Dossier zur Nutzenbewertung gemäß § 35a SGB V

Insulin icodec (Awiqli®)

Novo Nordisk Pharma GmbH

Modul 4 A – Anhang 4-G

Behandlung von Insulin-naiven Erwachsenen mit Typ 2 Diabetes mellitus ohne oder mit kardiovaskulärer Erkrankung

Stand: 29.08.2024

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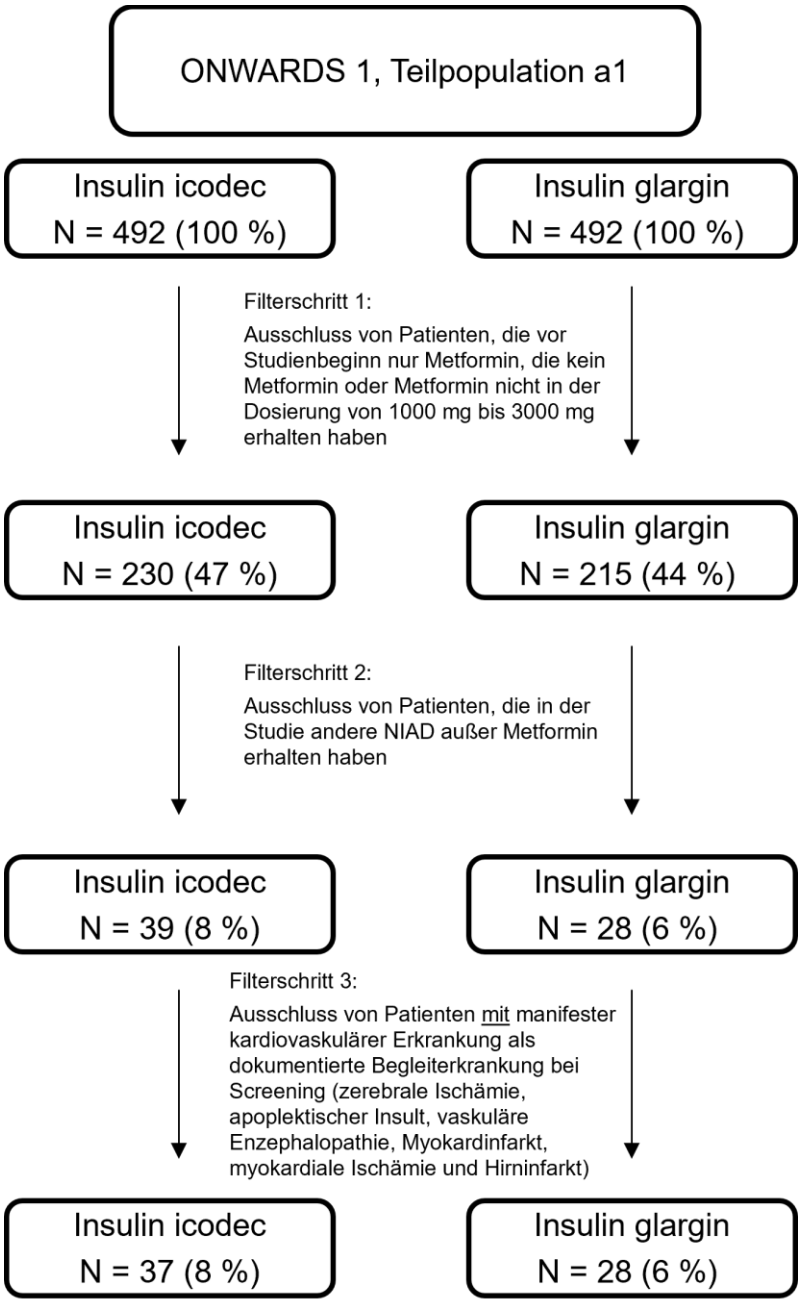
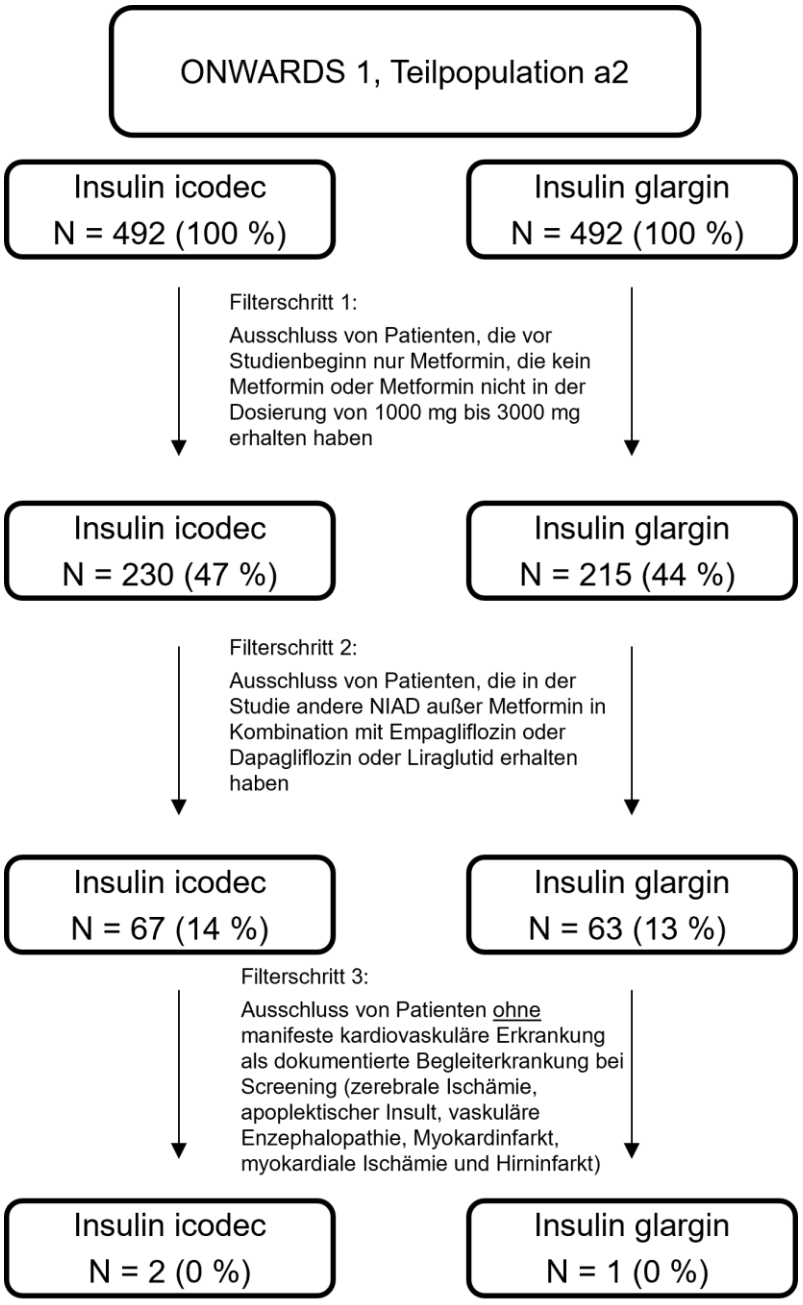
1.1 Auswertung der Teilpopulationen aus ONWARDS 1

1.1.1 Flow-Chart zur Auswertung der Teilpopulation a1



1.1.2 Flow-Chart zur Auswertung der Teilpopulation a2



1.2 Summary of label population 1 - Onwards 1 - Full analysis set

	Ico		IGlar	
	N	(%)	N	(%)
Full analysis set	492	(100)	492	(100)
Remaining subjects pre-treated with metformin and NIAD	230	(47)	215	(44)
Remaining subjects on metformin only post-baseline	39	(8)	28	(6)
Remaining subjects without specific CV disease medical history (population 1)	37	(8)	28	(6)

N: number of subjects, NIAD: Non-insulin antidiabetic drug. The medical history terms used to identify specific CV disease are cerebral ischaemia, cerebrovascular accident, vascular encephalopathy, cerebral infarction, myocardial infarction, and myocardial ischaemia.

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1.3 Summary of label population 2 - Onwards 1 - Full analysis set

	Ico		IGlar	
	N	(%)	N	(%)
Full analysis set	492	(100)	492	(100)
Remaining subjects pre-treated with metformin and NIAD	230	(47)	215	(44)
Remaining subjects on metformin in combination with Empa/ Dapa/Lira post-baseline	67	(14)	63	(13)
Remaining subjects with specific CV disease medical history (population 2)	2	(0)	1	(0)

N: number of subjects, NIAD: Non-insulin antidiabetic drug, Empa: Empagliflozin, Dapa: Dapagliflozin, Lira: Liraglutide. The medical history terms used to identify specific CV disease are cerebral ischaemia, cerebrovascular accident, vascular encephalopathy, cerebral infarction, myocardial infarction, and myocardial ischaemia.

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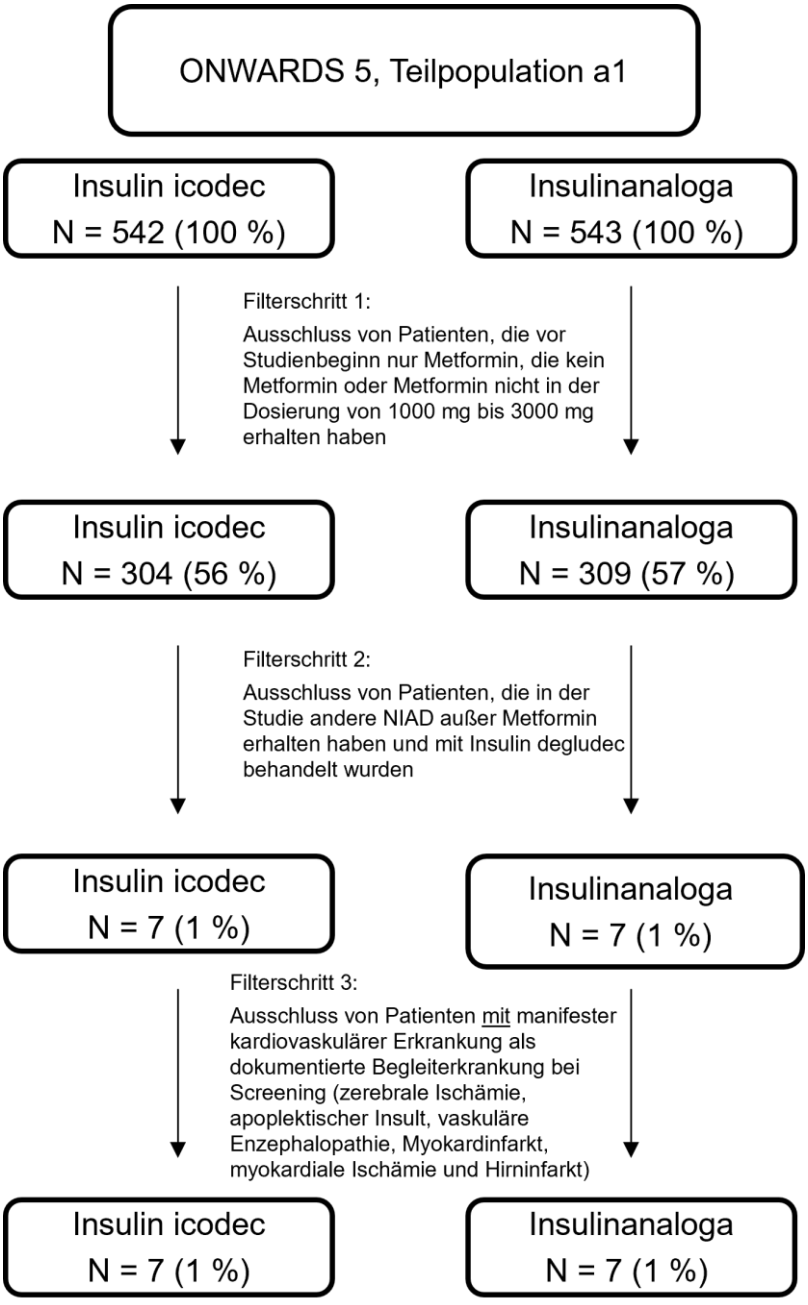
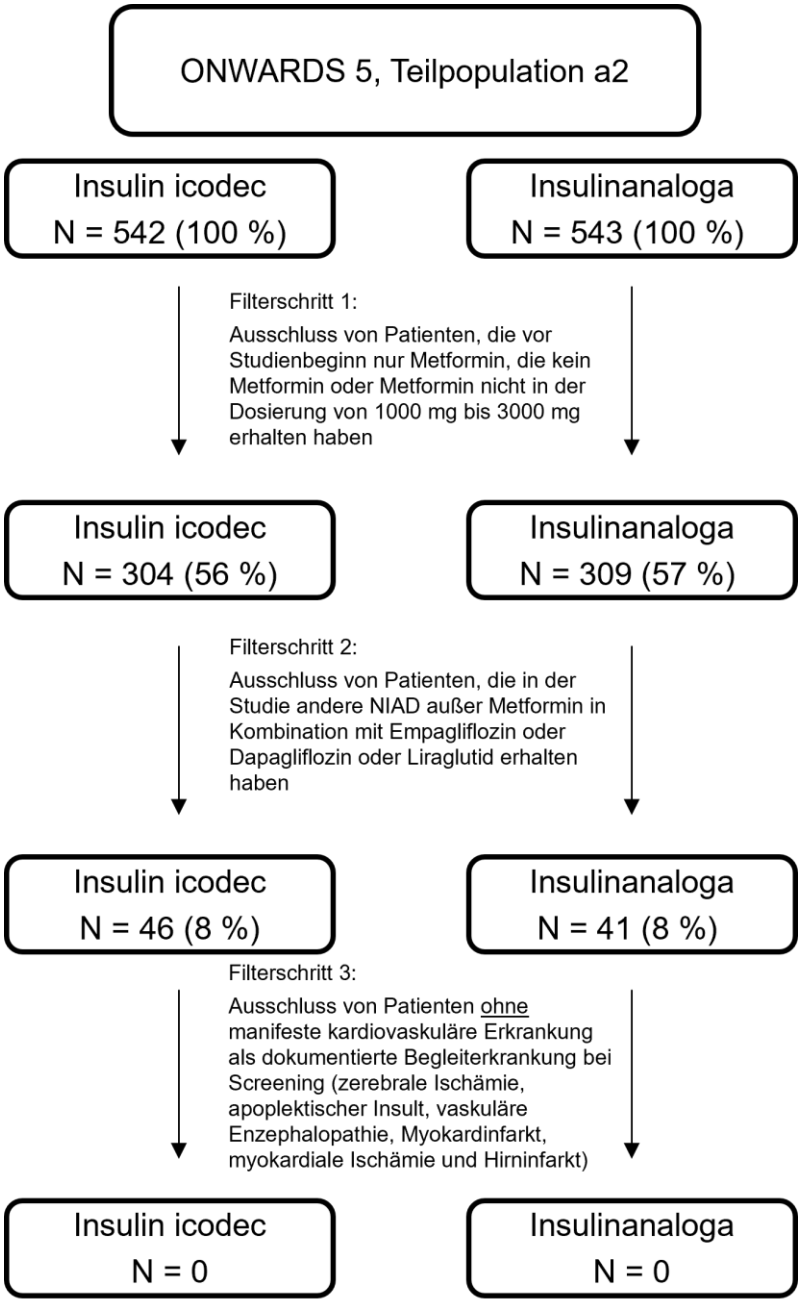
1.4 Auswertung der Teilpopulationen aus ONWARDS 5

1.4.1 Flow-Chart zur Auswertung der Teilpopulation a1



1.4.2 Flow-Chart zur Auswertung der Teilpopulation a2



1.5 Summary of label population 1 - Onwards 5 - Full analysis set

	Ico		OD analogues	
	N	(%)	N	(%)
Full analysis set	542	(100)	543	(100)
Remaining subjects pre-treated with metformin and NIAD	304	(56)	309	(57)
Remaining subjects on metformin only post-baseline	10	(2)	7	(1)
Remaining subjects who were not assigned insulin degludec at screening	7	(1)	7	(1)
Remaining subjects without specific CV disease medical history (population 1)	7	(1)	7	(1)

N: number of subjects, NIAD: Non-insulin antidiabetic drug. The medical history terms used to identify specific CV disease are cerebral ischaemia, cerebrovascular accident, vascular encephalopathy, cerebral infarction, myocardial infarction, and myocardial ischaemia.

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1.6 Summary of label population 2 - Onwards 5 - Full analysis set

	Ico		OD analogues	
	N	(%)	N	(%)
Full analysis set	542	(100)	543	(100)
Remaining subjects pre-treated with metformin and NIAD	304	(56)	309	(57)
Remaining subjects on metformin in combination with Empa/ Dapa/Lira post-baseline	46	(8)	41	(8)
Remaining subjects with specific CV disease medical history (population 2)	0	(0)	0	(0)

N: number of subjects, NIAD: Non-insulin antidiabetic drug, Empa: Empagliflozin, Dapa: Dapagliflozin, Lira: Liraglutide. The medical history terms used to identify specific CV disease are cerebral ischaemia, cerebrovascular accident, vascular encephalopathy, cerebral infarction, myocardial infarction, and myocardial ischaemia.

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2 Vollständige Auswertung zu Wirksamkeit und Sicherheit inkl. Subgruppenanalysen zur Teilpopulation a1 aus ONWARDS 1

2.1 Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar	
		N n	Mean (SD)	LS Mean (SE)	N n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
HbA1c (%)									
All subjects (total)	Week 10	37 37	-0.88 (1.24)		28 28	-0.82 (0.86)			0.05 [-0.44; 0.54]
	Week 18	37 36	-1.45 (1.05)		28 28	-1.14 (0.94)			0.30 [-0.19; 0.80]
	Week 26	37 37	-1.61 (0.92)		28 28	-1.48 (0.99)			0.13 [-0.36; 0.62]
	Week 36	37 35	-1.67 (0.87)		28 27	-1.52 (0.85)			0.17 [-0.32; 0.66]
	Week 44	37 37	-1.78 (0.95)		28 27	-1.50 (0.79)			0.31 [-0.18; 0.81]
	Week 52	37 37	-1.74 (0.99)		28 27	-1.71 (0.91)			0.04 [-0.45; 0.53]
	Week 62	37 37	-1.72 (1.13)		28 27	-1.74 (0.98)			-0.02 [-0.51; 0.47]
	Week 70	37 34	-1.62 (1.02)		28 27	-1.53 (0.96)			0.09 [-0.40; 0.58]
	Week 78	37 36	-1.64 (1.01)	-1.63 (0.15)	28 27	-1.67 (1.01)	-1.57 (0.17)	-0.05 [-0.49; 0.39] 0.8163	-0.03 [-0.52; 0.46]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
Gender											
Female	Week 10	17	17	-0.84 (1.04)		14	14	-0.74 (0.80)			0.10 [-0.60; 0.81]
	Week 18	17	16	-1.45 (0.99)		14	14	-0.95 (0.95)			0.50 [-0.22; 1.22]
	Week 26	17	17	-1.52 (0.94)		14	14	-1.35 (1.02)			0.17 [-0.54; 0.88]
	Week 36	17	15	-1.47 (0.93)		14	13	-1.48 (0.74)			-0.01 [-0.72; 0.70]
	Week 44	17	17	-1.63 (1.16)		14	13	-1.37 (0.81)			0.25 [-0.46; 0.96]
	Week 52	17	17	-1.53 (1.20)		14	13	-1.82 (0.99)			-0.25 [-0.96; 0.46]
	Week 62	17	17	-1.56 (1.39)		14	13	-1.87 (1.09)			-0.24 [-0.94; 0.47]
	Week 70	17	15	-1.50 (1.38)		14	13	-1.64 (1.03)			-0.11 [-0.82; 0.60]
	Week 78	17	16	-1.52 (1.28)	-1.59 (0.22)	14	13	-1.69 (1.02)	-1.60 (0.24)	0.02 [-0.63; 0.66] 0.9554	-0.14 [-0.85; 0.57] 0.7667
Male	Week 10	20	20	-0.92 (1.41)		14	14	-0.91 (0.93)			0.01 [-0.68; 0.69]
	Week 18	20	20	-1.46 (1.13)		14	14	-1.34 (0.93)			0.11 [-0.57; 0.79]
	Week 26	20	20	-1.68 (0.92)		14	14	-1.61 (0.97)			0.07 [-0.61; 0.75]
	Week 36	20	20	-1.82 (0.82)		14	14	-1.56 (0.96)			0.29 [-0.39; 0.98]
	Week 44	20	20	-1.90 (0.73)		14	14	-1.61 (0.79)			0.37 [-0.32; 1.06]
	Week 52	20	20	-1.93 (0.77)		14	14	-1.61 (0.86)			0.38 [-0.30; 1.07]
	Week 62	20	20	-1.85 (0.88)		14	14	-1.63 (0.89)			0.24 [-0.44; 0.93]
	Week 70	20	19	-1.72 (0.65)		14	14	-1.44 (0.92)			0.35 [-0.33; 1.04]
	Week 78	20	20	-1.74 (0.76)	-1.66 (0.20)	14	14	-1.65 (1.05)	-1.54 (0.24)	-0.12 [-0.73; 0.50] 0.7103	0.09 [-0.59; 0.78]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
Age											
<65 years	Week 10	26	26	-0.99 (1.29)		23	23	-0.73 (0.91)			0.23 [-0.33; 0.79]
	Week 18	26	25	-1.55 (0.98)		23	23	-1.04 (1.01)			0.50 [-0.07; 1.07]
	Week 26	26	26	-1.67 (0.82)		23	23	-1.42 (1.08)			0.25 [-0.31; 0.82]
	Week 36	26	26	-1.63 (0.87)		23	22	-1.42 (0.91)			0.23 [-0.33; 0.80]
	Week 44	26	26	-1.91 (0.85)		23	22	-1.45 (0.85)			0.52 [-0.05; 1.09]
	Week 52	26	26	-1.90 (0.85)		23	22	-1.70 (1.00)			0.20 [-0.36; 0.77]
	Week 62	26	26	-1.88 (1.06)		23	22	-1.74 (1.08)			0.13 [-0.43; 0.69]
	Week 70	26	23	-1.78 (0.88)		23	22	-1.50 (1.03)			0.29 [-0.27; 0.86]
	Week 78	26	25	-1.74 (0.92)	-1.64 (0.18)	23	22	-1.65 (1.09)	-1.52 (0.19)	-0.12 [-0.63; 0.39] 0.6456	0.08 [-0.48; 0.65] 0.5352
>=65 years	Week 10	11	11	-0.61 (1.12)		5	5	-1.24 (0.36)			-0.62 [-1.70; 0.46]
	Week 18	11	11	-1.23 (1.21)		5	5	-1.60 (0.32)			-0.34 [-1.40; 0.72]
	Week 26	11	11	-1.46 (1.15)		5	5	-1.74 (0.24)			-0.27 [-1.33; 0.79]
	Week 36	11	9	-1.78 (0.92)		5	5	-1.96 (0.17)			-0.22 [-1.28; 0.84]
	Week 44	11	11	-1.46 (1.12)		5	5	-1.68 (0.44)			-0.21 [-1.27; 0.85]
	Week 52	11	11	-1.38 (1.24)		5	5	-1.72 (0.36)			-0.30 [-1.36; 0.76]
	Week 62	11	11	-1.34 (1.25)		5	5	-1.78 (0.22)			-0.39 [-1.46; 0.67]
	Week 70	11	11	-1.29 (1.25)		5	5	-1.70 (0.66)			-0.35 [-1.41; 0.72]
	Week 78	11	11	-1.42 (1.22)	-1.58 (0.27)	5	5	-1.74 (0.63)	-1.80 (0.41)	0.22 [-0.73; 1.17] 0.6465	-0.28 [-1.34; 0.78]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico				IGlar				Ico - IGlar			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
HbA1c													
<=8,5%	Week 10	18	18	-0.33 (0.87)		9	9	-0.32 (0.96)				0.01 [-0.79; 0.81]	
	Week 18	18	17	-0.81 (0.68)		9	9	-0.74 (0.77)				0.09 [-0.71; 0.89]	
	Week 26	18	18	-1.08 (0.68)		9	9	-0.92 (0.72)				0.23 [-0.58; 1.03]	
	Week 36	18	17	-1.28 (0.78)		9	9	-1.01 (0.90)				0.32 [-0.48; 1.12]	
	Week 44	18	18	-1.10 (0.73)		9	9	-0.77 (0.58)				0.47 [-0.34; 1.28]	
	Week 52	18	18	-1.06 (0.79)		9	9	-1.01 (0.85)				0.06 [-0.74; 0.86]	
	Week 62	18	18	-0.94 (0.81)		9	9	-1.10 (1.09)				-0.17 [-0.97; 0.64]	
	Week 70	18	16	-0.91 (0.86)		9	9	-1.01 (1.08)				-0.10 [-0.90; 0.70]	
	Week 78	18	18	-0.92 (0.72)	-0.95 (0.21)	9	9	-1.22 (1.15)	-1.30 (0.29)	0.34 [-0.36; 1.04]	0.3382	-0.33 [-1.14; 0.47]	0.1498
>8,5%	Week 10	19	19	-1.40 (1.32)		19	19	-1.06 (0.71)				0.31 [-0.32; 0.95]	
	Week 18	19	19	-2.03 (1.00)		19	19	-1.33 (0.98)				0.69 [0.03; 1.34]	
	Week 26	19	19	-2.10 (0.85)		19	19	-1.74 (1.00)				0.38 [-0.26; 1.02]	
	Week 36	19	18	-2.03 (0.82)		19	18	-1.77 (0.72)				0.33 [-0.31; 0.97]	
	Week 44	19	19	-2.42 (0.63)		19	18	-1.86 (0.61)				0.88 [0.21; 1.54]	
	Week 52	19	19	-2.39 (0.70)		19	18	-2.06 (0.74)				0.46 [-0.19; 1.10]	
	Week 62	19	19	-2.45 (0.89)		19	18	-2.07 (0.76)				0.46 [-0.19; 1.10]	
	Week 70	19	18	-2.25 (0.70)		19	18	-1.79 (0.81)				0.59 [-0.06; 1.24]	
	Week 78	19	18	-2.36 (0.70)	-2.15 (0.21)	19	18	-1.89 (0.89)	-1.82 (0.21)	-0.33 [-0.92; 0.26]	0.2699	0.57 [-0.08; 1.22]	
Region													
Europe	Week 10	9	9	-0.48 (0.81)		6	6	-0.73 (1.12)				-0.26 [-1.29; 0.78]	
	Week 18	9	9	-1.12 (0.97)		6	6	-1.20 (1.03)				-0.07 [-1.11; 0.96]	
	Week 26	9	9	-1.19 (0.83)		6	6	-1.40 (1.03)				-0.22 [-1.25; 0.82]	
	Week 36	9	8	-1.32 (1.03)		6	6	-1.57 (0.76)				-0.24 [-1.28; 0.79]	
	Week 44	9	9	-1.32 (1.04)		6	6	-1.22 (0.83)				0.10 [-0.93; 1.14]	
	Week 52	9	9	-1.21 (1.08)		6	6	-1.63 (0.92)				-0.39 [-1.43; 0.65]	
	Week 62	9	9	-1.19 (1.21)		6	6	-1.45 (1.12)				-0.21 [-1.25; 0.83]	
	Week 70	9	8	-1.07 (1.33)		6	6	-1.48 (1.45)				-0.28 [-1.32; 0.76]	
	Week 78	9	8	-1.16 (1.19)	-1.14 (0.30)	6	6	-1.40 (1.39)	-1.54 (0.36)	0.40 [-0.52; 1.32]	0.3955	-0.18 [-1.21; 0.86]	0.5459
North and South America	Week 10	19	19	-0.79 (1.43)		17	17	-0.95 (0.78)				-0.13 [-0.78; 0.53]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
	Week 18	19	18	-1.42 (1.16)		17	17	-1.22 (0.96)			0.19 [-0.47; 0.84]
	Week 26	19	19	-1.72 (0.98)		17	17	-1.66 (0.88)			0.06 [-0.60; 0.71]
	Week 36	19	19	-1.63 (0.86)		17	16	-1.61 (0.83)			0.03 [-0.63; 0.68]
	Week 44	19	19	-1.81 (0.72)		17	16	-1.62 (0.77)			0.24 [-0.41; 0.90]
	Week 52	19	19	-1.76 (0.75)		17	16	-1.56 (0.77)			0.26 [-0.40; 0.92]
	Week 62	19	19	-1.68 (0.86)		17	16	-1.71 (0.80)			-0.03 [-0.69; 0.62]
	Week 70	19	17	-1.63 (0.73)		17	16	-1.52 (0.82)			0.14 [-0.52; 0.80]
	Week 78	19	19	-1.66 (0.82)	-1.71 (0.20)	17	16	-1.69 (0.90)	-1.52 (0.22)	-0.20 [-0.78; 0.38] 0.5057	-0.04 [-0.70; 0.61]
Asia	Week 10	9	9	-1.46 (1.04)		5	5	-0.50 (0.85)			0.91 [-0.23; 2.06]
	Week 18	9	9	-1.84 (0.87)		5	5	-0.82 (0.92)			1.08 [-0.09; 2.24]
	Week 26	9	9	-1.78 (0.83)		5	5	-0.94 (1.27)			0.78 [-0.35; 1.91]
	Week 36	9	8	-2.10 (0.62)		5	5	-1.18 (1.08)			1.08 [-0.09; 2.24]
	Week 44	9	9	-2.17 (1.17)		5	5	-1.44 (0.88)			0.63 [-0.49; 1.75]
	Week 52	9	9	-2.23 (1.20)		5	5	-2.26 (1.28)			-0.02 [-1.11; 1.07]
	Week 62	9	9	-2.33 (1.39)		5	5	-2.22 (1.35)			0.08 [-1.02; 1.17]
	Week 70	9	9	-2.09 (1.07)		5	5	-1.64 (0.94)			0.41 [-0.70; 1.51]
	Week 78	9	9	-2.03 (1.14)	-1.94 (0.29)	5	5	-1.92 (1.03)	-1.79 (0.39)	-0.14 [-1.10; 0.81] 0.7711	0.10 [-1.00; 1.19]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current

Change in HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
Race											
White	Week 10	23	23	-0.53 (1.26)		13	13	-0.99 (0.97)			-0.39 [-1.08; 0.29]
	Week 18	23	22	-1.24 (1.05)		13	13	-1.32 (1.17)			-0.08 [-0.76; 0.60]
	Week 26	23	23	-1.47 (0.86)		13	13	-1.78 (1.02)			-0.34 [-1.02; 0.34]
	Week 36	23	22	-1.51 (0.91)		13	12	-1.74 (0.74)			-0.27 [-0.95; 0.42]
	Week 44	23	23	-1.62 (0.80)		13	12	-1.62 (0.82)			0.00 [-0.68; 0.68]
	Week 52	23	23	-1.55 (0.88)		13	12	-1.80 (0.82)			-0.29 [-0.97; 0.40]
	Week 62	23	23	-1.50 (0.95)		13	12	-1.73 (0.96)			-0.23 [-0.92; 0.45]
	Week 70	23	20	-1.39 (0.95)		13	12	-1.61 (1.20)			-0.21 [-0.89; 0.47]
	Week 78	23	22	-1.48 (0.92)	-1.55 (0.22)	13	12	-1.65 (1.14)	-1.51 (0.28)	-0.04 [-0.67; 0.59] 0.9017	-0.17 [-0.85; 0.51] 0.8432
Not white	Week 10	14	14	-1.46 (0.98)		15	15	-0.67 (0.75)			0.88 [0.11; 1.64]
	Week 18	14	14	-1.79 (1.00)		15	15	-0.99 (0.70)			0.91 [0.15; 1.68]
	Week 26	14	14	-1.84 (1.00)		15	15	-1.21 (0.91)			0.63 [-0.11; 1.38]
	Week 36	14	13	-1.94 (0.77)		15	15	-1.34 (0.91)			0.69 [-0.06; 1.44]
	Week 44	14	14	-2.04 (1.13)		15	15	-1.40 (0.78)			0.64 [-0.11; 1.39]
	Week 52	14	14	-2.06 (1.12)		15	15	-1.63 (1.00)			0.40 [-0.34; 1.13]
	Week 62	14	14	-2.07 (1.35)		15	15	-1.75 (1.02)			0.26 [-0.47; 0.99]
	Week 70	14	14	-1.96 (1.06)		15	15	-1.47 (0.76)			0.51 [-0.23; 1.25]
	Week 78	14	14	-1.90 (1.13)	-1.76 (0.32)	15	15	-1.69 (0.95)	-1.63 (0.25)	-0.14 [-0.84; 0.57] 0.7043	0.20 [-0.53; 0.93]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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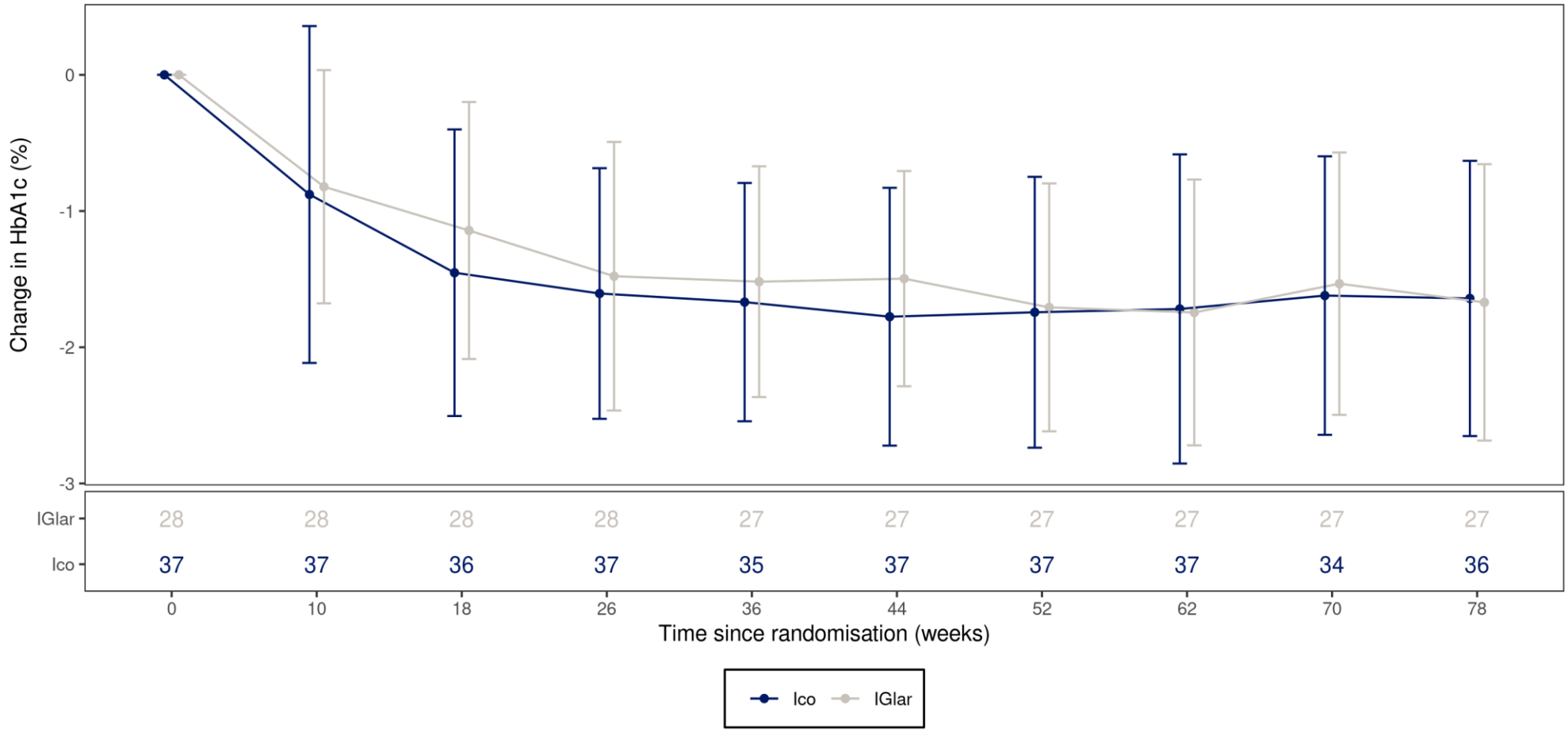
2.2 Change in HbA1c by treatment week - Mean plot - Onwards 1 - Population 1 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
HbA1c: Haemoglobin A1c.

nn1436/nn1436-amnog/current
23JAN2024:13:35:49 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/HBA1CBchg4477.png

2.3 Absolute HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
HbA1c (%)								
All subjects (total)	Week 0	37	37	8.73 (1.08)	28	28	8.86 (0.95)	0.13 [-0.36; 0.62]
	Week 10	37	37	7.85 (1.21)	28	28	8.04 (1.00)	0.17 [-0.32; 0.66]
	Week 18	37	36	7.31 (0.96)	28	28	7.72 (1.20)	0.38 [-0.11; 0.88]
	Week 26	37	37	7.12 (0.87)	28	28	7.39 (0.98)	0.28 [-0.21; 0.77]
	Week 36	37	35	7.07 (0.92)	28	27	7.27 (0.80)	0.22 [-0.27; 0.71]
	Week 44	37	37	6.95 (0.73)	28	27	7.29 (0.62)	0.48 [-0.02; 0.98]
	Week 52	37	37	6.99 (0.73)	28	27	7.08 (0.75)	0.12 [-0.37; 0.61]
	Week 62	37	37	7.01 (0.82)	28	27	7.04 (0.85)	0.04 [-0.46; 0.53]
	Week 70	37	34	7.10 (0.86)	28	27	7.25 (0.88)	0.18 [-0.32; 0.67]
	Week 78	37	36	7.06 (0.72)	28	27	7.11 (0.87)	0.07 [-0.42; 0.56]
Gender								
Female	Week 0	17	17	8.61 (1.26)	14	14	8.77 (1.07)	0.14 [-0.57; 0.84]
	Week 10	17	17	7.77 (0.86)	14	14	8.04 (1.24)	0.25 [-0.46; 0.96]
	Week 18	17	16	7.21 (0.59)	14	14	7.82 (1.52)	0.54 [-0.18; 1.26]
	Week 26	17	17	7.08 (0.76)	14	14	7.42 (1.29)	0.32 [-0.39; 1.03]
	Week 36	17	15	7.15 (0.90)	14	13	7.12 (0.93)	-0.03 [-0.74; 0.68]
	Week 44	17	17	6.98 (0.73)	14	13	7.23 (0.78)	0.33 [-0.38; 1.04]
	Week 52	17	17	7.08 (0.83)	14	13	6.78 (0.87)	-0.34 [-1.05; 0.38]
	Week 62	17	17	7.04 (1.03)	14	13	6.73 (0.90)	-0.31 [-1.02; 0.40]
	Week 70	17	15	7.05 (0.96)	14	13	6.96 (0.89)	-0.09 [-0.80; 0.62]
	Week 78	17	16	7.01 (0.75)	14	13	6.91 (0.89)	-0.12 [-0.83; 0.59]
Male	Week 0	20	20	8.84 (0.91)	14	14	8.96 (0.85)	0.13 [-0.55; 0.82]
	Week 10	20	20	7.92 (1.45)	14	14	8.05 (0.75)	0.10 [-0.58; 0.79]
	Week 18	20	20	7.38 (1.19)	14	14	7.62 (0.80)	0.22 [-0.46; 0.91]
	Week 26	20	20	7.16 (0.98)	14	14	7.35 (0.59)	0.22 [-0.47; 0.90]
	Week 36	20	20	7.02 (0.95)	14	14	7.40 (0.66)	0.45 [-0.25; 1.14]
	Week 44	20	20	6.93 (0.75)	14	14	7.34 (0.44)	0.62 [-0.08; 1.32]
	Week 52	20	20	6.91 (0.64)	14	14	7.35 (0.50)	0.73 [0.02; 1.43]
	Week 62	20	20	6.98 (0.61)	14	14	7.33 (0.70)	0.52 [-0.17; 1.21]
	Week 70	20	19	7.14 (0.80)	14	14	7.52 (0.80)	0.47 [-0.22; 1.16]
	Week 78	20	20	7.10 (0.72)	14	14	7.31 (0.84)	0.26 [-0.42; 0.95]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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Absolute HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Age								
<65 years	Week 0	26	26	8.77 (0.99)	23	23	8.87 (1.01)	0.10 [-0.46; 0.66]
	Week 10	26	26	7.78 (1.35)	23	23	8.14 (1.01)	0.30 [-0.27; 0.86]
	Week 18	26	25	7.26 (1.04)	23	23	7.83 (1.27)	0.48 [-0.08; 1.05]
	Week 26	26	26	7.11 (0.92)	23	23	7.45 (1.04)	0.35 [-0.22; 0.91]
	Week 36	26	26	7.14 (0.98)	23	22	7.36 (0.77)	0.24 [-0.32; 0.80]
	Week 44	26	26	6.87 (0.71)	23	22	7.32 (0.66)	0.65 [0.08; 1.23]
	Week 52	26	26	6.88 (0.70)	23	22	7.07 (0.79)	0.26 [-0.31; 0.82]
	Week 62	26	26	6.89 (0.84)	23	22	7.04 (0.88)	0.17 [-0.39; 0.73]
	Week 70	26	23	6.98 (0.82)	23	22	7.28 (0.93)	0.34 [-0.23; 0.90]
	Week 78	26	25	6.99 (0.70)	23	22	7.12 (0.89)	0.16 [-0.40; 0.72]
>=65 years	Week 0	11	11	8.63 (1.31)	5	5	8.82 (0.75)	0.16 [-0.90; 1.21]
	Week 10	11	11	8.02 (0.79)	5	5	7.58 (0.93)	-0.50 [-1.57; 0.57]
	Week 18	11	11	7.40 (0.80)	5	5	7.22 (0.68)	-0.22 [-1.28; 0.84]
	Week 26	11	11	7.16 (0.80)	5	5	7.08 (0.63)	-0.10 [-1.16; 0.95]
	Week 36	11	9	6.88 (0.72)	5	5	6.86 (0.86)	-0.02 [-1.08; 1.04]
	Week 44	11	11	7.16 (0.76)	5	5	7.14 (0.44)	-0.03 [-1.09; 1.02]
	Week 52	11	11	7.25 (0.76)	5	5	7.10 (0.56)	-0.19 [-1.25; 0.86]
	Week 62	11	11	7.29 (0.70)	5	5	7.04 (0.73)	-0.33 [-1.40; 0.73]
	Week 70	11	11	7.34 (0.95)	5	5	7.12 (0.68)	-0.23 [-1.29; 0.83]
	Week 78	11	11	7.21 (0.79)	5	5	7.08 (0.88)	-0.15 [-1.21; 0.91]
HbA1c								
<=8,5%	Week 0	18	18	7.84 (0.48)	9	9	7.78 (0.41)	-0.13 [-0.93; 0.67]
	Week 10	18	18	7.51 (0.85)	9	9	7.46 (0.94)	-0.06 [-0.86; 0.74]
	Week 18	18	17	7.04 (0.59)	9	9	7.03 (0.64)	0.00 [-0.80; 0.80]
	Week 26	18	18	6.76 (0.42)	9	9	6.86 (0.61)	0.20 [-0.60; 1.00]
	Week 36	18	17	6.61 (0.47)	9	9	6.77 (0.81)	0.26 [-0.54; 1.06]
	Week 44	18	18	6.74 (0.42)	9	9	7.01 (0.62)	0.53 [-0.28; 1.34]
	Week 52	18	18	6.78 (0.48)	9	9	6.77 (0.76)	-0.02 [-0.82; 0.78]
	Week 62	18	18	6.89 (0.52)	9	9	6.68 (0.93)	-0.31 [-1.11; 0.50]
	Week 70	18	16	6.85 (0.62)	9	9	6.77 (0.91)	-0.11 [-0.91; 0.69]
	Week 78	18	18	6.92 (0.48)	9	9	6.56 (0.92)	-0.53 [-1.35; 0.28]
>8,5%	Week 0	19	19	9.57 (0.74)	19	19	9.38 (0.64)	-0.27 [-0.91; 0.36]
	Week 10	19	19	8.17 (1.41)	19	19	8.32 (0.93)	0.12 [-0.52; 0.76]
	Week 18	19	19	7.55 (1.17)	19	19	8.05 (1.27)	0.40 [-0.24; 1.04]
	Week 26	19	19	7.47 (1.05)	19	19	7.64 (1.04)	0.15 [-0.48; 0.79]
	Week 36	19	18	7.52 (1.02)	19	18	7.52 (0.68)	0.00 [-0.64; 0.64]
	Week 44	19	19	7.16 (0.90)	19	18	7.43 (0.58)	0.35 [-0.29; 0.99]
	Week 52	19	19	7.18 (0.87)	19	18	7.23 (0.71)	0.06 [-0.58; 0.70]
	Week 62	19	19	7.12 (1.02)	19	18	7.22 (0.76)	0.11 [-0.53; 0.75]
	Week 70	19	18	7.32 (1.00)	19	18	7.49 (0.78)	0.19 [-0.44; 0.83]
	Week 78	19	18	7.20 (0.90)	19	18	7.39 (0.71)	0.23 [-0.40; 0.87]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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Absolute HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Region								
Europe	Week 0	9	9	8.59 (1.36)	6	6	8.53 (1.27)	-0.04 [-1.07; 0.99]
	Week 10	9	9	8.11 (0.93)	6	6	7.80 (1.22)	-0.28 [-1.32; 0.76]
	Week 18	9	9	7.47 (0.74)	6	6	7.33 (0.83)	-0.16 [-1.20; 0.87]
	Week 26	9	9	7.40 (0.74)	6	6	7.13 (0.80)	-0.33 [-1.37; 0.71]
	Week 36	9	8	7.09 (0.85)	6	6	6.97 (0.77)	-0.14 [-1.17; 0.90]
	Week 44	9	9	7.27 (0.69)	6	6	7.32 (0.81)	0.06 [-0.97; 1.10]
	Week 52	9	9	7.38 (0.72)	6	6	6.90 (0.91)	-0.56 [-1.61; 0.49]
	Week 62	9	9	7.40 (0.80)	6	6	7.08 (1.28)	-0.29 [-1.33; 0.74]
	Week 70	9	8	7.38 (0.83)	6	6	7.05 (1.26)	-0.30 [-1.34; 0.74]
	Week 78	9	8	7.28 (0.82)	6	6	7.13 (1.42)	-0.12 [-1.16; 0.91]
North and South America	Week 0	19	19	8.68 (1.02)	17	17	8.94 (0.91)	0.25 [-0.40; 0.91]
	Week 10	19	19	7.89 (1.43)	17	17	7.99 (0.98)	0.08 [-0.58; 0.73]
	Week 18	19	18	7.32 (1.22)	17	17	7.72 (1.34)	0.31 [-0.35; 0.96]
	Week 26	19	19	6.96 (1.04)	17	17	7.27 (0.85)	0.31 [-0.34; 0.97]
	Week 36	19	19	7.05 (1.08)	17	16	7.20 (0.79)	0.15 [-0.50; 0.81]
	Week 44	19	19	6.88 (0.76)	17	16	7.19 (0.61)	0.44 [-0.23; 1.10]
	Week 52	19	19	6.92 (0.75)	17	16	7.24 (0.70)	0.43 [-0.23; 1.10]
	Week 62	19	19	7.01 (0.78)	17	16	7.10 (0.74)	0.12 [-0.53; 0.78]
	Week 70	19	17	7.08 (0.98)	17	16	7.29 (0.87)	0.22 [-0.44; 0.87]
	Week 78	19	19	7.03 (0.72)	17	16	7.11 (0.78)	0.11 [-0.54; 0.77]
Asia	Week 0	9	9	8.97 (0.97)	5	5	9.02 (0.79)	0.05 [-1.04; 1.15]
	Week 10	9	9	7.51 (0.92)	5	5	8.52 (0.84)	1.05 [-0.11; 2.21]
	Week 18	9	9	7.12 (0.50)	5	5	8.20 (1.05)	1.37 [0.17; 2.58]
	Week 26	9	9	7.19 (0.56)	5	5	8.08 (1.44)	0.88 [-0.26; 2.02]
	Week 36	9	8	7.11 (0.61)	5	5	7.84 (0.69)	1.07 [-0.10; 2.23]
	Week 44	9	9	6.80 (0.69)	5	5	7.58 (0.37)	1.21 [0.03; 2.40]
	Week 52	9	9	6.73 (0.60)	5	5	6.76 (0.67)	0.04 [-1.05; 1.13]
	Week 62	9	9	6.63 (0.80)	5	5	6.80 (0.70)	0.20 [-0.89; 1.30]
	Week 70	9	9	6.88 (0.67)	5	5	7.38 (0.38)	0.80 [-0.33; 1.93]
	Week 78	9	9	6.93 (0.68)	5	5	7.10 (0.31)	0.27 [-0.83; 1.36]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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Absolute HbA1c by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Race								
White	Week 0	23	23	8.69 (1.18)	13	13	8.99 (1.10)	0.26 [-0.43; 0.94]
	Week 10	23	23	8.17 (1.28)	13	13	8.00 (1.22)	-0.13 [-0.81; 0.55]
	Week 18	23	22	7.50 (1.08)	13	13	7.67 (1.50)	0.13 [-0.55; 0.81]
	Week 26	23	23	7.23 (0.97)	13	13	7.21 (1.00)	-0.02 [-0.70; 0.66]
	Week 36	23	22	7.12 (1.10)	13	12	7.08 (0.80)	-0.04 [-0.72; 0.64]
	Week 44	23	23	7.07 (0.76)	13	12	7.21 (0.78)	0.17 [-0.51; 0.85]
	Week 52	23	23	7.14 (0.78)	13	12	7.03 (0.86)	-0.14 [-0.82; 0.54]
	Week 62	23	23	7.19 (0.82)	13	12	7.09 (1.07)	-0.10 [-0.78; 0.58]
	Week 70	23	20	7.28 (0.98)	13	12	7.22 (1.18)	-0.06 [-0.74; 0.62]
	Week 78	23	22	7.16 (0.79)	13	12	7.18 (1.15)	0.01 [-0.67; 0.69]
Not white	Week 0	14	14	8.79 (0.91)	15	15	8.75 (0.83)	-0.04 [-0.77; 0.68]
	Week 10	14	14	7.34 (0.89)	15	15	8.08 (0.82)	0.84 [0.08; 1.60]
	Week 18	14	14	7.00 (0.67)	15	15	7.77 (0.91)	0.93 [0.16; 1.69]
	Week 26	14	14	6.96 (0.70)	15	15	7.54 (0.98)	0.66 [-0.09; 1.41]
	Week 36	14	13	6.99 (0.53)	15	15	7.41 (0.79)	0.61 [-0.14; 1.35]
	Week 44	14	14	6.76 (0.65)	15	15	7.35 (0.47)	1.02 [0.25; 1.80]
	Week 52	14	14	6.73 (0.56)	15	15	7.12 (0.68)	0.61 [-0.13; 1.36]
	Week 62	14	14	6.72 (0.75)	15	15	7.00 (0.65)	0.39 [-0.35; 1.12]
	Week 70	14	14	6.84 (0.61)	15	15	7.28 (0.58)	0.73 [-0.03; 1.48]
	Week 78	14	14	6.89 (0.60)	15	15	7.07 (0.60)	0.28 [-0.45; 1.01]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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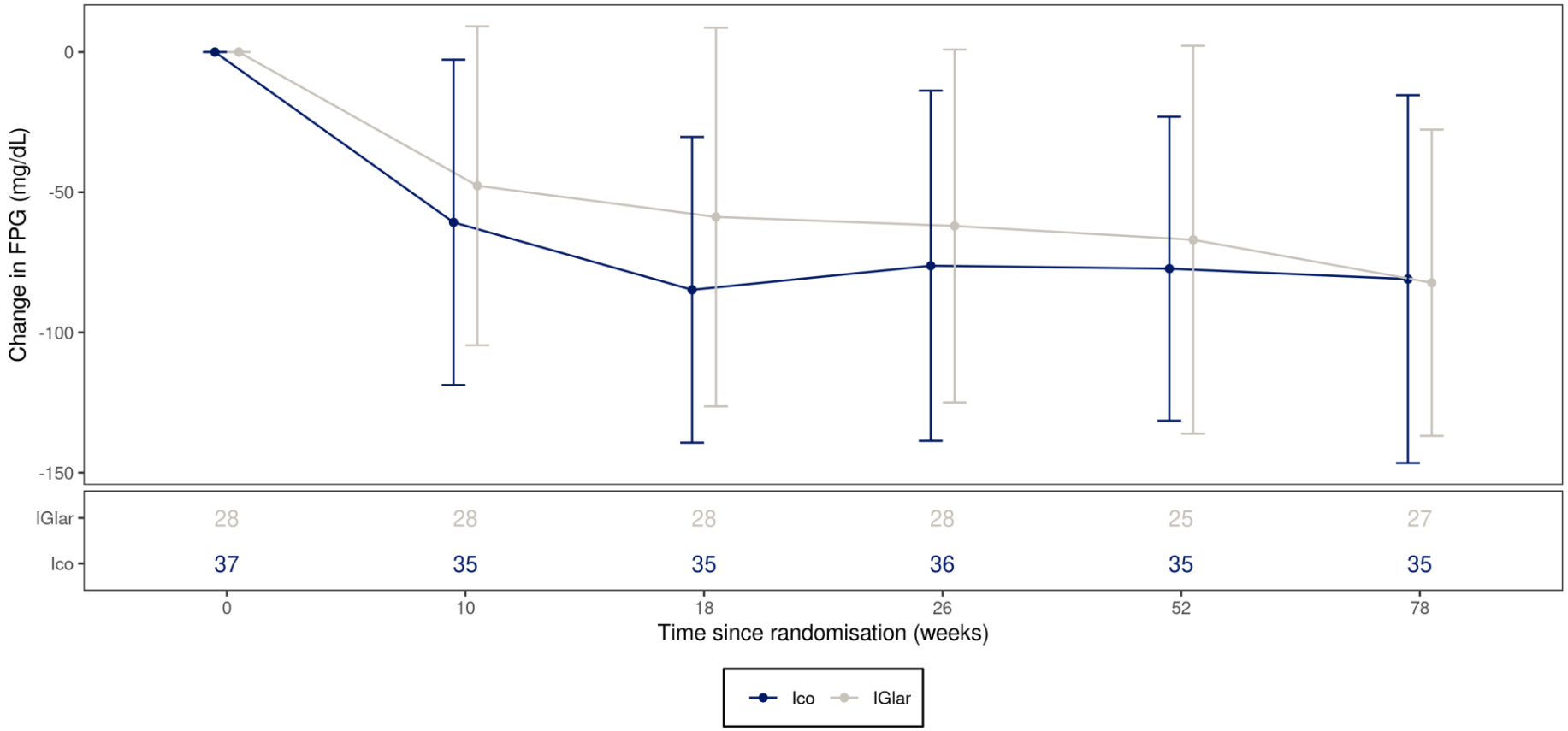
2.4 Change in fasting plasma glucose (FPG) by treatment week - Onwards 1 - in-trial - Population 1 - Full analysis set

	Week	Ico				IGlar				Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
FPG (mg/dL)												
All subjects (total)	Week 10	37	35	-60.75 (58.03)		28	28	-47.69 (56.89)				0.22 [-0.27; 0.72]
	Week 18	37	35	-84.80 (54.53)		28	28	-58.82 (67.54)				0.42 [-0.07; 0.92]
	Week 26	37	36	-76.23 (62.47)		28	28	-62.04 (62.94)				0.22 [-0.27; 0.72]
	Week 52	37	35	-77.28 (54.22)		28	25	-66.96 (69.18)				0.17 [-0.32; 0.66]
	Week 78	37	35	-80.99 (65.61)	-76.38 (6.14)	28	27	-82.29 (54.61)	-82.42 (6.99)	6.04 [-12.27; 24.35]	0.5181	-0.02 [-0.51; 0.47]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region use as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available on treatment (LAOT) values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:34:28 - /ChangeFPG_4477.txt

2.5 Change in fasting plasma glucose (FPG) by treatment week - Mean plot - Onwards 1 - Population 1 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
FPG : Fasting plasma glucose

nn1436/nn1436-amnog/current
23JAN2024:13:35:51 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/FPG2chg4477.png

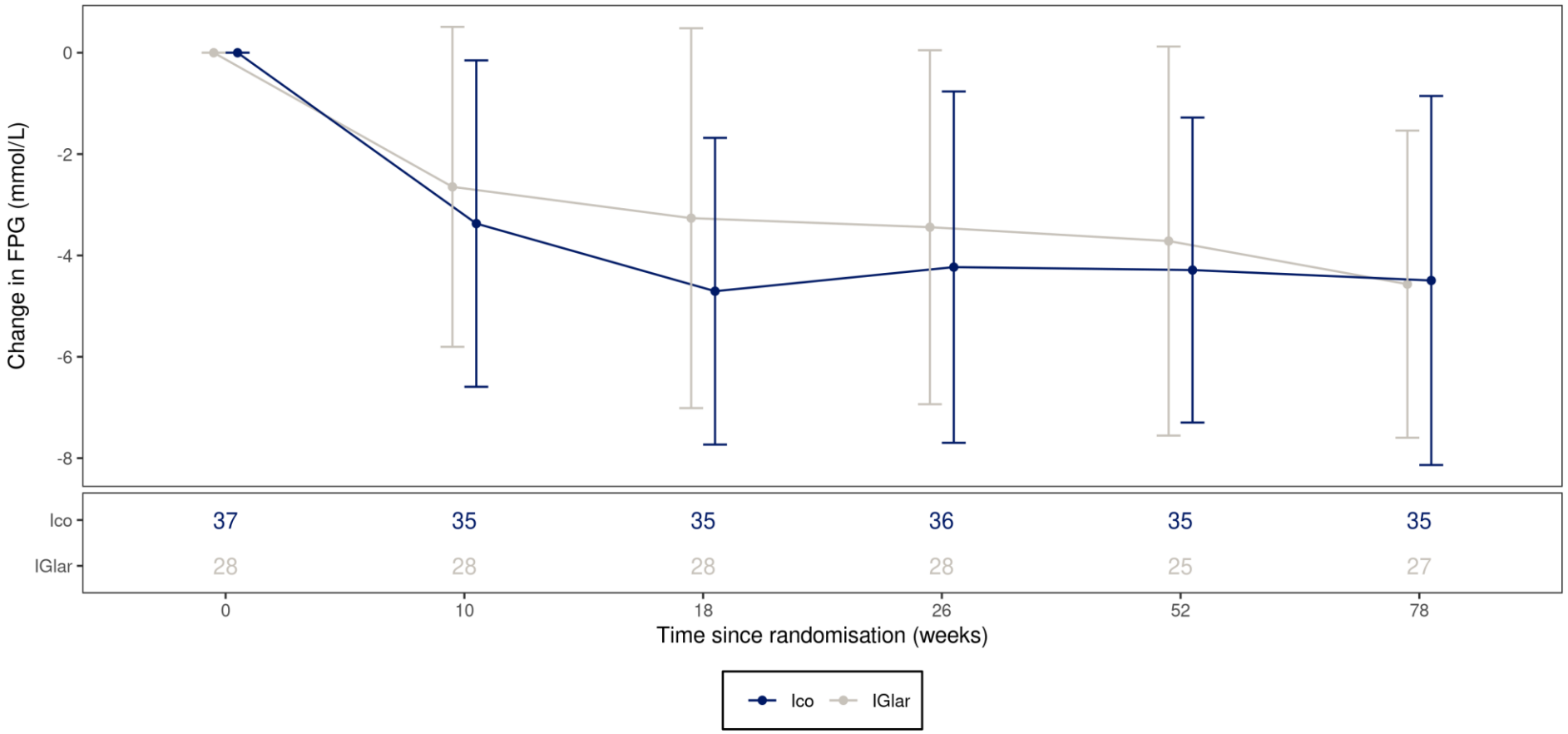
2.6 Change in fasting plasma glucose (FPG) by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

		Ico				IGlar				Ico - IGlar		
	Week	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]
FPG (mmol/L)												
All subjects (total)	Week 10	37	35	-3.37 (3.22)		28	28	-2.65 (3.16)				0.22 [-0.27; 0.72]
	Week 18	37	35	-4.71 (3.03)		28	28	-3.26 (3.75)				0.42 [-0.07; 0.92]
	Week 26	37	36	-4.23 (3.47)		28	28	-3.44 (3.49)				0.22 [-0.27; 0.72]
	Week 52	37	35	-4.29 (3.01)		28	25	-3.72 (3.84)				0.17 [-0.32; 0.66]
	Week 78	37	35	-4.49 (3.64)	-4.24 (0.34)	28	27	-4.57 (3.03)	-4.57 (0.39)	0.34 [-0.68; 1.35]	0.5181	-0.02 [-0.51; 0.47]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region use as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available on treatment (LAOT) values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
24JUL2023:15:23:48 - /ChangeFPG_4477.txt

2.7 Change in fasting plasma glucose (FPG) by treatment week - Mean plot - Onwards 1 - Population 1 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).
FPG : Fasting plasma glucose

nn1436/nn1436-amnog/current
21JUL2023:13:54:34 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/FPGchg4477.png

2.8 Absolute fasting plasma glucose (FPG) by treatment week - Onwards 1 - in-trial - Population 1 - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
FPG (mg/dL)								
All subjects (total)	Week 0	37	36	200.77 (56.51)	28	28	194.68 (57.82)	-0.11 [-0.60; 0.39]
	Week 10	37	36	140.11 (41.82)	28	28	146.99 (64.14)	0.13 [-0.36; 0.62]
	Week 18	37	36	116.63 (33.71)	28	28	135.86 (55.51)	0.43 [-0.07; 0.92]
	Week 26	37	37	124.24 (30.45)	28	28	132.64 (50.33)	0.21 [-0.29; 0.70]
	Week 52	37	36	122.39 (30.20)	28	25	126.72 (44.58)	0.12 [-0.38; 0.61]
	Week 78	37	35	118.31 (24.33)	28	27	109.25 (24.77)	-0.37 [-0.86; 0.13]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

nn1436/nn1436-amnog/current
23JAN2024:13:34:29 - /FPG_4477.txt

2.9 Absolute Fasting plasma glucose (FPG) by treatment week - Onwards 1 - in-trial - Population 1 - Full analysis set

		Ico			IGlar			Ico - IGlar
	Week	N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
FPG (mmol/L)								
All subjects (total)	Week 0	37	36	11.14 (3.14)	28	28	10.80 (3.21)	-0.11 [-0.60; 0.39]
	Week 10	37	36	7.78 (2.32)	28	28	8.16 (3.56)	0.13 [-0.36; 0.62]
	Week 18	37	36	6.47 (1.87)	28	28	7.54 (3.08)	0.43 [-0.07; 0.92]
	Week 26	37	37	6.89 (1.69)	28	28	7.36 (2.79)	0.21 [-0.29; 0.70]
	Week 52	37	36	6.79 (1.68)	28	25	7.03 (2.47)	0.12 [-0.38; 0.61]
	Week 78	37	35	6.57 (1.35)	28	27	6.06 (1.37)	-0.37 [-0.86; 0.13]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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24JUL2023:15:23:49 - /FPG_4477.txt

2.10 Change in body weight by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
Body weight (kg)													
All subjects (total)	Week 14	37	37	0.49 (2.36)		28	27	0.59 (2.37)				0.04 [-0.45; 0.53]	
	Week 26	37	37	0.99 (3.69)		28	28	1.92 (3.77)				0.25 [-0.25; 0.74]	
	Week 52	37	37	2.08 (4.33)		28	26	3.87 (4.45)				0.40 [-0.09; 0.90]	
	Week 78	37	36	2.55 (4.55)	2.52 (0.78)	28	27	3.46 (4.65)	3.26 (0.91)	-0.74 [-3.10; 1.61]	0.5368	0.20 [-0.30; 0.69]	
Gender													
Female	Week 14	17	17	0.49 (2.44)		14	14	0.57 (2.50)				0.03 [-0.68; 0.74]	
	Week 26	17	17	0.68 (4.19)		14	14	1.43 (4.05)				0.18 [-0.53; 0.89]	
	Week 52	17	17	1.96 (5.27)		14	12	3.71 (4.39)				0.35 [-0.37; 1.06]	
	Week 78	17	16	2.49 (6.04)	2.36 (1.23)	14	13	2.58 (3.40)	2.42 (1.38)	-0.06 [-3.53; 3.41]	0.9727	0.02 [-0.69; 0.73]	0.5826
Male	Week 14	20	20	0.50 (2.35)		14	13	0.60 (2.32)				0.05 [-0.64; 0.73]	
	Week 26	20	20	1.25 (3.29)		14	14	2.40 (3.56)				0.33 [-0.36; 1.02]	
	Week 52	20	20	2.18 (3.49)		14	14	4.01 (4.66)				0.45 [-0.25; 1.14]	
	Week 78	20	20	2.59 (3.06)	2.68 (1.12)	14	14	4.26 (5.58)	4.08 (1.33)	-1.40 [-4.68; 1.88]	0.4020	0.38 [-0.31; 1.07]	
Age													
<65 years	Week 14	26	26	0.85 (2.54)		23	22	0.26 (2.41)				-0.23 [-0.80; 0.33]	
	Week 26	26	26	1.75 (3.47)		23	23	1.99 (4.12)				0.06 [-0.50; 0.62]	
	Week 52	26	26	2.91 (4.45)		23	21	4.01 (4.76)				0.24 [-0.33; 0.80]	
	Week 78	26	25	3.29 (4.80)	3.32 (0.95)	23	22	3.48 (4.78)	3.32 (1.00)	0.00 [-2.70; 2.70]	0.9999	0.04 [-0.52; 0.60]	0.4426
>=65 years	Week 14	11	11	-0.35 (1.66)		5	5	2.00 (1.72)				1.33 [0.17; 2.48]	
	Week 26	11	11	-0.82 (3.72)		5	5	1.58 (1.57)				0.70 [-0.38; 1.78]	
	Week 52	11	11	0.13 (3.49)		5	5	3.26 (3.12)				0.88 [-0.22; 1.98]	
	Week 78	11	11	0.86 (3.56)	0.66 (1.43)	5	5	3.36 (4.56)	2.94 (2.19)	-2.27 [-7.39; 2.84]	0.3833	0.61 [-0.47; 1.69]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Change in body weight by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar		
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI] p-value	Hedges' g [95%-CI] p-value int.
HbA1c											
<=8,5%	Week 14	18	18	0.46 (2.55)		9	9	0.25 (2.74)			-0.08 [-0.88; 0.72]
	Week 26	18	18	0.14 (3.24)		9	9	1.99 (4.61)			0.48 [-0.33; 1.29]
	Week 52	18	18	0.96 (4.19)		9	9	3.85 (5.00)			0.63 [-0.19; 1.45]
	Week 78	18	18	1.67 (4.52)	1.40 (1.11)	9	9	1.87 (2.12)	1.69 (1.56)	-0.29 [-4.02; 3.44] 0.8777	0.05 [-0.75; 0.85] 0.9693
>8,5%	Week 14	19	19	0.53 (2.22)		19	18	0.75 (2.23)			0.10 [-0.54; 0.73]
	Week 26	19	19	1.79 (3.99)		19	19	1.88 (3.45)			0.02 [-0.61; 0.66]
	Week 52	19	19	3.15 (4.31)		19	17	3.88 (4.29)			0.17 [-0.47; 0.80]
	Week 78	19	18	3.42 (4.54)	3.60 (1.12)	19	18	4.25 (5.38)	3.99 (1.10)	-0.39 [-3.47; 2.69] 0.8049	0.16 [-0.47; 0.80]
Region											
Europe	Week 14	9	9	-1.03 (1.94)		6	6	-0.85 (1.70)			0.09 [-0.94; 1.13]
	Week 26	9	9	-0.53 (3.40)		6	6	1.80 (5.61)			0.50 [-0.55; 1.55]
	Week 52	9	9	-0.10 (3.94)		6	6	5.02 (5.86)			1.01 [-0.09; 2.10]
	Week 78	9	8	1.24 (4.16)	1.01 (1.64)	6	6	4.50 (5.67)	4.42 (1.90)	-3.41 [-8.30; 1.47] 0.1709	0.64 [-0.42; 1.70] 0.2507
North and South America	Week 14	19	19	1.06 (2.72)		17	16	0.76 (2.64)			-0.11 [-0.77; 0.54]
	Week 26	19	19	2.01 (4.28)		17	17	1.88 (3.74)			-0.03 [-0.69; 0.62]
	Week 52	19	19	3.57 (4.80)		17	15	3.52 (4.62)			-0.01 [-0.67; 0.64]
	Week 78	19	19	3.97 (5.15)	3.90 (1.07)	17	16	3.18 (5.08)	2.95 (1.16)	0.94 [-2.13; 4.02] 0.5475	-0.15 [-0.81; 0.51]
Asia	Week 14	9	9	0.82 (1.02)		5	5	1.76 (1.39)			0.76 [-0.37; 1.89]
	Week 26	9	9	0.34 (1.72)		5	5	2.18 (0.89)			1.15 [-0.02; 2.32]
	Week 52	9	9	1.12 (2.34)		5	5	3.56 (1.89)			1.04 [-0.12; 2.19]
	Week 78	9	9	0.71 (2.35)	0.90 (1.59)	5	5	3.08 (1.26)	3.36 (2.15)	-2.46 [-7.53; 2.61] 0.3422	1.08 [-0.08; 2.25]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:34:30 - /ChangeWeight_4477.txt

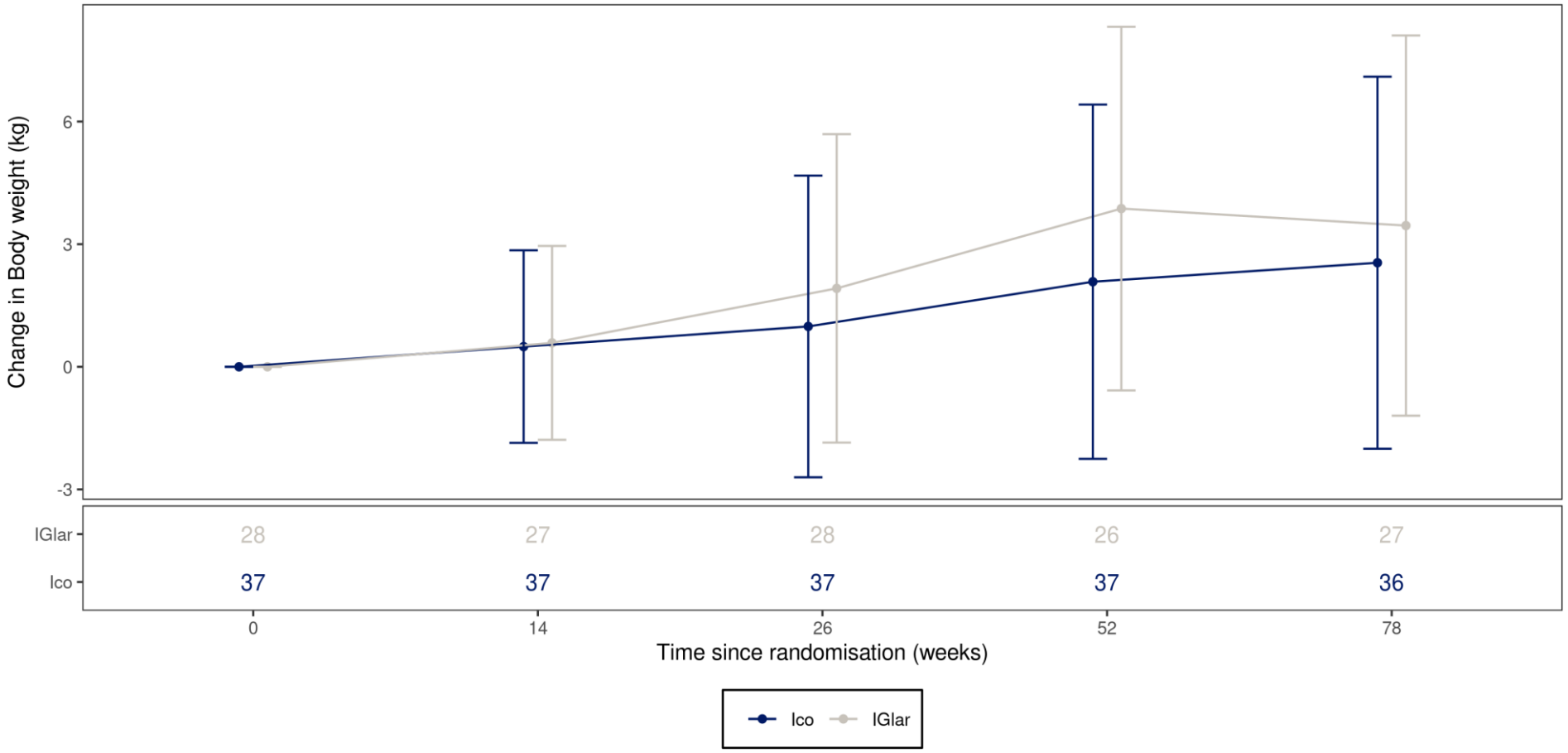
Change in body weight by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar			
		N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETD [95%-CI]	p-value	Hedges' g [95%-CI]	p-value int.
Race													
White	Week 14	23	23	0.13 (2.71)		13	12	-0.47 (2.07)				-0.23 [-0.92; 0.45]	
	Week 26	23	23	0.94 (4.29)		13	13	1.21 (4.60)				0.06 [-0.62; 0.74]	
	Week 52	23	23	2.62 (5.11)		13	11	4.48 (5.19)				0.35 [-0.33; 1.04]	
	Week 78	23	22	3.53 (5.24)	3.64 (1.18)	13	12	3.77 (6.37)	3.83 (1.49)	-0.20 [-3.56; 3.17]	0.9086	0.04 [-0.64; 0.72]	0.4406
Not white	Week 14	14	14	1.09 (1.52)		15	15	1.43 (2.31)				0.17 [-0.56; 0.90]	
	Week 26	14	14	1.06 (2.57)		15	15	2.53 (2.91)				0.52 [-0.22; 1.26]	
	Week 52	14	14	1.20 (2.53)		15	15	3.42 (3.95)				0.65 [-0.10; 1.39]	
	Week 78	14	14	1.00 (2.67)	0.62 (1.67)	15	15	3.21 (2.86)	2.83 (1.30)	-2.21 [-5.94; 1.52]	0.2465	0.77 [0.02; 1.53]	

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test), p-value int.: unadjusted two-sided p-value for test of no treatment by subgroup interaction (F-test). The change from baseline in response after 78 weeks is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and baseline response as covariate. Missing values at week 78 are imputed by the baseline value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the last available planned assessments. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:34:30 - /ChangeWeight_4477.txt

2.11 Change in body weight by treatment week - Mean plot - Onwards 1 - Population 1 - in-trial - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).

nn1436/nn1436-amnog/current
23JAN2024:13:35:52 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/WEIGHTchg4477.png

2.12 Absolute body weight by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Body weight (kg)								
All subjects (total)	Week 0	37	37	88.98 (18.43)	28	28	87.11 (19.10)	-0.10 [-0.59; 0.39]
	Week 14	37	37	89.47 (17.91)	28	27	86.12 (17.34)	-0.19 [-0.68; 0.30]
	Week 26	37	37	89.96 (18.47)	28	28	89.03 (19.16)	-0.05 [-0.54; 0.44]
	Week 52	37	37	91.06 (18.82)	28	26	92.13 (19.33)	0.06 [-0.44; 0.55]
	Week 78	37	36	91.38 (19.23)	28	27	91.04 (20.86)	-0.02 [-0.51; 0.47]
Gender								
Female	Week 0	17	17	82.71 (12.83)	14	14	77.94 (14.02)	-0.35 [-1.06; 0.37]
	Week 14	17	17	83.20 (13.22)	14	14	78.51 (14.05)	-0.34 [-1.05; 0.38]
	Week 26	17	17	83.39 (13.97)	14	14	79.37 (13.57)	-0.28 [-0.99; 0.43]
	Week 52	17	17	84.67 (14.12)	14	12	82.62 (14.38)	-0.14 [-0.85; 0.57]
	Week 78	17	16	84.49 (14.68)	14	13	80.81 (14.01)	-0.25 [-0.96; 0.46]
Male	Week 0	20	20	94.30 (20.97)	14	14	96.28 (19.48)	0.09 [-0.59; 0.78]
	Week 14	20	20	94.80 (19.89)	14	13	94.33 (17.23)	-0.02 [-0.71; 0.66]
	Week 26	20	20	95.55 (20.26)	14	14	98.68 (19.42)	0.15 [-0.53; 0.84]
	Week 52	20	20	96.48 (20.87)	14	14	100.29 (19.70)	0.18 [-0.50; 0.87]
	Week 78	20	20	96.89 (20.95)	14	14	100.54 (22.08)	0.17 [-0.52; 0.85]
Age								
<65 years	Week 0	26	26	87.75 (18.00)	23	23	88.26 (20.33)	0.03 [-0.53; 0.59]
	Week 14	26	26	88.60 (17.21)	23	22	86.65 (18.46)	-0.11 [-0.67; 0.45]
	Week 26	26	26	89.50 (18.02)	23	23	90.25 (20.50)	0.04 [-0.52; 0.60]
	Week 52	26	26	90.65 (18.00)	23	21	93.81 (20.74)	0.16 [-0.40; 0.72]
	Week 78	26	25	90.78 (18.11)	23	22	92.38 (22.65)	0.08 [-0.48; 0.64]
>=65 years	Week 0	11	11	91.88 (19.99)	5	5	81.81 (12.03)	-0.53 [-1.60; 0.55]
	Week 14	11	11	91.54 (20.19)	5	5	83.81 (12.55)	-0.40 [-1.46; 0.67]
	Week 26	11	11	91.06 (20.35)	5	5	83.39 (10.83)	-0.40 [-1.47; 0.67]
	Week 52	11	11	92.01 (21.52)	5	5	85.07 (10.37)	-0.35 [-1.41; 0.72]
	Week 78	11	11	92.74 (22.45)	5	5	85.17 (9.07)	-0.37 [-1.43; 0.70]
HbA1c								
<=8,5%	Week 0	18	18	91.53 (19.78)	9	9	91.00 (18.38)	-0.03 [-0.83; 0.77]
	Week 14	18	18	91.98 (19.13)	9	9	91.26 (17.30)	-0.04 [-0.84; 0.76]
	Week 26	18	18	91.67 (19.94)	9	9	92.99 (17.33)	0.07 [-0.73; 0.87]
	Week 52	18	18	92.49 (19.33)	9	9	94.86 (17.03)	0.12 [-0.68; 0.92]
	Week 78	18	18	93.20 (19.55)	9	9	92.87 (17.50)	-0.02 [-0.82; 0.78]
>8,5%	Week 0	19	19	86.56 (17.23)	19	19	85.26 (19.64)	-0.07 [-0.70; 0.57]
	Week 14	19	19	87.09 (16.83)	19	18	83.56 (17.26)	-0.20 [-0.84; 0.43]
	Week 26	19	19	88.35 (17.35)	19	19	87.15 (20.13)	-0.06 [-0.70; 0.57]
	Week 52	19	19	89.70 (18.75)	19	17	90.69 (20.79)	0.05 [-0.59; 0.68]
	Week 78	19	18	89.56 (19.29)	19	18	90.13 (22.78)	0.03 [-0.61; 0.66]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

nn1436/nn1436-amnog/current
23JAN2024:13:34:32 - /Weight_4477.txt

Absolute body weight by treatment week - Onwards 1 - Population 1 - in-trial - Full analysis set

	Week	Ico			IGlar			Ico - IGlar
		N	n	Mean (SD)	N	n	Mean (SD)	Hedges' g [95%-CI]
Region								
Europe	Week 0	9	9	94.13 (17.50)	6	6	92.92 (16.10)	-0.07 [-1.10; 0.97]
	Week 14	9	9	93.10 (17.82)	6	6	92.07 (16.16)	-0.06 [-1.09; 0.98]
	Week 26	9	9	93.60 (18.41)	6	6	94.72 (14.20)	0.06 [-0.97; 1.10]
	Week 52	9	9	94.03 (18.30)	6	6	97.93 (16.83)	0.21 [-0.83; 1.24]
	Week 78	9	8	95.38 (21.23)	6	6	97.42 (21.20)	0.09 [-0.94; 1.12]
North and South America	Week 0	19	19	92.34 (20.14)	17	17	89.68 (19.82)	-0.13 [-0.79; 0.52]
	Week 14	19	19	93.40 (19.33)	17	16	87.94 (17.77)	-0.29 [-0.94; 0.37]
	Week 26	19	19	94.35 (19.65)	17	17	91.56 (20.34)	-0.14 [-0.79; 0.52]
	Week 52	19	19	95.91 (20.00)	17	15	95.54 (19.42)	-0.02 [-0.67; 0.64]
	Week 78	19	19	96.30 (19.36)	17	16	93.83 (20.84)	-0.12 [-0.78; 0.53]
Asia	Week 0	9	9	76.72 (9.13)	5	5	71.40 (13.40)	-0.46 [-1.57; 0.64]
	Week 14	9	9	77.54 (8.56)	5	5	73.16 (12.94)	-0.40 [-1.50; 0.70]
	Week 26	9	9	77.07 (8.94)	5	5	73.58 (14.03)	-0.30 [-1.40; 0.80]
	Week 52	9	9	77.84 (9.80)	5	5	74.96 (14.07)	-0.24 [-1.33; 0.86]
	Week 78	9	9	77.43 (9.33)	5	5	74.48 (14.26)	-0.25 [-1.34; 0.85]
Race								
White	Week 0	23	23	95.60 (18.86)	13	13	89.18 (19.03)	-0.33 [-1.02; 0.35]
	Week 14	23	23	95.73 (18.24)	13	12	85.35 (15.42)	-0.59 [-1.28; 0.11]
	Week 26	23	23	96.55 (18.67)	13	13	90.39 (19.99)	-0.31 [-1.00; 0.37]
	Week 52	23	23	98.22 (18.81)	13	11	96.77 (20.75)	-0.07 [-0.75; 0.61]
	Week 78	23	22	99.20 (19.25)	13	12	94.20 (23.59)	-0.23 [-0.92; 0.45]
Not white	Week 0	14	14	78.09 (11.52)	15	15	85.31 (19.63)	0.43 [-0.30; 1.17]
	Week 14	14	14	79.18 (11.91)	15	15	86.74 (19.25)	0.46 [-0.28; 1.19]
	Week 26	14	14	79.15 (12.32)	15	15	87.84 (19.03)	0.52 [-0.22; 1.26]
	Week 52	14	14	79.29 (11.90)	15	15	88.73 (18.18)	0.59 [-0.15; 1.34]
	Week 78	14	14	79.09 (11.41)	15	15	88.52 (18.86)	0.58 [-0.16; 1.33]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval.

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2.13 Total weekly insulin dose by treatment week (U) - Onwards 1 - Population 1 - on-treatment - Full analysis set

Week	Ico				IGlar				Ico / IGlar	Ico - IGlar
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Weekly insulin dose (U)										
All subjects (total) Week 1	37	37	71.62 (7.27)		28	28	71.16 (4.93)			-0.07 [-0.56; 0.42]
Week 2	37	37	94.05 (56.15)		28	28	87.92 (18.52)			-0.14 [-0.63; 0.35]
Week 3	37	37	101.22 (17.85)		28	28	103.68 (23.87)			0.12 [-0.37; 0.61]
Week 4	37	37	118.38 (21.54)		28	28	120.71 (31.01)			0.09 [-0.40; 0.58]
Week 5	37	37	130.81 (28.71)		28	28	134.71 (40.44)			0.11 [-0.38; 0.60]
Week 6	37	37	142.43 (35.47)		28	28	146.61 (51.65)			0.10 [-0.40; 0.59]
Week 7	37	37	155.14 (40.66)		28	28	159.51 (58.13)			0.09 [-0.40; 0.58]
Week 8	37	37	166.49 (48.32)		28	28	169.64 (65.72)			0.06 [-0.44; 0.55]
Week 9	37	37	176.22 (55.24)		28	28	180.93 (72.87)			0.07 [-0.42; 0.56]
Week 10	37	37	187.57 (61.84)		28	28	190.29 (81.14)			0.04 [-0.45; 0.53]
Week 11	37	37	197.30 (69.35)		28	28	202.68 (86.20)			0.07 [-0.42; 0.56]
Week 12	37	37	204.05 (74.10)		28	28	216.07 (90.11)			0.15 [-0.35; 0.64]
Week 13	37	37	211.62 (81.33)		28	27	219.27 (94.25)			0.09 [-0.40; 0.58]
Week 14	37	37	217.03 (87.49)		28	27	229.68 (98.63)			0.14 [-0.36; 0.63]
Week 15	37	37	222.70 (94.09)		28	27	239.63 (104.38)			0.17 [-0.32; 0.66]
Week 16	37	37	229.19 (97.73)		28	27	247.22 (111.21)			0.17 [-0.32; 0.66]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test).The log-transformed response at week 78 is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and log-transformed screening response as covariate. Missing mean values at week 78 are imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly insulin dose by treatment week (U) - Onwards 1 - Population 1 - on-treatment - Full analysis set

Week	Ico				IGlar				Ico / IGlar	Ico - IGlar
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 17	37	37	234.05 (102.37)		28	28	255.18 (116.63)			0.19 [-0.30; 0.68]
Week 18	37	37	238.38 (106.47)		28	28	262.11 (120.81)			0.21 [-0.28; 0.70]
Week 19	37	37	242.16 (110.46)		28	28	267.04 (124.73)			0.21 [-0.28; 0.70]
Week 20	37	37	244.86 (115.29)		28	28	270.13 (130.90)			0.20 [-0.29; 0.70]
Week 21	37	37	249.19 (120.59)		28	28	273.79 (132.87)			0.19 [-0.30; 0.68]
Week 22	37	37	254.05 (128.94)		28	28	278.18 (136.29)			0.18 [-0.31; 0.67]
Week 23	37	36	261.39 (132.28)		28	28	283.61 (140.86)			0.16 [-0.33; 0.65]
Week 24	37	37	263.24 (135.50)		28	28	287.39 (145.33)			0.17 [-0.32; 0.66]
Week 25	37	37	268.38 (138.05)		28	28	289.00 (146.89)			0.14 [-0.35; 0.64]
Week 26	37	37	268.38 (142.37)		28	28	291.36 (149.87)			0.16 [-0.34; 0.65]
Week 27	37	37	272.16 (145.95)		28	28	295.13 (154.91)			0.15 [-0.34; 0.64]
Week 28	37	37	275.95 (150.67)		28	28	299.93 (160.43)			0.15 [-0.34; 0.64]
Week 29	37	37	278.92 (154.90)		28	28	303.14 (164.03)			0.15 [-0.34; 0.64]
Week 30	37	37	282.43 (161.41)		28	28	305.61 (166.61)			0.14 [-0.35; 0.63]
Week 31	37	37	285.68 (163.61)		28	27	295.11 (159.79)			0.06 [-0.43; 0.55]
Week 32	37	37	288.92 (169.90)		28	27	299.00 (163.19)			0.06 [-0.43; 0.55]
Week 34	37	36	301.67 (173.61)		28	27	303.96 (169.71)			0.01 [-0.48; 0.50]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test).The log-transformed response at week 78 is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and log-transformed screening response as covariate. Missing mean values at week 78 are imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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Total weekly insulin dose by treatment week (U) - Onwards 1 - Population 1 - on-treatment - Full analysis set

Week	Ico				IGlar				Ico / IGlar	Ico - IGlar
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI] p-value	Hedges' g [95%-CI]
Week 36	37	36	304.17 (178.09)		28	27	307.30 (176.04)			0.02 [-0.47; 0.51]
Week 38	37	36	303.89 (176.67)		28	27	312.52 (180.89)			0.05 [-0.44; 0.54]
Week 40	37	36	306.94 (177.42)		28	27	313.30 (184.29)			0.03 [-0.46; 0.53]
Week 42	37	36	308.89 (179.44)		28	27	313.48 (187.91)			0.02 [-0.47; 0.52]
Week 44	37	36	309.72 (178.91)		28	27	320.19 (195.38)			0.06 [-0.44; 0.55]
Week 46	37	36	311.67 (183.05)		28	27	322.11 (200.09)			0.05 [-0.44; 0.55]
Week 48	37	36	313.89 (185.09)		28	27	324.89 (205.91)			0.06 [-0.44; 0.55]
Week 49	37	36	315.83 (184.68)		28	27	328.20 (205.21)			0.06 [-0.43; 0.55]
Week 50	37	36	317.50 (183.98)		28	27	331.89 (207.69)			0.07 [-0.42; 0.56]
Week 51	37	36	318.33 (186.60)		28	27	335.22 (209.46)			0.08 [-0.41; 0.58]
Week 52	37	36	319.31 (185.03)		28	27	338.11 (210.75)			0.09 [-0.40; 0.59]
Week 54	37	36	318.61 (186.34)		28	27	343.56 (210.11)			0.13 [-0.37; 0.62]
Week 56	37	36	317.22 (188.36)		28	27	345.00 (214.81)			0.14 [-0.35; 0.63]
Week 58	37	36	317.22 (189.57)		28	27	346.67 (216.85)			0.14 [-0.35; 0.64]
Week 60	37	35	308.57 (182.36)		28	27	346.89 (217.70)			0.19 [-0.30; 0.68]
Week 62	37	35	324.00 (195.10)		28	27	349.22 (220.28)			0.12 [-0.37; 0.61]
Week 64	37	36	321.67 (191.84)		28	27	351.57 (224.53)			0.14 [-0.35; 0.63]
Week 66	37	36	323.61 (192.74)		28	27	353.81 (225.47)			0.14 [-0.35; 0.64]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test).The log-transformed response at week 78 is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and log-transformed screening response as covariate. Missing mean values at week 78 are imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

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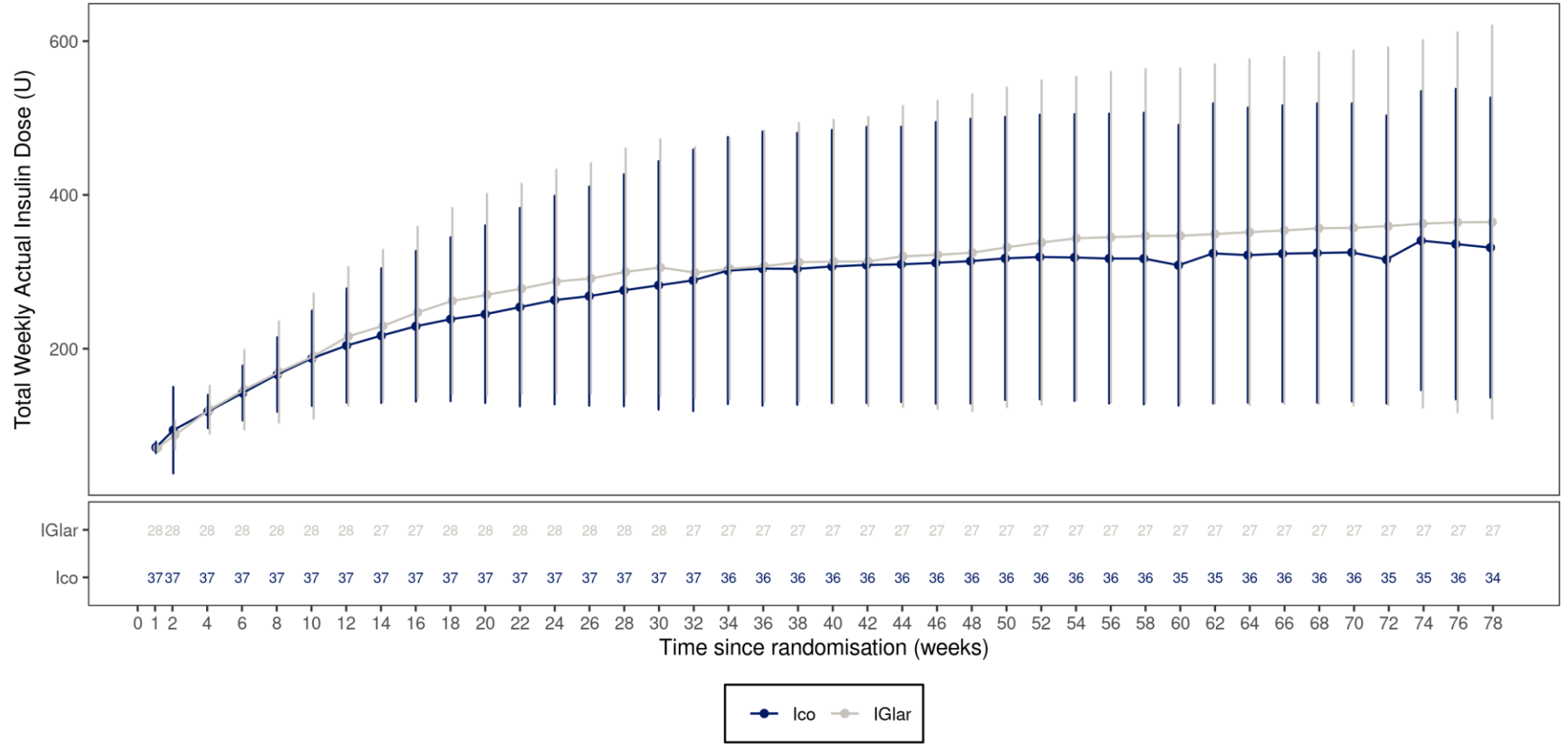
Total weekly insulin dose by treatment week (U) - Onwards 1 - Population 1 - on-treatment - Full analysis set

Week	Ico				IGlar				Ico / IGlar		Ico - IGlar
	N	n	Mean (SD)	LS Mean (SE)	N	n	Mean (SD)	LS Mean (SE)	ETR [95%-CI]	p-value	Hedges' g [95%-CI]
Week 68	37	36	324.44 (194.59)		28	27	356.67 (228.54)				0.15 [-0.34; 0.64]
Week 70	37	36	325.28 (193.63)		28	27	357.26 (230.72)				0.15 [-0.34; 0.64]
Week 72	37	35	316.00 (187.16)		28	27	359.46 (232.17)				0.21 [-0.29; 0.70]
Week 74	37	35	340.57 (194.30)		28	27	362.59 (238.78)				0.10 [-0.39; 0.59]
Week 75	37	34	344.41 (198.36)		28	27	361.00 (241.55)				0.08 [-0.42; 0.57]
Week 76	37	36	336.11 (201.73)		28	27	364.37 (246.84)				0.13 [-0.37; 0.62]
Week 77	37	36	337.50 (201.49)		28	27	362.81 (253.03)				0.11 [-0.38; 0.60]
Week 78	37	34	331.47 (195.00)	276.66 (0.11)	28	27	364.70 (255.55)	293.89 (0.12)	0.94 [0.68;1.30]	0.7165	0.15 [-0.34; 0.64]

N: number of subjects in the analysis set, n: number of subjects with an observation, SD: Standard deviation, SE: Standard error, CI: confidence interval, p-value: unadjusted two-sided p-value for test of no difference from 0 (t-test).The log-transformed response at week 78 is analysed using an analysis of covariance (ANCOVA) model with treatment and region as fixed factors, and log-transformed screening response as covariate. Missing mean values at week 78 are imputed by the log-transformed screening value and a random term, using multiple imputation. The random term is normally distributed with mean 0 and standard deviation equal to the estimated residual standard deviation from the ANCOVA model fitted to the log-transformed LAOT values. The model includes the same factors and covariates as the model used for analysis. Each imputed dataset is analysed separately and estimates are combined using Rubin's rules.

nn1436/nn1436-amnog/current
23JAN2024:13:34:33 - /TotInsDose_4477.txt

2.14 Total weekly insulin dose by treatment week (U) - Mean plot - Onwards 1 - Population 1 - on-treatment - Full analysis set



Observed data. Number of subjects contributing to data points appears in the bottom panel. Legend: Mean(symbol) and mean ± standard deviation (error bars).

nn1436/nn1436-amnog/current
23JAN2024:13:35:48 - P:/nn1436/nn1436-amnog/current/stats/program/nonctrprog/meanplot_descriptive.R/INSDWACtotal4477.png

2.15 All-cause mortality - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:21 - /ACM_4477.txt

2.16 Adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	33 (89.2)	28	21 (75.0)	2.75 (0.72, 10.55)	1.19 (0.93, 1.51)	14.19 (-4.71, 33.09)	0.1552	
Gender									0.1288
Female	17	16 (94.1)	14	9 (64.3)	8.89 (0.89, 88.40)	1.46 (0.97, 2.20)	29.83 (2.35, 57.31)	0.0410	
Male	20	17 (85.0)	14	12 (85.7)	0.94 (0.14, 6.54)	0.99 (0.75, 1.31)	-0.71 (-24.82, 23.39)	0.9967	
Age									0.9632
<65 years	26	23 (88.5)	23	17 (73.9)	2.71 (0.59, 12.39)	1.20 (0.90, 1.58)	14.55 (-7.20, 36.29)	0.2195	
>=65 years	11	10 (90.9)	5	4 (80.0)	2.50 (0.12, 50.44)	1.14 (0.71, 1.83)	10.91 (-28.05, 49.87)	0.7310	
HbA1c									0.3178
<=8,5%	18	15 (83.3)	9	7 (77.8)	1.43 (0.19, 10.57)	1.07 (0.71, 1.61)	5.56 (-26.60, 37.71)	0.8234	
>8,5%	19	18 (94.7)	19	14 (73.7)	6.43 (0.67, 61.47)	1.29 (0.96, 1.72)	21.05 (-1.15, 43.25)	0.1061	
Region									0.4277
Europe	9	7 (77.8)	6	5 (83.3)	0.70 (0.05, 10.01)	0.93 (0.57, 1.54)	-5.56 (-45.89, 34.78)	0.9148	
North and South America	19	18 (94.7)	17	13 (76.5)	5.54 (0.55, 55.49)	1.24 (0.93, 1.65)	18.27 (-4.26, 40.79)	0.1377	
Asia	9	8 (88.9)	5	3 (60.0)	5.33 (0.34, 82.83)	1.48 (0.70, 3.14)	28.89 (-18.71, 76.49)	0.2920	
Race									0.5610
White	23	20 (87.0)	13	10 (76.9)	2.00 (0.34, 11.76)	1.13 (0.81, 1.58)	10.03 (-16.69, 36.75)	0.4864	
Not white	14	13 (92.9)	15	11 (73.3)	4.73 (0.46, 48.77)	1.27 (0.90, 1.78)	19.52 (-6.61, 45.65)	0.2292	

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N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:21 - /AE_4477.txt

2.17 Severe adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	2 (5.4)	28	0 (0.0)	4.01 (0.19, 87.00)	3.82 (0.19, 76.46)	5.41 (-1.88, 12.69)	0.2588	
Gender									NA
Female	17	1 (5.9)	14	0 (0.0)	2.64 (0.10, 69.88)	2.50 (0.11, 56.98)	5.88 (-5.30, 17.07)	0.5137	
Male	20	1 (5.0)	14	0 (0.0)	2.23 (0.08, 58.81)	2.14 (0.09, 49.08)	5.00 (-4.55, 14.55)	0.5668	
Age									NA
<65 years	26	0 (0.0)	23	0 (0.0)	0.89 (0.02, 46.48)	0.89 (0.02, 43.09)	0.00 (0.00, 0.00)	NA	
>=65 years	11	2 (18.2)	5	0 (0.0)	2.89 (0.12, 71.93)	2.50 (0.14, 44.26)	18.18 (-4.61, 40.97)	0.3865	
HbA1c									NA
<=8,5%	18	1 (5.6)	9	0 (0.0)	1.63 (0.06, 44.01)	1.58 (0.07, 35.32)	5.56 (-5.03, 16.14)	0.5904	
>8,5%	19	1 (5.3)	19	0 (0.0)	3.16 (0.12, 82.64)	3.00 (0.13, 69.31)	5.26 (-4.78, 15.30)	0.5257	
Region									NA
Europe	9	1 (11.1)	6	0 (0.0)	2.29 (0.08, 66.02)	2.10 (0.10, 44.40)	11.11 (-9.42, 31.64)	0.5602	
North and South America	19	1 (5.3)	17	0 (0.0)	2.84 (0.11, 74.42)	2.70 (0.12, 62.17)	5.26 (-4.78, 15.30)	0.5134	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									NA
White	23	2 (8.7)	13	0 (0.0)	3.14 (0.14, 70.51)	2.92 (0.15, 56.51)	8.70 (-2.82, 20.21)	0.3983	
Not white	14	0 (0.0)	15	0 (0.0)	1.07 (0.02, 57.48)	1.07 (0.02, 50.43)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:23 - /SevAE_4477.txt

2.18 Serious adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	3 (8.1)	28	2 (7.1)	1.15 (0.18, 7.37)	1.14 (0.20, 6.34)	0.97 (-12.01, 13.94)	0.9624	
Gender									0.7663
Female	17	1 (5.9)	14	1 (7.1)	0.81 (0.05, 14.28)	0.82 (0.06, 12.01)	-1.26 (-18.78, 16.26)	0.9647	
Male	20	2 (10.0)	14	1 (7.1)	1.44 (0.12, 17.67)	1.40 (0.14, 13.98)	2.86 (-15.98, 21.69)	0.8234	
Age									0.2818
<65 years	26	0 (0.0)	23	1 (4.3)	0.28 (0.01, 7.30)	0.30 (0.01, 6.94)	-4.35 (-12.68, 3.99)	0.3529	
>=65 years	11	3 (27.3)	5	1 (20.0)	1.50 (0.12, 19.44)	1.36 (0.18, 10.09)	7.27 (-36.57, 51.11)	0.8207	
HbA1c									1.0000
<=8,5%	18	2 (11.1)	9	1 (11.1)	1.00 (0.08, 12.76)	1.00 (0.10, 9.61)	0.00 (-25.15, 25.15)	1.0000	
>8,5%	19	1 (5.3)	19	1 (5.3)	1.00 (0.06, 17.25)	1.00 (0.07, 14.85)	0.00 (-14.20, 14.20)	1.0000	
Region									NA
Europe	9	2 (22.2)	6	0 (0.0)	4.33 (0.17, 107.69)	3.50 (0.20, 62.27)	22.22 (-4.94, 49.38)	0.3198	
North and South America	19	1 (5.3)	17	2 (11.8)	0.42 (0.03, 5.06)	0.45 (0.04, 4.50)	-6.50 (-24.81, 11.81)	0.5912	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									0.2722
White	23	3 (13.0)	13	1 (7.7)	1.80 (0.17, 19.33)	1.70 (0.20, 14.68)	5.35 (-14.63, 25.33)	0.6788	
Not white	14	0 (0.0)	15	1 (6.7)	0.33 (0.01, 8.88)	0.36 (0.02, 8.07)	-6.67 (-19.29, 5.96)	0.5256	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:24 - /SerAE_4477.txt

2.19 Serious adverse events - hypoglycaemia - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:26 - /SerAEhyp_4477.txt

2.20 Adverse events leading to permanent trial product discontinuation - Onwards 1 - Population 1 - in- trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:26 - /AEdisc_4477.txt

2.21 Adverse events leading to study withdrawal - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:27 - /AEwith_4477.txt

2.22 Adverse events excluding disease-associated events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	33 (89.2)	28	21 (75.0)	2.75 (0.72, 10.55)	1.19 (0.93, 1.51)	14.19 (-4.71, 33.09)	0.1552	
Gender									0.1288
Female	17	16 (94.1)	14	9 (64.3)	8.89 (0.89, 88.40)	1.46 (0.97, 2.20)	29.83 (2.35, 57.31)	0.0410	
Male	20	17 (85.0)	14	12 (85.7)	0.94 (0.14, 6.54)	0.99 (0.75, 1.31)	-0.71 (-24.82, 23.39)	0.9967	
Age									0.9632
<65 years	26	23 (88.5)	23	17 (73.9)	2.71 (0.59, 12.39)	1.20 (0.90, 1.58)	14.55 (-7.20, 36.29)	0.2195	
>=65 years	11	10 (90.9)	5	4 (80.0)	2.50 (0.12, 50.44)	1.14 (0.71, 1.83)	10.91 (-28.05, 49.87)	0.7310	
HbA1c									0.3178
<=8,5%	18	15 (83.3)	9	7 (77.8)	1.43 (0.19, 10.57)	1.07 (0.71, 1.61)	5.56 (-26.60, 37.71)	0.8234	
>8,5%	19	18 (94.7)	19	14 (73.7)	6.43 (0.67, 61.47)	1.29 (0.96, 1.72)	21.05 (-1.15, 43.25)	0.1061	
Region									0.4277
Europe	9	7 (77.8)	6	5 (83.3)	0.70 (0.05, 10.01)	0.93 (0.57, 1.54)	-5.56 (-45.89, 34.78)	0.9148	
North and South America	19	18 (94.7)	17	13 (76.5)	5.54 (0.55, 55.49)	1.24 (0.93, 1.65)	18.27 (-4.26, 40.79)	0.1377	
Asia	9	8 (88.9)	5	3 (60.0)	5.33 (0.34, 82.83)	1.48 (0.70, 3.14)	28.89 (-18.71, 76.49)	0.2920	
Race									0.5610
White	23	20 (87.0)	13	10 (76.9)	2.00 (0.34, 11.76)	1.13 (0.81, 1.58)	10.03 (-16.69, 36.75)	0.4864	
Not white	14	13 (92.9)	15	11 (73.3)	4.73 (0.46, 48.77)	1.27 (0.90, 1.78)	19.52 (-6.61, 45.65)	0.2292	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:28 - /AEexcl_4477.txt

2.23 Severe adverse events excluding disease-associated events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	2 (5.4)	28	0 (0.0)	4.01 (0.19, 87.00)	3.82 (0.19, 76.46)	5.41 (-1.88, 12.69)	0.2588	
Gender									NA
Female	17	1 (5.9)	14	0 (0.0)	2.64 (0.10, 69.88)	2.50 (0.11, 56.98)	5.88 (-5.30, 17.07)	0.5137	
Male	20	1 (5.0)	14	0 (0.0)	2.23 (0.08, 58.81)	2.14 (0.09, 49.08)	5.00 (-4.55, 14.55)	0.5668	
Age									NA
<65 years	26	0 (0.0)	23	0 (0.0)	0.89 (0.02, 46.48)	0.89 (0.02, 43.09)	0.00 (0.00, 0.00)	NA	
>=65 years	11	2 (18.2)	5	0 (0.0)	2.89 (0.12, 71.93)	2.50 (0.14, 44.26)	18.18 (-4.61, 40.97)	0.3865	
HbA1c									NA
<=8,5%	18	1 (5.6)	9	0 (0.0)	1.63 (0.06, 44.01)	1.58 (0.07, 35.32)	5.56 (-5.03, 16.14)	0.5904	
>8,5%	19	1 (5.3)	19	0 (0.0)	3.16 (0.12, 82.64)	3.00 (0.13, 69.31)	5.26 (-4.78, 15.30)	0.5257	
Region									NA
Europe	9	1 (11.1)	6	0 (0.0)	2.29 (0.08, 66.02)	2.10 (0.10, 44.40)	11.11 (-9.42, 31.64)	0.5602	
North and South America	19	1 (5.3)	17	0 (0.0)	2.84 (0.11, 74.42)	2.70 (0.12, 62.17)	5.26 (-4.78, 15.30)	0.5134	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									NA
White	23	2 (8.7)	13	0 (0.0)	3.14 (0.14, 70.51)	2.92 (0.15, 56.51)	8.70 (-2.82, 20.21)	0.3983	
Not white	14	0 (0.0)	15	0 (0.0)	1.07 (0.02, 57.48)	1.07 (0.02, 50.43)	0.00 (0.00, 0.00)	NA	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:28 - /SevAEexcl_4477.txt

2.24 Serious adverse events excluding disease-associated events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	3 (8.1)	28	2 (7.1)	1.15 (0.18, 7.37)	1.14 (0.20, 6.34)	0.97 (-12.01, 13.94)	0.9624	
Gender									0.7663
Female	17	1 (5.9)	14	1 (7.1)	0.81 (0.05, 14.28)	0.82 (0.06, 12.01)	-1.26 (-18.78, 16.26)	0.9647	
Male	20	2 (10.0)	14	1 (7.1)	1.44 (0.12, 17.67)	1.40 (0.14, 13.98)	2.86 (-15.98, 21.69)	0.8234	
Age									0.2818
<65 years	26	0 (0.0)	23	1 (4.3)	0.28 (0.01, 7.30)	0.30 (0.01, 6.94)	-4.35 (-12.68, 3.99)	0.3529	
>=65 years	11	3 (27.3)	5	1 (20.0)	1.50 (0.12, 19.44)	1.36 (0.18, 10.09)	7.27 (-36.57, 51.11)	0.8207	
HbA1c									1.0000
<=8,5%	18	2 (11.1)	9	1 (11.1)	1.00 (0.08, 12.76)	1.00 (0.10, 9.61)	0.00 (-25.15, 25.15)	1.0000	
>8,5%	19	1 (5.3)	19	1 (5.3)	1.00 (0.06, 17.25)	1.00 (0.07, 14.85)	0.00 (-14.20, 14.20)	1.0000	
Region									NA
Europe	9	2 (22.2)	6	0 (0.0)	4.33 (0.17, 107.69)	3.50 (0.20, 62.27)	22.22 (-4.94, 49.38)	0.3198	
North and South America	19	1 (5.3)	17	2 (11.8)	0.42 (0.03, 5.06)	0.45 (0.04, 4.50)	-6.50 (-24.81, 11.81)	0.5912	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									0.2722
White	23	3 (13.0)	13	1 (7.7)	1.80 (0.17, 19.33)	1.70 (0.20, 14.68)	5.35 (-14.63, 25.33)	0.6788	
Not white	14	0 (0.0)	15	1 (6.7)	0.33 (0.01, 8.88)	0.36 (0.02, 8.07)	-6.67 (-19.29, 5.96)	0.5256	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:29 - /SerAEexcl_4477.txt

2.25 Non-severe hypoglycaemic episodes (G-BA definition) - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:30 - /nonsevhypo_4477.txt

2.26 Severe hypoglycaemic episodes (G-BA definition) - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:32 - /sevhypo_4477.txt

2.27 EAC evaluated cardiovascular events - Onwards 1 - Population 1 -in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:34 - /allEAC_4477.txt

2.28 EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:35 - /allEACacs_4477.txt

2.29 EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:35 - /allEACce_4477.txt

2.30 EAC evaluated cardiovascular events - Heart failure - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:36 - /allEAChf_4477.txt

2.31 EAC evaluated cardiovascular events - Death - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:36 - /allEACd_4477.txt

2.32 Severe EAC evaluated cardiovascular events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:37 - /SevEAC_4477.txt

2.33 Severe EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:38 - /SevEACacs_4477.txt

2.34 Severe EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 1 - Population 1 - in- trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:38 - /SevEACce_4477.txt

2.35 Severe EAC evaluated cardiovascular events - Heart failure - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:39 - /SevEAChf_4477.txt

2.36 Severe EAC evaluated cardiovascular events - Death - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:40 - /SevEACd_4477.txt

2.37 Serious EAC evaluated cardiovascular events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:44 - /SerEAC_4477.txt

2.38 Serious EAC evaluated cardiovascular events - Acute coronary syndrome - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:44 - /SerEACacs_4477.txt

2.39 Serious EAC evaluated cardiovascular events - Cerebrovascular event - Onwards 1 - Population 1 - in- trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:45 - /SerEACce_4477.txt

2.40 Serious EAC evaluated cardiovascular events - Heart failure - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:45 - /SerEAChf_4477.txt

2.41 Serious EAC evaluated cardiovascular events - Death - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:46 - /SerEACd_4477.txt

2.42 Hypersensitivity adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	1 (2.7)	28	4 (14.3)	0.17 (0.02, 1.58)	0.19 (0.02, 1.60)	-11.58 (-25.56, 2.39)	0.0920	
Gender									0.3889
Female	17	0 (0.0)	14	2 (14.3)	0.14 (0.01, 3.24)	0.17 (0.01, 3.21)	-14.29 (-32.62, 4.04)	0.1410	
Male	20	1 (5.0)	14	2 (14.3)	0.32 (0.03, 3.87)	0.35 (0.04, 3.50)	-9.29 (-29.96, 11.38)	0.4196	
Age									0.1980
<65 years	26	1 (3.8)	23	2 (8.7)	0.42 (0.04, 4.96)	0.44 (0.04, 4.56)	-4.85 (-18.53, 8.83)	0.5930	
>=65 years	11	0 (0.0)	5	2 (40.0)	0.06 (0.00, 1.59)	0.10 (0.01, 1.77)	-40.00 (-82.94, 2.94)	0.0291	
HbA1c									0.0750
<=8,5%	18	0 (0.0)	9	3 (33.3)	0.05 (0.00, 1.11)	0.08 (0.00, 1.32)	-33.33 (-64.13, -2.54)	0.0104	
>8,5%	19	1 (5.3)	19	1 (5.3)	1.00 (0.06, 17.25)	1.00 (0.07, 14.85)	0.00 (-14.20, 14.20)	1.0000	
Region									NA
Europe	9	0 (0.0)	6	0 (0.0)	0.68 (0.01, 39.07)	0.70 (0.02, 31.26)	0.00 (0.00, 0.00)	NA	
North and South America	19	1 (5.3)	17	4 (23.5)	0.18 (0.02, 1.81)	0.22 (0.03, 1.81)	-18.27 (-40.79, 4.26)	0.1377	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									NA
White	23	0 (0.0)	13	0 (0.0)	0.57 (0.01, 30.64)	0.58 (0.01, 27.80)	0.00 (0.00, 0.00)	NA	
Not white	14	1 (7.1)	15	4 (26.7)	0.21 (0.02, 2.18)	0.27 (0.03, 2.12)	-19.52 (-45.65, 6.61)	0.2292	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:47 - /allCQ01_4477.txt

2.43 Severe hypersensitivity adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:48 - /SevCQ01_4477.txt

2.44 Serious hypersensitivity adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:49 - /SerCQ01_4477.txt

2.45 Injection site reactions adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar				
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value	p-value int.
All subjects (total)	37	1 (2.7)	28	0 (0.0)	2.34 (0.09, 59.69)	2.29 (0.10, 54.18)	2.70 (-2.52, 7.93)	0.5169	
Gender									NA
Female	17	0 (0.0)	14	0 (0.0)	0.83 (0.02, 44.40)	0.83 (0.02, 39.54)	0.00 (0.00, 0.00)	NA	
Male	20	1 (5.0)	14	0 (0.0)	2.23 (0.08, 58.81)	2.14 (0.09, 49.08)	5.00 (-4.55, 14.55)	0.5668	
Age									NA
<65 years	26	1 (3.8)	23	0 (0.0)	2.76 (0.11, 71.25)	2.67 (0.11, 62.42)	3.85 (-3.55, 11.24)	0.5141	
>=65 years	11	0 (0.0)	5	0 (0.0)	0.48 (0.01, 27.44)	0.50 (0.01, 22.25)	0.00 (0.00, 0.00)	NA	
HbA1c									NA
<=8,5%	18	0 (0.0)	9	0 (0.0)	0.51 (0.01, 27.96)	0.53 (0.01, 24.60)	0.00 (0.00, 0.00)	NA	
>8,5%	19	1 (5.3)	19	0 (0.0)	3.16 (0.12, 82.64)	3.00 (0.13, 69.31)	5.26 (-4.78, 15.30)	0.5257	
Region									NA
Europe	9	0 (0.0)	6	0 (0.0)	0.68 (0.01, 39.07)	0.70 (0.02, 31.26)	0.00 (0.00, 0.00)	NA	
North and South America	19	1 (5.3)	17	0 (0.0)	2.84 (0.11, 74.42)	2.70 (0.12, 62.17)	5.26 (-4.78, 15.30)	0.5134	
Asia	9	0 (0.0)	5	0 (0.0)	0.58 (0.01, 33.50)	0.60 (0.01, 26.47)	0.00 (0.00, 0.00)	NA	
Race									NA
White	23	0 (0.0)	13	0 (0.0)	0.57 (0.01, 30.64)	0.58 (0.01, 27.80)	0.00 (0.00, 0.00)	NA	
Not white	14	1 (7.1)	15	0 (0.0)	3.44 (0.13, 91.79)	3.20 (0.14, 72.62)	7.14 (-6.35, 20.63)	0.3519	

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand.

nn1436/nn1436-amnog/current
21FEB2024:13:14:50 - /allCQ02_4477.txt

2.46 Severe injection site reactions adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:51 - /SevCQ02_4477.txt

2.47 Serious injection site reactions adverse events - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:14:53 - /SerCQ02_4477.txt

2.48 Adverse events by preferred term - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
Back pain								
All subjects (total)	37	5 (13.5)	28	3 (10.7)	1.30 (0.28, 5.98)	1.26 (0.33, 4.84)	2.80 (-13.09, 18.69)	0.7930
COVID-19								
All subjects (total)	37	6 (16.2)	28	1 (3.6)	5.23 (0.59, 46.18)	4.54 (0.58, 35.60)	12.64 (-1.08, 26.37)	0.1146
Arthralgia								
All subjects (total)	37	5 (13.5)	28	1 (3.6)	4.22 (0.46, 38.35)	3.78 (0.47, 30.60)	9.94 (-3.04, 22.93)	0.1791
Hypertriglyceridaemia								
All subjects (total)	37	4 (10.8)	28	1 (3.6)	3.27 (0.35, 31.04)	3.03 (0.36, 25.62)	7.24 (-4.90, 19.38)	0.3539

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. Preferred terms are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
21FEB2024:13:16:13 - /AEbyPT_4477.txt

2.49 Adverse events by system organ class - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
Infections and infestations								
All subjects (total)	37	12 (32.4)	28	11 (39.3)	0.74 (0.27, 2.07)	0.83 (0.43, 1.59)	-6.85 (-30.41, 16.70)	0.6046
Musculoskeletal and connective tissue disorders								
All subjects (total)	37	15 (40.5)	28	6 (21.4)	2.50 (0.82, 7.63)	1.89 (0.84, 4.25)	19.11 (-2.83, 41.05)	0.1085
Metabolism and nutrition disorders								
All subjects (total)	37	5 (13.5)	28	5 (17.9)	0.72 (0.19, 2.77)	0.76 (0.24, 2.36)	-4.34 (-22.30, 13.62)	0.6721
Gastrointestinal disorders								
All subjects (total)	37	5 (13.5)	28	4 (14.3)	0.94 (0.23, 3.87)	0.95 (0.28, 3.20)	-0.77 (-17.78, 16.24)	0.9659
Injury, poisoning and procedural complications								
All subjects (total)	37	7 (18.9)	28	2 (7.1)	3.03 (0.58, 15.90)	2.65 (0.60, 11.79)	11.78 (-4.04, 27.60)	0.1946
Eye disorders								
All subjects (total)	37	7 (18.9)	28	1 (3.6)	6.30 (0.73, 54.56)	5.30 (0.69, 40.62)	15.35 (0.98, 29.72)	0.0687
Nervous system disorders								
All subjects (total)	37	6 (16.2)	28	1 (3.6)	5.23 (0.59, 46.18)	4.54 (0.58, 35.60)	12.64 (-1.08, 26.37)	0.1146
Respiratory, thoracic and mediastinal disorders								
All subjects (total)	37	4 (10.8)	28	3 (10.7)	1.01 (0.21, 4.93)	1.01 (0.25, 4.15)	0.10 (-15.11, 15.31)	1.0000

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. System organ classes are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
21FEB2024:13:16:14 - /AEbySOC_4477.txt

Adverse events by system organ class - Onwards 1 - Population 1 - in-trial - Safety analysis set

	Ico		IGlar		Ico vs. IGlar			
	N	n (%)	N	n (%)	OR (95% CI)	RR (95% CI)	RD (95% CI)	p-value
General disorders and administration site conditions								
All subjects (total)	37	4 (10.8)	28	1 (3.6)	3.27 (0.35, 31.04)	3.03 (0.36, 25.62)	7.24 (-4.90, 19.38)	0.3539
Psychiatric disorders								
All subjects (total)	37	4 (10.8)	28	1 (3.6)	3.27 (0.35, 31.04)	3.03 (0.36, 25.62)	7.24 (-4.90, 19.38)	0.3539
Investigations								
All subjects (total)	37	1 (2.7)	28	3 (10.7)	0.23 (0.02, 2.36)	0.25 (0.03, 2.30)	-8.01 (-20.60, 4.58)	0.2135
Skin and subcutaneous tissue disorders								
All subjects (total)	37	1 (2.7)	28	3 (10.7)	0.23 (0.02, 2.36)	0.25 (0.03, 2.30)	-8.01 (-20.60, 4.58)	0.2135

N: number of subjects, n: number of subjects with at least one event, OR: Odds Ratio, RR: Relative Risk, RD: Risk Difference, CI: Confidence Interval. The relative risk, odds ratio, risk difference estimates and confidence limits were derived based on a non-parametric analysis (2x2 contingency tables) of the binary response (had an event in the in-trial observation period or not). To calculate odds ratios and relative risks in the event of zero cells, the correction value of 0.5 was added to each cell frequency of the corresponding fourfold table. P-values (two-sided) are based on Barnard's unconditional exact test if the minimum of the four cell counts in the 2x2 contingency table is <= 5 or the sum of the four cell counts is <= 200. Otherwise, Fisher's exact test is applied. P-value (two-sided) for the interaction of subgroups is calculated using the Breslow-Day test for homogeneity across 2x2xk contingency tables for k levels of each subgroup. In-trial onset is captured on or after the day of randomisation and no later than week 83 (or week 78 for treatment discontinuation) or withdrawal/death date for subjects that withdraws/dies beforehand. System organ classes are ordered by total number of events in descending sequence.

nn1436/nn1436-amnog/current
21FEB2024:13:16:14 - /AEbySOC_4477.txt

2.50 Serious adverse events by preferred term - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:15 - /SAEbyPT_4477.txt

2.51 Serious adverse events by system organ class - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:16 - /SAEbySOC_4477.txt

2.52 Severe adverse events by preferred term - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:17 - /SevAEbyPT_4477.txt

2.53 Severe adverse events by system organ class - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:17 - /SevAEbySOC_4477.txt

2.54 Adverse events leading to permanent trial product discontinuation by preferred term - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:20 - /AEDiscbyPT_4477.txt

2.55 Adverse events leading to permanent trial product discontinuation by system organ class - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:20 - /AEDiscbySOC_4477.txt

2.56 Adverse events leading to study withdrawal by preferred term - Onwards 1 - Population 1 - in-trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:21 - /AEWithbyPT_4477.txt

2.57 Adverse events leading to study withdrawal by system organ class - Onwards 1 - Population 1 - in- trial - Safety analysis set

There is no data for this output

nn1436/nn1436-amnog/current
21FEB2024:13:16:22 - /AEWithbySOC_4477.txt

3 Auswertung zum Anteil von Patienten, die in deutschen Studienzentren rekrutiert wurden

3.1 Summary of subjects from Germany in the insulin icodec RCT pool

Study	N	n DE	% DE
ONWARDS 1	984	0	0
ONWARDS 2	526	45	8,6
ONWARDS 3	588	0	0
ONWARDS 4	582	0	0
ONWARDS 5	1085	101	9,3
ONWARDS 6	582	46	7,9
NN1436-4466	154	32	20,8
NN1436-4465	205	38	18,5
NN1436-4462	43	0	0
NN1436-4422	24	0	0
NN1436-4383	247	0	0
NN1436-4314 (I287)	48	48	100
NN1436-4225	66	66	100
NN1436-4057	49	49	100
NN1436-3955 (part 1 and 2 combined)	69	69	100
Sum	**5252**	**494**	**9,4**

N is given as all subjects in the study, independent of having insulin icodec or comparative investigational medicinal product.
DE: Deutschland (Germany); N: number of subjects; n: number of subjects from Germany;
RCT: randomized controlled trial