0)	0 (0.0)	0 (0.0)
Osteoporosis	1 (2.5)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.5)	0 (0.0)	1 (2.5)
Malignant melanoma	0 (0.0)	0 (0.0)	1 (2.5)
Skin papilloma	1 (2.5)	0 (0.0)	0 (0.0)
Nervous system disorders	12 (30.0)	2 (5.0)	0 (0.0)
Headache	11 (27.5)	1 (2.5)	0 (0.0)
Loss of consciousness	0 (0.0)	1 (2.5)	0 (0.0)
Dizziness	1 (2.5)	0 (0.0)	0 (0.0)
Memory impairment	1 (2.5)	0 (0.0)	0 (0.0)
Syncope	1 (2.5)	0 (0.0)	0 (0.0)

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Table 14.3.1-1.3 (Page 10 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 Mild n(%)	Moderate n(%)	Severe n(%)
Psychiatric disorders	2 (5.0)	0 (0.0)	0 (0.0)
Bipolar disorder	1 (2.5)	0 (0.0)	0 (0.0)
Insomnia	1 (2.5)	0 (0.0)	0 (0.0)
Renal and urinary disorders	5 (12.5)	1 (2.5)	0 (0.0)
Proteinuria	0 (0.0)	1 (2.5)	0 (0.0)
Ureterolithiasis	2 (5.0)	0 (0.0)	0 (0.0)
Haemorrhage urinary tract	1 (2.5)	0 (0.0)	0 (0.0)
Microalbuminuria	1 (2.5)	0 (0.0)	0 (0.0)
Renal disorder	1 (2.5)	0 (0.0)	0 (0.0)
Renal impairment	1 (2.5)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	2 (5.0)	0 (0.0)	0 (0.0)
Heavy menstrual bleeding	2 (5.0)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
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Table 14.3.1-1.3 (Page 11 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Dysmenorrhoea	1 (2.5)	0 (0.0)	0 (0.0)
Menstrual disorder	1 (2.5)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	6 (15.0)	1 (2.5)	0 (0.0)
Epistaxis	1 (2.5)	1 (2.5)	0 (0.0)
Nasal dryness	0 (0.0)	1 (2.5)	0 (0.0)
Nasal congestion	2 (5.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	1 (2.5)	0 (0.0)	0 (0.0)
Rhinorrhoea	1 (2.5)	0 (0.0)	0 (0.0)
Sneezing	1 (2.5)	0 (0.0)	0 (0.0)
Skin and subcutaneous tissue disorders	5 (12.5)	4 (10.0)	0 (0.0)
Dermatitis allergic	0 (0.0)	2 (5.0)	0 (0.0)
Acne	0 (0.0)	1 (2.5)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
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Table 14.3.1-1.3 (Page 12 of 12)
Treatment-emergent adverse events by primary system organ class, preferred term and severity
Safety Analysis Set

	LNP023 200mg b.i.d. N=40		
Primary system organ class Preferred term	**Mild n(%)**	**Moderate n(%)**	**Severe n(%)**
Erythema multiforme	0 (0.0)	1 (2.5)	0 (0.0)
Urticaria	0 (0.0)	1 (2.5)	0 (0.0)
Haemorrhage subcutaneous	1 (2.5)	0 (0.0)	0 (0.0)
Nail disorder	1 (2.5)	0 (0.0)	0 (0.0)
Pruritus	1 (2.5)	0 (0.0)	0 (0.0)
Rash	1 (2.5)	0 (0.0)	0 (0.0)
Rash maculo-papular	1 (2.5)	0 (0.0)	0 (0.0)
Skin discolouration	1 (2.5)	0 (0.0)	0 (0.0)
Vascular disorders	2 (5.0)	0 (0.0)	0 (0.0)
Hypertension	2 (5.0)	0 (0.0)	0 (0.0)

- A patient with multiple severities for an AE is only counted under the maximum severity.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
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3.11.3 Schwerwiegende UE nach SOC und PT

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Serious treatment-emergent adverse events
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Number of patients with at least one event	8 (20.0)
Blood and lymphatic system disorders	1 (2.5)
Breakthrough haemolysis	1 (2.5)
Eye disorders	1 (2.5)
Cataract	1 (2.5)
Infections and infestations	5 (12.5)
COVID-19	2 (5.0)
Infection	1 (2.5)
Pneumonia	1 (2.5)
Pneumonia bacterial	1 (2.5)
Metabolism and nutrition disorders	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
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Table 14.3.1-1.2 (Page 2 of 2)
Serious treatment-emergent adverse events
by primary system organ class and preferred term
Safety Analysis Set

Primary system organ class **Preferred term**	**LNP023 200mg b.i.d.** **N=40** **n (%)**
Type 2 diabetes mellitus	1 (2.5)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.5)
Malignant melanoma	1 (2.5)

- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.
- A patient with multiple occurrences of an AE is counted only once in this AE category.
- System organ classes are presented in alphabetical order; preferred terms are sorted within system organ class in descending frequency of AEs.
- MedDRA version 26.0 has been used for the reporting of adverse events.
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3.11.4 Unerwünschte Ereignisse von besonderem Interesse (AESI)

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Table 14.3.1-2.1 (Page 1 of 3)
Treatment-emergent adverse events of special interest by risk level terms and preferred term
Safety Analysis Set

Risk Preferred term	name	LNP023 200mg b.i.d. N=40 n (%)
Number of patients with at least one event		11 (27.5)
Haemolysis in PNH patients (Broad)		3 (7.5)
Breakthrough haemolysis		2 (5.0)
Blood creatinine increased		1 (2.5)
Haemolysis in PNH patients (Narrow)		2 (5.0)
Breakthrough haemolysis		2 (5.0)
Hypersensitivity		4 (10.0)
Dermatitis allergic		2 (5.0)
Erythema multiforme		1 (2.5)
Rash		1 (2.5)
Rash maculo-papular		1 (2.5)

- A patient with multiple adverse events within risk is counted only once in the total row.
- A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment.
- Risks are presented in alphabetical order; preferred terms are sorted within risk in descending frequency of AEs in the LNP023 column.
- MedDRA version 26.0 has been used for the reporting of adverse events.
- Treatment Emergent Adverse Event (TEAE) is defined as event started during on-treatment period. On-treatment period for LNP023 is from first dose date until 7 days after the date of last dose administered.
- A patient with multiple occurrences of a risk under one treatment is counted only once for the same risk for that treatment.
- Compound Case Retrieval Strategy Sheet as of 29-Apr-2023.

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Table 14.3.1-2.1 (Page 2 of 3)
Treatment-emergent adverse events of special interest by risk level terms and preferred term
Safety Analysis Set

Risk name Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Urticaria	1 (2.5)
Infections caused by encapsulated bacteria	2 (5.0)
Pneumonia bacterial	1 (2.5)
Staphylococcal skin infection	1 (2.5)
Serious or severe infections	5 (12.5)
COVID-19	2 (5.0)
Infection	1 (2.5)
Pneumonia	1 (2.5)
Pneumonia bacterial	1 (2.5)
Testicular effects	1 (2.5)
Blood follicle stimulating hormone increased	1 (2.5)

- A patient with multiple adverse events within risk is counted only once in the total row.
- A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment.
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Table 14.3.1-2.1 (Page 3 of 3)
Treatment-emergent adverse events of special interest by risk level terms and preferred term
Safety Analysis Set

Risk name Preferred term	LNP023 200mg b.i.d. N=40 n (%)
Dihydrotestosterone decreased	1 (2.5)
Thyroid changes	1 (2.5)
Reverse tri-iodothyronine increased	1 (2.5)

- A patient with multiple adverse events within risk is counted only once in the total row.
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- A patient with multiple occurrences of a risk under one treatment is counted only once for the same risk for that treatment.
- Compound Case Retrieval Strategy Sheet as of 29-Apr-2023.

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