Modul 4A Anhang 4-G

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Iptacopan (Fabhalta®)

Novartis Pharma GmbH

Modul 4 A – Anhang 4-G

***Vorbehandelte** erwachsene Patienten mit paroxysmaler nächtlicher Hämoglobinurie (PNH), die eine hämolytische Anämie aufweisen*

Ergänzende Analysen zur Studie APPLY-PNH

Stand: 26.06.2024

Iptacopan in patients with PNH and residual anemia despite anti-C5 antibody therapy

Study CLNP023C12302 (APPLY-PNH)

AMNOG initial full dossier submission

TFLs

Cut-off date:	06th Mar 2023
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1 Patient disposition, demographic and disease characteristics, follow-up times, PRO compliance rates and treatments

Table 1-1 Follow-up time (Full Analysis Set)

	Treatment Groups		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Total (N = 97)**
Follow-up time (days)			
n	62	35	97
Mean ± SD	168.9 ± 2.00	171.5 ± 6.31	169.9 ± 4.26
Median	169.0	169.0	169.0
Range 1st to 3rd quartile	169.0 to 169.0	169.0 to 170.0	169.0 to 169.0
Range minimum to maximum	166.0 to 183.0	166.0 to 195.0	166.0 to 195.0

N: Number of patients in the analysis set
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Follow-up time [days] = minimum (date of completion or discontinuation from randomized treatment period, death date, cut-off date) – date of first exposure to treatment + 1

Cut-off date for analysis: 06-Mar-2023

Table 1-2.1 FACIT Fatigue: return rates (Full Analysis Set)

	Treatment Groups		
	Iptacopan (N = 62) n (%)	**Anti-C5 antibody (N = 35) n (%)**	**Total (N = 97) n (%)**
FACIT Fatigue			
Baseline	62 (100.0)	33 (94.3)	95 (97.9)
Day 7	60 (96.8)	27 (77.1)	87 (89.7)
Day 14	57 (91.9)	28 (80.0)	85 (87.6)
Day 42	61 (98.4)	32 (91.4)	93 (95.9)
Day 84	57 (91.9)	29 (82.9)	86 (88.7)
Day 126	58 (93.5)	29 (82.9)	87 (89.7)
Day 140	59 (95.2)	28 (80.0)	87 (89.7)
Day 154	56 (90.3)	28 (80.0)	84 (86.6)
Day 168	60 (96.8)	30 (85.7)	90 (92.8)
Baseline and at least one post-baseline assessment	62 (100.0)	33 (94.3)	95 (97.9)

N: Number of patients in the analysis set
n: Number of returns
.....

The number of returns is the number of patients with non-missing data at the respective visit.
N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

Table 1-2.2 EORTC QLQ-C30: return rates (Full Analysis Set)

	Treatment Groups		
	Iptacopan (N = 62) n (%)	**Anti-C5 antibody (N = 35) n (%)**	**Total (N = 97) n (%)**
EORTC QLQ-C30			
Baseline	62 (100.0)	33 (94.3)	95 (97.9)
Day 14	57 (91.9)	28 (80.0)	85 (87.6)
Day 42	61 (98.4)	32 (91.4)	93 (95.9)
Day 84	57 (91.9)	29 (82.9)	86 (88.7)
Day 126	58 (93.5)	29 (82.9)	87 (89.7)
Day 140	59 (95.2)	28 (80.0)	87 (89.7)
Day 154	56 (90.3)	28 (80.0)	84 (86.6)
Day 168	60 (96.8)	30 (85.7)	90 (92.8)
Baseline and at least one post-baseline assessment	62 (100.0)	33 (94.3)	95 (97.9)

N: Number of patients in the analysis set
n: Number of returns
.....

The number of returns is the number of patients with non-missing data (i.e. at least one [sub-]score present) at the respective visit.
N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

Table 1-2.3 EQ-5D VAS: return rates (Full Analysis Set)

	Treatment Groups		
	Iptacopan (N = 62) n (%)	**Anti-C5 antibody (N = 35) n (%)**	**Total (N = 97) n (%)**
EQ-5D VAS			
Baseline	62 (100.0)	33 (94.3)	95 (97.9)
Day 14	56 (90.3)	28 (80.0)	84 (86.6)
Day 42	61 (98.4)	32 (91.4)	93 (95.9)
Day 84	57 (91.9)	29 (82.9)	86 (88.7)
Day 126	58 (93.5)	29 (82.9)	87 (89.7)
Day 140	59 (95.2)	28 (80.0)	87 (89.7)
Day 154	56 (90.3)	28 (80.0)	84 (86.6)
Day 168	60 (96.8)	30 (85.7)	90 (92.8)
Baseline and at least one post-baseline assessment	62 (100.0)	33 (94.3)	95 (97.9)

N: Number of patients in the analysis set
n: Number of returns
.....

The number of returns is the number of patients with non-missing data at the respective visit.
N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

Table 1-3 Dose of study treatment for patients receiving Ravulizumab by body weight (Safety Set)

	Treatment Group
	Anti-C5 antibody (N = 35) n (%)
Patients receiving Ravulizumab by body weight category	
Ravulizumab 3000mg	5 (14.3)
≥ 40 to < 60 kg	4 (11.4)
≥ 60 to < 100 kg	1 (2.9)
≥ 100 kg	0 (0.0)
Ravulizumab 3300mg	6 (17.1)
≥ 40 to < 60 kg	0 (0.0)
≥ 60 to < 100 kg	6 (17.1)
≥ 100 kg	0 (0.0)
Ravulizumab 3600mg	1 (2.9)
≥ 40 to < 60 kg	0 (0.0)
≥ 60 to < 100 kg	0 (0.0)
≥ 100 kg	1 (2.9)

N: Number of patients in the analysis set
n: Number of patients in the respective category
.....

N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

Table 1-4.1 Prior medications by ATC class and Preferred Term (Safety Set)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
Number of subjects with at least one medication	**62 (100.0)**	**35 (100.0)**	**97 (100.0)**
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	**62 (100.0)**	**35 (100.0)**	**97 (100.0)**
IMMUNOSUPPRESSANTS	62 (100.0)	35 (100.0)	97 (100.0)
IMMUNOSUPPRESSANTS	62 (100.0)	35 (100.0)	97 (100.0)
CALCINEURIN INHIBITORS	1 (1.6)	1 (2.9)	2 (2.1)
CICLOSPORIN	1 (1.6)	1 (2.9)	2 (2.1)
SELECTIVE IMMUNOSUPPRESSANTS	62 (100.0)	35 (100.0)	97 (100.0)
ECULIZUMAB	50 (80.6)	28 (80.0)	78 (80.4)
RAVULIZUMAB	23 (37.1)	12 (34.3)	35 (36.1)
ANTIINFECTIVES FOR SYSTEMIC USE	**16 (25.8)**	**13 (37.1)**	**29 (29.9)**
VACCINES	15 (24.2)	12 (34.3)	27 (27.8)
BACTERIAL VACCINES	1 (1.6)	0	1 (1.0)
PERTUSSIS VACCINES	1 (1.6)	0	1 (1.0)
DIPHTHERIA VACCINE TOXOID;PERTUSSIS VACCINE ACELLULAR;TETANUS VACCINE TOXOID	1 (1.6)	0	1 (1.0)
VIRAL VACCINES	15 (24.2)	12 (34.3)	27 (27.8)
INFLUENZA VACCINES	2 (3.2)	0	2 (2.1)
INFLUENZA VACCINE	1 (1.6)	0	1 (1.0)
INFLUENZA VACCINE INACT SPLIT 4V	1 (1.6)	0	1 (1.0)
OTHER VIRAL VACCINES	15 (24.2)	12 (34.3)	27 (27.8)
COVID-19 VACCINE	2 (3.2)	1 (2.9)	3 (3.1)
COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19)	1 (1.6)	3 (8.6)	4 (4.1)
ELASOMERAN	3 (4.8)	1 (2.9)	4 (4.1)
TOZINAMERAN	10 (16.1)	8 (22.9)	18 (18.6)
VARICELLA ZOSTER VACCINES	1 (1.6)	0	1 (1.0)
VARICELLA ZOSTER VACCINE RGE (CHO)	1 (1.6)	0	1 (1.0)
ANTIBACTERIALS FOR SYSTEMIC USE	2 (3.2)	3 (8.6)	5 (5.2)
BETA-LACTAM ANTIBACTERIALS, PENICILLINS	0	1 (2.9)	1 (1.0)
BETA-LACTAMASE RESISTANT PENICILLINS	0	1 (2.9)	1 (1.0)
FLUCLOXACILLIN	0	1 (2.9)	1 (1.0)
OTHER BETA-LACTAM ANTIBACTERIALS	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
THIRD-GENERATION CEPHALOSPORINS	1 (1.6)	0	1 (1.0)
CEFIXIME	1 (1.6)	0	1 (1.0)
QUINOLONE ANTIBACTERIALS	1 (1.6)	1 (2.9)	2 (2.1)
FLUOROQUINOLONES	1 (1.6)	1 (2.9)	2 (2.1)
LEVOFLOXACIN	1 (1.6)	1 (2.9)	2 (2.1)
TETRACYCLINES	0	1 (2.9)	1 (1.0)
TETRACYCLINES	0	1 (2.9)	1 (1.0)
DOXYCYCLINE	0	1 (2.9)	1 (1.0)
ANTIVIRALS FOR SYSTEMIC USE	1 (1.6)	1 (2.9)	2 (2.1)
DIRECT ACTING ANTIVIRALS	1 (1.6)	1 (2.9)	2 (2.1)
NUCLEOSIDES AND NUCLEOTIDES EXCL. REVERSE TRANSCRIPTASE INHIBITORS	1 (1.6)	1 (2.9)	2 (2.1)
REMDESIVIR	1 (1.6)	1 (2.9)	2 (2.1)
NERVOUS SYSTEM	**6 (9.7)**	**1 (2.9)**	**7 (7.2)**
ANALGESICS	6 (9.7)	0	6 (6.2)
OTHER ANALGESICS AND ANTIPYRETICS	6 (9.7)	0	6 (6.2)
ANILIDES	5 (8.1)	0	5 (5.2)
PARACETAMOL	5 (8.1)	0	5 (5.2)
PYRAZOLONES	1 (1.6)	0	1 (1.0)
METAMIZOLE SODIUM	1 (1.6)	0	1 (1.0)
PSYCHOANALEPTICS	0	1 (2.9)	1 (1.0)
ANTIDEPRESSANTS	0	1 (2.9)	1 (1.0)
OTHER ANTIDEPRESSANTS	0	1 (2.9)	1 (1.0)
VENLAFAXINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
ALIMENTARY TRACT AND METABOLISM	**3 (4.8)**	**2 (5.7)**	**5 (5.2)**
VITAMINS	2 (3.2)	0	2 (2.1)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO	1 (1.6)	0	1 (1.0)
VITAMIN D AND ANALOGUES	1 (1.6)	0	1 (1.0)
COLECALCIFEROL	1 (1.6)	0	1 (1.0)
VITAMIN B-COMPLEX, INCL. COMBINATIONS	1 (1.6)	0	1 (1.0)
VITAMIN B-COMPLEX, PLAIN	1 (1.6)	0	1 (1.0)
VITAMIN B COMPLEX	1 (1.6)	0	1 (1.0)
ANABOLIC AGENTS FOR SYSTEMIC USE	0	1 (2.9)	1 (1.0)
ANABOLIC STEROIDS	0	1 (2.9)	1 (1.0)
ANDROSTAN DERIVATIVES	0	1 (2.9)	1 (1.0)
OXYMETHOLONE	0	1 (2.9)	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	0	1 (2.9)	1 (1.0)
ANTIPROPULSIVES	0	1 (2.9)	1 (1.0)
ANTIPROPULSIVES	0	1 (2.9)	1 (1.0)
LOPERAMIDE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
BILE AND LIVER THERAPY	0	1 (2.9)	1 (1.0)
BILE THERAPY	0	1 (2.9)	1 (1.0)
BILE ACIDS AND DERIVATIVES	0	1 (2.9)	1 (1.0)
URSODEOXYCHOLIC ACID	0	1 (2.9)	1 (1.0)
DRUGS FOR ACID RELATED DISORDERS	1 (1.6)	0	1 (1.0)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	1 (1.6)	0	1 (1.0)
PROTON PUMP INHIBITORS	1 (1.6)	0	1 (1.0)
ESOMEPRAZOLE MAGNESIUM	1 (1.6)	0	1 (1.0)
BLOOD AND BLOOD FORMING ORGANS	**3 (4.8)**	**2 (5.7)**	**5 (5.2)**
ANTITHROMBOTIC AGENTS	1 (1.6)	2 (5.7)	3 (3.1)
ANTITHROMBOTIC AGENTS	1 (1.6)	2 (5.7)	3 (3.1)
HEPARIN GROUP	1 (1.6)	1 (2.9)	2 (2.1)
ENOXAPARIN	1 (1.6)	0	1 (1.0)
TINZAPARIN	0	1 (2.9)	1 (1.0)
VITAMIN K ANTAGONISTS	0	1 (2.9)	1 (1.0)
WARFARIN POTASSIUM	0	1 (2.9)	1 (1.0)
ANTIANEMIC PREPARATIONS	2 (3.2)	0	2 (2.1)
OTHER ANTIANEMIC PREPARATIONS	1 (1.6)	0	1 (1.0)
OTHER ANTIANEMIC PREPARATIONS	1 (1.6)	0	1 (1.0)
ERYTHROPOIETIN	1 (1.6)	0	1 (1.0)
VITAMIN B12 AND FOLIC ACID	1 (1.6)	0	1 (1.0)
FOLIC ACID AND DERIVATIVES	1 (1.6)	0	1 (1.0)
FOLIC ACID	1 (1.6)	0	1 (1.0)
VARIOUS	**2 (3.2)**	**3 (8.6)**	**5 (5.2)**
ALL OTHER THERAPEUTIC PRODUCTS	1 (1.6)	3 (8.6)	4 (4.1)
ALL OTHER THERAPEUTIC PRODUCTS	1 (1.6)	3 (8.6)	4 (4.1)
IRON CHELATING AGENTS	1 (1.6)	3 (8.6)	4 (4.1)
DEFERASIROX	1 (1.6)	2 (5.7)	3 (3.1)
DEFEROXAMINE MESILATE	0	2 (5.7)	2 (2.1)
GENERAL NUTRIENTS	1 (1.6)	0	1 (1.0)
OTHER NUTRIENTS	1 (1.6)	0	1 (1.0)
AMINO ACIDS, INCL. COMBINATIONS WITH POLYPEPTIDES	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
LYSINE	1 (1.6)	0	1 (1.0)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	**3 (4.8)**	**1 (2.9)**	**4 (4.1)**
CORTICOSTEROIDS FOR SYSTEMIC USE	3 (4.8)	1 (2.9)	4 (4.1)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	3 (4.8)	1 (2.9)	4 (4.1)
GLUCOCORTICOIDS	3 (4.8)	1 (2.9)	4 (4.1)
METHYLPREDNISOLONE	2 (3.2)	0	2 (2.1)
PREDNISOLONE	0	1 (2.9)	1 (1.0)
PREDNISONE	2 (3.2)	0	2 (2.1)
RESPIRATORY SYSTEM	**1 (1.6)**	**1 (2.9)**	**2 (2.1)**
ANTIHISTAMINES FOR SYSTEMIC USE	0	1 (2.9)	1 (1.0)
ANTIHISTAMINES FOR SYSTEMIC USE	0	1 (2.9)	1 (1.0)
OTHER ANTIHISTAMINES FOR SYSTEMIC USE	0	1 (2.9)	1 (1.0)
OLOPATADINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
COUGH AND COLD PREPARATIONS	1 (1.6)	0	1 (1.0)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS	1 (1.6)	0	1 (1.0)
OPIUM ALKALOIDS AND DERIVATIVES	1 (1.6)	0	1 (1.0)
CODEINE	1 (1.6)	0	1 (1.0)
SENSORY ORGANS	**1 (1.6)**	**1 (2.9)**	**2 (2.1)**
OPHTHALMOLOGICALS	1 (1.6)	1 (2.9)	2 (2.1)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	0	1 (2.9)	1 (1.0)
PARASYMPATHOMIMETICS	0	1 (2.9)	1 (1.0)
NEOSTIGMINE METILSULFATE	0	1 (2.9)	1 (1.0)
ANTIINFECTIVES	0	1 (2.9)	1 (1.0)
ANTIBIOTICS	0	1 (2.9)	1 (1.0)
TETRACYCLINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
DECONGESTANTS AND ANTIALLERGICS	0	1 (2.9)	1 (1.0)
SYMPATHOMIMETICS USED AS DECONGESTANTS	0	1 (2.9)	1 (1.0)
ANTAZOLINE PHOSPHATE;CHLORHEXIDINE GLUCONATE;TETRYZOLINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
MYDRIATICS AND CYCLOPLEGICS	1 (1.6)	0	1 (1.0)
ANTICHOLINERGICS	1 (1.6)	0	1 (1.0)
TROPICAMIDE	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
SYMPATHOMIMETICS EXCL. ANTIGLAUCOMA PREPARATIONS	1 (1.6)	0	1 (1.0)
PHENYLEPHRINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
OTHER OPHTHALMOLOGICALS	0	1 (2.9)	1 (1.0)
OTHER OPHTHALMOLOGICALS	0	1 (2.9)	1 (1.0)
PIRENOXINE	0	1 (2.9)	1 (1.0)
GENITO URINARY SYSTEM AND SEX HORMONES	**0**	**1 (2.9)**	**1 (1.0)**
UROLOGICALS	0	1 (2.9)	1 (1.0)
UROLOGICALS	0	1 (2.9)	1 (1.0)
DRUGS FOR URINARY FREQUENCY AND INCONTINENCE	0	1 (2.9)	1 (1.0)
MIRABEGRON	0	1 (2.9)	1 (1.0)
MUSCULO-SKELETAL SYSTEM	**1 (1.6)**	**0**	**1 (1.0)**
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	1 (1.6)	0	1 (1.0)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	1 (1.6)	0	1 (1.0)
PROPIONIC ACID DERIVATIVES	1 (1.6)	0	1 (1.0)
IBUPROFEN	1 (1.6)	0	1 (1.0)

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Prior medication is defined as any medication with a start date and end date before Day 1.
Anatomical Therapeutic Chemical (ATC) classes are classified as per WHO drug dictionary version DDEBApr22.
A patient with multiple occurrences within an ATC class is counted only once in the total row.

Cut-off date for analysis: 06-Mar-2023

Table 1-4.2 Concomitant medications by ATC class and Preferred Term (Safety Set)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
Number of subjects with at least one medication	**61 (98.4)**	**35 (100.0)**	**96 (99.0)**
BLOOD AND BLOOD FORMING ORGANS	**53 (85.5)**	**31 (88.6)**	**84 (86.6)**
ANTIANEMIC PREPARATIONS	43 (69.4)	27 (77.1)	70 (72.2)
IRON PREPARATIONS	5 (8.1)	1 (2.9)	6 (6.2)
IRON BIVALENT, ORAL PREPARATIONS	4 (6.5)	1 (2.9)	5 (5.2)
FERRIC SULFATE	1 (1.6)	0	1 (1.0)
FERROUS SODIUM CITRATE	1 (1.6)	0	1 (1.0)
FERROUS SULFATE	2 (3.2)	0	2 (2.1)
IRON	0	1 (2.9)	1 (1.0)
IRON, PARENTERAL PREPARATIONS	1 (1.6)	0	1 (1.0)
FERRIC CARBOXYMALTOSE	1 (1.6)	0	1 (1.0)
OTHER ANTIANEMIC PREPARATIONS	2 (3.2)	5 (14.3)	7 (7.2)
OTHER ANTIANEMIC PREPARATIONS	2 (3.2)	5 (14.3)	7 (7.2)
DARBEPOETIN ALFA	1 (1.6)	1 (2.9)	2 (2.1)
EPOETIN ALFA	0	1 (2.9)	1 (1.0)
EPOETIN ZETA	1 (1.6)	1 (2.9)	2 (2.1)
ERYTHROPOIETIN	0	2 (5.7)	2 (2.1)
VITAMIN B12 AND FOLIC ACID	41 (66.1)	26 (74.3)	67 (69.1)
FOLIC ACID AND DERIVATIVES	41 (66.1)	26 (74.3)	67 (69.1)
CALCIUM FOLINATE	1 (1.6)	0	1 (1.0)
FOLIC ACID	40 (64.5)	26 (74.3)	66 (68.0)
VITAMIN B12 (CYANOCOBALAMIN AND ANALOGUES)	11 (17.7)	4 (11.4)	15 (15.5)
CYANOCOBALAMIN	7 (11.3)	1 (2.9)	8 (8.2)
MECOBALAMIN	1 (1.6)	0	1 (1.0)
VITAMIN B12 NOS	3 (4.8)	3 (8.6)	6 (6.2)
ANTITHROMBOTIC AGENTS	18 (29.0)	11 (31.4)	29 (29.9)
ANTITHROMBOTIC AGENTS	18 (29.0)	11 (31.4)	29 (29.9)
DIRECT FACTOR XA INHIBITORS	4 (6.5)	2 (5.7)	6 (6.2)
APIXABAN	1 (1.6)	0	1 (1.0)
EDOXABAN TOSILATE	1 (1.6)	1 (2.9)	2 (2.1)
RIVAROXABAN	2 (3.2)	1 (2.9)	3 (3.1)
DIRECT THROMBIN INHIBITORS	0	1 (2.9)	1 (1.0)
DABIGATRAN ETEXILATE MESILATE	0	1 (2.9)	1 (1.0)
HEPARIN GROUP	4 (6.5)	4 (11.4)	8 (8.2)
ENOXAPARIN	1 (1.6)	0	1 (1.0)
ENOXAPARIN SODIUM	3 (4.8)	2 (5.7)	5 (5.2)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
HEPARIN CALCIUM	0	1 (2.9)	1 (1.0)
TINZAPARIN	0	1 (2.9)	1 (1.0)
OTHER ANTITHROMBOTIC AGENTS	1 (1.6)	0	1 (1.0)
FONDAPARINUX	1 (1.6)	0	1 (1.0)
PLATELET AGGREGATION INHIBITORS EXCL. HEPARIN	2 (3.2)	2 (5.7)	4 (4.1)
ACETYLSALICYLIC ACID	1 (1.6)	1 (2.9)	2 (2.1)
CILOSTAZOL	1 (1.6)	0	1 (1.0)
DIPYRIDAMOLE	0	1 (2.9)	1 (1.0)
VITAMIN K ANTAGONISTS	8 (12.9)	2 (5.7)	10 (10.3)
FLUINDIONE	0	1 (2.9)	1 (1.0)
PHENPROCOUMON	1 (1.6)	0	1 (1.0)
WARFARIN	5 (8.1)	0	5 (5.2)
WARFARIN POTASSIUM	1 (1.6)	0	1 (1.0)
WARFARIN SODIUM	1 (1.6)	1 (2.9)	2 (2.1)
ANTIHEMORRHAGICS	5 (8.1)	2 (5.7)	7 (7.2)
ANTIFIBRINOLYTICS	1 (1.6)	1 (2.9)	2 (2.1)
AMINO ACIDS	1 (1.6)	1 (2.9)	2 (2.1)
TRANEXAMIC ACID	1 (1.6)	1 (2.9)	2 (2.1)
VITAMIN K AND OTHER HEMOSTATICS	4 (6.5)	1 (2.9)	5 (5.2)
BLOOD COAGULATION FACTORS	1 (1.6)	0	1 (1.0)
THROMBIN	1 (1.6)	0	1 (1.0)
LOCAL HEMOSTATICS	1 (1.6)	0	1 (1.0)
EPINEPHRINE	1 (1.6)	0	1 (1.0)
OTHER SYSTEMIC HEMOSTATICS	2 (3.2)	1 (2.9)	3 (3.1)
ELTROMBOPAG	2 (3.2)	1 (2.9)	3 (3.1)
ELTROMBOPAG OLAMINE	1 (1.6)	0	1 (1.0)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	4 (6.5)	1 (2.9)	5 (5.2)
I.V. SOLUTION ADDITIVES	1 (1.6)	0	1 (1.0)
ELECTROLYTE SOLUTIONS	1 (1.6)	0	1 (1.0)
MAGNESIUM SULFATE	1 (1.6)	0	1 (1.0)
I.V. SOLUTIONS	4 (6.5)	1 (2.9)	5 (5.2)
SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE	4 (6.5)	1 (2.9)	5 (5.2)
CALCIUM CHLORIDE DIHYDRATE;MAGNESIUM CHLORIDE HEXAHYDRATE;MALIC ACID;POTASSIUM CHLORIDE;SODIUM ACETATE TRIHYDRATE;SODIUM CHLORIDE	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
CALCIUM GLUCONATE MONOHYDRATE;GLUCOSE;MAGNESIUM CHLORIDE HEXAHYDRATE;POTASSIUM CHLORIDE;SODIUM ACETATE;SODIUM CHLORIDE;SODIUM CITRATE DIHYDRATE	1 (1.6)	0	1 (1.0)
SODIUM BICARBONATE	1 (1.6)	0	1 (1.0)
SODIUM CHLORIDE	2 (3.2)	1 (2.9)	3 (3.1)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
CARBOHYDRATES NOS;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	1 (1.6)	0	1 (1.0)
ANTIINFECTIVES FOR SYSTEMIC USE	**43 (69.4)**	**20 (57.1)**	**63 (64.9)**
ANTIBACTERIALS FOR SYSTEMIC USE	32 (51.6)	14 (40.0)	46 (47.4)
AMINOGLYCOSIDE ANTIBACTERIALS	0	1 (2.9)	1 (1.0)
OTHER AMINOGLYCOSIDES	0	1 (2.9)	1 (1.0)
AMIKACIN	0	1 (2.9)	1 (1.0)
GENTAMICIN	0	1 (2.9)	1 (1.0)
BETA-LACTAM ANTIBACTERIALS, PENICILLINS	20 (32.3)	10 (28.6)	30 (30.9)
BETA-LACTAMASE INHIBITORS	2 (3.2)	0	2 (2.1)
CLAVULANIC ACID	2 (3.2)	0	2 (2.1)
BETA-LACTAMASE RESISTANT PENICILLINS	0	1 (2.9)	1 (1.0)
FLUCLOXACILLIN	0	1 (2.9)	1 (1.0)
BETA-LACTAMASE SENSITIVE PENICILLINS	8 (12.9)	5 (14.3)	13 (13.4)
PHENOXYMETHYLPENICILLIN	8 (12.9)	4 (11.4)	12 (12.4)
PHENOXYMETHYLPENICILLIN POTASSIUM	0	1 (2.9)	1 (1.0)
COMBINATIONS OF PENICILLINS, INCL. BETA-LACTAMASE INHIBITORS	7 (11.3)	2 (5.7)	9 (9.3)
AMOXICILLIN SODIUM;CLAVULANATE POTASSIUM	1 (1.6)	0	1 (1.0)
AMOXICILLIN TRIHYDRATE;CLAVULANATE POTASSIUM	2 (3.2)	1 (2.9)	3 (3.1)
AMOXICILLIN;CLAVULANATE POTASSIUM	1 (1.6)	1 (2.9)	2 (2.1)
AMOXICILLIN;CLAVULANIC ACID	2 (3.2)	0	2 (2.1)
PIPERACILLIN SODIUM;TAZOBACTAM SODIUM	1 (1.6)	0	1 (1.0)
PIPERACILLIN;TAZOBACTAM	0	1 (2.9)	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
PENICILLIN NOS	1 (1.6)	0	1 (1.0)
PENICILLINS WITH EXTENDED SPECTRUM	7 (11.3)	2 (5.7)	9 (9.3)
AMOXICILLIN	7 (11.3)	2 (5.7)	9 (9.3)
MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS	5 (8.1)	0	5 (5.2)
MACROLIDES	5 (8.1)	0	5 (5.2)
AZITHROMYCIN	4 (6.5)	0	4 (4.1)
CLARITHROMYCIN	1 (1.6)	0	1 (1.0)
OTHER ANTIBACTERIALS	2 (3.2)	1 (2.9)	3 (3.1)
IMIDAZOLE DERIVATIVES	0	1 (2.9)	1 (1.0)
METRONIDAZOLE	0	1 (2.9)	1 (1.0)
NITROFURAN DERIVATIVES	2 (3.2)	0	2 (2.1)
NITROFURANTOIN	2 (3.2)	0	2 (2.1)
OTHER ANTIBACTERIALS	0	1 (2.9)	1 (1.0)
DAPTOMYCIN	0	1 (2.9)	1 (1.0)
LINEZOLID	0	1 (2.9)	1 (1.0)
RIFAMPICIN	0	1 (2.9)	1 (1.0)
OTHER BETA-LACTAM ANTIBACTERIALS	5 (8.1)	2 (5.7)	7 (7.2)
FIRST-GENERATION CEPHALOSPORINS	1 (1.6)	1 (2.9)	2 (2.1)
CEFAZOLIN	0	1 (2.9)	1 (1.0)
CEFAZOLIN SODIUM	1 (1.6)	0	1 (1.0)
SECOND-GENERATION CEPHALOSPORINS	1 (1.6)	1 (2.9)	2 (2.1)
CEFUROXIME	0	1 (2.9)	1 (1.0)
CEFUROXIME AXETIL	1 (1.6)	0	1 (1.0)
THIRD-GENERATION CEPHALOSPORINS	3 (4.8)	1 (2.9)	4 (4.1)
CEFTAZIDIME	0	1 (2.9)	1 (1.0)
CEFTRIAXONE	1 (1.6)	1 (2.9)	2 (2.1)
CEFTRIAXONE SODIUM	1 (1.6)	0	1 (1.0)
CEFTRIAXONE SODIUM SESQUATERHYDRATE	1 (1.6)	0	1 (1.0)
QUINOLONE ANTIBACTERIALS	11 (17.7)	5 (14.3)	16 (16.5)
FLUOROQUINOLONES	11 (17.7)	5 (14.3)	16 (16.5)
CIPROFLOXACIN	6 (9.7)	5 (14.3)	11 (11.3)
CIPROFLOXACIN LACTATE	1 (1.6)	0	1 (1.0)
LEVOFLOXACIN	5 (8.1)	0	5 (5.2)
SULFONAMIDES AND TRIMETHOPRIM	1 (1.6)	1 (2.9)	2 (2.1)
COMBINATIONS OF SULFONAMIDES AND TRIMETHOPRIM, INCL. DERIVATIVES	1 (1.6)	1 (2.9)	2 (2.1)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
SULFAMETHOXAZOLE;TRIMETHOPRIM	1 (1.6)	1 (2.9)	2 (2.1)
TETRACYCLINES	1 (1.6)	2 (5.7)	3 (3.1)
TETRACYCLINES	1 (1.6)	2 (5.7)	3 (3.1)
DOXYCYCLINE	1 (1.6)	2 (5.7)	3 (3.1)
VACCINES	23 (37.1)	8 (22.9)	31 (32.0)
BACTERIAL VACCINES	1 (1.6)	0	1 (1.0)
TETANUS VACCINES	1 (1.6)	0	1 (1.0)
TETANUS VACCINE TOXOID	1 (1.6)	0	1 (1.0)
VIRAL VACCINES	23 (37.1)	8 (22.9)	31 (32.0)
INFLUENZA VACCINES	3 (4.8)	0	3 (3.1)
INFLUENZA VACCINE	1 (1.6)	0	1 (1.0)
INFLUENZA VACCINE INACT SPLIT 3V	2 (3.2)	0	2 (2.1)
OTHER VIRAL VACCINES	22 (35.5)	8 (22.9)	30 (30.9)
COVID-19 VACCINE	2 (3.2)	1 (2.9)	3 (3.1)
COVID-19 VACCINE NRVV AD (CHADOX1 NCOV-19)	1 (1.6)	0	1 (1.0)
ELASOMERAN	4 (6.5)	1 (2.9)	5 (5.2)
TOZINAMERAN	15 (24.2)	6 (17.1)	21 (21.6)
ANTIVIRALS FOR SYSTEMIC USE	4 (6.5)	4 (11.4)	8 (8.2)
DIRECT ACTING ANTIVIRALS	4 (6.5)	4 (11.4)	8 (8.2)
NEURAMINIDASE INHIBITORS	0	1 (2.9)	1 (1.0)
OSELTAMIVIR	0	1 (2.9)	1 (1.0)
NUCLEOSIDE AND NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS	1 (1.6)	0	1 (1.0)
ENTECAVIR	1 (1.6)	0	1 (1.0)
NUCLEOSIDES AND NUCLEOTIDES EXCL. REVERSE TRANSCRIPTASE INHIBITORS	2 (3.2)	2 (5.7)	4 (4.1)
ACICLOVIR	2 (3.2)	2 (5.7)	4 (4.1)
PROTEASE INHIBITORS	1 (1.6)	1 (2.9)	2 (2.1)
NIRMATRELVIR	1 (1.6)	0	1 (1.0)
NIRMATRELVIR;RITONAVIR	0	1 (2.9)	1 (1.0)
RITONAVIR	1 (1.6)	0	1 (1.0)
IMMUNE SERA AND IMMUNOGLOBULINS	1 (1.6)	0	1 (1.0)
IMMUNOGLOBULINS	1 (1.6)	0	1 (1.0)
IMMUNOGLOBULINS, NORMAL HUMAN	1 (1.6)	0	1 (1.0)
IMMUNOGLOBULIN HUMAN NORMAL	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
IMMUNOGLOBULINS NOS	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
ALIMENTARY TRACT AND METABOLISM	**31 (50.0)**	**16 (45.7)**	**47 (48.5)**
DRUGS FOR ACID RELATED DISORDERS	15 (24.2)	10 (28.6)	25 (25.8)
ANTACIDS	0	1 (2.9)	1 (1.0)
MAGNESIUM COMPOUNDS	0	1 (2.9)	1 (1.0)
MAGNESIUM OXIDE	0	1 (2.9)	1 (1.0)
DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	15 (24.2)	10 (28.6)	25 (25.8)
H2-RECEPTOR ANTAGONISTS	1 (1.6)	0	1 (1.0)
FAMOTIDINE	1 (1.6)	0	1 (1.0)
OTHER DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)	2 (3.2)	0	2 (2.1)
REBAMIPIDE	1 (1.6)	0	1 (1.0)
SODIUM BICARBONATE;SODIUM GUALENATE	1 (1.6)	0	1 (1.0)
PROTON PUMP INHIBITORS	13 (21.0)	10 (28.6)	23 (23.7)
ESOMEPRAZOLE	1 (1.6)	1 (2.9)	2 (2.1)
ESOMEPRAZOLE MAGNESIUM	1 (1.6)	1 (2.9)	2 (2.1)
LANSOPRAZOLE	1 (1.6)	0	1 (1.0)
OMEPRAZOLE	3 (4.8)	1 (2.9)	4 (4.1)
PANTOPRAZOLE	4 (6.5)	5 (14.3)	9 (9.3)
PANTOPRAZOLE SODIUM SESQUIHYDRATE	2 (3.2)	1 (2.9)	3 (3.1)
RABEPRAZOLE SODIUM	1 (1.6)	1 (2.9)	2 (2.1)
VITAMINS	16 (25.8)	8 (22.9)	24 (24.7)
ASCORBIC ACID (VITAMIN C), INCL. COMBINATIONS	4 (6.5)	0	4 (4.1)
ASCORBIC ACID (VITAMIN C), COMBINATIONS	1 (1.6)	0	1 (1.0)
ASCORBIC ACID;CALCIUM PANTOTHENATE	1 (1.6)	0	1 (1.0)
ASCORBIC ACID (VITAMIN C), PLAIN	3 (4.8)	0	3 (3.1)
ASCORBIC ACID	3 (4.8)	0	3 (3.1)
MULTIVITAMINS, PLAIN	2 (3.2)	0	2 (2.1)
MULTIVITAMINS, PLAIN	2 (3.2)	0	2 (2.1)
VITAMINS NOS	2 (3.2)	0	2 (2.1)
OTHER PLAIN VITAMIN PREPARATIONS	2 (3.2)	0	2 (2.1)
OTHER PLAIN VITAMIN PREPARATIONS	2 (3.2)	0	2 (2.1)
PANTETHINE	1 (1.6)	0	1 (1.0)
TOCOPHEROL	1 (1.6)	0	1 (1.0)
OTHER VITAMIN PRODUCTS, COMBINATIONS	0	2 (5.7)	2 (2.1)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
COMBINATIONS OF VITAMINS	0	2 (5.7)	2 (2.1)
FURSULTIAMINE;RIBOFLAVIN	0	1 (2.9)	1 (1.0)
VITAMIN B NOS	0	1 (2.9)	1 (1.0)
VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO	12 (19.4)	5 (14.3)	17 (17.5)
VITAMIN D AND ANALOGUES	12 (19.4)	5 (14.3)	17 (17.5)
ALFACALCIDOL	1 (1.6)	0	1 (1.0)
CALCIFEDIOL	0	1 (2.9)	1 (1.0)
CALCITRIOL	0	1 (2.9)	1 (1.0)
COLECALCIFEROL	9 (14.5)	2 (5.7)	11 (11.3)
VITAMIN D NOS	2 (3.2)	1 (2.9)	3 (3.1)
VITAMIN B1, PLAIN AND IN COMBINATION WITH VITAMIN B6 AND B12	2 (3.2)	1 (2.9)	3 (3.1)
VITAMIN B1 IN COMBINATION WITH VITAMIN B6 AND/OR VITAMIN B12	2 (3.2)	0	2 (2.1)
CYANOCOBALAMIN;PYRIDOXINE HYDROCHLORIDE;THIAMINE HYDROCHLORIDE	2 (3.2)	0	2 (2.1)
VITAMIN B1, PLAIN	0	1 (2.9)	1 (1.0)
VITAMIN B NOS	0	1 (2.9)	1 (1.0)
MINERAL SUPPLEMENTS	7 (11.3)	2 (5.7)	9 (9.3)
CALCIUM	1 (1.6)	1 (2.9)	2 (2.1)
CALCIUM	1 (1.6)	1 (2.9)	2 (2.1)
CALCIUM	0	1 (2.9)	1 (1.0)
CALCIUM GLUCONATE	1 (1.6)	0	1 (1.0)
OTHER MINERAL SUPPLEMENTS	4 (6.5)	1 (2.9)	5 (5.2)
MAGNESIUM	3 (4.8)	1 (2.9)	4 (4.1)
MAGNESIUM	2 (3.2)	0	2 (2.1)
MAGNESIUM OXIDE	1 (1.6)	1 (2.9)	2 (2.1)
ZINC	1 (1.6)	0	1 (1.0)
ZINC	1 (1.6)	0	1 (1.0)
POTASSIUM	3 (4.8)	1 (2.9)	4 (4.1)
POTASSIUM	3 (4.8)	1 (2.9)	4 (4.1)
POTASSIUM CHLORIDE	3 (4.8)	1 (2.9)	4 (4.1)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	3 (4.8)	2 (5.7)	5 (5.2)
ANTIDIARRHEAL MICROORGANISMS	2 (3.2)	1 (2.9)	3 (3.1)
ANTIDIARRHEAL MICROORGANISMS	1 (1.6)	1 (2.9)	2 (2.1)
ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE	0	1 (2.9)	1 (1.0)
PROBIOTICS NOS	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
LACTOMIN	1 (1.6)	0	1 (1.0)
INTESTINAL ANTIINFLAMMATORY AGENTS	1 (1.6)	1 (2.9)	2 (2.1)
AMINOSALICYLIC ACID AND SIMILAR AGENTS	0	1 (2.9)	1 (1.0)
MESALAZINE	0	1 (2.9)	1 (1.0)
CORTICOSTEROIDS ACTING LOCALLY	1 (1.6)	0	1 (1.0)
HYDROCORTISONE ACETATE	1 (1.6)	0	1 (1.0)
OTHER ANTIDIARRHEALS	0	1 (2.9)	1 (1.0)
OTHER ANTIDIARRHEALS	0	1 (2.9)	1 (1.0)
COLESTYRAMINE	0	1 (2.9)	1 (1.0)
BILE AND LIVER THERAPY	3 (4.8)	2 (5.7)	5 (5.2)
BILE THERAPY	3 (4.8)	2 (5.7)	5 (5.2)
BILE ACIDS AND DERIVATIVES	3 (4.8)	2 (5.7)	5 (5.2)
URSODEOXYCHOLIC ACID	3 (4.8)	2 (5.7)	5 (5.2)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	4 (6.5)	1 (2.9)	5 (5.2)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	3 (4.8)	1 (2.9)	4 (4.1)
HERBAL CARMINATIVES	1 (1.6)	0	1 (1.0)
ANGELICA ARCHANGELICA ROOT;CARUM CARVI FRUIT;CHELIDONIUM MAJUS HERB;GLYCYRRHIZA GLABRA ROOT;IBERIS AMARA;MATRICARIA CHAMOMILLA FLOWER;MELISSA OFFICINALIS LEAF;MENTHA X PIPERITA LEAF;	1 (1.6)	0	1 (1.0)
OTHER DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	1 (1.6)	1 (2.9)	2 (2.1)
DIMETICONE	1 (1.6)	1 (2.9)	2 (2.1)
SYNTHETIC ANTICHOLINERGICS, ESTERS WITH TERTIARY AMINO GROUP	1 (1.6)	0	1 (1.0)
MEBEVERINE	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	1 (1.6)	0	1 (1.0)
PROPULSIVES	0	1 (2.9)	1 (1.0)
PROPULSIVES	0	1 (2.9)	1 (1.0)
METOCLOPRAMIDE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
ANTIEMETICS AND ANTINAUSEANTS	2 (3.2)	0	2 (2.1)
ANTIEMETICS AND ANTINAUSEANTS	2 (3.2)	0	2 (2.1)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
METOCLOPRAMIDE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
SEROTONIN (5HT3) ANTAGONISTS	1 (1.6)	0	1 (1.0)
ONDANSETRON	1 (1.6)	0	1 (1.0)
DRUGS FOR CONSTIPATION	1 (1.6)	1 (2.9)	2 (2.1)
DRUGS FOR CONSTIPATION	1 (1.6)	1 (2.9)	2 (2.1)
CONTACT LAXATIVES	0	1 (2.9)	1 (1.0)
SENNOSIDE A+B	0	1 (2.9)	1 (1.0)
OSMOTICALLY ACTING LAXATIVES	1 (1.6)	1 (2.9)	2 (2.1)
MAGNESIUM OXIDE	1 (1.6)	1 (2.9)	2 (2.1)
OTHER DRUGS FOR CONSTIPATION	1 (1.6)	0	1 (1.0)
ELOBIXIBAT	1 (1.6)	0	1 (1.0)
STOMATOLOGICAL PREPARATIONS	1 (1.6)	1 (2.9)	2 (2.1)
STOMATOLOGICAL PREPARATIONS	1 (1.6)	1 (2.9)	2 (2.1)
CORTICOSTEROIDS FOR LOCAL ORAL TREATMENT	1 (1.6)	1 (2.9)	2 (2.1)
TRIAMCINOLONE ACETONIDE	1 (1.6)	1 (2.9)	2 (2.1)
ANABOLIC AGENTS FOR SYSTEMIC USE	0	1 (2.9)	1 (1.0)
ANABOLIC STEROIDS	0	1 (2.9)	1 (1.0)
ANDROSTAN DERIVATIVES	0	1 (2.9)	1 (1.0)
METENOLONE ACETATE	0	1 (2.9)	1 (1.0)
DRUGS USED IN DIABETES	0	1 (2.9)	1 (1.0)
BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS	0	1 (2.9)	1 (1.0)
BIGUANIDES	0	1 (2.9)	1 (1.0)
METFORMIN	0	1 (2.9)	1 (1.0)
NERVOUS SYSTEM	**25 (40.3)**	**17 (48.6)**	**42 (43.3)**
ANALGESICS	15 (24.2)	12 (34.3)	27 (27.8)
ANTIMIGRAINE PREPARATIONS	1 (1.6)	1 (2.9)	2 (2.1)
OTHER ANTIMIGRAINE PREPARATIONS	0	1 (2.9)	1 (1.0)
PROPRANOLOL	0	1 (2.9)	1 (1.0)
SELECTIVE SEROTONIN (5HT1) AGONISTS	1 (1.6)	0	1 (1.0)
ZOLMITRIPTAN	1 (1.6)	0	1 (1.0)
OPIOIDS	3 (4.8)	2 (5.7)	5 (5.2)
NATURAL OPIUM ALKALOIDS	2 (3.2)	1 (2.9)	3 (3.1)
CODEINE PHOSPHATE	1 (1.6)	0	1 (1.0)
MORPHINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
MORPHINE SULFATE	0	1 (2.9)	1 (1.0)
OXYCODONE	0	1 (2.9)	1 (1.0)
OPIOIDS IN COMBINATION WITH NON-OPIOID ANALGESICS	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
CAFFEINE;CODEINE PHOSPHATE;PARACETAMOL	1 (1.6)	0	1 (1.0)
OTHER OPIOIDS	0	1 (2.9)	1 (1.0)
TRAMADOL HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
OTHER ANALGESICS AND ANTIPYRETICS	14 (22.6)	12 (34.3)	26 (26.8)
ANILIDES	12 (19.4)	9 (25.7)	21 (21.6)
BUTALBITAL;CAFFEINE;PARACETAMOL	0	1 (2.9)	1 (1.0)
CAFFEINE;PARACETAMOL;PROMETHAZINE METHYLENE DISALICYLATE;SALICYLAMIDE	1 (1.6)	0	1 (1.0)
PARACETAMOL	12 (19.4)	8 (22.9)	20 (20.6)
OTHER ANALGESICS AND ANTIPYRETICS	1 (1.6)	1 (2.9)	2 (2.1)
AMITRIPTYLINE	1 (1.6)	0	1 (1.0)
AMITRIPTYLINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
GABAPENTIN	0	1 (2.9)	1 (1.0)
NEFOPAM	0	1 (2.9)	1 (1.0)
PYRAZOLONES	2 (3.2)	2 (5.7)	4 (4.1)
METAMIZOLE	1 (1.6)	0	1 (1.0)
METAMIZOLE SODIUM	1 (1.6)	2 (5.7)	3 (3.1)
SALICYLIC ACID AND DERIVATIVES	0	2 (5.7)	2 (2.1)
ACETYLSALICYLIC ACID	0	2 (5.7)	2 (2.1)
PSYCHOANALEPTICS	6 (9.7)	4 (11.4)	10 (10.3)
ANTIDEPRESSANTS	6 (9.7)	4 (11.4)	10 (10.3)
NON-SELECTIVE MONOAMINE REUPTAKE INHIBITORS	1 (1.6)	1 (2.9)	2 (2.1)
OPIPRAMOL	0	1 (2.9)	1 (1.0)
OPIPRAMOL HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
OTHER ANTIDEPRESSANTS	2 (3.2)	2 (5.7)	4 (4.1)
TRAZODONE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
VENLAFAXINE	1 (1.6)	1 (2.9)	2 (2.1)
VENLAFAXINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
SELECTIVE SEROTONIN REUPTAKE INHIBITORS	3 (4.8)	1 (2.9)	4 (4.1)
FLUOXETINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
PAROXETINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
SERTRALINE	0	1 (2.9)	1 (1.0)
SERTRALINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
PSYCHOSTIMULANTS, AGENTS USED FOR ADHD AND NOOTROPICS	1 (1.6)	0	1 (1.0)
CENTRALLY ACTING SYMPATHOMIMETICS	1 (1.6)	0	1 (1.0)
METHYLPHENIDATE	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
PSYCHOLEPTICS	7 (11.3)	3 (8.6)	10 (10.3)
ANXIOLYTICS	4 (6.5)	3 (8.6)	7 (7.2)
BENZODIAZEPINE DERIVATIVES	2 (3.2)	1 (2.9)	3 (3.1)
ALPRAZOLAM	1 (1.6)	0	1 (1.0)
BROMAZEPAM	1 (1.6)	0	1 (1.0)
LORAZEPAM	1 (1.6)	1 (2.9)	2 (2.1)
DIPHENYLMETHANE DERIVATIVES	1 (1.6)	0	1 (1.0)
HYDROXYZINE	1 (1.6)	0	1 (1.0)
OTHER ANXIOLYTICS	1 (1.6)	2 (5.7)	3 (3.1)
ESCITALOPRAM OXALATE	1 (1.6)	0	1 (1.0)
ETIFOXINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
PROPRANOLOL HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
HYPNOTICS AND SEDATIVES	4 (6.5)	1 (2.9)	5 (5.2)
BENZODIAZEPINE DERIVATIVES	1 (1.6)	1 (2.9)	2 (2.1)
LORMETAZEPAM	0	1 (2.9)	1 (1.0)
MIDAZOLAM	1 (1.6)	0	1 (1.0)
BENZODIAZEPINE RELATED DRUGS	2 (3.2)	0	2 (2.1)
ESZOPICLONE	1 (1.6)	0	1 (1.0)
ZOLPIDEM	1 (1.6)	0	1 (1.0)
MELATONIN RECEPTOR AGONISTS	1 (1.6)	0	1 (1.0)
MELATONIN	1 (1.6)	0	1 (1.0)
ANESTHETICS	4 (6.5)	0	4 (4.1)
ANESTHETICS, GENERAL	1 (1.6)	0	1 (1.0)
OPIOID ANESTHETICS	1 (1.6)	0	1 (1.0)
REMIFENTANIL	1 (1.6)	0	1 (1.0)
OTHER GENERAL ANESTHETICS	1 (1.6)	0	1 (1.0)
PROPOFOL	1 (1.6)	0	1 (1.0)
ANESTHETICS, LOCAL	4 (6.5)	0	4 (4.1)
AMIDES	4 (6.5)	0	4 (4.1)
ARTICAINE HYDROCHLORIDE;EPINEPHRINE BITARTRATE	1 (1.6)	0	1 (1.0)
EPINEPHRINE;LIDOCAINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
LIDOCAINE	1 (1.6)	0	1 (1.0)
LIDOCAINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
ANTIEPILEPTICS	1 (1.6)	1 (2.9)	2 (2.1)
ANTIEPILEPTICS	1 (1.6)	1 (2.9)	2 (2.1)
OTHER ANTIEPILEPTICS	1 (1.6)	1 (2.9)	2 (2.1)
LEVETIRACETAM	1 (1.6)	1 (2.9)	2 (2.1)
ANTI-PARKINSON DRUGS	1 (1.6)	0	1 (1.0)
DOPAMINERGIC AGENTS	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
DOPAMINE AGONISTS	1 (1.6)	0	1 (1.0)
PRAMIPEXOLE	1 (1.6)	0	1 (1.0)
CARDIOVASCULAR SYSTEM	**16 (25.8)**	**10 (28.6)**	**26 (26.8)**
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	8 (12.9)	7 (20.0)	15 (15.5)
ACE INHIBITORS, COMBINATIONS	1 (1.6)	0	1 (1.0)
ACE INHIBITORS AND CALCIUM CHANNEL BLOCKERS	1 (1.6)	0	1 (1.0)
AMLODIPINE BESILATE;PERINDOPRIL ARGININE	1 (1.6)	0	1 (1.0)
ACE INHIBITORS, PLAIN	2 (3.2)	2 (5.7)	4 (4.1)
ACE INHIBITORS, PLAIN	2 (3.2)	2 (5.7)	4 (4.1)
ENALAPRIL MALEATE	1 (1.6)	0	1 (1.0)
RAMIPRIL	1 (1.6)	2 (5.7)	3 (3.1)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS), COMBINATIONS	3 (4.8)	0	3 (3.1)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS) AND CALCIUM CHANNEL BLOCKERS	1 (1.6)	0	1 (1.0)
AMLODIPINE BESILATE;OLMESARTAN MEDOXOMIL	1 (1.6)	0	1 (1.0)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS) AND DIURETICS	1 (1.6)	0	1 (1.0)
HYDROCHLOROTHIAZIDE;LOSARTAN POTASSIUM	1 (1.6)	0	1 (1.0)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS), OTHER COMBINATIONS	1 (1.6)	0	1 (1.0)
SACUBITRIL;VALSARTAN	1 (1.6)	0	1 (1.0)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS), PLAIN	2 (3.2)	6 (17.1)	8 (8.2)
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBS), PLAIN	2 (3.2)	6 (17.1)	8 (8.2)
CANDESARTAN	1 (1.6)	0	1 (1.0)
LOSARTAN	0	1 (2.9)	1 (1.0)
LOSARTAN POTASSIUM	1 (1.6)	0	1 (1.0)
OLMESARTAN	0	1 (2.9)	1 (1.0)
OLMESARTAN MEDOXOMIL	0	1 (2.9)	1 (1.0)
TELMISARTAN	0	3 (8.6)	3 (3.1)
BETA BLOCKING AGENTS	6 (9.7)	4 (11.4)	10 (10.3)
BETA BLOCKING AGENTS	6 (9.7)	4 (11.4)	10 (10.3)
ALPHA AND BETA BLOCKING AGENTS	1 (1.6)	0	1 (1.0)
CARVEDILOL	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
BETA BLOCKING AGENTS, NON-SELECTIVE	1 (1.6)	0	1 (1.0)
PROPRANOLOL	1 (1.6)	0	1 (1.0)
BETA BLOCKING AGENTS, SELECTIVE	4 (6.5)	4 (11.4)	8 (8.2)
BISOPROLOL	1 (1.6)	2 (5.7)	3 (3.1)
BISOPROLOL FUMARATE	1 (1.6)	2 (5.7)	3 (3.1)
METOPROLOL TARTRATE	2 (3.2)	0	2 (2.1)
CALCIUM CHANNEL BLOCKERS	6 (9.7)	4 (11.4)	10 (10.3)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CARDIAC EFFECTS	0	1 (2.9)	1 (1.0)
PHENYLALKYLAMINE DERIVATIVES	0	1 (2.9)	1 (1.0)
VERAPAMIL HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS	6 (9.7)	4 (11.4)	10 (10.3)
DIHYDROPYRIDINE DERIVATIVES	6 (9.7)	4 (11.4)	10 (10.3)
AMLODIPINE	3 (4.8)	1 (2.9)	4 (4.1)
AMLODIPINE BESILATE	3 (4.8)	1 (2.9)	4 (4.1)
LERCANIDIPINE	0	1 (2.9)	1 (1.0)
NICARDIPINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
DIURETICS	2 (3.2)	2 (5.7)	4 (4.1)
ALDOSTERONE ANTAGONISTS AND OTHER POTASSIUM-SPARING AGENTS	1 (1.6)	1 (2.9)	2 (2.1)
ALDOSTERONE ANTAGONISTS	1 (1.6)	1 (2.9)	2 (2.1)
POTASSIUM CANRENOATE	0	1 (2.9)	1 (1.0)
SPIRONOLACTONE	1 (1.6)	0	1 (1.0)
HIGH-CEILING DIURETICS	2 (3.2)	2 (5.7)	4 (4.1)
SULFONAMIDES, PLAIN	2 (3.2)	2 (5.7)	4 (4.1)
AZOSEMIDE	1 (1.6)	0	1 (1.0)
FUROSEMIDE	0	2 (5.7)	2 (2.1)
TORASEMIDE	1 (1.6)	0	1 (1.0)
LOW-CEILING DIURETICS, THIAZIDES	0	1 (2.9)	1 (1.0)
THIAZIDES, PLAIN	0	1 (2.9)	1 (1.0)
HYDROCHLOROTHIAZIDE	0	1 (2.9)	1 (1.0)
LIPID MODIFYING AGENTS	4 (6.5)	0	4 (4.1)
LIPID MODIFYING AGENTS, COMBINATIONS	1 (1.6)	0	1 (1.0)
COMBINATIONS OF VARIOUS LIPID MODIFYING AGENTS	1 (1.6)	0	1 (1.0)
EZETIMIBE;SIMVASTATIN	1 (1.6)	0	1 (1.0)
LIPID MODIFYING AGENTS, PLAIN	3 (4.8)	0	3 (3.1)
HMG COA REDUCTASE INHIBITORS	3 (4.8)	0	3 (3.1)
ROSUVASTATIN	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
SIMVASTATIN	2 (3.2)	0	2 (2.1)
CARDIAC THERAPY	2 (3.2)	1 (2.9)	3 (3.1)
ANTIARRHYTHMICS, CLASS I AND III	1 (1.6)	1 (2.9)	2 (2.1)
ANTIARRHYTHMICS, CLASS IC	0	1 (2.9)	1 (1.0)
FLECAINIDE ACETATE	0	1 (2.9)	1 (1.0)
ANTIARRHYTHMICS, CLASS III	1 (1.6)	0	1 (1.0)
AMIODARONE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
CARDIAC STIMULANTS EXCL. CARDIAC GLYCOSIDES	1 (1.6)	0	1 (1.0)
ADRENERGIC AND DOPAMINERGIC AGENTS	1 (1.6)	0	1 (1.0)
EPHEDRINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
PHENYLEPHRINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
ANTIHYPERTENSIVES	2 (3.2)	0	2 (2.1)
ANTIADRENERGIC AGENTS, CENTRALLY ACTING	1 (1.6)	0	1 (1.0)
IMIDAZOLINE RECEPTOR AGONISTS	1 (1.6)	0	1 (1.0)
CLONIDINE	1 (1.6)	0	1 (1.0)
OTHER ANTIHYPERTENSIVES	1 (1.6)	0	1 (1.0)
ANTIHYPERTENSIVES FOR PULMONARY ARTERIAL HYPERTENSION	1 (1.6)	0	1 (1.0)
SILDENAFIL	1 (1.6)	0	1 (1.0)
VASOPROTECTIVES	0	2 (5.7)	2 (2.1)
AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSURES FOR TOPICAL USE	0	1 (2.9)	1 (1.0)
LOCAL ANESTHETICS	0	1 (2.9)	1 (1.0)
BENZOCAINE;BISMUTH SUBGALLATE;DIPHENHYDRAMINE HYDROCHLORIDE;ZINC OXIDE	0	1 (2.9)	1 (1.0)
CAPILLARY STABILIZING AGENTS	0	1 (2.9)	1 (1.0)
BIOFLAVONOIDS	0	1 (2.9)	1 (1.0)
DIOSMIN	0	1 (2.9)	1 (1.0)
VARIOUS	**14 (22.6)**	**9 (25.7)**	**23 (23.7)**
ALL OTHER THERAPEUTIC PRODUCTS	10 (16.1)	9 (25.7)	19 (19.6)
ALL OTHER THERAPEUTIC PRODUCTS	10 (16.1)	9 (25.7)	19 (19.6)
ANTIDOTES	1 (1.6)	0	1 (1.0)
SUGAMMADEX SODIUM	1 (1.6)	0	1 (1.0)
DRUGS FOR TREATMENT OF HYPERKALEMIA AND HYPERPHOSPHATEMIA	0	1 (2.9)	1 (1.0)
GLUCOSE;INSULIN	0	1 (2.9)	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
IRON CHELATING AGENTS	8 (12.9)	8 (22.9)	16 (16.5)
DEFERASIROX	8 (12.9)	6 (17.1)	14 (14.4)
DEFERIPRONE	0	1 (2.9)	1 (1.0)
DEFEROXAMINE	0	1 (2.9)	1 (1.0)
DEFEROXAMINE MESILATE	0	1 (2.9)	1 (1.0)
MEDICAL GASES	1 (1.6)	0	1 (1.0)
OXYGEN	1 (1.6)	0	1 (1.0)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	2 (3.2)	1 (2.9)	3 (3.1)
NOT SPECIFIED	2 (3.2)	1 (2.9)	3 (3.1)
NOT SPECIFIED	2 (3.2)	1 (2.9)	3 (3.1)
CAMELLIA SINENSIS	1 (1.6)	0	1 (1.0)
HERBAL NOS	1 (1.6)	0	1 (1.0)
ORIGANUM MINUTIFLORUM OIL	1 (1.6)	0	1 (1.0)
PLATYCODON GRANDIFLORUS ROOT FLUID EXTRACT	0	1 (2.9)	1 (1.0)
GENERAL NUTRIENTS	2 (3.2)	0	2 (2.1)
OTHER NUTRIENTS	2 (3.2)	0	2 (2.1)
AMINO ACIDS, INCL. COMBINATIONS WITH POLYPEPTIDES	1 (1.6)	0	1 (1.0)
PEPTIDES NOS	1 (1.6)	0	1 (1.0)
OTHER COMBINATIONS OF NUTRIENTS	1 (1.6)	0	1 (1.0)
DOCOSAHEXAENOIC ACID	1 (1.6)	0	1 (1.0)
HOMEOPATHIC PREPARATION	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
HOMEOPATHICS NOS	1 (1.6)	0	1 (1.0)
MUSCULO-SKELETAL SYSTEM	**16 (25.8)**	**6 (17.1)**	**22 (22.7)**
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	8 (12.9)	1 (2.9)	9 (9.3)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS	8 (12.9)	1 (2.9)	9 (9.3)
ACETIC ACID DERIVATIVES AND RELATED SUBSTANCES	1 (1.6)	1 (2.9)	2 (2.1)
DICLOFENAC DIETHYLAMINE	0	1 (2.9)	1 (1.0)
INDOMETACIN	1 (1.6)	0	1 (1.0)
HERBAL ANTIINFLAMMATORY AND ANTIRHEUMATIC REMEDIES	1 (1.6)	0	1 (1.0)
CURCUMA LONGA RHIZOME	1 (1.6)	0	1 (1.0)
PROPIONIC ACID DERIVATIVES	6 (9.7)	0	6 (6.2)
IBUPROFEN	6 (9.7)	0	6 (6.2)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	5 (8.1)	3 (8.6)	8 (8.2)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	5 (8.1)	3 (8.6)	8 (8.2)
ANTIINFLAMMATORY PREPARATIONS, NON-STEROIDS FOR TOPICAL USE	4 (6.5)	2 (5.7)	6 (6.2)
DICLOFENAC	1 (1.6)	0	1 (1.0)
DICLOFENAC SODIUM	1 (1.6)	0	1 (1.0)
INDOMETACIN	0	1 (2.9)	1 (1.0)
KETOPROFEN	0	1 (2.9)	1 (1.0)
LOXOPROFEN SODIUM DIHYDRATE	1 (1.6)	0	1 (1.0)
PIROXICAM	1 (1.6)	0	1 (1.0)
OTHER TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	1 (1.6)	1 (2.9)	2 (2.1)
CHONDROITIN SULFATE;GLUCOSAMINE HYDROCHLORIDE;METHYLSULFONYL METHANE	1 (1.6)	0	1 (1.0)
HEPARINOID	0	1 (2.9)	1 (1.0)
ANTIGOUT PREPARATIONS	3 (4.8)	1 (2.9)	4 (4.1)
ANTIGOUT PREPARATIONS	3 (4.8)	1 (2.9)	4 (4.1)
PREPARATIONS INHIBITING URIC ACID PRODUCTION	3 (4.8)	1 (2.9)	4 (4.1)
ALLOPURINOL	1 (1.6)	1 (2.9)	2 (2.1)
FEBUXOSTAT	2 (3.2)	0	2 (2.1)
MUSCLE RELAXANTS	3 (4.8)	1 (2.9)	4 (4.1)
MUSCLE RELAXANTS, CENTRALLY ACTING AGENTS	2 (3.2)	1 (2.9)	3 (3.1)
CARBAMIC ACID ESTERS	1 (1.6)	0	1 (1.0)
METHOCARBAMOL	1 (1.6)	0	1 (1.0)
OTHER CENTRALLY ACTING AGENTS	0	1 (2.9)	1 (1.0)
BACLOFEN	0	1 (2.9)	1 (1.0)
OXAZOL, THIAZINE, AND TRIAZINE DERIVATIVES	1 (1.6)	0	1 (1.0)
CHLORZOXAZONE;PARACETAMOL	1 (1.6)	0	1 (1.0)
MUSCLE RELAXANTS, PERIPHERALLY ACTING AGENTS	1 (1.6)	0	1 (1.0)
OTHER QUATERNARY AMMONIUM COMPOUNDS	1 (1.6)	0	1 (1.0)
ROCURONIUM BROMIDE	1 (1.6)	0	1 (1.0)
DRUGS FOR TREATMENT OF BONE DISEASES	2 (3.2)	0	2 (2.1)
DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION	2 (3.2)	0	2 (2.1)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
BISPHOSPHONATES	2 (3.2)	0	2 (2.1)
ALENDRONATE SODIUM	1 (1.6)	0	1 (1.0)
ALENDRONIC ACID	1 (1.6)	0	1 (1.0)
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS	**16 (25.8)**	**5 (14.3)**	**21 (21.6)**
CORTICOSTEROIDS FOR SYSTEMIC USE	10 (16.1)	2 (5.7)	12 (12.4)
CORTICOSTEROIDS FOR SYSTEMIC USE, COMBINATIONS	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS FOR SYSTEMIC USE, COMBINATIONS	1 (1.6)	0	1 (1.0)
BETAMETHASONE;CHLORPHENAMINE MALEATE	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN	9 (14.5)	2 (5.7)	11 (11.3)
GLUCOCORTICOIDS	9 (14.5)	2 (5.7)	11 (11.3)
DEXAMETHASONE	1 (1.6)	0	1 (1.0)
METHYLPREDNISOLONE	2 (3.2)	0	2 (2.1)
PREDNISOLONE	4 (6.5)	0	4 (4.1)
PREDNISONE	2 (3.2)	2 (5.7)	4 (4.1)
MINERALOCORTICOIDS	1 (1.6)	0	1 (1.0)
FLUDROCORTISONE ACETATE	1 (1.6)	0	1 (1.0)
THYROID THERAPY	7 (11.3)	3 (8.6)	10 (10.3)
NOT SPECIFIED	0	1 (2.9)	1 (1.0)
NOT SPECIFIED	0	1 (2.9)	1 (1.0)
LEVOTHYROXINE SODIUM;POTASSIUM IODIDE	0	1 (2.9)	1 (1.0)
THYROID PREPARATIONS	7 (11.3)	2 (5.7)	9 (9.3)
THYROID HORMONES	7 (11.3)	2 (5.7)	9 (9.3)
LEVOTHYROXINE	0	2 (5.7)	2 (2.1)
LEVOTHYROXINE SODIUM	7 (11.3)	0	7 (7.2)
CALCIUM HOMEOSTASIS	0	1 (2.9)	1 (1.0)
ANTI-PARATHYROID AGENTS	0	1 (2.9)	1 (1.0)
OTHER ANTI-PARATHYROID AGENTS	0	1 (2.9)	1 (1.0)
CINACALCET HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
RESPIRATORY SYSTEM	**10 (16.1)**	**6 (17.1)**	**16 (16.5)**
ANTIHISTAMINES FOR SYSTEMIC USE	4 (6.5)	5 (14.3)	9 (9.3)
ANTIHISTAMINES FOR SYSTEMIC USE	4 (6.5)	5 (14.3)	9 (9.3)
AMINOALKYL ETHERS	0	1 (2.9)	1 (1.0)
DIPHENHYDRAMINE	0	1 (2.9)	1 (1.0)
NOT SPECIFIED	0	1 (2.9)	1 (1.0)
ANTIHISTAMINES	0	1 (2.9)	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
OTHER ANTIHISTAMINES FOR SYSTEMIC USE	1 (1.6)	1 (2.9)	2 (2.1)
BEPOTASTINE BESILATE	1 (1.6)	0	1 (1.0)
BILASTINE	0	1 (2.9)	1 (1.0)
FEXOFENADINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
PIPERAZINE DERIVATIVES	3 (4.8)	2 (5.7)	5 (5.2)
BUCLIZINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
CETIRIZINE	1 (1.6)	1 (2.9)	2 (2.1)
CETIRIZINE HYDROCHLORIDE	1 (1.6)	0	1 (1.0)
LEVOCETIRIZINE	1 (1.6)	1 (2.9)	2 (2.1)
NASAL PREPARATIONS	4 (6.5)	3 (8.6)	7 (7.2)
DECONGESTANTS AND OTHER NASAL PREPARATIONS FOR TOPICAL USE	3 (4.8)	3 (8.6)	6 (6.2)
CORTICOSTEROIDS	2 (3.2)	3 (8.6)	5 (5.2)
DEXAMETHASONE CIPECILATE	1 (1.6)	0	1 (1.0)
FLUTICASONE FUROATE	0	2 (5.7)	2 (2.1)
FLUTICASONE PROPIONATE	0	1 (2.9)	1 (1.0)
MOMETASONE FUROATE	1 (1.6)	0	1 (1.0)
OTHER NASAL PREPARATIONS	1 (1.6)	0	1 (1.0)
SODIUM CHLORIDE	1 (1.6)	0	1 (1.0)
NASAL DECONGESTANTS FOR SYSTEMIC USE	1 (1.6)	0	1 (1.0)
SYMPATHOMIMETICS	1 (1.6)	0	1 (1.0)
LORATADINE;PSEUDOEPHEDRINE SULFATE	1 (1.6)	0	1 (1.0)
COUGH AND COLD PREPARATIONS	4 (6.5)	1 (2.9)	5 (5.2)
COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS	1 (1.6)	1 (2.9)	2 (2.1)
OPIUM ALKALOIDS AND DERIVATIVES	1 (1.6)	1 (2.9)	2 (2.1)
DEXTROMETHORPHAN HYDROBROMIDE	0	1 (2.9)	1 (1.0)
DEXTROMETHORPHAN HYDROBROMIDE;LYSOZYME CHLORIDE;POTASSIUM CRESOLSULFONATE	1 (1.6)	0	1 (1.0)
EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS	3 (4.8)	1 (2.9)	4 (4.1)
EXPECTORANTS	1 (1.6)	0	1 (1.0)
HEDERA HELIX LEAF	1 (1.6)	0	1 (1.0)
MUCOLYTICS	2 (3.2)	1 (2.9)	3 (3.1)
ACETYLCYSTEINE	2 (3.2)	1 (2.9)	3 (3.1)
HERBAL COUGH AND COLD REMEDIES, OTHER	1 (1.6)	0	1 (1.0)
HERBAL DIAPHORETICS AND OTHER HERBAL COUGH AND COLD REMEDIES	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
GENTIANA LUTEA ROOT;PRIMULA SPP.;RUMEX SPP.;SAMBUCUS NIGRA FLOWER;VERBENA OFFICINALIS	1 (1.6)	0	1 (1.0)
PELARGONIUM SIDOIDES ROOT	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
COUGH AND COLD PREPARATIONS	1 (1.6)	0	1 (1.0)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	2 (3.2)	0	2 (2.1)
OTHER SYSTEMIC DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	2 (3.2)	0	2 (2.1)
LEUKOTRIENE RECEPTOR ANTAGONISTS	2 (3.2)	0	2 (2.1)
MONTELUKAST	2 (3.2)	0	2 (2.1)
THROAT PREPARATIONS	1 (1.6)	1 (2.9)	2 (2.1)
THROAT PREPARATIONS	1 (1.6)	1 (2.9)	2 (2.1)
ANTISEPTICS	1 (1.6)	0	1 (1.0)
SODIUM GUALENATE HYDRATE	1 (1.6)	0	1 (1.0)
OTHER THROAT PREPARATIONS	0	1 (2.9)	1 (1.0)
BENZYDAMINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
DERMATOLOGICALS	**10 (16.1)**	**2 (5.7)**	**12 (12.4)**
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	4 (6.5)	2 (5.7)	6 (6.2)
CORTICOSTEROIDS, PLAIN	4 (6.5)	2 (5.7)	6 (6.2)
CORTICOSTEROIDS, MODERATELY POTENT (GROUP II)	2 (3.2)	0	2 (2.1)
DEXAMETHASONE VALERATE	1 (1.6)	0	1 (1.0)
TRIAMCINOLONE ACETONIDE	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS, POTENT (GROUP III)	2 (3.2)	1 (2.9)	3 (3.1)
DIFLUPREDNATE	0	1 (2.9)	1 (1.0)
FLUOCINONIDE	1 (1.6)	0	1 (1.0)
HYDROCORTISONE	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS, VERY POTENT (GROUP IV)	0	1 (2.9)	1 (1.0)
CLOBETASOL	0	1 (2.9)	1 (1.0)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	5 (8.1)	0	5 (5.2)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	5 (8.1)	0	5 (5.2)
ANESTHETICS FOR TOPICAL USE	3 (4.8)	0	3 (3.1)
LIDOCAINE	2 (3.2)	0	2 (2.1)
LIDOCAINE;PRILOCAINE	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
ANTIHISTAMINES FOR TOPICAL USE	2 (3.2)	0	2 (2.1)
DIMETINDENE MALEATE	1 (1.6)	0	1 (1.0)
DIPHENHYDRAMINE HYDROCHLORIDE;ZINC ACETATE	1 (1.6)	0	1 (1.0)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	3 (4.8)	1 (2.9)	4 (4.1)
ANTIBIOTICS FOR TOPICAL USE	2 (3.2)	0	2 (2.1)
OTHER ANTIBIOTICS FOR TOPICAL USE	2 (3.2)	0	2 (2.1)
BACITRACIN ZINC;NEOMYCIN SULFATE;POLYMYXIN B SULFATE	1 (1.6)	0	1 (1.0)
GENTAMICIN SULFATE	1 (1.6)	0	1 (1.0)
CHEMOTHERAPEUTICS FOR TOPICAL USE	2 (3.2)	1 (2.9)	3 (3.1)
ANTIVIRALS	2 (3.2)	1 (2.9)	3 (3.1)
ACICLOVIR	1 (1.6)	0	1 (1.0)
VIDARABINE	1 (1.6)	1 (2.9)	2 (2.1)
ANTIFUNGALS FOR DERMATOLOGICAL USE	3 (4.8)	0	3 (3.1)
ANTIFUNGALS FOR TOPICAL USE	3 (4.8)	0	3 (3.1)
IMIDAZOLE AND TRIAZOLE DERIVATIVES	3 (4.8)	0	3 (3.1)
BETAMETHASONE DIPROPIONATE;CLOTRIMAZOLE	1 (1.6)	0	1 (1.0)
CLOTRIMAZOLE	1 (1.6)	0	1 (1.0)
MICONAZOLE	1 (1.6)	0	1 (1.0)
ANTI-ACNE PREPARATIONS	2 (3.2)	0	2 (2.1)
ANTI-ACNE PREPARATIONS FOR TOPICAL USE	2 (3.2)	0	2 (2.1)
ANTIINFECTIVES FOR TREATMENT OF ACNE	2 (3.2)	0	2 (2.1)
CLINDAMYCIN	1 (1.6)	0	1 (1.0)
CLINDAMYCIN PHOSPHATE	1 (1.6)	0	1 (1.0)
PEROXIDES	2 (3.2)	0	2 (2.1)
BENZOYL PEROXIDE	2 (3.2)	0	2 (2.1)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	2 (3.2)	0	2 (2.1)
CICATRIZANTS	2 (3.2)	0	2 (2.1)
OTHER CICATRIZANTS	2 (3.2)	0	2 (2.1)
ALPROSTADIL	1 (1.6)	0	1 (1.0)
HYALURONATE SODIUM	1 (1.6)	0	1 (1.0)
MEDICATED DRESSINGS	1 (1.6)	0	1 (1.0)
MEDICATED DRESSINGS	1 (1.6)	0	1 (1.0)
MEDICATED DRESSINGS WITH ANTIINFECTIVES	1 (1.6)	0	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
FRAMYCETIN SULFATE	1 (1.6)	0	1 (1.0)
GENITO URINARY SYSTEM AND SEX HORMONES	**10 (16.1)**	**2 (5.7)**	**12 (12.4)**
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	7 (11.3)	0	7 (7.2)
HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE	7 (11.3)	0	7 (7.2)
NOT SPECIFIED	1 (1.6)	0	1 (1.0)
ORAL CONTRACEPTIVE NOS	1 (1.6)	0	1 (1.0)
PROGESTOGENS	5 (8.1)	0	5 (5.2)
DESOGESTREL	5 (8.1)	0	5 (5.2)
PROGESTOGENS AND ESTROGENS, FIXED COMBINATIONS	1 (1.6)	0	1 (1.0)
ETHINYLESTRADIOL;LEVONORGESTREL	1 (1.6)	0	1 (1.0)
UROLOGICALS	3 (4.8)	1 (2.9)	4 (4.1)
DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY	1 (1.6)	0	1 (1.0)
HERBAL DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY	1 (1.6)	0	1 (1.0)
CUCURBITA PEPO OIL;SERENOA REPENS;ZINC GLUCONATE	1 (1.6)	0	1 (1.0)
UROLOGICALS	2 (3.2)	1 (2.9)	3 (3.1)
DRUGS FOR URINARY FREQUENCY AND INCONTINENCE	2 (3.2)	0	2 (2.1)
FESOTERODINE FUMARATE	1 (1.6)	0	1 (1.0)
TROSPIUM CHLORIDE	1 (1.6)	0	1 (1.0)
DRUGS USED IN ERECTILE DYSFUNCTION	0	1 (2.9)	1 (1.0)
SILDENAFIL CITRATE	0	1 (2.9)	1 (1.0)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	0	1 (2.9)	1 (1.0)
ANTIINFECTIVES AND ANTISEPTICS, EXCL. COMBINATIONS WITH CORTICOSTEROIDS	0	1 (2.9)	1 (1.0)
ANTIBIOTICS	0	1 (2.9)	1 (1.0)
CIPROFLOXACIN	0	1 (2.9)	1 (1.0)
SENSORY ORGANS	**5 (8.1)**	**2 (5.7)**	**7 (7.2)**
OPHTHALMOLOGICALS	4 (6.5)	2 (5.7)	6 (6.2)
ANTIGLAUCOMA PREPARATIONS AND MIOTICS	1 (1.6)	2 (5.7)	3 (3.1)
BETA BLOCKING AGENTS	0	1 (2.9)	1 (1.0)
BIMATOPROST;TIMOLOL MALEATE	0	1 (2.9)	1 (1.0)

First ATC Level Second ATC Level Third ATC Level Fourth ATC Level Preferred Term	Iptacopan (N=62) n (%)	Anti-C5 Antibody (N=35) n (%)	Overall (N=97) n (%)
CARBONIC ANHYDRASE INHIBITORS	0	1 (2.9)	1 (1.0)
DORZOLAMIDE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
PARASYMPATHOMIMETICS	0	1 (2.9)	1 (1.0)
NEOSTIGMINE METILSULFATE	0	1 (2.9)	1 (1.0)
PROSTAGLANDIN ANALOGUES	1 (1.6)	0	1 (1.0)
LATANOPROST	1 (1.6)	0	1 (1.0)
ANTIINFECTIVES	1 (1.6)	1 (2.9)	2 (2.1)
ANTIBIOTICS	1 (1.6)	1 (2.9)	2 (2.1)
GENTAMICIN SULFATE	1 (1.6)	0	1 (1.0)
TETRACYCLINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
FLUOROQUINOLONES	0	1 (2.9)	1 (1.0)
LEVOFLOXACIN	0	1 (2.9)	1 (1.0)
DECONGESTANTS AND ANTIALLERGICS	0	1 (2.9)	1 (1.0)
SYMPATHOMIMETICS USED AS DECONGESTANTS	0	1 (2.9)	1 (1.0)
ANTAZOLINE PHOSPHATE;CHLORHEXIDINE GLUCONATE;TETRYZOLINE HYDROCHLORIDE	0	1 (2.9)	1 (1.0)
OTHER OPHTHALMOLOGICALS	2 (3.2)	1 (2.9)	3 (3.1)
OTHER OPHTHALMOLOGICALS	2 (3.2)	1 (2.9)	3 (3.1)
CARMELLOSE SODIUM	1 (1.6)	0	1 (1.0)
HYPROMELLOSE	1 (1.6)	0	1 (1.0)
PIRENOXINE	0	1 (2.9)	1 (1.0)
OTOLOGICALS	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION	1 (1.6)	0	1 (1.0)
CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION	1 (1.6)	0	1 (1.0)
HYDROCORTISONE;NEOMYCIN;POLYMYXIN B	1 (1.6)	0	1 (1.0)
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	**4 (6.5)**	**2 (5.7)**	**6 (6.2)**
IMMUNOSUPPRESSANTS	3 (4.8)	2 (5.7)	5 (5.2)
IMMUNOSUPPRESSANTS	3 (4.8)	2 (5.7)	5 (5.2)
CALCINEURIN INHIBITORS	2 (3.2)	2 (5.7)	4 (4.1)
CICLOSPORIN	2 (3.2)	1 (2.9)	3 (3.1)
TACROLIMUS	0	1 (2.9)	1 (1.0)
OTHER IMMUNOSUPPRESSANTS	0	1 (2.9)	1 (1.0)
AZATHIOPRINE	0	1 (2.9)	1 (1.0)
SELECTIVE IMMUNOSUPPRESSANTS	1 (1.6)	0	1 (1.0)
ECULIZUMAB	1 (1.6)	0	1 (1.0)
IMMUNOSTIMULANTS	1 (1.6)	0	1 (1.0)

First ATC Level **Second ATC Level** **Third ATC Level** **Fourth ATC Level** Preferred Term	**Iptacopan (N=62) n (%)**	**Anti-C5 Antibody (N=35) n (%)**	**Overall (N=97) n (%)**
IMMUNOSTIMULANTS	1 (1.6)	0	1 (1.0)
COLONY STIMULATING FACTORS	1 (1.6)	0	1 (1.0)
FILGRASTIM	1 (1.6)	0	1 (1.0)

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Concomitant medication is defined as any medication with end date on or after Day 1 or ongoing at the end of treatment or missing end date and start date before the end of treatment in the randomized period.
Anatomical Therapeutic Chemical (ATC) classes are classified as per WHO drug dictionary version DDEBApr22.
A patient with multiple occurrences within an ATC class is counted only once in the total row.

Cut-off date for analysis: 06-Mar-2023

Table 1-4.3 Post-treatment medications by ATC class and Preferred Term (Safety Set)

First ATC Level **Second ATC Level** **Third ATC Level** **Fourth ATC Level** Preferred Term	**Iptacopan (N=62) n (%)**	**Anti-C5 Antibody (N=35) n (%)**	**Overall (N=97) n (%)**
Number of subjects with at least one medication	**1 (1.6)**	**0**	**1 (1.0)**
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	**1 (1.6)**	**0**	**1 (1.0)**
IMMUNOSUPPRESSANTS	1 (1.6)	0	1 (1.0)
IMMUNOSUPPRESSANTS	1 (1.6)	0	1 (1.0)
SELECTIVE IMMUNOSUPPRESSANTS	1 (1.6)	0	1 (1.0)
ECULIZUMAB	1 (1.6)	0	1 (1.0)

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Post-treatment medication is defined as any medication with start date after the end of treatment in the randomized period.
Anatomical Therapeutic Chemical (ATC) classes are classified as per WHO drug dictionary version DDEBApr22.
A patient with multiple occurrences within an ATC class is counted only once in the total row.

Cut-off date for analysis: 06-Mar-2023

Table 1-5 Subgroups (Full Analysis Set)

	Treatment Groups		
	Iptacopan (N = 62)	**Anti-C5 Antibody (N = 35)**	**Overall (N = 97)**
Length of time since diagnosis, n (%)			
< 5 years	18 (29.0)	11 (31.4)	29 (29.9)
≥ 5 years	44 (71.0)	24 (68.6)	68 (70.1)
Age categories, n (%)			
< 45 years	25 (40.3)	16 (45.7)	41 (42.3)
≥ 45 years	37 (59.7)	19 (54.3)	56 (57.7)
Sex, n (%)			
Male	19 (30.6)	11 (31.4)	30 (30.9)
Female	43 (69.4)	24 (68.6)	67 (69.1)
Baseline hemoglobin, n (%)			
< 9 g/dL	32 (51.6)	18 (51.4)	50 (51.5)
≥ 9 g/dL	30 (48.4)	17 (48.6)	47 (48.5)
History of MAVE prior to screening, n (%)			
No	50 (80.6)	25 (71.4)	75 (77.3)
Yes	12 (19.4)	10 (28.6)	22 (22.7)
Anti-C5 medication history 6 months prior to randomization, n (%)			
Eculizumab	40 (64.5)	23 (65.7)	63 (64.9)
Ravulizumab	22 (35.5)	12 (34.3)	34 (35.1)
Transfusion in the last 6 months prior to randomization, n (%)			
No	27 (43.5)	14 (40.0)	41 (42.3)
Yes	35 (56.5)	21 (60.0)	56 (57.7)
Number of transfusions in the last 6 months prior to randomization, n (%)			
< 2	38 (61.3)	21 (60.0)	59 (60.8)
≥ 2	24 (38.7)	14 (40.0)	38 (39.2)
Duration of anti-C5 treatment, n (%)			
< 12 months	11 (17.7)	6 (17.1)	17 (17.5)
≥ 12 months	51 (82.3)	29 (82.9)	80 (82.5)

N: Number of patients in the analysis set
MAVE: Major Adverse Vascular Event
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N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

2 Efficacy

2-1 Sustained Hb ≥ 8 g/dL

Table 2-1 Achievement of sustained Hb ≥ 8 g/dL in patients with severe residual anemia at baseline (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value
Achievement of sustained Hb ≥ 8 g/dL						
n / N' (%)	5 / 7 (71.4)	0 / 7 (0.0)	OR	33.00	[1.31; 833.87]	0.034
			RR	11.00	[0.72; 167.68]	0.084
			RD	0.7143	[0.3796; 1.0489]	<0.001

N: Number of patients in the analysis set
N': Number of patients with severe residual anemia (i.e. Hb < 8 g/dL) at baseline and with response variable defined based on non-missing data (evaluable patients)
n: Number of patients with response based on non-missing data
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
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Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

Response is defined as having hemoglobin ≥ 8 g/dL assessed at three out of four visits between Day 126 and Day 168 in the absence of packed red blood cell transfusions between Day 14 and Day 168.

Cut-off date for analysis: 06-Mar-2023

2-2 Reticulocyte counts

Table 2-2.1 Reticulocyte counts: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
Reticulocytes (10^9/L)		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 193.22 (83.64)	35 | 190.59 (80.92)
Day 7	61 | 92.91 (39.92)	28 | 203.39 (98.95)
Day 14	58 | 58.49 (41.68)	27 | 167.10 (62.30)
Day 28	60 | 43.64 (49.53)	32 | 183.95 (81.57)
Day 42	59 | 50.65 (61.80)	31 | 191.59 (82.20)
Day 56	59 | 62.28 (58.51)	31 | 187.00 (76.49)
Day 84	60 | 75.88 (72.94)	33 | 184.14 (71.51)
Day 112	56 | 73.15 (54.53)	27 | 188.54 (70.03)
Day 126	59 | 70.67 (59.40)	34 | 184.19 (82.65)
Day 140	56 | 70.37 (41.93)	32 | 187.02 (74.82)
Day 154	56 | 70.88 (39.84)	32 | 181.95 (70.72)
Day 168	58 | 73.61 (42.76)	34 | 178.11 (81.07)
Day 126 - 168	**62 | 71.16 (42.37)**	**35 | 186.69 (76.55)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation
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Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 06-Mar-2023

Table 2-2.2 Reticulocyte counts: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
Reticulocytes (10^9/L)					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 7	61 | -93.65 (6.91)	28 | 7.71 (9.25)	-101.36	[-123.40; -79.31]	<0.001
Day 14	58 | -128.30 (6.39)	27 | 0.89 (8.46)	-129.19	[-149.38; -109.00]	<0.001
Day 28	60 | -141.52 (6.45)	32 | 5.25 (8.31)	-146.77	[-166.66; -126.88]	<0.001
Day 42	59 | -137.23 (7.30)	31 | 14.00 (9.51)	-151.23	[-174.15; -128.30]	<0.001
Day 56	59 | -124.82 (6.44)	31 | -0.09 (8.32)	-124.73	[-144.63; -104.84]	<0.001
Day 84	60 | -111.44 (6.84)	33 | -4.09 (8.85)	-107.36	[-128.64; -86.07]	<0.001
Day 112	56 | -114.42 (6.15)	27 | 1.66 (8.02)	-116.08	[-135.14; -97.02]	<0.001
Day 126	59 | -115.88 (6.23)	34 | -3.56 (7.95)	-112.31	[-131.34; -93.28]	<0.001
Day 140	56 | -116.56 (5.89)	32 | 9.96 (7.48)	-126.52	[-144.34; -108.69]	<0.001
Day 154	56 | -116.24 (5.49)	32 | 0.94 (6.95)	-117.17	[-133.62; -100.72]	<0.001
Day 168	58 | -113.80 (6.03)	34 | -5.00 (7.66)	-108.80	[-127.10; -90.50]	<0.001
Day 126 - 168	**62 | -115.87 (5.43)**	**35 | 0.33 (6.85)**	**-116.20**	**[-132.37; -100.02]**	**<0.001**
Hedges' G			**-3.02**	**[-3.61; -2.43]**	

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

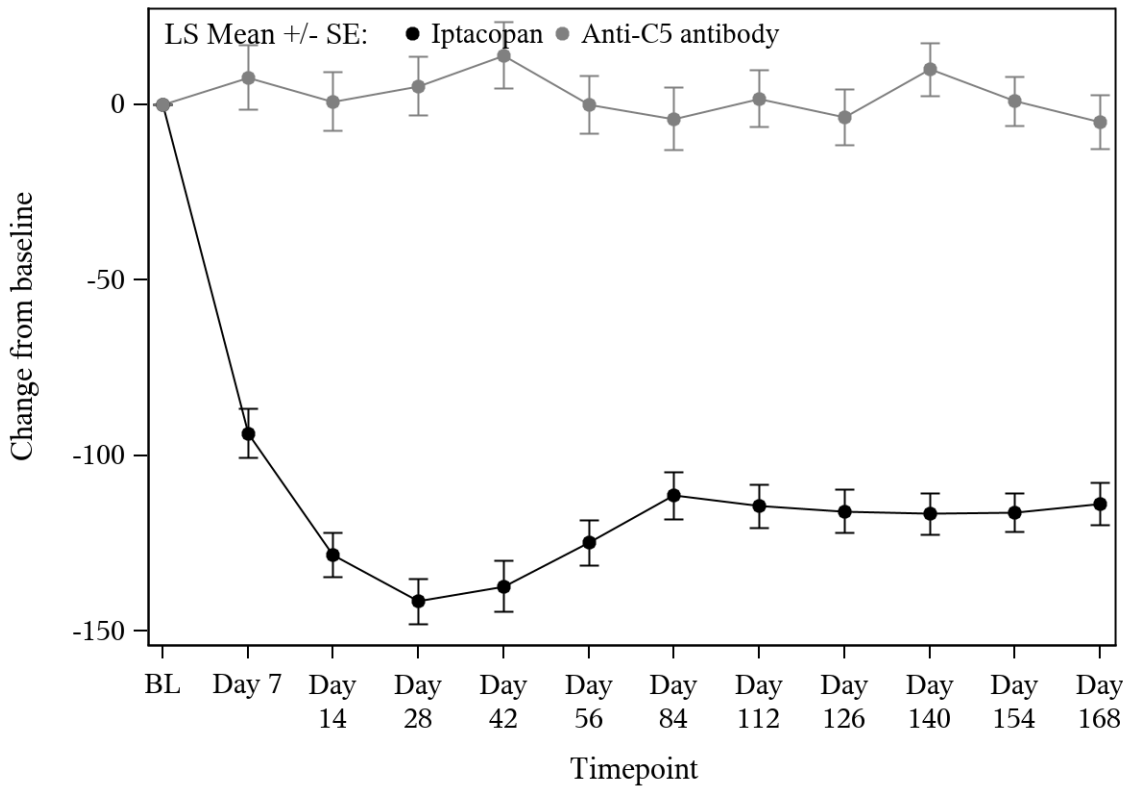
Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

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

Cut-off date for analysis: 06-Mar-2023

Figure 2-2.2 Reticulocyte counts: line chart of least squares mean change from baseline (Full Analysis Set)

Reticulocytes (10^9/L)



	BL	Day 7	Day 14	Day 28	Day 42	Day 56	Day 84	Day 112	Day 126	Day 140	Day 154	Day 168
Iptacopan	62	61	58	60	59	59	60	56	59	56	56	58
Anti-C5 antibody	35	28	27	32	31	31	33	27	34	32	32	34

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

2-3 Transfusion avoidance

Table 2-3 Transfusion avoidance between Day 14 and Day 336: logistic model analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value
Transfusion avoidance between Day 14 and Day 336						
n / N' (%)	57 / 62 (91.9)	14 / 35 (40.0)	OR	16.83	[5.21; 54.37]	<0.001
Predict. % [95% CI]	90.3 [82.3; 96.4]	40.7 [25.7; 56.6]	RR	2.23	[1.57; 3.51]	
			RD	0.4950	[0.3162; 0.6519]	

N: Number of patients in the analysis set
N': Number of patients included in the analysis
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
.....

Analysis methods:
OR, RR and RD from logistic regression model using Firth's penalized maximum likelihood estimation:
Logit(proportion) = treatment + baseline hemoglobin (indicator of hemoglobin ≥ 9 g/dL) + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value from model linear predictor of treatment.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group. Then RR and RD were calculated from predicted proportions. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Cut-off date for analysis: 06-Mar-2023

3 PRO

3-1 FACIT Fatigue

Table 3-1.1 FACIT Fatigue: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
FACIT Fatigue		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 34.69 (9.82)	33 | 30.85 (11.45)
Day 7	60 | 39.10 (7.83)	27 | 32.59 (11.15)
Day 14	57 | 40.40 (7.98)	28 | 33.79 (10.95)
Day 42	61 | 43.20 (7.53)	32 | 30.59 (10.93)
Day 84	57 | 43.58 (7.37)	29 | 31.59 (11.78)
Day 126	58 | 43.09 (7.53)	29 | 33.66 (11.20)
Day 140	59 | 41.68 (7.72)	28 | 30.96 (13.19)
Day 154	56 | 42.48 (8.62)	28 | 32.86 (12.31)
Day 168	60 | 43.17 (7.85)	30 | 31.13 (12.71)
Day 126 - 168	**62 | 42.73 (7.46)**	**31 | 31.81 (12.27)**

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-1.2 FACIT Fatigue: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
FACIT Fatigue					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 7	60 | 4.70 (0.87)	27 | 1.46 (1.18)	3.24	[0.45; 6.03]	0.024
Day 14	57 | 5.87 (0.94)	28 | 0.84 (1.26)	5.03	[2.03; 8.03]	0.001
Day 42	61 | 9.02 (1.00)	32 | -1.07 (1.33)	10.08	[6.90; 13.27]	<0.001
Day 84	57 | 9.23 (1.04)	29 | 0.61 (1.40)	8.61	[5.26; 11.96]	<0.001
Day 126	58 | 8.98 (0.98)	29 | 0.65 (1.31)	8.33	[5.21; 11.45]	<0.001
Day 140	59 | 7.58 (1.07)	28 | -1.15 (1.46)	8.74	[5.26; 12.22]	<0.001
Day 154	56 | 8.85 (1.13)	28 | 1.35 (1.54)	7.50	[3.80; 11.20]	<0.001
Day 168	60 | 8.86 (1.09)	30 | 0.07 (1.48)	8.78	[5.24; 12.33]	<0.001
Day 126 - 168	**62 | 8.62 (0.97)**	**31 | 0.28 (1.29)**	**8.34**	**[5.26; 11.41]**	**<0.001**
Hedges' G			**1.18**	**[0.72; 1.65]**	

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

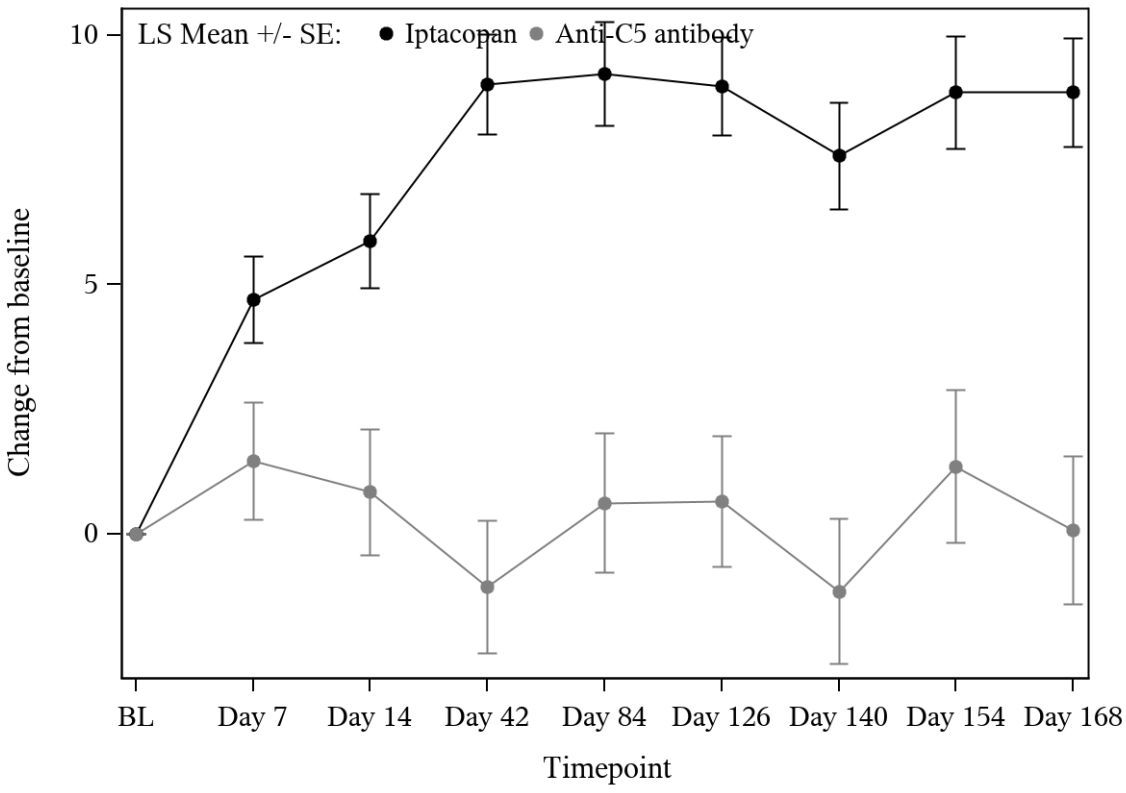
Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

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

Cut-off date for analysis: 06-Mar-2023

Figure 3-1.2 FACIT Fatigue: line chart of least squares mean change from baseline (Full Analysis Set)

FACIT Fatigue



Iptacopan	62	60	57	61	57	58	59	56	60
Anti-C5 antibody	33	27	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-1.3 FACIT Fatigue responder analysis (improvement defined as ≥ 8 point increase from baseline): GLMM analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
FACIT Fatigue						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 7	19 / 60 (31.7)	4 / 27 (14.8)	OR	11.54	[2.32; 57.44]	0.003
	35.2 [25.0; 46.1]	12.6 [3.4; 23.6]	RR	2.76	[1.47; 9.84]	
			RD	0.2179	[0.1011; 0.3559]	
Day 14	17 / 57 (29.8)	5 / 28 (17.9)	OR	15.03	[3.43; 65.73]	<0.001
	35.2 [25.5; 45.4]	11.9 [3.7; 22.1]	RR	2.89	[1.60; 9.06]	
			RD	0.2274	[0.1202; 0.3496]	
Day 42	29 / 61 (47.5)	4 / 32 (12.5)	OR	34.49	[8.46; 140.51]	<0.001
	46.2 [35.4; 56.5]	11.9 [4.5; 20.9]	RR	3.89	[2.21; 10.04]	
			RD	0.3411	[0.2278; 0.4562]	
Day 84	29 / 57 (50.9)	3 / 29 (10.3)	OR	61.09	[12.39; 301.13]	<0.001
	52.7 [40.3; 64.6]	12.4 [4.6; 20.9]	RR	4.19	[2.44; 11.30]	
			RD	0.4003	[0.2725; 0.5261]	
Day 126	30 / 58 (51.7)	7 / 29 (24.1)	OR	48.18	[12.19; 190.47]	<0.001
	54.6 [43.7; 66.0]	14.4 [6.2; 23.4]	RR	3.74	[2.34; 8.72]	
			RD	0.4002	[0.2826; 0.5241]	
Day 140	26 / 59 (44.1)	5 / 28 (17.9)	OR	37.19	[10.24; 135.01]	<0.001
	55.0 [44.2; 65.3]	15.5 [6.7; 24.7]	RR	3.53	[2.22; 8.04]	
			RD	0.3933	[0.2740; 0.5242]	
Day 154	29 / 56 (51.8)	6 / 28 (21.4)	OR	26.23	[6.99; 98.50]	<0.001
	52.9 [41.7; 62.9]	16.1 [6.6; 25.8]	RR	3.30	[2.07; 8.03]	
			RD	0.3677	[0.2453; 0.5073]	
Day 168	33 / 60 (55.0)	5 / 30 (16.7)	OR	16.91	[3.54; 80.80]	<0.001
	52.9 [41.0; 63.4]	19.8 [7.1; 32.0]	RR	2.65	[1.62; 7.37]	
			RD	0.3305	[0.1740; 0.4891]	
Day 126 - 168	**62**	**31**	**OR**	**29.86**	**[8.28; 107.69]**	**<0.001**
	53.8 [43.3; 63.6]	**16.5 [7.4; 25.6]**	**RR**	**3.23**	**[2.10; 7.36]**	
			RD	**0.3736**	**[0.2534; 0.5035]**	

Treatment Groups		Comparison			
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
GLMM: Generalized linear mixed model
.....

Analysis methods:
OR, RR and RD from logistic GLMM with random intercept and week as continuous covariate:
Logit(proportion) = treatment + baseline value + treatment * week + baseline value * week + treatment * week * week + baseline value * week * week
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value were calculated from model linear predictors, at Day 126 - 168 from a linear function of linear predictors.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group at each visit. Then predicted proportions were averaged over the four visits Day 126 - 168. Then RR and RD were calculated for each visit and for Day 126 - 168. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Response (improvement) is defined as ≥ 8 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

Table 3-1.4 FACIT Fatigue responder analysis (improvement defined as ≥ 8 point increase from baseline): raw relative risk (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
FACIT Fatigue					
Day 7					
n / N' (%)	19 / 60 (31.7)	4 / 27 (14.8)	2.14	[0.80; 5.68]	0.128
Day 14					
n / N' (%)	17 / 57 (29.8)	5 / 28 (17.9)	1.67	[0.69; 4.06]	0.258
Day 42					
n / N' (%)	29 / 61 (47.5)	4 / 32 (12.5)	3.80	[1.47; 9.87]	0.006
Day 84					
n / N' (%)	29 / 57 (50.9)	3 / 29 (10.3)	4.92	[1.63; 14.80]	0.005
Day 126					
n / N' (%)	30 / 58 (51.7)	7 / 29 (24.1)	2.14	[1.07; 4.28]	0.031
Day 140					
n / N' (%)	26 / 59 (44.1)	5 / 28 (17.9)	2.47	[1.06; 5.74]	0.036
Day 154					
n / N' (%)	29 / 56 (51.8)	6 / 28 (21.4)	2.42	[1.14; 5.13]	0.022
Day 168					
n / N' (%)	33 / 60 (55.0)	5 / 30 (16.7)	3.30	[1.44; 7.58]	0.005
Day 126 - Day 168					
n / N' (%)	**32 / 62 (51.6)**	**3 / 31 (9.7)**	**5.33**	**[1.77; 16.06]**	**0.003**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis methods:
RR was calculated without adjustment with Wald 95% CI and p-value. In case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.
For Day 126 - 168, observed responders per treatment group were derived from change from baseline of the average of the last four visits. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

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

Response (improvement) is defined as ≥ 8 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

3-2 EORTC QLQ-C30 Symptoms

Table 3-2.1 EORTC QLQ-C30 Symptoms: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
QLQ-C30 - Fatigue		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 41.85 (23.99)	33 | 51.01 (26.59)
Day 14	57 | 29.82 (20.16)	28 | 42.86 (25.43)
Day 42	61 | 24.77 (19.07)	32 | 52.08 (24.51)
Day 84	57 | 22.42 (18.12)	29 | 49.04 (27.14)
Day 126	58 | 23.75 (17.96)	29 | 45.21 (26.21)
Day 140	59 | 27.31 (19.39)	28 | 49.21 (29.54)
Day 154	56 | 24.60 (20.51)	28 | 47.22 (28.47)
Day 168	60 | 24.26 (19.89)	30 | 47.78 (25.30)
Day 126 - 168	**62 | 24.88 (17.32)**	**31 | 47.88 (26.62)**
QLQ-C30 - Nausea and vomiting		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 4.44 (8.50)	33 | 8.33 (11.60)
Day 14	57 | 5.26 (12.66)	28 | 5.36 (10.20)
Day 42	61 | 3.28 (8.51)	32 | 9.90 (16.32)
Day 84	57 | 3.80 (9.97)	29 | 8.62 (15.18)
Day 126	58 | 2.30 (7.29)	29 | 5.17 (11.87)
Day 140	59 | 5.37 (12.55)	28 | 8.33 (15.38)
Day 154	56 | 5.36 (14.94)	28 | 7.74 (13.21)
Day 168	60 | 4.17 (10.90)	30 | 6.67 (10.36)
Day 126 - 168	**62 | 4.44 (9.07)**	**31 | 7.35 (11.65)**
QLQ-C30 - Pain		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 13.84 (20.58)	33 | 24.24 (27.98)
Day 14	57 | 9.94 (17.78)	28 | 19.05 (27.49)
Day 42	61 | 8.74 (14.47)	32 | 26.04 (33.58)
Day 84	57 | 8.19 (15.15)	29 | 21.84 (25.63)
Day 126	58 | 8.05 (18.79)	29 | 18.39 (23.29)
Day 140	59 | 11.30 (19.44)	28 | 22.02 (28.71)
Day 154	56 | 9.82 (16.14)	28 | 17.26 (23.78)
Day 168	60 | 8.61 (14.55)	30 | 21.11 (28.68)
Day 126 - 168	**62 | 9.50 (14.79)**	**31 | 21.01 (25.04)**

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
QLQ-C30 - Dyspnoea		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 37.90 (28.18)	33 | 40.91 (28.59)
Day 14	57 | 19.30 (24.35)	28 | 41.67 (28.15)
Day 42	61 | 14.75 (21.54)	32 | 40.63 (30.21)
Day 84	57 | 13.45 (19.78)	29 | 39.08 (30.95)
Day 126	58 | 14.37 (23.46)	29 | 37.93 (30.50)
Day 140	59 | 14.69 (21.68)	28 | 40.48 (34.38)
Day 154	56 | 13.10 (17.61)	28 | 36.90 (24.58)
Day 168	60 | 13.33 (20.54)	30 | 36.67 (29.49)
Day 126 - 168	**62 | 14.16 (19.15)**	**31 | 38.80 (27.20)**
QLQ-C30 - Insomnia		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 35.48 (28.71)	33 | 28.28 (29.31)
Day 14	57 | 29.24 (29.59)	28 | 21.43 (24.37)
Day 42	61 | 25.68 (26.80)	32 | 19.79 (27.90)
Day 84	57 | 22.22 (23.00)	29 | 24.14 (30.73)
Day 126	58 | 24.14 (28.47)	29 | 20.69 (22.56)
Day 140	59 | 24.29 (29.58)	28 | 16.67 (23.13)
Day 154	56 | 23.81 (27.50)	28 | 20.24 (26.20)
Day 168	60 | 23.33 (26.25)	30 | 23.33 (29.23)
Day 126 - 168	**62 | 23.66 (23.81)**	**31 | 21.77 (23.58)**
QLQ-C30 - Appetite loss		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 9.14 (15.59)	33 | 17.17 (21.03)
Day 14	57 | 3.51 (12.09)	28 | 13.10 (18.90)
Day 42	61 | 2.73 (9.22)	32 | 13.54 (23.74)
Day 84	57 | 5.85 (14.26)	29 | 13.79 (24.43)
Day 126	58 | 3.45 (10.24)	29 | 6.90 (13.74)
Day 140	59 | 6.78 (17.26)	28 | 14.29 (26.34)
Day 154	56 | 4.17 (12.81)	28 | 9.52 (17.82)
Day 168	60 | 3.89 (10.79)	30 | 16.67 (27.33)
Day 126 - 168	**62 | 4.48 (9.29)**	**31 | 12.46 (18.84)**

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
QLQ-C30 - Constipation		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 6.72 (15.23)	33 | 10.10 (18.61)
Day 14	57 | 5.85 (14.26)	28 | 8.33 (21.52)
Day 42	61 | 5.46 (13.85)	32 | 11.46 (26.25)
Day 84	57 | 5.85 (14.26)	29 | 14.94 (26.10)
Day 126	58 | 5.75 (14.15)	29 | 16.09 (27.63)
Day 140	59 | 6.21 (13.09)	28 | 14.29 (27.86)
Day 154	56 | 7.74 (15.56)	28 | 14.29 (23.00)
Day 168	60 | 6.67 (14.78)	30 | 11.11 (20.22)
Day 126 - 168	**62 | 6.32 (11.30)**	**31 | 13.89 (22.73)**
QLQ-C30 - Diarrhoea		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 6.18 (13.91)	33 | 11.11 (17.51)
Day 14	57 | 10.53 (21.96)	28 | 11.90 (20.72)
Day 42	61 | 9.84 (21.38)	32 | 20.83 (31.40)
Day 84	57 | 9.36 (21.60)	29 | 14.94 (27.58)
Day 126	58 | 8.62 (19.31)	29 | 11.49 (20.46)
Day 140	59 | 14.12 (26.41)	28 | 11.90 (24.37)
Day 154	56 | 11.90 (21.49)	28 | 9.52 (15.33)
Day 168	60 | 7.78 (17.75)	30 | 11.11 (18.22)
Day 126 - 168	**62 | 10.75 (18.26)**	**31 | 11.74 (17.31)**

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-2.2 EORTC QLQ-C30 Symptoms: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
QLQ-C30 - Fatigue					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -14.29 (2.42)	28 | -4.19 (3.28)	-10.10	[-17.92; -2.28]	0.012
Day 42	61 | -19.30 (2.39)	32 | 2.11 (3.20)	-21.41	[-29.05; -13.78]	<0.001
Day 84	57 | -21.44 (2.57)	29 | -1.61 (3.48)	-19.83	[-28.19; -11.48]	<0.001
Day 126	58 | -20.19 (2.33)	29 | -1.50 (3.11)	-18.68	[-26.09; -11.27]	<0.001
Day 140	59 | -16.91 (2.42)	28 | 0.13 (3.31)	-17.04	[-24.90; -9.19]	<0.001
Day 154	56 | -19.74 (2.75)	28 | -3.44 (3.76)	-16.30	[-25.32; -7.28]	<0.001
Day 168	60 | -19.71 (2.51)	30 | -3.07 (3.41)	-16.64	[-24.78; -8.50]	<0.001
Day 126 - 168	**62 | -19.17 (2.16)**	**31 | -2.01 (2.88)**	**-17.17**	**[-23.96; -10.37]**	**<0.001**
Hedges' G			**-1.10**	**[-1.56; -0.65]**	
QLQ-C30 - Nausea and vomiting					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -0.54 (1.31)	28 | -2.32 (1.82)	1.78	[-2.60; 6.16]	0.421
Day 42	61 | -2.75 (1.48)	32 | 2.22 (2.03)	-4.97	[-9.89; -0.05]	0.048
Day 84	57 | -1.82 (1.39)	29 | -0.20 (1.92)	-1.62	[-6.26; 3.02]	0.489
Day 126	58 | -3.31 (1.10)	29 | -1.78 (1.47)	-1.53	[-5.07; 2.00]	0.391
Day 140	59 | -0.16 (1.55)	28 | 0.45 (2.18)	-0.61	[-5.85; 4.63]	0.817
Day 154	56 | -0.42 (1.72)	28 | 0.33 (2.40)	-0.75	[-6.56; 5.07]	0.799
Day 168	60 | -1.64 (1.26)	30 | -1.20 (1.73)	-0.44	[-4.63; 3.74]	0.833
Day 126 - 168	**62 | -1.46 (1.09)**	**31 | -0.63 (1.47)**	**-0.83**	**[-4.35; 2.68]**	**0.639**
Hedges' G			**-0.10**	**[-0.54; 0.33]**	
QLQ-C30 - Pain					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -5.25 (2.70)	28 | -0.18 (3.69)	-5.07	[-13.87; 3.73]	0.255
Day 42	61 | -6.66 (2.76)	32 | 5.93 (3.71)	-12.59	[-21.46; -3.71]	0.006
Day 84	57 | -7.07 (2.54)	29 | 2.00 (3.44)	-9.08	[-17.28; -0.87]	0.031
Day 126	58 | -6.96 (2.58)	29 | 1.46 (3.47)	-8.42	[-16.70; -0.14]	0.046
Day 140	59 | -4.06 (2.77)	28 | 3.48 (3.78)	-7.54	[-16.55; 1.46]	0.099
Day 154	56 | -5.81 (2.53)	28 | -1.43 (3.41)	-4.38	[-12.50; 3.73]	0.286
Day 168	60 | -6.71 (2.56)	30 | 1.37 (3.45)	-8.08	[-16.29; 0.12]	0.053
Day 126 - 168	**62 | -6.32 (2.29)**	**31 | 0.78 (3.03)**	**-7.11**	**[-14.28; 0.06]**	**0.052**
Hedges' G			**-0.43**	**[-0.87; 0.00]**	

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
QLQ-C30 - Dyspnoea					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -19.80 (2.97)	28 | 1.28 (4.01)	-21.08	[-30.60; -11.56]	<0.001
Day 42	61 | -24.23 (3.00)	32 | -0.93 (3.99)	-23.30	[-32.81; -13.79]	<0.001
Day 84	57 | -24.51 (3.10)	29 | -3.63 (4.18)	-20.87	[-30.87; -10.88]	<0.001
Day 126	58 | -24.79 (3.07)	29 | -0.71 (4.15)	-24.07	[-33.93; -14.21]	<0.001
Day 140	59 | -24.61 (3.16)	28 | -0.63 (4.34)	-23.98	[-34.26; -13.70]	<0.001
Day 154	56 | -25.22 (2.63)	28 | -3.48 (3.51)	-21.74	[-30.04; -13.45]	<0.001
Day 168	60 | -25.86 (2.80)	30 | -5.79 (3.77)	-20.08	[-28.99; -11.16]	<0.001
Day 126 - 168	**62 | -25.00 (2.48)**	**31 | -2.53 (3.29)**	**-22.47**	**[-30.18; -14.76]**	**<0.001**
Hedges' G			**-1.27**	**[-1.74; -0.81]**	
QLQ-C30 - Insomnia					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -7.50 (2.49)	28 | -7.07 (3.39)	-0.42	[-8.54; 7.69]	0.918
Day 42	61 | -10.30 (2.74)	32 | -12.56 (3.66)	2.25	[-6.51; 11.01]	0.611
Day 84	57 | -12.92 (2.60)	29 | -7.94 (3.51)	-4.98	[-13.34; 3.38]	0.240
Day 126	58 | -12.79 (2.96)	29 | -7.58 (4.05)	-5.21	[-14.96; 4.53]	0.291
Day 140	59 | -11.84 (3.34)	28 | -10.71 (4.67)	-1.12	[-12.34; 10.09]	0.843
Day 154	56 | -12.28 (3.23)	28 | -11.33 (4.46)	-0.95	[-11.67; 9.76]	0.860
Day 168	60 | -13.01 (3.11)	30 | -8.66 (4.26)	-4.35	[-14.59; 5.90]	0.401
Day 126 - 168	**62 | -12.53 (2.53)**	**31 | -9.62 (3.42)**	**-2.91**	**[-11.05; 5.24]**	**0.480**
Hedges' G			**-0.16**	**[-0.59; 0.28]**	
QLQ-C30 - Appetite loss					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -7.01 (1.84)	28 | 1.43 (2.53)	-8.43	[-14.55; -2.32]	0.008
Day 42	61 | -7.76 (1.97)	32 | 0.09 (2.69)	-7.85	[-14.35; -1.35]	0.019
Day 84	57 | -4.03 (2.23)	29 | -0.96 (3.09)	-3.07	[-10.62; 4.48]	0.422
Day 126	58 | -7.05 (1.45)	29 | -5.39 (1.94)	-1.66	[-6.32; 3.00]	0.481
Day 140	59 | -2.97 (2.43)	28 | 0.47 (3.47)	-3.45	[-11.84; 4.94]	0.416
Day 154	56 | -6.44 (1.93)	28 | -3.08 (2.67)	-3.36	[-9.80; 3.08]	0.302
Day 168	60 | -6.32 (2.21)	30 | 3.10 (3.06)	-9.42	[-16.83; -2.00]	0.013
Day 126 - 168	**62 | -5.87 (1.51)**	**31 | -1.40 (2.03)**	**-4.47**	**[-9.34; 0.40]**	**0.072**
Hedges' G			**-0.40**	**[-0.84; 0.03]**	

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
QLQ-C30 - Constipation					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | -1.53 (1.41)	28 | -1.40 (1.87)	-0.13	[-4.58; 4.31]	0.953
Day 42	61 | -1.76 (1.85)	32 | 1.40 (2.47)	-3.16	[-9.09; 2.77]	0.293
Day 84	57 | -0.84 (1.84)	29 | 5.44 (2.48)	-6.27	[-12.22; -0.33]	0.039
Day 126	58 | -1.24 (1.75)	29 | 5.65 (2.37)	-6.89	[-12.56; -1.22]	0.018
Day 140	59 | -1.10 (1.94)	28 | 3.83 (2.68)	-4.94	[-11.34; 1.46]	0.129
Day 154	56 | 0.47 (1.82)	28 | 4.14 (2.47)	-3.67	[-9.60; 2.26]	0.222
Day 168	60 | -0.95 (1.96)	30 | 1.26 (2.68)	-2.21	[-8.64; 4.23]	0.498
Day 126 - 168	**62 | -0.68 (1.49)**	**31 | 3.74 (1.97)**	**-4.42**	**[-9.10; 0.25]**	**0.063**
Hedges' G			**-0.41**	**[-0.85; 0.02]**	
QLQ-C30 - Diarrhoea					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 3.79 (2.52)	28 | 0.89 (3.46)	2.90	[-5.41; 11.21]	0.489
Day 42	61 | 3.31 (2.70)	32 | 8.95 (3.65)	-5.64	[-14.42; 3.14]	0.205
Day 84	57 | 2.85 (2.45)	29 | 2.79 (3.31)	0.06	[-7.87; 7.98]	0.989
Day 126	58 | 2.84 (2.46)	29 | 3.43 (3.31)	-0.59	[-8.50; 7.32]	0.883
Day 140	59 | 6.93 (3.08)	28 | 2.96 (4.27)	3.97	[-6.27; 14.21]	0.443
Day 154	56 | 4.66 (2.47)	28 | 0.80 (3.36)	3.86	[-4.18; 11.90]	0.343
Day 168	60 | 0.99 (2.31)	30 | 1.43 (3.12)	-0.43	[-7.88; 7.01]	0.908
Day 126 - 168	**62 | 3.80 (2.09)**	**31 | 2.10 (2.77)**	**1.70**	**[-4.86; 8.27]**	**0.608**
Hedges' G			**0.11**	**[-0.32; 0.54]**	

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

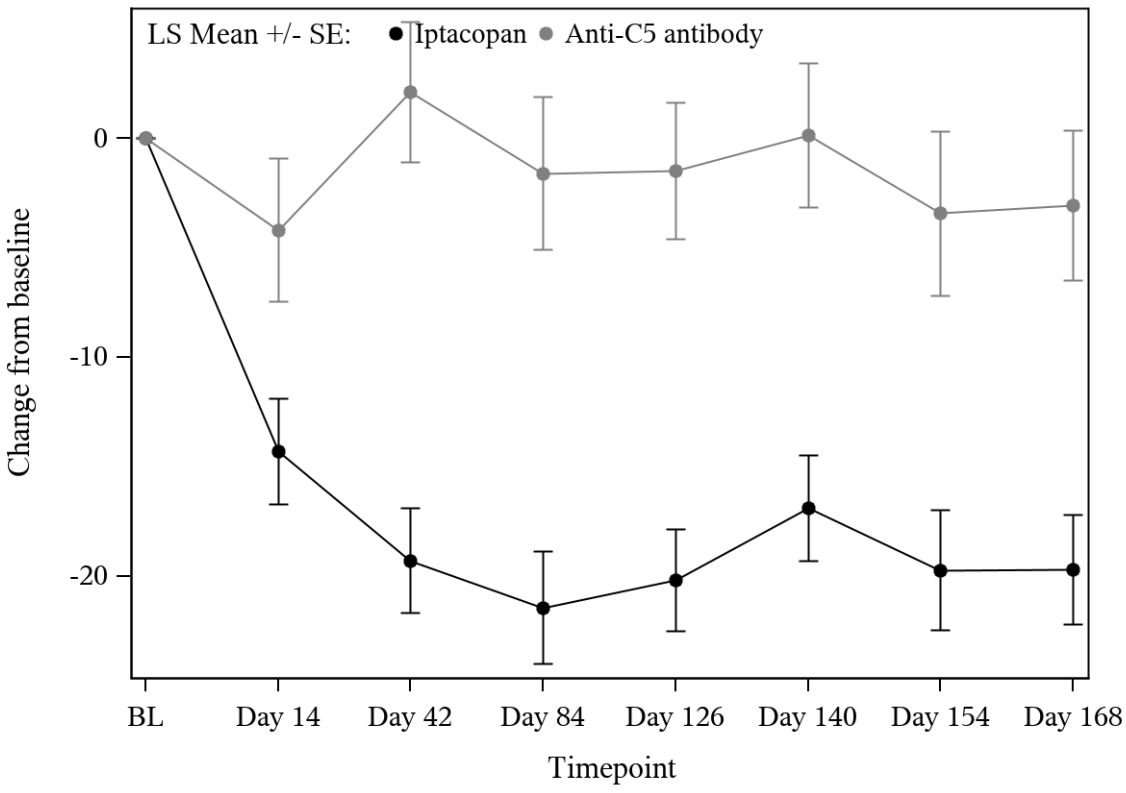
Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

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

Cut-off date for analysis: 06-Mar-2023

Figure 3-2.2 EORTC QLQ-C30 Symptoms: line chart of least squares mean change from baseline (Full Analysis Set)

QLQ-C30 - Fatigue



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

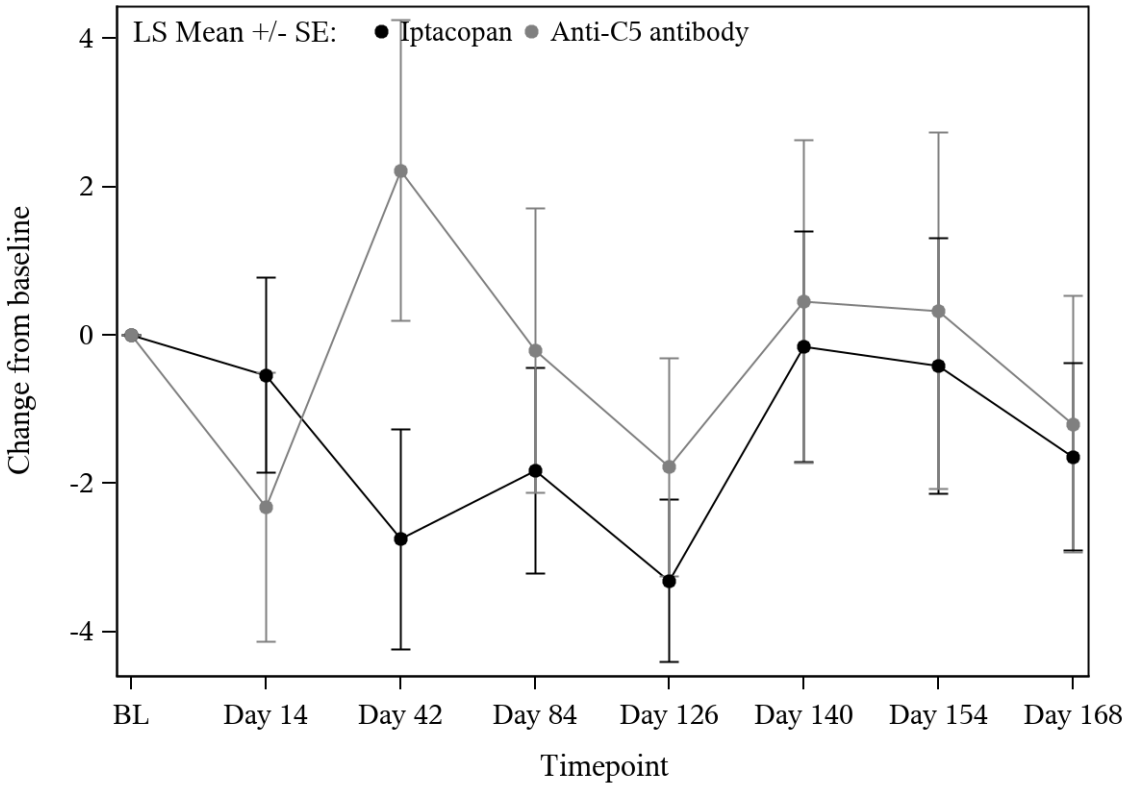
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Nausea and vomiting



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

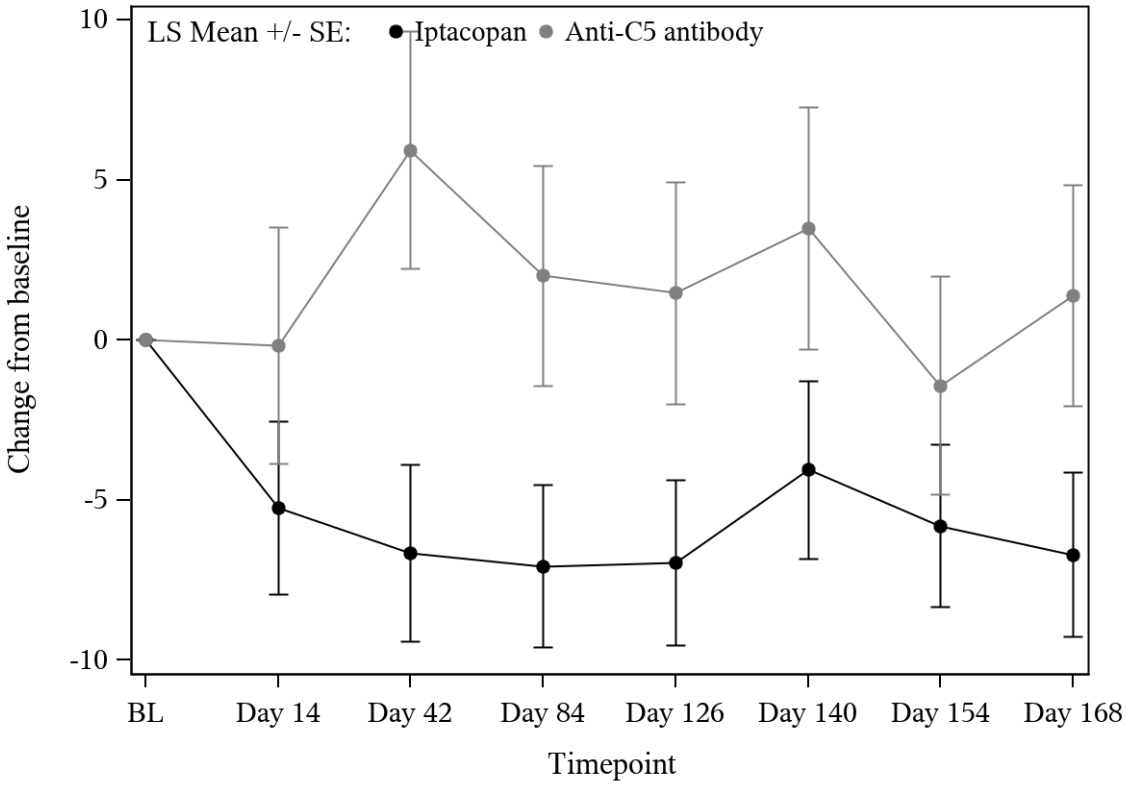
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Pain



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

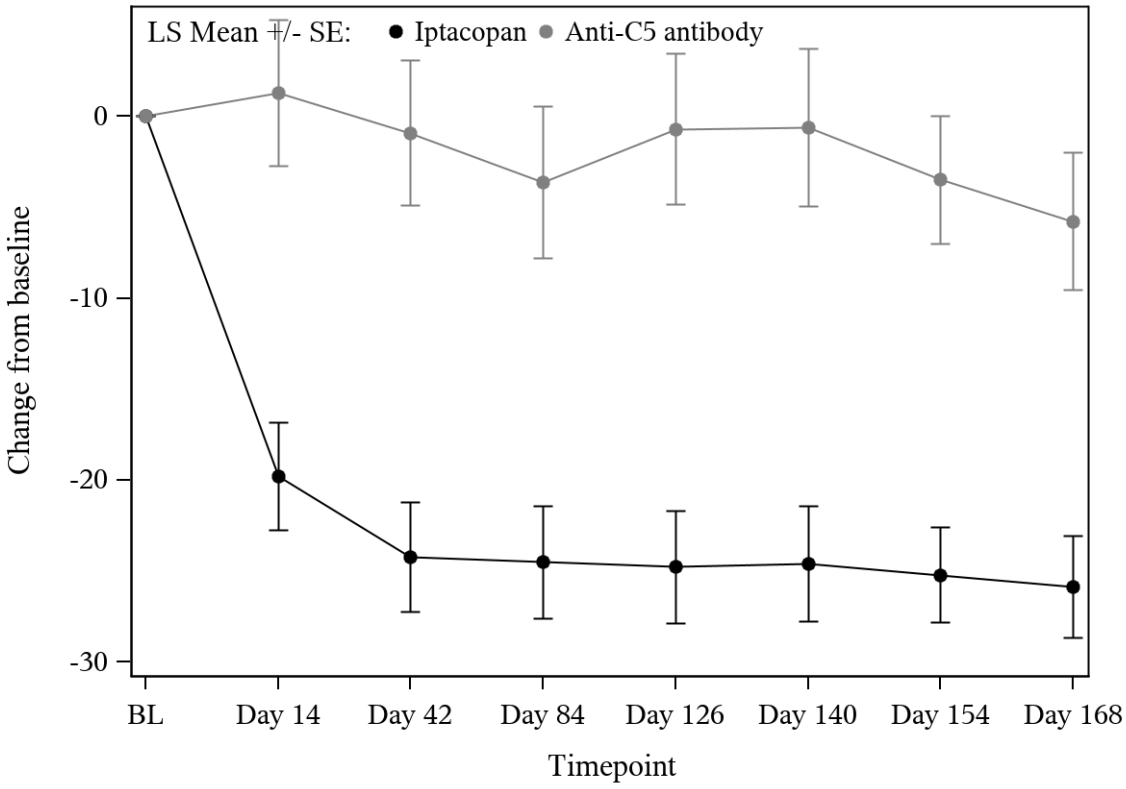
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Dyspnoea



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

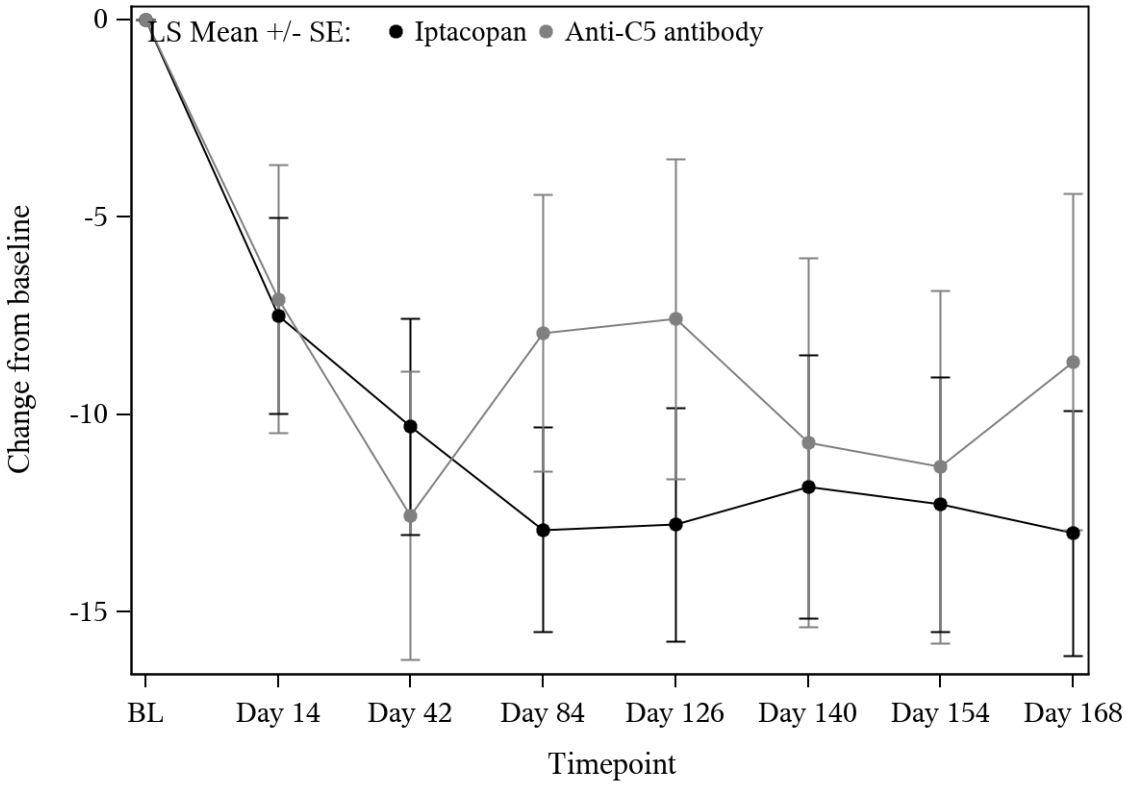
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Insomnia



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

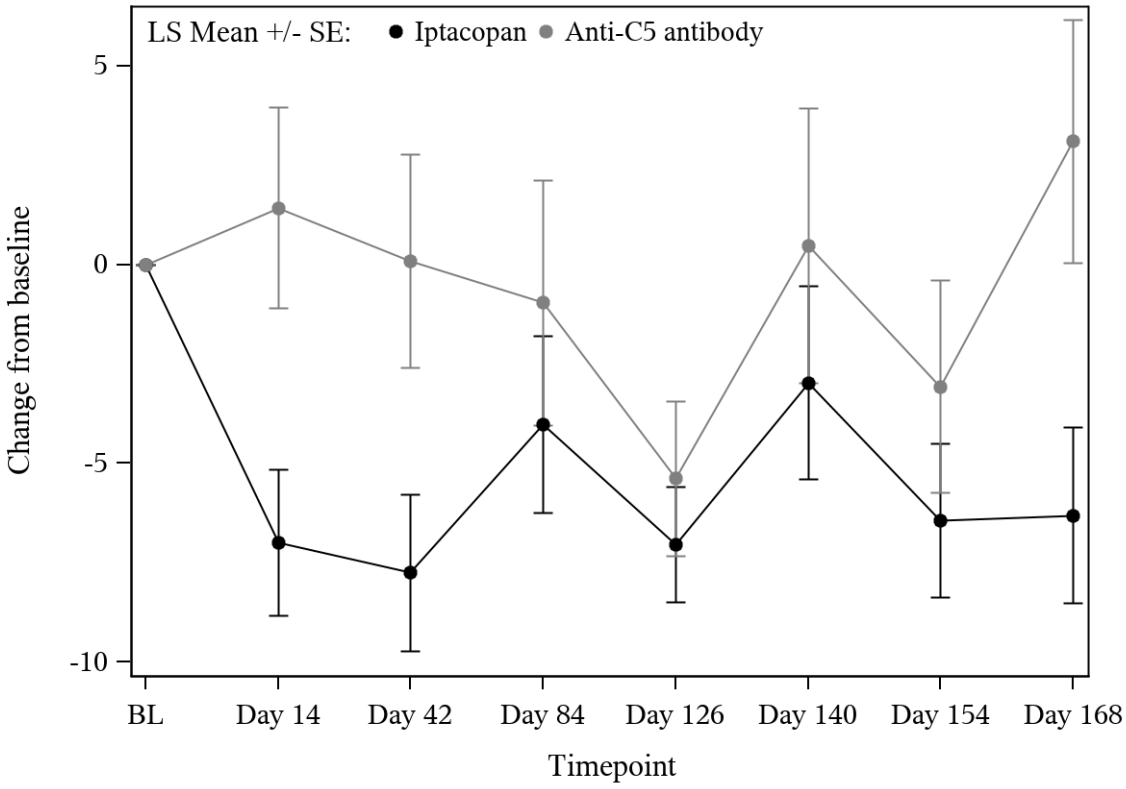
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Appetite loss



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

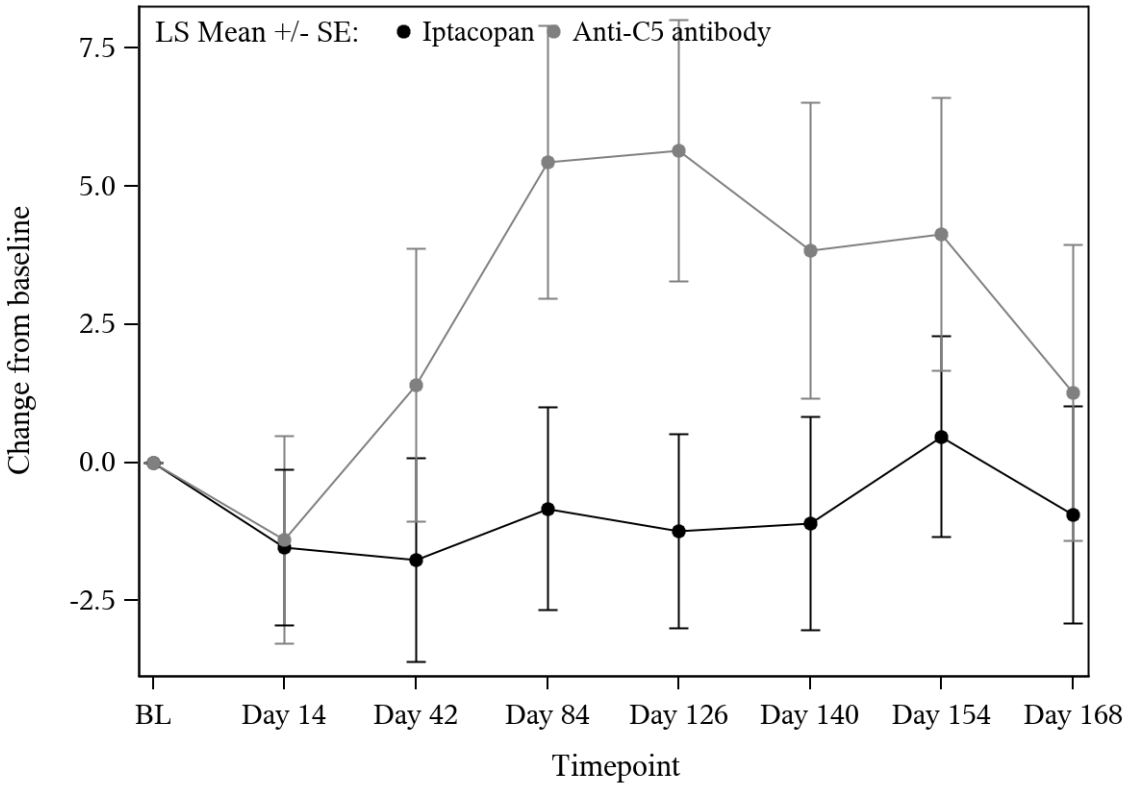
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Constipation



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

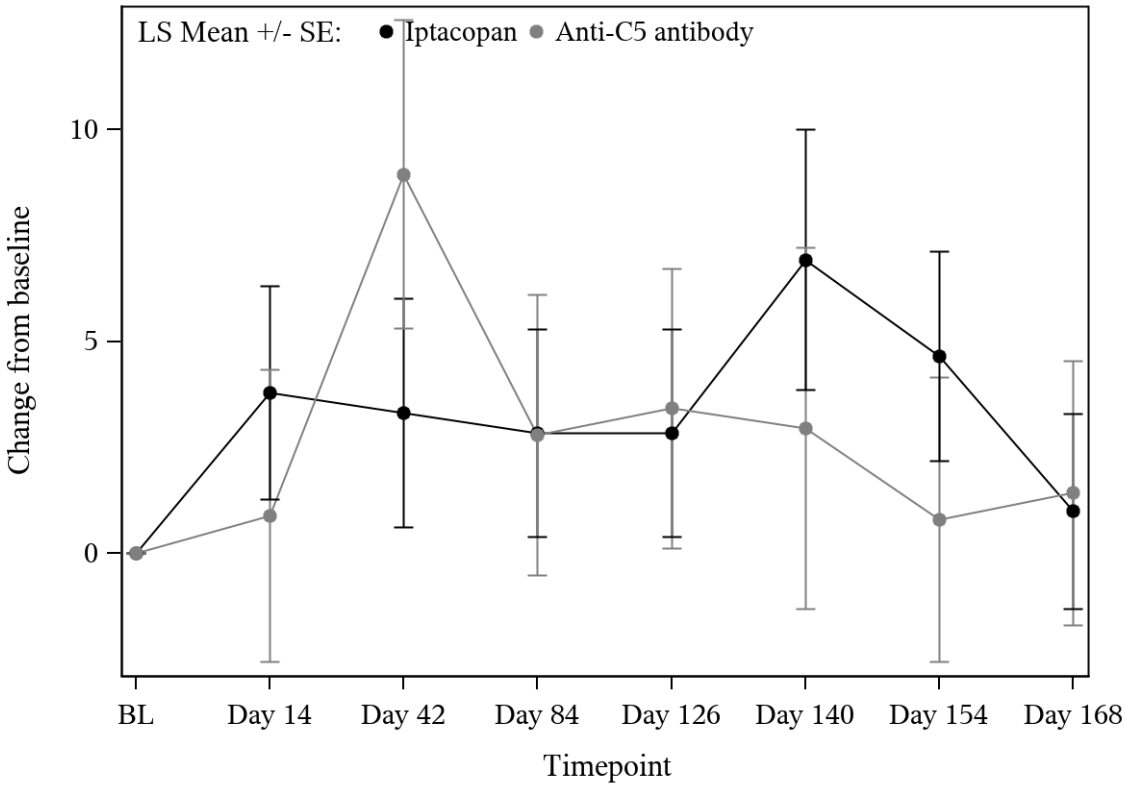
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Diarrhoea



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-2.3 EORTC QLQ-C30 Symptoms responder analysis (improvement defined as ≥ 10 point decrease from baseline): GLMM analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Fatigue						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	30 / 57 (52.6)	11 / 28 (39.3)	OR	5.23	[1.11; 24.74]	0.037
	54.4 [43.2; 65.3]	35.5 [23.0; 49.9]	RR	1.51	[1.12; 2.41]	
			RD	0.1827	[0.0513; 0.3366]	
Day 42	35 / 61 (57.4)	13 / 32 (40.6)	OR	7.74	[2.29; 26.14]	0.001
	60.8 [51.0; 70.0]	35.0 [22.8; 48.1]	RR	1.72	[1.30; 2.64]	
			RD	0.2570	[0.1393; 0.3993]	
Day 84	36 / 57 (63.2)	12 / 29 (41.4)	OR	10.88	[2.91; 40.70]	<0.001
	65.8 [55.2; 75.6]	35.2 [23.0; 47.8]	RR	1.86	[1.40; 2.79]	
			RD	0.3030	[0.1827; 0.4389]	
Day 126	40 / 58 (69.0)	12 / 29 (41.4)	OR	11.39	[3.51; 37.03]	<0.001
	68.6 [58.8; 77.2]	37.8 [25.3; 49.5]	RR	1.79	[1.43; 2.62]	
			RD	0.3028	[0.1995; 0.4378]	
Day 140	37 / 59 (62.7)	13 / 28 (46.4)	OR	10.83	[3.52; 33.38]	<0.001
	69.4 [59.8; 77.7]	38.9 [25.9; 50.6]	RR	1.77	[1.41; 2.64]	
			RD	0.3019	[0.1941; 0.4380]	
Day 154	38 / 56 (67.9)	10 / 28 (35.7)	OR	9.97	[3.07; 32.36]	<0.001
	68.8 [58.3; 78.4]	39.0 [24.8; 51.4]	RR	1.76	[1.36; 2.77]	
			RD	0.2966	[0.1700; 0.4561]	
Day 168	41 / 60 (68.3)	15 / 30 (50.0)	OR	8.88	[2.17; 36.38]	0.002
	70.5 [59.1; 80.9]	42.8 [26.8; 56.1]	RR	1.64	[1.25; 2.63]	
			RD	0.2741	[0.1285; 0.4547]	
Day 126 - 168	**62**	**31**	**OR**	**10.22**	**[3.29; 31.76]**	**<0.001**
	69.4 [59.4; 78.3]	**39.5 [26.4; 51.6]**	**RR**	**1.74**	**[1.38; 2.59]**	
			RD	**0.2946**	**[0.1788; 0.4407]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Nausea and vomiting						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	4 / 57 (7.0)	3 / 28 (10.7)	OR	3.34	[0.21; 53.61]	0.393
	10.5 [3.7; 18.0]	6.4 [0.5; 14.8]	RR	1.62	[0.53; 18.20]	
			RD	0.0374	[-.0489; 0.1225]	
Day 42	7 / 61 (11.5)	3 / 32 (9.4)	OR	2.16	[0.23; 19.91]	0.497
	10.7 [4.7; 16.7]	7.9 [2.2; 13.8]	RR	1.32	[0.61; 4.84]	
			RD	0.0259	[-.0360; 0.1027]	
Day 84	4 / 57 (7.0)	4 / 29 (13.8)	OR	1.74	[0.16; 18.58]	0.646
	10.8 [4.2; 18.4]	9.3 [3.2; 16.1]	RR	1.15	[0.54; 2.72]	
			RD	0.0146	[-.0478; 0.0877]	
Day 126	5 / 58 (8.6)	2 / 29 (6.9)	OR	2.39	[0.28; 20.64]	0.428
	8.8 [3.0; 15.2]	6.7 [1.9; 12.4]	RR	1.30	[0.70; 3.49]	
			RD	0.0197	[-.0228; 0.0785]	
Day 140	5 / 59 (8.5)	3 / 28 (10.7)	OR	2.99	[0.37; 24.30]	0.305
	11.3 [4.7; 17.6]	7.9 [2.2; 13.8]	RR	1.42	[0.77; 4.32]	
			RD	0.0331	[-.0201; 0.0993]	
Day 154	6 / 56 (10.7)	4 / 28 (14.3)	OR	3.97	[0.43; 36.34]	0.222
	12.0 [4.7; 19.4]	7.3 [2.0; 12.7]	RR	1.62	[0.85; 6.41]	
			RD	0.0461	[-.0130; 0.1237]	
Day 168	6 / 60 (10.0)	1 / 30 (3.3)	OR	5.58	[0.40; 77.31]	0.199
	10.7 [3.3; 18.2]	5.2 [0.9; 10.4]	RR	1.91	[0.75; 11.70]	
			RD	0.0503	[-.0137; 0.1372]	
Day 126 - 168	**62**	**31**	**OR**	**3.55**	**[0.42; 29.86]**	**0.244**
	10.6 [4.3; 17.0]	**6.8 [2.0; 11.9]**	**RR**	**1.55**	**[0.84; 4.75]**	
			RD	**0.0374**	**[-.0120; 0.1051]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Pain						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	14 / 57 (24.6)	9 / 28 (32.1)	OR	1.87	[0.29; 12.26]	0.513
	27.0 [17.2; 37.2]	23.2 [11.9; 34.0]	RR	1.16	[0.81; 2.05]	
			RD	0.0378	[-.0492; 0.1421]	
Day 42	12 / 61 (19.7)	8 / 32 (25.0)	OR	1.97	[0.44; 8.85]	0.378
	25.6 [16.5; 35.8]	21.0 [11.5; 31.1]	RR	1.21	[0.86; 2.01]	
			RD	0.0455	[-.0340; 0.1368]	
Day 84	13 / 57 (22.8)	7 / 29 (24.1)	OR	2.38	[0.44; 12.76]	0.310
	24.7 [15.1; 35.5]	19.2 [11.5; 28.1]	RR	1.28	[0.87; 2.01]	
			RD	0.0538	[-.0273; 0.1472]	
Day 126	13 / 58 (22.4)	8 / 29 (27.6)	OR	3.32	[0.73; 15.13]	0.121
	24.1 [14.8; 33.9]	16.8 [9.5; 25.2]	RR	1.41	[1.01; 2.32]	
			RD	0.0708	[0.0025; 0.1503]	
Day 140	12 / 59 (20.3)	3 / 28 (10.7)	OR	3.83	[0.90; 16.36]	0.070
	24.1 [15.0; 33.3]	15.8 [8.7; 24.4]	RR	1.48	[1.07; 2.62]	
			RD	0.0780	[0.0129; 0.1621]	
Day 154	11 / 56 (19.6)	8 / 28 (28.6)	OR	4.48	[0.98; 20.50]	0.053
	25.5 [16.3; 35.8]	16.4 [8.1; 26.0]	RR	1.51	[1.06; 2.92]	
			RD	0.0893	[0.0125; 0.1804]	
Day 168	17 / 60 (28.3)	5 / 30 (16.7)	OR	5.33	[0.87; 32.66]	0.070
	28.9 [18.5; 40.2]	17.6 [7.5; 29.2]	RR	1.59	[1.00; 3.74]	
			RD	0.1091	[0.0009; 0.2383]	
Day 126 - 168	**62**	**31**	**OR**	**4.18**	**[0.97; 18.04]**	**0.055**
	25.6 [16.6; 35.3]	**16.7 [8.8; 25.5]**	**RR**	**1.50**	**[1.08; 2.75]**	
			RD	**0.0871**	**[0.0148; 0.1769]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Dyspnoea						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	36 / 57 (63.2)	8 / 28 (28.6)	OR	10.49	[2.47; 44.58]	0.002
	65.0 [52.6; 76.4]	32.7 [19.3; 45.3]	RR	1.98	[1.39; 3.40]	
			RD	0.3218	[0.1649; 0.4891]	
Day 42	42 / 61 (68.9)	10 / 32 (31.3)	OR	11.72	[3.69; 37.24]	<0.001
	66.7 [55.7; 75.8]	32.9 [20.3; 44.6]	RR	2.03	[1.47; 3.27]	
			RD	0.3400	[0.1926; 0.4869]	
Day 84	38 / 57 (66.7)	11 / 29 (37.9)	OR	12.81	[3.62; 45.39]	<0.001
	67.1 [55.7; 77.1]	32.7 [20.4; 45.9]	RR	2.03	[1.47; 3.25]	
			RD	0.3404	[0.1945; 0.4866]	
Day 126	42 / 58 (72.4)	9 / 29 (31.0)	OR	12.74	[4.13; 39.28]	<0.001
	71.2 [61.2; 81.1]	38.5 [26.7; 49.4]	RR	1.85	[1.45; 2.61]	
			RD	0.3274	[0.2082; 0.4533]	
Day 140	41 / 59 (69.5)	9 / 28 (32.1)	OR	12.46	[4.25; 36.49]	<0.001
	73.5 [63.5; 82.7]	40.6 [29.7; 51.2]	RR	1.81	[1.44; 2.44]	
			RD	0.3280	[0.2118; 0.4527]	
Day 154	41 / 56 (73.2)	12 / 28 (42.9)	OR	12.05	[3.90; 37.22]	<0.001
	75.5 [65.1; 84.9]	44.8 [33.2; 55.7]	RR	1.67	[1.38; 2.33]	
			RD	0.3042	[0.1890; 0.4398]	
Day 168	47 / 60 (78.3)	14 / 30 (46.7)	OR	11.53	[2.97; 44.74]	<0.001
	76.0 [64.2; 85.6]	45.8 [31.2; 58.4]	RR	1.65	[1.29; 2.44]	
			RD	0.2979	[0.1637; 0.4632]	
Day 126 - 168	**62**	**31**	**OR**	**12.19**	**[4.12; 36.04]**	**<0.001**
	73.9 [63.7; 83.1]	**42.3 [31.6; 52.5]**	**RR**	**1.74**	**[1.40; 2.39]**	
			RD	**0.3163**	**[0.2014; 0.4411]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Insomnia						
	n / N' (%) **Predict. % [95% CI]**	**n / N' (%)** **Predict. % [95% CI]**				
Day 14	20 / 57 (35.1)	10 / 28 (35.7)	OR	0.43	[0.08; 2.20]	0.312
	35.4 [24.3; 46.7]	44.8 [29.8; 59.7]	RR	0.78	[0.55; 1.17]	
			RD	-.0967	[-.2376; 0.0543]	
Day 42	25 / 61 (41.0)	17 / 32 (53.1)	OR	0.46	[0.13; 1.65]	0.233
	39.2 [30.4; 48.5]	48.2 [35.3; 60.7]	RR	0.82	[0.64; 1.05]	
			RD	-.0869	[-.2015; 0.0196]	
Day 84	26 / 57 (45.6)	12 / 29 (41.4)	OR	0.52	[0.13; 2.13]	0.365
	42.4 [32.5; 53.0]	49.1 [35.6; 62.2]	RR	0.86	[0.67; 1.11]	
			RD	-.0696	[-.1893; 0.0437]	
Day 126	28 / 58 (48.3)	12 / 29 (41.4)	OR	0.62	[0.17; 2.24]	0.469
	45.4 [35.4; 55.5]	50.4 [37.7; 62.7]	RR	0.90	[0.73; 1.13]	
			RD	-.0519	[-.1542; 0.0531]	
Day 140	25 / 59 (42.4)	13 / 28 (46.4)	OR	0.67	[0.20; 2.28]	0.520
	47.2 [36.7; 57.1]	51.8 [39.0; 63.6]	RR	0.91	[0.74; 1.15]	
			RD	-.0463	[-.1460; 0.0627]	
Day 154	27 / 56 (48.2)	12 / 28 (42.9)	OR	0.72	[0.20; 2.59]	0.615
	43.3 [32.7; 53.7]	47.4 [32.1; 59.7]	RR	0.92	[0.71; 1.26]	
			RD	-.0390	[-.1612; 0.0868]	
Day 168	29 / 60 (48.3)	14 / 30 (46.7)	OR	0.78	[0.17; 3.54]	0.748
	46.0 [34.3; 56.8]	49.1 [33.2; 62.5]	RR	0.94	[0.70; 1.36]	
			RD	-.0312	[-.1630; 0.1207]	
Day 126 - 168	**62**	**31**	**OR**	**0.70**	**[0.20; 2.39]**	**0.564**
	45.4 [35.2; 55.4]	**49.7 [36.4; 61.4]**	**RR**	**0.92**	**[0.73; 1.19]**	
			RD	**-.0412**	**[-.1497; 0.0719]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Appetite loss						
	n / N' (%) **Predict. % [95% CI]**	**n / N' (%)** **Predict. % [95% CI]**				
Day 14	15 / 57 (26.3)	7 / 28 (25.0)	OR	5.69	[0.65; 49.85]	0.116
	30.3 [20.1; 41.1]	21.3 [10.8; 31.9]	RR	1.40	[0.97; 2.67]	
			RD	0.0865	[-.0081; 0.2152]	
Day 42	16 / 61 (26.2)	11 / 32 (34.4)	OR	2.38	[0.45; 12.66]	0.310
	29.4 [19.6; 39.1]	24.2 [14.4; 33.2]	RR	1.22	[0.90; 1.93]	
			RD	0.0528	[-.0274; 0.1539]	
Day 84	10 / 57 (17.5)	9 / 29 (31.0)	OR	1.19	[0.20; 7.09]	0.847
	23.6 [15.3; 32.0]	22.5 [12.6; 32.5]	RR	1.04	[0.75; 1.62]	
			RD	0.0095	[-.0681; 0.0980]	
Day 126	13 / 58 (22.4)	11 / 29 (37.9)	OR	1.26	[0.25; 6.32]	0.780
	25.7 [16.9; 34.7]	24.6 [15.8; 33.6]	RR	1.04	[0.80; 1.52]	
			RD	0.0096	[-.0529; 0.0932]	
Day 140	11 / 59 (18.6)	7 / 28 (25.0)	OR	1.51	[0.32; 7.19]	0.603
	25.7 [17.4; 34.3]	23.8 [15.3; 32.5]	RR	1.08	[0.82; 1.55]	
			RD	0.0196	[-.0436; 0.0955]	
Day 154	14 / 56 (25.0)	10 / 28 (35.7)	OR	1.97	[0.38; 10.27]	0.419
	26.6 [17.2; 36.0]	23.4 [14.5; 32.5]	RR	1.13	[0.86; 1.65]	
			RD	0.0317	[-.0364; 0.1098]	
Day 168	14 / 60 (23.3)	9 / 30 (30.0)	OR	2.80	[0.39; 20.22]	0.308
	27.8 [18.5; 37.5]	22.9 [13.4; 32.2]	RR	1.20	[0.87; 1.93]	
			RD	0.0484	[-.0332; 0.1465]	
Day 126 - 168	**62**	**31**	**OR**	**1.80**	**[0.37; 8.77]**	**0.467**
	26.5 [17.9; 35.5]	**23.7 [15.4; 32.0]**	**RR**	**1.11**	**[0.86; 1.55]**	
			RD	**0.0265**	**[-.0372; 0.1044]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Constipation						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	4 / 57 (7.0)	3 / 28 (10.7)	OR	2.07	[0.08; 51.83]	0.658
	10.7 [5.2; 17.5]	8.7 [2.2; 17.0]	RR	1.21	[0.58; 3.94]	
			RD	0.0184	[-.0527; 0.0943]	
Day 42	8 / 61 (13.1)	4 / 32 (12.5)	OR	1.77	[0.17; 18.37]	0.632
	10.9 [5.4; 17.2]	9.4 [2.5; 16.6]	RR	1.14	[0.63; 4.05]	
			RD	0.0133	[-.0435; 0.0911]	
Day 84	5 / 57 (8.8)	4 / 29 (13.8)	OR	1.86	[0.16; 21.33]	0.619
	11.6 [5.5; 18.6]	10.1 [2.7; 18.0]	RR	1.12	[0.62; 4.08]	
			RD	0.0130	[-.0493; 0.0880]	
Day 126	6 / 58 (10.3)	2 / 29 (6.9)	OR	2.73	[0.29; 25.75]	0.381
	11.0 [5.5; 17.5]	8.2 [2.3; 14.7]	RR	1.25	[0.81; 4.37]	
			RD	0.0222	[-.0211; 0.1008]	
Day 140	5 / 59 (8.5)	3 / 28 (10.7)	OR	3.34	[0.37; 30.29]	0.283
	11.2 [5.7; 18.2]	7.9 [2.3; 14.5]	RR	1.33	[0.86; 4.60]	
			RD	0.0280	[-.0137; 0.1090]	
Day 154	6 / 56 (10.7)	2 / 28 (7.1)	OR	4.25	[0.39; 46.27]	0.235
	11.4 [5.8; 18.8]	7.1 [1.6; 13.5]	RR	1.52	[0.89; 7.85]	
			RD	0.0397	[-.0112; 0.1230]	
Day 168	7 / 60 (11.7)	4 / 30 (13.3)	OR	5.61	[0.30; 103.65]	0.246
	13.1 [6.8; 21.1]	8.1 [2.3; 15.3]	RR	1.58	[0.88; 5.67]	
			RD	0.0490	[-.0136; 0.1329]	
Day 126 - 168	**62**	**31**	**OR**	**3.84**	**[0.40; 37.23]**	**0.246**
	11.8 [6.2; 18.8]	**7.9 [2.2; 14.0]**	**RR**	**1.42**	**[0.87; 4.94]**	
			RD	**0.0347**	**[-.0124; 0.1113]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Diarrhoea						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	5 / 57 (8.8)	4 / 28 (14.3)	OR	1.39	[0.15; 12.48]	0.768
	11.1 [3.9; 20.2]	9.6 [2.2; 17.4]	RR	1.14	[0.35; 4.82]	
			RD	0.0131	[-.0770; 0.1140]	
Day 42	9 / 61 (14.8)	2 / 32 (6.3)	OR	1.82	[0.33; 10.17]	0.494
	13.2 [6.3; 21.0]	10.0 [3.9; 16.7]	RR	1.30	[0.71; 3.16]	
			RD	0.0309	[-.0321; 0.1124]	
Day 84	6 / 57 (10.5)	5 / 29 (17.2)	OR	1.95	[0.31; 12.31]	0.476
	14.5 [7.0; 23.4]	10.8 [4.1; 18.2]	RR	1.33	[0.70; 3.57]	
			RD	0.0379	[-.0424; 0.1248]	
Day 126	9 / 58 (15.5)	4 / 29 (13.8)	OR	1.40	[0.27; 7.35]	0.689
	14.2 [7.1; 22.1]	12.5 [5.1; 20.4]	RR	1.11	[0.68; 2.54]	
			RD	0.0143	[-.0470; 0.0983]	
Day 140	8 / 59 (13.6)	3 / 28 (10.7)	OR	1.15	[0.23; 5.62]	0.864
	14.3 [7.4; 22.2]	13.5 [6.0; 21.8]	RR	1.03	[0.65; 2.11]	
			RD	0.0046	[-.0495; 0.0870]	
Day 154	7 / 56 (12.5)	7 / 28 (25.0)	OR	0.90	[0.17; 4.72]	0.900
	15.0 [8.0; 22.9]	15.5 [7.5; 24.2]	RR	0.96	[0.61; 1.71]	
			RD	-.0068	[-.0661; 0.0690]	
Day 168	8 / 60 (13.3)	5 / 30 (16.7)	OR	0.67	[0.09; 4.82]	0.694
	13.6 [6.7; 21.4]	15.5 [7.6; 23.9]	RR	0.88	[0.53; 1.63]	
			RD	-.0187	[-.0862; 0.0598]	
Day 126 - 168	**62**	**31**	**OR**	**0.99**	**[0.20; 4.92]**	**0.994**
	14.2 [7.6; 21.7]	**14.3 [6.9; 22.1]**	**RR**	**0.99**	**[0.64; 1.85]**	
			RD	**-.0019**	**[-.0562; 0.0749]**	

Treatment Groups		Comparison			
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
GLMM: Generalized linear mixed model
.....

Analysis methods:
OR, RR and RD from logistic GLMM with random intercept and week as continuous covariate:
Logit(proportion) = treatment + baseline value + treatment * week + baseline value * week + treatment * week * week + baseline value * week * week
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value were calculated from model linear predictors, at Day 126 - 168 from a linear function of linear predictors.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group at each visit. Then predicted proportions were averaged over the four visits Day 126 - 168. Then RR and RD were calculated for each visit and for Day 126 - 168. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Response (improvement) is defined as ≥ 10 point decrease from baseline.

Cut-off date for analysis: 06-Mar-2023

Table 3-2.4 EORTC QLQ-C30 Symptoms responder analysis (improvement defined as ≥ 10 point decrease from baseline): raw relative risk (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
QLQ-C30 - Fatigue					
Day 14					
n / N' (%)	30 / 57 (52.6)	11 / 28 (39.3)	1.34	[0.79; 2.26]	0.272
Day 42					
n / N' (%)	35 / 61 (57.4)	13 / 32 (40.6)	1.41	[0.88; 2.26]	0.151
Day 84					
n / N' (%)	36 / 57 (63.2)	12 / 29 (41.4)	1.53	[0.95; 2.46]	0.082
Day 126					
n / N' (%)	40 / 58 (69.0)	12 / 29 (41.4)	1.67	[1.05; 2.66]	0.032
Day 140					
n / N' (%)	37 / 59 (62.7)	13 / 28 (46.4)	1.35	[0.87; 2.11]	0.184
Day 154					
n / N' (%)	38 / 56 (67.9)	10 / 28 (35.7)	1.90	[1.12; 3.22]	0.017
Day 168					
n / N' (%)	41 / 60 (68.3)	15 / 30 (50.0)	1.37	[0.92; 2.03]	0.123
Day 126 - Day 168					
n / N' (%)	**40 / 62 (64.5)**	**12 / 31 (38.7)**	**1.67**	**[1.03; 2.69]**	**0.037**
QLQ-C30 - Nausea and vomiting					
Day 14					
n / N' (%)	4 / 57 (7.0)	3 / 28 (10.7)	0.65	[0.16; 2.73]	0.561
Day 42					
n / N' (%)	7 / 61 (11.5)	3 / 32 (9.4)	1.22	[0.34; 4.42]	0.757
Day 84					
n / N' (%)	4 / 57 (7.0)	4 / 29 (13.8)	0.51	[0.14; 1.89]	0.313
Day 126					
n / N' (%)	5 / 58 (8.6)	2 / 29 (6.9)	1.25	[0.26; 6.06]	0.782
Day 140					
n / N' (%)	5 / 59 (8.5)	3 / 28 (10.7)	0.79	[0.20; 3.08]	0.735
Day 154					
n / N' (%)	6 / 56 (10.7)	4 / 28 (14.3)	0.75	[0.23; 2.44]	0.633
Day 168					
n / N' (%)	6 / 60 (10.0)	1 / 30 (3.3)	3.00	[0.38; 23.80]	0.299
Day 126 - Day 168					
n / N' (%)	**8 / 62 (12.9)**	**4 / 31 (12.9)**	**1.00**	**[0.33; 3.07]**	**1.000**
QLQ-C30 - Pain					
Day 14					
n / N' (%)	14 / 57 (24.6)	9 / 28 (32.1)	0.76	[0.38; 1.55]	0.454

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
Day 42					
n / N' (%)	12 / 61 (19.7)	8 / 32 (25.0)	0.79	[0.36; 1.73]	0.550
Day 84					
n / N' (%)	13 / 57 (22.8)	7 / 29 (24.1)	0.94	[0.42; 2.11]	0.890
Day 126					
n / N' (%)	13 / 58 (22.4)	8 / 29 (27.6)	0.81	[0.38; 1.74]	0.592
Day 140					
n / N' (%)	12 / 59 (20.3)	3 / 28 (10.7)	1.90	[0.58; 6.19]	0.288
Day 154					
n / N' (%)	11 / 56 (19.6)	8 / 28 (28.6)	0.69	[0.31; 1.51]	0.352
Day 168					
n / N' (%)	17 / 60 (28.3)	5 / 30 (16.7)	1.70	[0.69; 4.16]	0.246
Day 126 - Day 168					
n / N' (%)	**16 / 62 (25.8)**	**6 / 31 (19.4)**	**1.33**	**[0.58; 3.07]**	**0.499**
QLQ-C30 - Dyspnoea					
Day 14					
n / N' (%)	36 / 57 (63.2)	8 / 28 (28.6)	2.21	[1.19; 4.10]	0.012
Day 42					
n / N' (%)	42 / 61 (68.9)	10 / 32 (31.3)	2.20	[1.28; 3.78]	0.004
Day 84					
n / N' (%)	38 / 57 (66.7)	11 / 29 (37.9)	1.76	[1.07; 2.90]	0.027
Day 126					
n / N' (%)	42 / 58 (72.4)	9 / 29 (31.0)	2.33	[1.33; 4.11]	0.003
Day 140					
n / N' (%)	41 / 59 (69.5)	9 / 28 (32.1)	2.16	[1.23; 3.80]	0.007
Day 154					
n / N' (%)	41 / 56 (73.2)	12 / 28 (42.9)	1.71	[1.08; 2.70]	0.021
Day 168					
n / N' (%)	47 / 60 (78.3)	14 / 30 (46.7)	1.68	[1.12; 2.52]	0.012
Day 126 - Day 168					
n / N' (%)	**44 / 62 (71.0)**	**10 / 31 (32.3)**	**2.20**	**[1.29; 3.75]**	**0.004**
QLQ-C30 - Insomnia					
Day 14					
n / N' (%)	20 / 57 (35.1)	10 / 28 (35.7)	0.98	[0.53; 1.81]	0.955
Day 42					
n / N' (%)	25 / 61 (41.0)	17 / 32 (53.1)	0.77	[0.50; 1.20]	0.251
Day 84					
n / N' (%)	26 / 57 (45.6)	12 / 29 (41.4)	1.10	[0.66; 1.85]	0.712
Day 126					
n / N' (%)	28 / 58 (48.3)	12 / 29 (41.4)	1.17	[0.70; 1.94]	0.552
Day 140					
n / N' (%)	25 / 59 (42.4)	13 / 28 (46.4)	0.91	[0.56; 1.50]	0.718

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
Day 154					
n / N' (%)	27 / 56 (48.2)	12 / 28 (42.9)	1.13	[0.68; 1.87]	0.649
Day 168					
n / N' (%)	29 / 60 (48.3)	14 / 30 (46.7)	1.04	[0.65; 1.65]	0.882
Day 126 - Day 168					
n / N' (%)	**30 / 62 (48.4)**	**12 / 31 (38.7)**	**1.25**	**[0.75; 2.09]**	**0.393**
QLQ-C30 - Appetite loss					
Day 14					
n / N' (%)	15 / 57 (26.3)	7 / 28 (25.0)	1.05	[0.49; 2.28]	0.897
Day 42					
n / N' (%)	16 / 61 (26.2)	11 / 32 (34.4)	0.76	[0.40; 1.44]	0.406
Day 84					
n / N' (%)	10 / 57 (17.5)	9 / 29 (31.0)	0.57	[0.26; 1.24]	0.153
Day 126					
n / N' (%)	13 / 58 (22.4)	11 / 29 (37.9)	0.59	[0.30; 1.15]	0.123
Day 140					
n / N' (%)	11 / 59 (18.6)	7 / 28 (25.0)	0.75	[0.32; 1.72]	0.491
Day 154					
n / N' (%)	14 / 56 (25.0)	10 / 28 (35.7)	0.70	[0.36; 1.37]	0.299
Day 168					
n / N' (%)	14 / 60 (23.3)	9 / 30 (30.0)	0.78	[0.38; 1.59]	0.490
Day 126 - Day 168					
n / N' (%)	**15 / 62 (24.2)**	**8 / 31 (25.8)**	**0.94**	**[0.45; 1.97]**	**0.865**
QLQ-C30 - Constipation					
Day 14					
n / N' (%)	4 / 57 (7.0)	3 / 28 (10.7)	0.65	[0.16; 2.73]	0.561
Day 42					
n / N' (%)	8 / 61 (13.1)	4 / 32 (12.5)	1.05	[0.34; 3.22]	0.933
Day 84					
n / N' (%)	5 / 57 (8.8)	4 / 29 (13.8)	0.64	[0.18; 2.19]	0.473
Day 126					
n / N' (%)	6 / 58 (10.3)	2 / 29 (6.9)	1.50	[0.32; 6.98]	0.605
Day 140					
n / N' (%)	5 / 59 (8.5)	3 / 28 (10.7)	0.79	[0.20; 3.08]	0.735
Day 154					
n / N' (%)	6 / 56 (10.7)	2 / 28 (7.1)	1.50	[0.32; 6.96]	0.605
Day 168					
n / N' (%)	7 / 60 (11.7)	4 / 30 (13.3)	0.88	[0.28; 2.76]	0.820
Day 126 - Day 168					
n / N' (%)	**6 / 62 (9.7)**	**2 / 31 (6.5)**	**1.50**	**[0.32; 7.00]**	**0.606**

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
QLQ-C30 - Diarrhoea					
Day 14					
n / N' (%)	5 / 57 (8.8)	4 / 28 (14.3)	0.61	[0.18; 2.11]	0.439
Day 42					
n / N' (%)	9 / 61 (14.8)	2 / 32 (6.3)	2.36	[0.54; 10.28]	0.253
Day 84					
n / N' (%)	6 / 57 (10.5)	5 / 29 (17.2)	0.61	[0.20; 1.83]	0.379
Day 126					
n / N' (%)	9 / 58 (15.5)	4 / 29 (13.8)	1.13	[0.38; 3.35]	0.832
Day 140					
n / N' (%)	8 / 59 (13.6)	3 / 28 (10.7)	1.27	[0.36; 4.41]	0.712
Day 154					
n / N' (%)	7 / 56 (12.5)	7 / 28 (25.0)	0.50	[0.19; 1.29]	0.150
Day 168					
n / N' (%)	8 / 60 (13.3)	5 / 30 (16.7)	0.80	[0.29; 2.24]	0.670
Day 126 - Day 168					
n / N' (%)	**6 / 62 (9.7)**	**4 / 31 (12.9)**	**0.75**	**[0.23; 2.46]**	**0.635**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
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Analysis methods:
RR was calculated without adjustment with Wald 95% CI and p-value. In case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.
For Day 126 - 168, observed responders per treatment group were derived from change from baseline of the average of the last four visits. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

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

Response (improvement) is defined as ≥ 10 point decrease from baseline.

Cut-off date for analysis: 06-Mar-2023

3-3 EORTC QLQ-C30 QoL

Table 3-3.1 EORTC QLQ-C30 QoL: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
QLQ-C30 - Global health status		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 58.80 (19.34)	33 | 57.70 (19.63)
Day 14	57 | 68.13 (17.62)	28 | 58.33 (18.56)
Day 42	61 | 74.73 (16.94)	32 | 54.95 (21.26)
Day 84	57 | 76.75 (17.38)	29 | 57.18 (20.74)
Day 126	58 | 77.30 (14.71)	29 | 61.78 (16.89)
Day 140	59 | 71.33 (17.25)	28 | 58.33 (20.54)
Day 154	56 | 74.11 (16.64)	27 | 60.80 (22.62)
Day 168	60 | 74.03 (16.32)	30 | 57.22 (21.19)
Day 126 - 168	**62 | 74.26 (14.15)**	**31 | 58.89 (19.22)**
QLQ-C30 - Physical functioning		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 73.23 (19.08)	33 | 66.16 (22.11)
Day 14	57 | 83.27 (16.38)	28 | 69.05 (19.56)
Day 42	61 | 86.01 (14.84)	32 | 67.08 (21.55)
Day 84	57 | 87.25 (13.17)	29 | 67.59 (20.83)
Day 126	58 | 88.16 (13.68)	29 | 70.80 (19.31)
Day 140	59 | 88.36 (12.90)	28 | 67.62 (23.50)
Day 154	56 | 85.83 (19.32)	28 | 69.52 (20.48)
Day 168	60 | 87.44 (15.58)	30 | 68.44 (21.44)
Day 126 - 168	**62 | 87.49 (13.71)**	**31 | 68.55 (20.40)**
QLQ-C30 - Role functioning		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 68.68 (25.95)	33 | 63.13 (30.83)
Day 14	57 | 76.02 (23.78)	28 | 64.29 (26.73)
Day 42	61 | 83.61 (21.19)	32 | 61.98 (29.70)
Day 84	57 | 85.38 (21.84)	29 | 65.52 (29.19)
Day 126	58 | 85.06 (18.39)	29 | 66.67 (25.97)
Day 140	59 | 81.64 (23.71)	28 | 61.31 (29.42)
Day 154	56 | 83.04 (26.49)	28 | 61.31 (30.45)
Day 168	60 | 83.89 (22.54)	30 | 61.11 (30.74)
Day 126 - 168	**62 | 83.49 (20.07)**	**31 | 61.83 (27.17)**

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
QLQ-C30 - Emotional functioning		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 68.95 (23.14)	33 | 72.85 (22.99)
Day 14	57 | 75.73 (20.31)	28 | 68.75 (22.86)
Day 42	61 | 80.46 (18.44)	32 | 71.61 (25.03)
Day 84	57 | 82.60 (16.61)	29 | 70.40 (24.15)
Day 126	58 | 78.74 (21.81)	29 | 75.86 (17.44)
Day 140	59 | 75.56 (21.99)	28 | 71.73 (24.36)
Day 154	56 | 78.72 (19.13)	28 | 72.32 (24.01)
Day 168	60 | 79.58 (21.34)	30 | 73.89 (26.24)
Day 126 - 168	**62 | 78.13 (19.39)**	**31 | 72.72 (23.05)**
QLQ-C30 - Cognitive functioning		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 75.27 (21.60)	33 | 70.96 (27.01)
Day 14	57 | 82.75 (17.53)	28 | 73.21 (26.19)
Day 42	61 | 83.33 (16.39)	32 | 70.31 (26.00)
Day 84	57 | 83.63 (19.79)	29 | 69.54 (28.89)
Day 126	58 | 86.21 (16.85)	29 | 68.97 (28.43)
Day 140	59 | 83.05 (18.44)	28 | 69.64 (28.35)
Day 154	56 | 83.93 (18.25)	28 | 66.07 (29.91)
Day 168	60 | 84.44 (17.86)	30 | 67.22 (29.52)
Day 126 - 168	**62 | 84.54 (16.35)**	**31 | 68.10 (27.18)**
QLQ-C30 - Social functioning		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 70.43 (30.32)	33 | 64.65 (29.69)
Day 14	57 | 78.95 (24.30)	28 | 70.24 (26.20)
Day 42	61 | 83.88 (23.17)	32 | 64.06 (31.99)
Day 84	57 | 87.72 (19.80)	29 | 64.37 (33.55)
Day 126	58 | 83.91 (22.07)	29 | 69.54 (27.84)
Day 140	59 | 83.33 (21.66)	28 | 66.67 (29.75)
Day 154	56 | 85.42 (23.58)	28 | 67.26 (29.91)
Day 168	60 | 87.22 (20.21)	30 | 61.67 (32.50)
Day 126 - 168	**62 | 84.86 (19.63)**	**31 | 65.59 (27.89)**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
SD: Standard deviation
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Analysis methods:
Descriptive means Day 126 - 168 were calculated by averaging first over the four visits for each patient and then averaging over the treatment group. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

Cut-off date for analysis: 06-Mar-2023

Table 3-3.2 EORTC QLQ-C30 QoL: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
QLQ-C30 - Global health status					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 10.07 (1.75)	28 | 0.15 (2.36)	9.92	[4.34; 15.50]	<0.001
Day 42	61 | 16.76 (2.01)	32 | -1.74 (2.69)	18.49	[12.10; 24.89]	<0.001
Day 84	57 | 18.53 (2.14)	29 | 1.33 (2.90)	17.21	[10.28; 24.13]	<0.001
Day 126	58 | 19.30 (1.93)	29 | 2.24 (2.60)	17.06	[10.88; 23.24]	<0.001
Day 140	59 | 13.59 (2.00)	28 | -0.49 (2.76)	14.08	[7.55; 20.62]	<0.001
Day 154	56 | 15.94 (2.09)	27 | 4.04 (2.87)	11.90	[5.08; 18.73]	<0.001
Day 168	60 | 15.90 (1.95)	30 | 0.32 (2.64)	15.57	[9.32; 21.83]	<0.001
Day 126 - 168	**62 | 16.27 (1.65)**	**31 | 1.61 (2.19)**	**14.66**	**[9.52; 19.79]**	**<0.001**
Hedges' G			**1.25**	**[0.78; 1.72]**	
QLQ-C30 - Physical functioning					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 11.27 (1.52)	28 | -0.85 (2.01)	12.12	[7.34; 16.89]	<0.001
Day 42	61 | 14.15 (1.79)	32 | -0.06 (2.39)	14.21	[8.48; 19.95]	<0.001
Day 84	57 | 15.82 (1.76)	29 | 0.92 (2.34)	14.90	[9.29; 20.51]	<0.001
Day 126	58 | 16.87 (1.63)	29 | 1.25 (2.15)	15.61	[10.49; 20.74]	<0.001
Day 140	59 | 16.93 (1.68)	28 | -0.63 (2.27)	17.56	[12.16; 22.96]	<0.001
Day 154	56 | 14.53 (2.24)	28 | 1.99 (3.09)	12.54	[5.08; 19.99]	0.001
Day 168	60 | 15.74 (1.81)	30 | 1.38 (2.44)	14.36	[8.51; 20.21]	<0.001
Day 126 - 168	**62 | 16.12 (1.52)**	**31 | 1.10 (2.00)**	**15.02**	**[10.26; 19.78]**	**<0.001**
Hedges' G			**1.38**	**[0.91; 1.85]**	
QLQ-C30 - Role functioning					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 8.41 (2.36)	28 | -3.85 (3.16)	12.26	[4.78; 19.74]	0.002
Day 42	61 | 15.94 (2.55)	32 | -1.58 (3.40)	17.52	[9.43; 25.61]	<0.001
Day 84	57 | 17.65 (2.73)	29 | 2.78 (3.67)	14.86	[6.10; 23.63]	0.001
Day 126	58 | 17.87 (2.44)	29 | -0.37 (3.26)	18.23	[10.49; 25.97]	<0.001
Day 140	59 | 14.25 (2.91)	28 | -3.96 (4.02)	18.22	[8.62; 27.81]	<0.001
Day 154	56 | 16.27 (3.32)	28 | -1.73 (4.57)	18.00	[7.02; 28.97]	0.002
Day 168	60 | 16.24 (2.65)	30 | -2.33 (3.59)	18.57	[10.01; 27.13]	<0.001
Day 126 - 168	**62 | 16.21 (2.38)**	**31 | -2.04 (3.18)**	**18.25**	**[10.72; 25.79]**	**<0.001**
Hedges' G			**1.06**	**[0.60; 1.52]**	

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
QLQ-C30 - Emotional functioning					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 6.26 (2.23)	28 | -1.71 (3.00)	7.97	[0.88; 15.05]	0.028
Day 42	61 | 10.83 (2.25)	32 | 0.37 (2.97)	10.46	[3.45; 17.48]	0.004
Day 84	57 | 12.22 (2.38)	29 | 1.49 (3.20)	10.73	[3.12; 18.33]	0.006
Day 126	58 | 8.66 (2.51)	29 | 2.90 (3.41)	5.76	[-2.34; 13.86]	0.161
Day 140	59 | 6.97 (2.58)	28 | -0.71 (3.53)	7.68	[-0.71; 16.06]	0.072
Day 154	56 | 9.06 (2.50)	28 | 1.25 (3.38)	7.81	[-0.24; 15.86]	0.057
Day 168	60 | 10.15 (2.40)	30 | 3.34 (3.24)	6.80	[-0.89; 14.49]	0.082
Day 126 - 168	**62 | 8.58 (2.25)**	**31 | 1.57 (3.00)**	**7.01**	**[-0.09; 14.11]**	**0.053**
Hedges' G			**0.43**	**[-0.00; 0.87]**	
QLQ-C30 - Cognitive functioning					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 7.59 (2.13)	28 | -0.42 (2.86)	8.02	[1.23; 14.80]	0.021
Day 42	61 | 8.48 (2.29)	32 | -1.48 (3.06)	9.96	[2.69; 17.23]	0.008
Day 84	57 | 7.76 (2.34)	29 | 0.37 (3.16)	7.39	[-0.14; 14.92]	0.054
Day 126	58 | 11.06 (2.14)	29 | -4.66 (2.87)	15.72	[8.93; 22.51]	<0.001
Day 140	59 | 8.61 (2.18)	28 | -1.74 (2.97)	10.35	[3.33; 17.36]	0.004
Day 154	56 | 10.01 (2.48)	28 | -4.64 (3.37)	14.64	[6.61; 22.68]	<0.001
Day 168	60 | 9.26 (2.17)	30 | -3.54 (2.93)	12.80	[5.87; 19.72]	<0.001
Day 126 - 168	**62 | 9.66 (1.92)**	**31 | -3.72 (2.54)**	**13.38**	**[7.42; 19.34]**	**<0.001**
Hedges' G			**0.98**	**[0.53; 1.43]**	
QLQ-C30 - Social functioning					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	57 | 12.35 (2.73)	28 | 1.88 (3.67)	10.47	[1.75; 19.18]	0.019
Day 42	61 | 17.05 (2.82)	32 | 1.24 (3.74)	15.81	[6.95; 24.67]	<0.001
Day 84	57 | 20.30 (3.02)	29 | 2.41 (4.07)	17.89	[8.19; 27.60]	<0.001
Day 126	58 | 17.32 (2.71)	29 | 4.14 (3.62)	13.18	[4.61; 21.75]	0.003
Day 140	59 | 17.06 (2.79)	28 | 1.69 (3.79)	15.36	[6.42; 24.31]	<0.001
Day 154	56 | 18.91 (2.90)	28 | 4.94 (3.91)	13.97	[4.69; 23.25]	0.004
Day 168	60 | 20.44 (2.84)	30 | -0.13 (3.81)	20.57	[11.55; 29.59]	<0.001
Day 126 - 168	**62 | 18.38 (2.41)**	**31 | 2.61 (3.18)**	**15.77**	**[8.34; 23.20]**	**<0.001**
Hedges' G			**0.93**	**[0.48; 1.38]**	

Treatment Groups		Comparison		
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

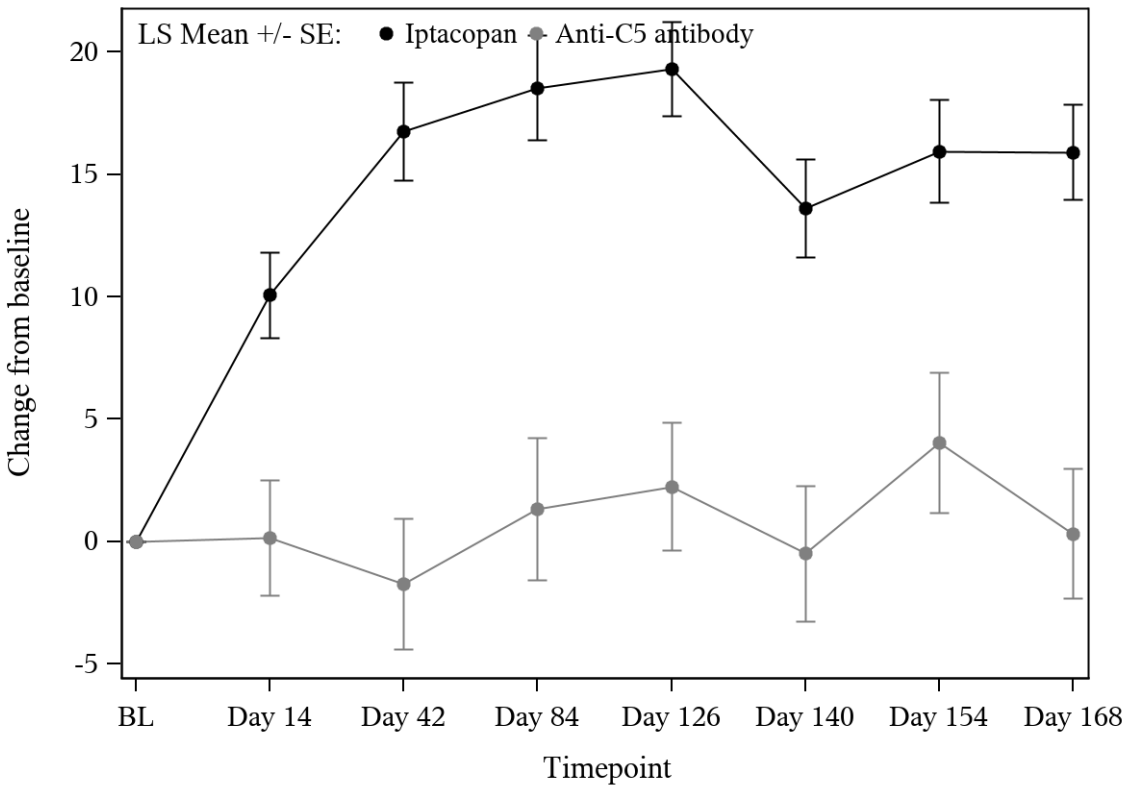
Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

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

Cut-off date for analysis: 06-Mar-2023

Figure 3-3.2 EORTC QLQ-C30 QoL: line chart of least squares mean change from baseline (Full Analysis Set)

QLQ-C30 - Global health status



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	27	30

LS Mean: Least square mean
SE: Standard error
.....

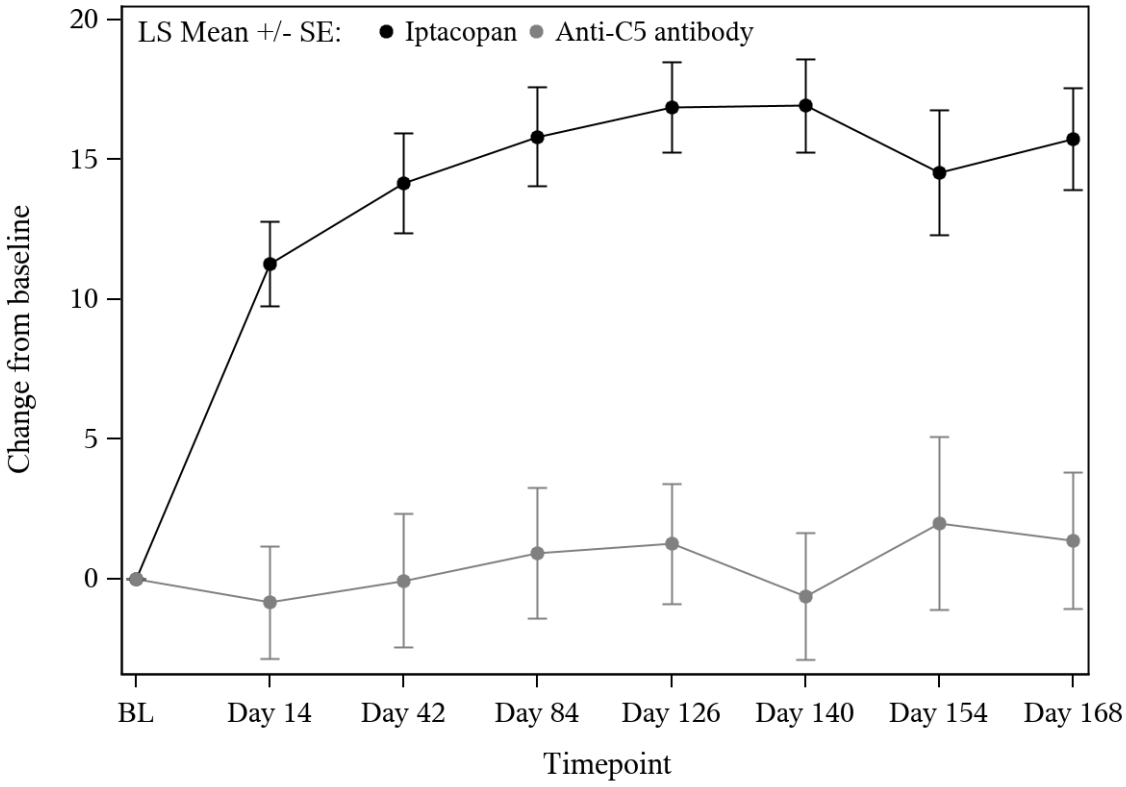
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Physical functioning



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

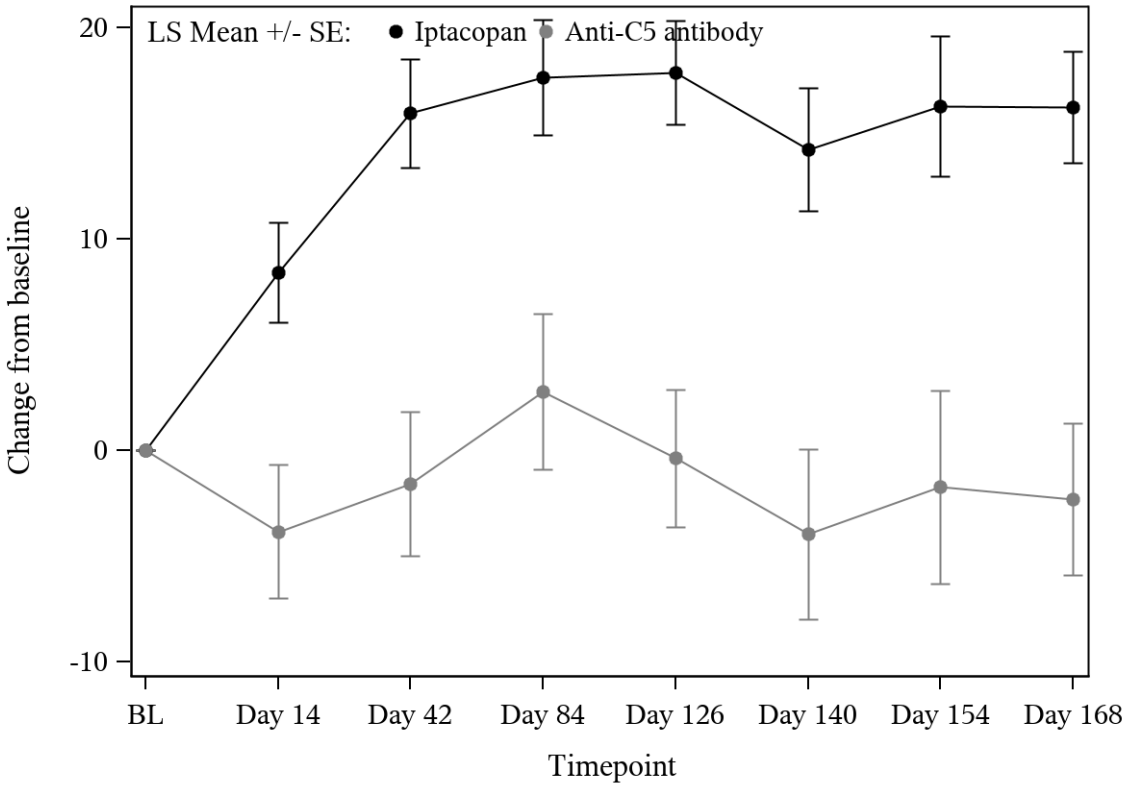
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Role functioning



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

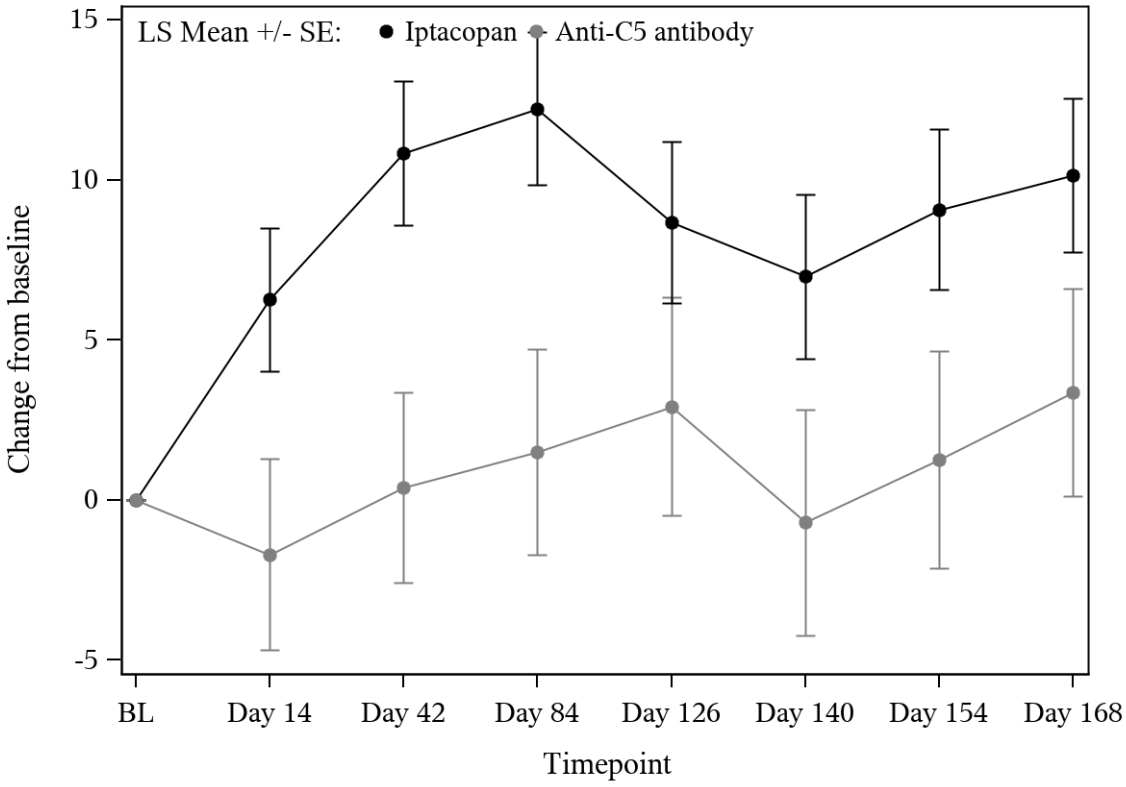
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Emotional functioning



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

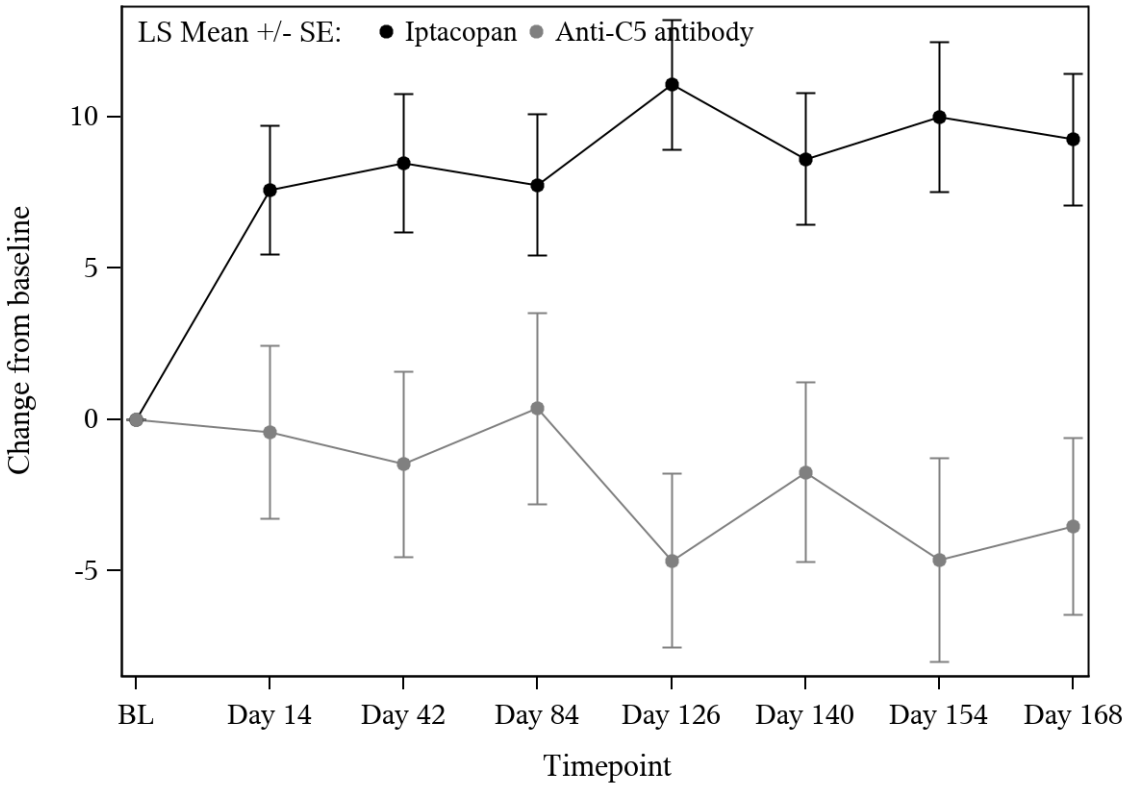
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Cognitive functioning



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

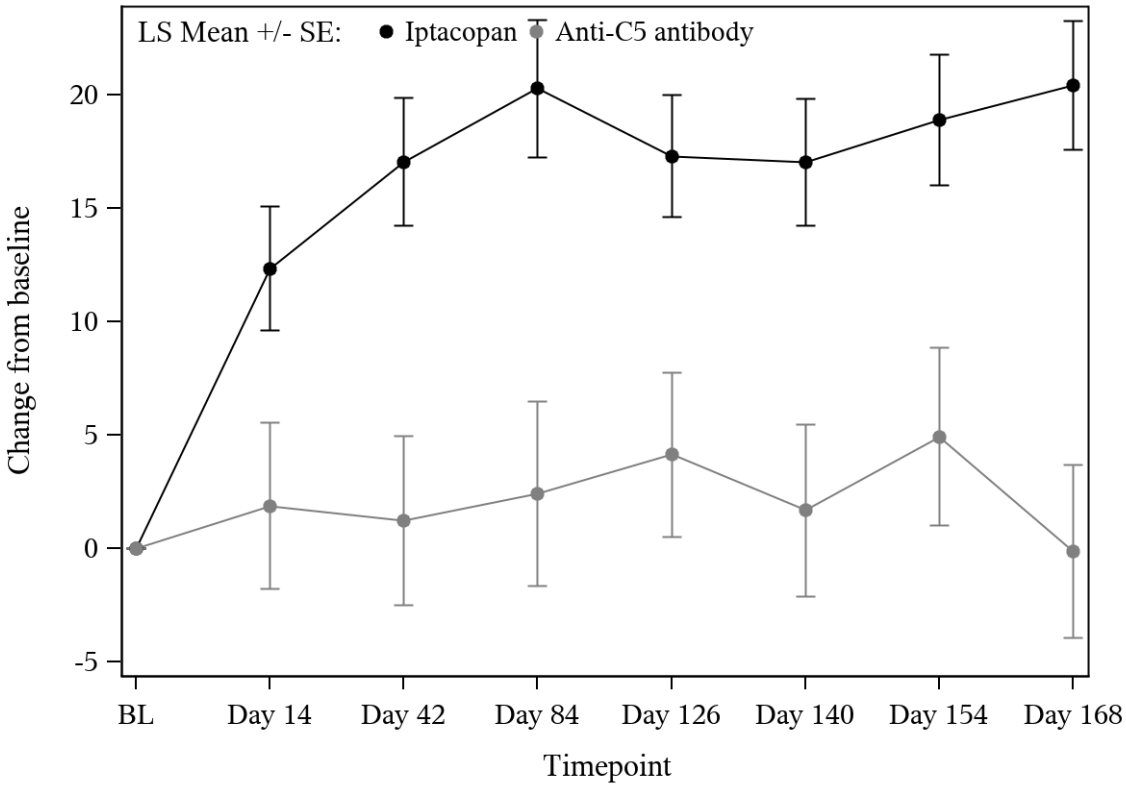
Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

QLQ-C30 - Social functioning



Iptacopan	62	57	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-3.3 EORTC QLQ-C30 QoL responder analysis (improvement defined as ≥ 10 point increase from baseline): GLMM analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Global health status						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	23 / 57 (40.4)	3 / 28 (10.7)	OR	8.98	[1.96; 41.08]	0.005
	40.1 [29.6; 51.3]	13.1 [3.4; 24.6]	RR	3.07	[1.61; 11.59]	
			RD	0.2717	[0.1334; 0.4155]	
Day 42	33 / 61 (54.1)	7 / 32 (21.9)	OR	12.37	[4.01; 38.18]	<0.001
	52.4 [42.7; 61.7]	18.4 [8.1; 27.8]	RR	2.86	[1.91; 6.66]	
			RD	0.3428	[0.2307; 0.4601]	
Day 84	37 / 57 (64.9)	7 / 29 (24.1)	OR	15.06	[4.45; 50.92]	<0.001
	62.2 [50.8; 72.1]	24.5 [12.7; 35.2]	RR	2.51	[1.76; 4.69]	
			RD	0.3750	[0.2533; 0.5124]	
Day 126	36 / 58 (62.1)	8 / 29 (27.6)	OR	13.06	[4.50; 37.89]	<0.001
	63.0 [52.5; 72.7]	28.3 [16.2; 39.1]	RR	2.24	[1.63; 3.81]	
			RD	0.3485	[0.2274; 0.4877]	
Day 140	33 / 59 (55.9)	6 / 28 (21.4)	OR	11.55	[4.27; 31.25]	<0.001
	63.4 [52.7; 72.7]	28.6 [16.7; 40.3]	RR	2.22	[1.58; 3.74]	
			RD	0.3483	[0.2219; 0.4837]	
Day 154	35 / 56 (62.5)	9 / 27 (33.3)	OR	9.83	[3.50; 27.60]	<0.001
	60.5 [50.3; 70.3]	26.6 [15.1; 38.5]	RR	2.28	[1.56; 4.07]	
			RD	0.3375	[0.1990; 0.4791]	
Day 168	37 / 60 (61.7)	8 / 30 (26.7)	OR	8.07	[2.29; 28.40]	0.001
	58.8 [47.8; 69.6]	28.1 [15.2; 42.3]	RR	2.07	[1.35; 3.79]	
			RD	0.3041	[0.1430; 0.4682]	
Day 126 - 168	**62**	**31**	**OR**	**10.46**	**[3.88; 28.20]**	**<0.001**
	61.5 [51.5; 70.7]	**27.8 [16.5; 39.2]**	**RR**	**2.20**	**[1.56; 3.77]**	
			RD	**0.3350**	**[0.2064; 0.4720]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Physical functioning						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	26 / 57 (45.6)	4 / 28 (14.3)	OR	8.72	[1.66; 45.89]	0.011
	43.8 [33.0; 54.8]	18.5 [7.3; 30.5]	RR	2.35	[1.38; 5.89]	
			RD	0.2519	[0.1106; 0.3944]	
Day 42	31 / 61 (50.8)	9 / 32 (28.1)	OR	21.91	[5.48; 87.53]	<0.001
	54.3 [44.3; 64.4]	19.8 [10.5; 30.3]	RR	2.71	[1.77; 4.86]	
			RD	0.3424	[0.2202; 0.4647]	
Day 84	31 / 57 (54.4)	6 / 29 (20.7)	OR	51.92	[10.11; 266.58]	<0.001
	58.6 [47.4; 69.1]	19.1 [10.0; 28.7]	RR	3.07	[2.00; 5.94]	
			RD	0.3938	[0.2656; 0.5174]	
Day 126	35 / 58 (60.3)	8 / 29 (27.6)	OR	66.02	[15.18; 287.03]	<0.001
	59.8 [49.0; 69.8]	20.3 [11.7; 30.0]	RR	2.96	[2.01; 5.09]	
			RD	0.3969	[0.2709; 0.5162]	
Day 140	34 / 59 (57.6)	5 / 28 (17.9)	OR	62.28	[15.36; 252.45]	<0.001
	60.6 [49.7; 70.3]	19.5 [11.5; 28.8]	RR	3.11	[2.07; 5.18]	
			RD	0.4097	[0.2840; 0.5286]	
Day 154	33 / 56 (58.9)	6 / 28 (21.4)	OR	54.82	[12.68; 236.99]	<0.001
	59.4 [47.9; 69.3]	17.5 [9.3; 26.4]	RR	3.40	[2.23; 6.31]	
			RD	0.4164	[0.2833; 0.5414]	
Day 168	34 / 60 (56.7)	7 / 30 (23.3)	OR	45.03	[7.76; 261.25]	<0.001
	59.8 [47.3; 70.9]	19.1 [9.1; 29.5]	RR	3.11	[1.97; 6.75]	
			RD	0.4038	[0.2552; 0.5556]	
Day 126 - 168	**62**	**31**	**OR**	**56.44**	**[13.84; 230.26]**	**<0.001**
	59.9 [49.0; 69.3]	**19.0 [11.2; 27.5]**	**RR**	**3.16**	**[2.13; 5.32]**	
			RD	**0.4084**	**[0.2820; 0.5259]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Role functioning						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	17 / 57 (29.8)	3 / 28 (10.7)	OR	6.88	[1.29; 36.70]	0.024
	31.4 [20.7; 43.1]	13.0 [2.8; 25.7]	RR	2.42	[1.19; 11.68]	
			RD	0.1834	[0.0439; 0.3328]	
Day 42	29 / 61 (47.5)	7 / 32 (21.9)	OR	7.35	[2.07; 26.05]	0.002
	44.7 [34.2; 55.1]	22.8 [11.7; 34.1]	RR	1.93	[1.32; 3.56]	
			RD	0.2160	[0.0983; 0.3373]	
Day 84	26 / 57 (45.6)	11 / 29 (37.9)	OR	7.62	[1.96; 29.64]	0.003
	50.2 [38.1; 61.8]	31.3 [19.6; 43.0]	RR	1.60	[1.20; 2.39]	
			RD	0.1869	[0.0762; 0.3134]	
Day 126	29 / 58 (50.0)	9 / 29 (31.0)	OR	7.32	[2.22; 24.18]	0.001
	52.2 [41.0; 63.0]	31.7 [21.2; 42.5]	RR	1.63	[1.25; 2.42]	
			RD	0.2004	[0.0926; 0.3302]	
Day 140	28 / 59 (47.5)	7 / 28 (25.0)	OR	7.11	[2.33; 21.68]	<0.001
	51.9 [40.3; 62.1]	30.3 [20.3; 40.3]	RR	1.70	[1.31; 2.55]	
			RD	0.2118	[0.1073; 0.3420]	
Day 154	27 / 56 (48.2)	9 / 28 (32.1)	OR	6.84	[2.19; 21.39]	<0.001
	49.9 [38.2; 60.4]	26.8 [16.8; 36.6]	RR	1.83	[1.39; 2.93]	
			RD	0.2271	[0.1258; 0.3758]	
Day 168	28 / 60 (46.7)	6 / 30 (20.0)	OR	6.53	[1.67; 25.48]	0.007
	46.7 [35.2; 57.5]	23.3 [12.1; 35.1]	RR	1.96	[1.30; 3.79]	
			RD	0.2282	[0.0947; 0.3915]	
Day 126 - 168	**62**	**31**	**OR**	**6.94**	**[2.30; 20.97]**	**<0.001**
	50.2 [38.9; 59.9]	**28.1 [18.6; 37.5]**	**RR**	**1.77**	**[1.38; 2.65]**	
			RD	**0.2176**	**[0.1223; 0.3499]**	

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Emotional functioning						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	21 / 57 (36.8)	2 / 28 (7.1)	OR	6.23	[1.36; 28.61]	0.019
	37.8 [27.0; 50.1]	18.8 [8.4; 31.1]	RR	1.98	[1.17; 4.58]	
			RD	0.1871	[0.0420; 0.3314]	
Day 42	26 / 61 (42.6)	8 / 32 (25.0)	OR	3.78	[1.23; 11.59]	0.020
	36.9 [27.8; 47.4]	22.9 [13.5; 32.8]	RR	1.62	[1.11; 2.73]	
			RD	0.1404	[0.0308; 0.2615]	
Day 84	25 / 57 (43.9)	7 / 29 (24.1)	OR	2.42	[0.75; 7.86]	0.139
	37.0 [26.1; 47.7]	27.4 [16.8; 37.8]	RR	1.36	[0.93; 2.14]	
			RD	0.0955	[-.0227; 0.2144]	
Day 126	18 / 58 (31.0)	5 / 29 (17.2)	OR	2.25	[0.81; 6.30]	0.121
	35.0 [24.5; 45.1]	25.4 [15.4; 35.3]	RR	1.38	[0.95; 2.14]	
			RD	0.0956	[-.0167; 0.1963]	
Day 140	20 / 59 (33.9)	4 / 28 (14.3)	OR	2.39	[0.91; 6.26]	0.076
	37.3 [27.0; 47.5]	26.5 [17.3; 36.3]	RR	1.40	[0.99; 2.14]	
			RD	0.1068	[-.0016; 0.2138]	
Day 154	23 / 56 (41.1)	6 / 28 (21.4)	OR	2.64	[0.97; 7.15]	0.057
	38.5 [27.5; 48.5]	25.8 [16.4; 35.7]	RR	1.49	[1.03; 2.39]	
			RD	0.1255	[0.0122; 0.2426]	
Day 168	27 / 60 (45.0)	8 / 30 (26.7)	OR	3.03	[0.90; 10.18]	0.072
	39.8 [27.1; 50.5]	24.7 [13.6; 36.9]	RR	1.60	[1.01; 2.92]	
			RD	0.1469	[0.0030; 0.2869]	
Day 126 - 168	**62**	**31**	**OR**	**2.56**	**[0.98; 6.70]**	**0.055**
	37.6 [27.4; 47.1]	**25.5 [16.3; 34.9]**	**RR**	**1.46**	**[1.03; 2.32]**	
			RD	**0.1184**	**[0.0083; 0.2271]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Cognitive functioning						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	20 / 57 (35.1)	8 / 28 (28.6)	OR	3.52	[0.65; 19.01]	0.143
	36.9 [25.5; 46.8]	24.5 [13.2; 35.3]	RR	1.51	[1.03; 2.64]	
			RD	0.1229	[0.0090; 0.2434]	
Day 42	22 / 61 (36.1)	8 / 32 (25.0)	OR	3.68	[0.97; 14.00]	0.056
	37.2 [27.4; 47.2]	25.4 [13.6; 36.1]	RR	1.47	[1.05; 2.54]	
			RD	0.1198	[0.0172; 0.2383]	
Day 84	19 / 57 (33.3)	10 / 29 (34.5)	OR	3.89	[0.92; 16.51]	0.065
	38.6 [27.6; 50.0]	26.1 [12.9; 38.9]	RR	1.47	[1.04; 2.71]	
			RD	0.1219	[0.0124; 0.2592]	
Day 126	21 / 58 (36.2)	6 / 29 (20.7)	OR	4.08	[1.14; 14.65]	0.031
	36.9 [26.5; 46.5]	24.0 [12.3; 34.7]	RR	1.52	[1.13; 2.71]	
			RD	0.1266	[0.0388; 0.2482]	
Day 140	23 / 59 (39.0)	8 / 28 (28.6)	OR	4.13	[1.23; 13.94]	0.022
	38.6 [27.8; 49.1]	24.9 [13.0; 34.9]	RR	1.55	[1.17; 2.62]	
			RD	0.1367	[0.0505; 0.2503]	
Day 154	21 / 56 (37.5)	10 / 28 (35.7)	OR	4.18	[1.17; 14.90]	0.027
	38.5 [28.1; 48.6]	25.2 [13.9; 35.5]	RR	1.51	[1.13; 2.49]	
			RD	0.1300	[0.0405; 0.2346]	
Day 168	22 / 60 (36.7)	7 / 30 (23.3)	OR	4.23	[0.92; 19.42]	0.064
	38.8 [28.6; 49.6]	24.8 [12.7; 37.2]	RR	1.57	[1.03; 2.92]	
			RD	0.1396	[0.0100; 0.2749]	
Day 126 - 168	**62**	**31**	**OR**	**4.16**	**[1.22; 14.12]**	**0.023**
	38.2 [27.8; 48.3]	**24.7 [13.2; 34.9]**	**RR**	**1.53**	**[1.16; 2.55]**	
			RD	**0.1328**	**[0.0484; 0.2391]**	

Treatment Groups			Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
QLQ-C30 - Social functioning						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	17 / 57 (29.8)	8 / 28 (28.6)	OR	1.70	[0.33; 8.75]	0.524
	33.7 [23.6; 44.4]	28.1 [13.9; 41.0]	RR	1.20	[0.77; 2.42]	
			RD	0.0557	[-.0843; 0.2222]	
Day 42	24 / 61 (39.3)	12 / 32 (37.5)	OR	1.31	[0.37; 4.67]	0.674
	37.0 [27.3; 46.9]	34.5 [22.1; 45.4]	RR	1.06	[0.80; 1.68]	
			RD	0.0226	[-.0762; 0.1645]	
Day 84	24 / 57 (42.1)	10 / 29 (34.5)	OR	1.58	[0.40; 6.31]	0.518
	39.9 [29.9; 49.7]	36.6 [25.1; 47.5]	RR	1.08	[0.84; 1.54]	
			RD	0.0306	[-.0693; 0.1489]	
Day 126	21 / 58 (36.2)	10 / 29 (34.5)	OR	3.78	[1.07; 13.32]	0.039
	43.8 [33.1; 54.1]	32.3 [20.7; 43.5]	RR	1.35	[1.02; 2.00]	
			RD	0.1147	[0.0077; 0.2303]	
Day 140	27 / 59 (45.8)	8 / 28 (28.6)	OR	5.89	[1.70; 20.41]	0.005
	45.5 [34.5; 55.0]	29.4 [17.7; 41.1]	RR	1.54	[1.11; 2.42]	
			RD	0.1616	[0.0442; 0.2848]	
Day 154	25 / 56 (44.6)	7 / 28 (25.0)	OR	9.91	[2.54; 38.70]	0.001
	45.1 [33.5; 55.1]	24.0 [13.3; 35.6]	RR	1.86	[1.26; 3.24]	
			RD	0.2088	[0.0812; 0.3409]	
Day 168	29 / 60 (48.3)	5 / 30 (16.7)	OR	18.00	[3.35; 96.74]	<0.001
	45.8 [34.4; 56.4]	20.0 [9.7; 31.5]	RR	2.28	[1.46; 4.71]	
			RD	0.2559	[0.1153; 0.4006]	
Day 126 - 168	**62**	**31**	**OR**	**7.94**	**[2.19; 28.80]**	**0.002**
	45.0 [34.0; 54.6]	**26.4 [15.7; 37.3]**	**RR**	**1.69**	**[1.21; 2.71]**	
			RD	**0.1861**	**[0.0690; 0.3074]**	

Treatment Groups		Comparison			
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
GLMM: Generalized linear mixed model
.....

Analysis methods:
OR, RR and RD from logistic GLMM with random intercept and week as continuous covariate:
Logit(proportion) = treatment + baseline value + treatment * week + baseline value * week + treatment * week * week + baseline value * week * week
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value were calculated from model linear predictors, at Day 126 - 168 from a linear function of linear predictors.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group at each visit. Then predicted proportions were averaged over the four visits Day 126 - 168. Then RR and RD were calculated for each visit and for Day 126 - 168. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Response (improvement) is defined as ≥ 10 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

Table 3-3.4 EORTC QLQ-C30 QoL responder analysis (improvement defined as ≥ 10 point increase from baseline): raw relative risk (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
QLQ-C30 - Global health status					
Day 14					
n / N' (%)	23 / 57 (40.4)	3 / 28 (10.7)	3.77	[1.24; 11.48]	0.020
Day 42					
n / N' (%)	33 / 61 (54.1)	7 / 32 (21.9)	2.47	[1.24; 4.95]	0.011
Day 84					
n / N' (%)	37 / 57 (64.9)	7 / 29 (24.1)	2.69	[1.37; 5.27]	0.004
Day 126					
n / N' (%)	36 / 58 (62.1)	8 / 29 (27.6)	2.25	[1.21; 4.20]	0.011
Day 140					
n / N' (%)	33 / 59 (55.9)	6 / 28 (21.4)	2.61	[1.24; 5.50]	0.012
Day 154					
n / N' (%)	35 / 56 (62.5)	9 / 27 (33.3)	1.88	[1.06; 3.32]	0.031
Day 168					
n / N' (%)	37 / 60 (61.7)	8 / 30 (26.7)	2.31	[1.24; 4.32]	0.009
Day 126 - Day 168					
n / N' (%)	**37 / 62 (59.7)**	**7 / 31 (22.6)**	**2.64**	**[1.33; 5.23]**	**0.005**
QLQ-C30 - Physical functioning					
Day 14					
n / N' (%)	26 / 57 (45.6)	4 / 28 (14.3)	3.19	[1.23; 8.26]	0.017
Day 42					
n / N' (%)	31 / 61 (50.8)	9 / 32 (28.1)	1.81	[0.99; 3.31]	0.056
Day 84					
n / N' (%)	31 / 57 (54.4)	6 / 29 (20.7)	2.63	[1.24; 5.57]	0.012
Day 126					
n / N' (%)	35 / 58 (60.3)	8 / 29 (27.6)	2.19	[1.17; 4.09]	0.014
Day 140					
n / N' (%)	34 / 59 (57.6)	5 / 28 (17.9)	3.23	[1.42; 7.36]	0.005
Day 154					
n / N' (%)	33 / 56 (58.9)	6 / 28 (21.4)	2.75	[1.31; 5.78]	0.008
Day 168					
n / N' (%)	34 / 60 (56.7)	7 / 30 (23.3)	2.43	[1.22; 4.82]	0.011
Day 126 - Day 168					
n / N' (%)	**38 / 62 (61.3)**	**7 / 31 (22.6)**	**2.71**	**[1.37; 5.36]**	**0.004**
QLQ-C30 - Role functioning					
Day 14					
n / N' (%)	17 / 57 (29.8)	3 / 28 (10.7)	2.78	[0.89; 8.71]	0.079

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
Day 42					
n / N' (%)	29 / 61 (47.5)	7 / 32 (21.9)	2.17	[1.07; 4.40]	0.031
Day 84					
n / N' (%)	26 / 57 (45.6)	11 / 29 (37.9)	1.20	[0.70; 2.07]	0.507
Day 126					
n / N' (%)	29 / 58 (50.0)	9 / 29 (31.0)	1.61	[0.88; 2.94]	0.120
Day 140					
n / N' (%)	28 / 59 (47.5)	7 / 28 (25.0)	1.90	[0.95; 3.81]	0.071
Day 154					
n / N' (%)	27 / 56 (48.2)	9 / 28 (32.1)	1.50	[0.82; 2.74]	0.187
Day 168					
n / N' (%)	28 / 60 (46.7)	6 / 30 (20.0)	2.33	[1.09; 5.01]	0.030
Day 126 - Day 168					
n / N' (%)	**31 / 62 (50.0)**	**8 / 31 (25.8)**	**1.94**	**[1.01; 3.70]**	**0.045**
QLQ-C30 - Emotional functioning					
Day 14					
n / N' (%)	21 / 57 (36.8)	2 / 28 (7.1)	5.16	[1.30; 20.46]	0.020
Day 42					
n / N' (%)	26 / 61 (42.6)	8 / 32 (25.0)	1.70	[0.88; 3.32]	0.117
Day 84					
n / N' (%)	25 / 57 (43.9)	7 / 29 (24.1)	1.82	[0.89; 3.69]	0.099
Day 126					
n / N' (%)	18 / 58 (31.0)	5 / 29 (17.2)	1.80	[0.74; 4.36]	0.193
Day 140					
n / N' (%)	20 / 59 (33.9)	4 / 28 (14.3)	2.37	[0.90; 6.29]	0.082
Day 154					
n / N' (%)	23 / 56 (41.1)	6 / 28 (21.4)	1.92	[0.88; 4.16]	0.100
Day 168					
n / N' (%)	27 / 60 (45.0)	8 / 30 (26.7)	1.69	[0.88; 3.25]	0.118
Day 126 - Day 168					
n / N' (%)	**25 / 62 (40.3)**	**4 / 31 (12.9)**	**3.13**	**[1.19; 8.19]**	**0.020**
QLQ-C30 - Cognitive functioning					
Day 14					
n / N' (%)	20 / 57 (35.1)	8 / 28 (28.6)	1.23	[0.62; 2.43]	0.556
Day 42					
n / N' (%)	22 / 61 (36.1)	8 / 32 (25.0)	1.44	[0.73; 2.87]	0.296
Day 84					
n / N' (%)	19 / 57 (33.3)	10 / 29 (34.5)	0.97	[0.52; 1.80]	0.915
Day 126					
n / N' (%)	21 / 58 (36.2)	6 / 29 (20.7)	1.75	[0.79; 3.86]	0.165
Day 140					
n / N' (%)	23 / 59 (39.0)	8 / 28 (28.6)	1.36	[0.70; 2.66]	0.361

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
Day 154					
n / N' (%)	21 / 56 (37.5)	10 / 28 (35.7)	1.05	[0.58; 1.92]	0.874
Day 168					
n / N' (%)	22 / 60 (36.7)	7 / 30 (23.3)	1.57	[0.76; 3.26]	0.224
Day 126 - Day 168					
n / N' (%)	**22 / 62 (35.5)**	**9 / 31 (29.0)**	**1.22**	**[0.64; 2.33]**	**0.542**
QLQ-C30 - Social functioning					
Day 14					
n / N' (%)	17 / 57 (29.8)	8 / 28 (28.6)	1.04	[0.51; 2.12]	0.905
Day 42					
n / N' (%)	24 / 61 (39.3)	12 / 32 (37.5)	1.05	[0.61; 1.81]	0.863
Day 84					
n / N' (%)	24 / 57 (42.1)	10 / 29 (34.5)	1.22	[0.68; 2.20]	0.505
Day 126					
n / N' (%)	21 / 58 (36.2)	10 / 29 (34.5)	1.05	[0.57; 1.93]	0.875
Day 140					
n / N' (%)	27 / 59 (45.8)	8 / 28 (28.6)	1.60	[0.84; 3.06]	0.154
Day 154					
n / N' (%)	25 / 56 (44.6)	7 / 28 (25.0)	1.79	[0.88; 3.61]	0.107
Day 168					
n / N' (%)	29 / 60 (48.3)	5 / 30 (16.7)	2.90	[1.25; 6.73]	0.013
Day 126 - Day 168					
n / N' (%)	**27 / 62 (43.5)**	**8 / 31 (25.8)**	**1.69**	**[0.87; 3.27]**	**0.121**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis methods:
RR was calculated without adjustment with Wald 95% CI and p-value. In case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.
For Day 126 - 168, observed responders per treatment group were derived from change from baseline of the average of the last four visits. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

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

Response (improvement) is defined as ≥ 10 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

3-4 EQ-5D VAS

Table 3-4.1 EQ-5D VAS: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
EQ-5D VAS		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 63.31 (18.33)	33 | 59.58 (20.65)
Day 14	56 | 70.55 (15.40)	28 | 58.61 (20.84)
Day 42	61 | 73.97 (16.50)	32 | 58.25 (19.35)
Day 84	57 | 76.86 (15.83)	29 | 57.45 (21.01)
Day 126	58 | 78.03 (13.12)	29 | 62.59 (19.00)
Day 140	59 | 74.90 (13.42)	28 | 59.43 (22.68)
Day 154	56 | 75.36 (15.91)	28 | 59.82 (21.49)
Day 168	60 | 76.30 (15.43)	30 | 57.73 (21.35)
Day 126 - 168	**62 | 76.24 (13.16)**	**31 | 59.27 (20.51)**

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-4.2 EQ-5D VAS: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
EQ-5D VAS					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 14	56 | 8.47 (1.58)	28 | -2.14 (2.07)	10.61	[5.73; 15.49]	<0.001
Day 42	61 | 12.40 (2.01)	32 | -0.68 (2.68)	13.08	[6.70; 19.46]	<0.001
Day 84	57 | 15.44 (2.08)	29 | -0.74 (2.81)	16.18	[9.47; 22.90]	<0.001
Day 126	58 | 16.16 (1.79)	29 | 1.29 (2.38)	14.87	[9.22; 20.52]	<0.001
Day 140	59 | 13.70 (1.98)	28 | -1.04 (2.70)	14.75	[8.34; 21.15]	<0.001
Day 154	56 | 14.32 (2.05)	28 | 0.60 (2.77)	13.72	[7.11; 20.33]	<0.001
Day 168	60 | 14.62 (2.03)	30 | -1.11 (2.75)	15.73	[9.17; 22.29]	<0.001
Day 126 - 168	**62 | 14.72 (1.77)**	**31 | -0.05 (2.35)**	**14.77**	**[9.20; 20.34]**	**<0.001**
Hedges' G			**1.16**	**[0.70; 1.62]**	

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

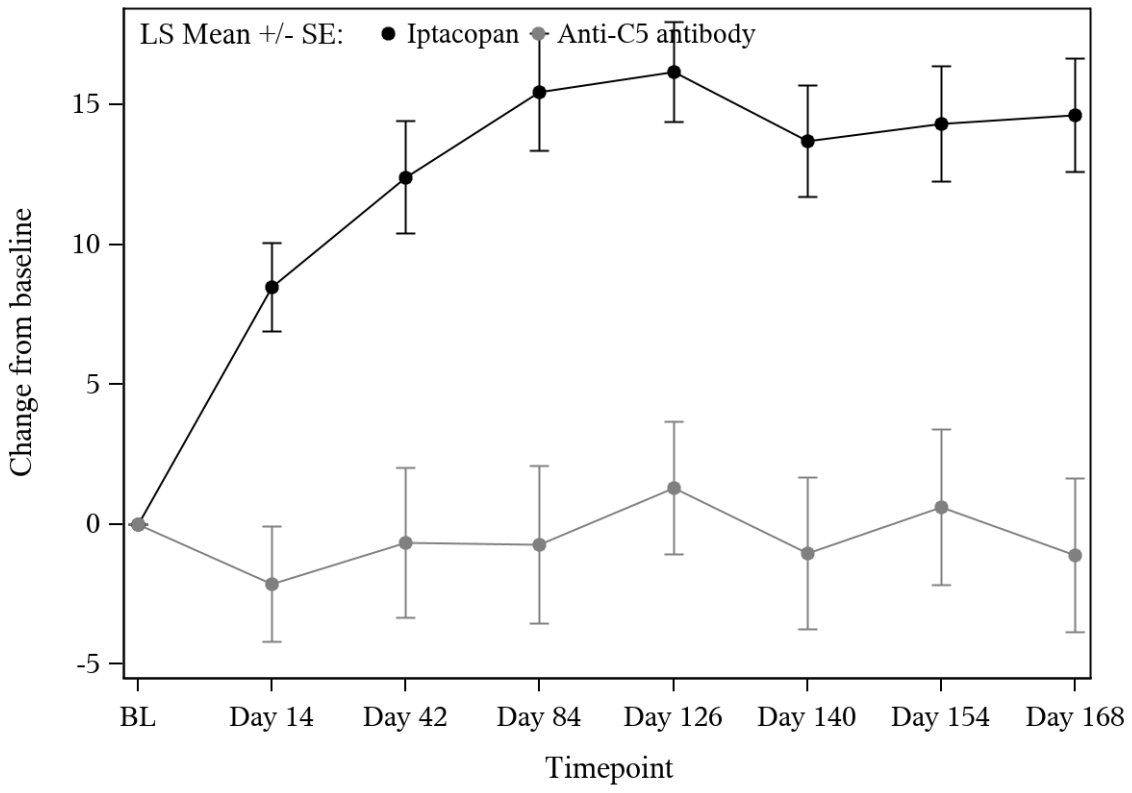
Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

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

Cut-off date for analysis: 06-Mar-2023

Figure 3-4.2 EQ-5D VAS: line chart of least squares mean change from baseline (Full Analysis Set)

EQ-5D VAS



Iptacopan	62	56	61	57	58	59	56	60
Anti-C5 antibody	33	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-4.3 EQ-5D VAS responder analysis (improvement defined as ≥ 15 point increase from baseline): GLMM analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
EQ-5D VAS						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 14	11 / 56 (19.6)	1 / 28 (3.6)	OR	28.83	[1.95; 426.06]	0.015
	21.1 [12.5; 31.7]	5.5 [1.2; 12.3]	RR	3.80	[1.63; 17.88]	
			RD	0.1536	[0.0572; 0.2670]	
Day 42	20 / 61 (32.8)	4 / 32 (12.5)	OR	33.65	[5.08; 222.68]	<0.001
	31.9 [22.5; 42.6]	7.6 [2.2; 15.0]	RR	4.19	[2.08; 13.99]	
			RD	0.2434	[0.1441; 0.3545]	
Day 84	23 / 57 (40.4)	2 / 29 (6.9)	OR	42.29	[6.40; 279.56]	<0.001
	42.0 [30.8; 53.9]	9.6 [3.0; 17.5]	RR	4.37	[2.28; 14.06]	
			RD	0.3256	[0.1961; 0.4569]	
Day 126	25 / 58 (43.1)	4 / 29 (13.8)	OR	52.98	[10.00; 280.79]	<0.001
	46.3 [35.2; 57.8]	12.1 [4.3; 20.3]	RR	3.85	[2.34; 10.27]	
			RD	0.3433	[0.2240; 0.4584]	
Day 140	28 / 59 (47.5)	2 / 28 (7.1)	OR	57.07	[11.74; 277.35]	<0.001
	48.3 [37.1; 58.3]	11.7 [4.1; 20.1]	RR	4.09	[2.42; 11.80]	
			RD	0.3637	[0.2435; 0.4743]	
Day 154	25 / 56 (44.6)	4 / 28 (14.3)	OR	61.45	[11.64; 324.50]	<0.001
	47.8 [36.3; 57.6]	9.9 [2.3; 18.5]	RR	4.72	[2.58; 20.38]	
			RD	0.3754	[0.2536; 0.4899]	
Day 168	28 / 60 (46.7)	3 / 30 (10.0)	OR	66.15	[8.62; 507.69]	<0.001
	47.0 [34.7; 57.2]	10.4 [1.9; 20.1]	RR	4.46	[2.28; 24.80]	
			RD	0.3656	[0.2294; 0.5002]	
Day 126 - 168	**62**	**31**	**OR**	**59.21**	**[12.03; 291.53]**	**<0.001**
	47.4 [36.7; 57.0]	**11.0 [3.7; 19.4]**	**RR**	**4.25**	**[2.44; 12.88]**	
			RD	**0.3628**	**[0.2452; 0.4705]**	

Treatment Groups		Comparison			
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
GLMM: Generalized linear mixed model
.....

Analysis methods:
OR, RR and RD from logistic GLMM with random intercept and week as continuous covariate:
Logit(proportion) = treatment + baseline value + treatment * week + baseline value * week + treatment * week * week + baseline value * week * week
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value were calculated from model linear predictors, at Day 126 - 168 from a linear function of linear predictors.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group at each visit. Then predicted proportions were averaged over the four visits Day 126 - 168. Then RR and RD were calculated for each visit and for Day 126 - 168. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Response (improvement) is defined as ≥ 15 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

Table 3-4.4 EQ-5D VAS responder analysis (improvement defined as ≥ 15 point increase from baseline): raw relative risk (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
EQ-5D VAS					
Day 14					
n / N' (%)	11 / 56 (19.6)	1 / 28 (3.6)	5.50	[0.75; 40.49]	0.094
Day 42					
n / N' (%)	20 / 61 (32.8)	4 / 32 (12.5)	2.62	[0.98; 7.02]	0.055
Day 84					
n / N' (%)	23 / 57 (40.4)	2 / 29 (6.9)	5.85	[1.48; 23.12]	0.012
Day 126					
n / N' (%)	25 / 58 (43.1)	4 / 29 (13.8)	3.13	[1.20; 8.13]	0.020
Day 140					
n / N' (%)	28 / 59 (47.5)	2 / 28 (7.1)	6.64	[1.70; 25.94]	0.006
Day 154					
n / N' (%)	25 / 56 (44.6)	4 / 28 (14.3)	3.13	[1.20; 8.10]	0.019
Day 168					
n / N' (%)	28 / 60 (46.7)	3 / 30 (10.0)	4.67	[1.54; 14.12]	0.006
Day 126 - Day 168					
n / N' (%)	**26 / 62 (41.9)**	**3 / 31 (9.7)**	**4.33**	**[1.42; 13.21]**	**0.010**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis methods:
RR was calculated without adjustment with Wald 95% CI and p-value. In case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.
For Day 126 - 168, observed responders per treatment group were derived from change from baseline of the average of the last four visits. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

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

Response (improvement) is defined as ≥ 15 point increase from baseline.

Cut-off date for analysis: 06-Mar-2023

3-5 PGIS

Table 3-5.1 PGIS: descriptive statistics by timepoint (Full Analysis Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**
PGIS		
	N' | Mean (SD)	**N' | Mean (SD)**
Baseline	62 | 1.55 (0.88)	33 | 1.70 (1.07)
Day 7	60 | 1.30 (0.89)	27 | 1.63 (0.79)
Day 14	57 | 1.07 (0.88)	28 | 1.71 (0.90)
Day 42	61 | 0.92 (0.76)	32 | 1.88 (0.98)
Day 84	57 | 0.77 (0.71)	29 | 1.66 (0.86)
Day 126	58 | 0.81 (0.74)	29 | 1.59 (0.87)
Day 140	58 | 0.91 (0.80)	28 | 1.71 (0.98)
Day 154	56 | 0.82 (0.79)	28 | 1.64 (0.99)
Day 168	60 | 0.73 (0.80)	30 | 1.57 (0.90)
Day 126 - 168	**62 | 0.82 (0.71)**	**31 | 1.67 (0.85)**

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

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-5.2 PGIS: MMRM analysis of change from baseline (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Adj. mean difference**	**[95% CI]**	**p-value**
PGIS					
	N' | LS Mean (SE)	**N' | LS Mean (SE)**			
Day 7	60 | -0.25 (0.09)	27 | -0.09 (0.13)	-0.16	[-0.47; 0.15]	0.303
Day 14	57 | -0.47 (0.11)	28 | 0.16 (0.14)	-0.63	[-0.98; -0.29]	<0.001
Day 42	61 | -0.64 (0.10)	32 | 0.21 (0.14)	-0.85	[-1.17; -0.52]	<0.001
Day 84	57 | -0.80 (0.10)	29 | -0.01 (0.14)	-0.79	[-1.12; -0.46]	<0.001
Day 126	58 | -0.75 (0.10)	29 | 0.02 (0.13)	-0.77	[-1.08; -0.46]	<0.001
Day 140	58 | -0.64 (0.11)	28 | 0.10 (0.14)	-0.75	[-1.09; -0.41]	<0.001
Day 154	56 | -0.78 (0.11)	28 | 0.01 (0.15)	-0.79	[-1.14; -0.44]	<0.001
Day 168	60 | -0.82 (0.10)	30 | -0.13 (0.14)	-0.68	[-1.02; -0.35]	<0.001
Day 126 - 168	**62 | -0.75 (0.09)**	**31 | -0.00 (0.12)**	**-0.75**	**[-1.03; -0.47]**	**<0.001**
Hedges' G			**-1.18**	**[-1.64; -0.72]**	

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

Analysis methods:
Adjusted mean (LS Mean) change from baseline and difference obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Anti-C5 antibody was the reference group for treatment group comparison.
LS Means and comparisons at Day 126 - 168 were calculated as linear function of the parameter estimates.

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

Hedges' G was calculated as model obtained adjusted mean difference / pooled SD with pooled SD = SE / sqrt (1/n1 + 1/n2) where SE is the standard error of the adjusted mean difference and n1 and n2 are the numbers of patients included in the analysis between Day 126 and 168 in treatment group 1 and 2, respectively.

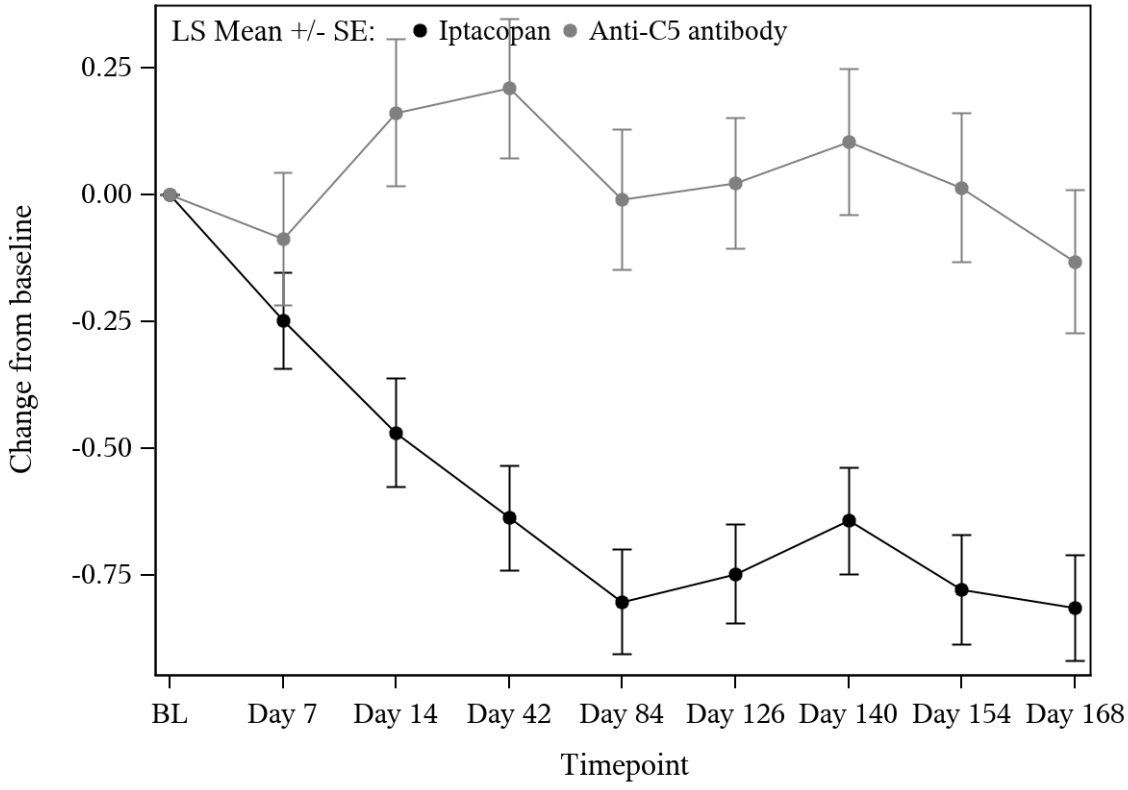
Intercurrent events stemming from discontinuation of treatment, breakthrough haemolysis events, MAVEs and red blood cell transfusions were handled with a treatment policy strategy, i.e. data obtained after the occurrence were not replaced by imputed values.
Missing values were not imputed, i.e. the analysis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

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

Cut-off date for analysis: 06-Mar-2023

Figure 3-5.2 PGIS: line chart of least squares mean change from baseline (Full Analysis Set)

PGIS



Iptacopan	62	60	57	61	57	58	58	56	60
Anti-C5 antibody	33	27	28	32	29	29	28	28	30

LS Mean: Least square mean
SE: Standard error
.....

Adjusted mean (LS Mean) change from baseline obtained from MMRM with unstructured covariance matrix:
Change from baseline = treatment + visit + treatment * visit + baseline value + baseline value * visit + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)

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

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

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

Cut-off date for analysis: 06-Mar-2023

Table 3-5.3 PGIS responder analysis (improvement defined as ≥ 1 step decrease in severity level from baseline): GLMM analysis (Full Analysis Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
PGIS						
	n / N' (%) Predict. % [95% CI]	**n / N' (%) Predict. % [95% CI]**				
Day 7	24 / 60 (40.0)	8 / 27 (29.6)	OR	6.15	[1.51; 25.06]	0.011
	43.6 [32.1; 54.9]	22.3 [7.7; 35.7]	RR	1.97	[1.20; 5.23]	
			RD	0.2108	[0.0699; 0.3604]	
Day 14	27 / 57 (47.4)	3 / 28 (10.7)	OR	8.61	[2.35; 31.62]	0.001
	42.8 [32.3; 53.1]	19.6 [7.8; 30.4]	RR	2.19	[1.42; 5.13]	
			RD	0.2307	[0.1122; 0.3556]	
Day 42	32 / 61 (52.5)	6 / 32 (18.8)	OR	24.76	[6.82; 89.92]	<0.001
	52.4 [42.8; 61.7]	18.2 [9.7; 26.8]	RR	2.85	[1.99; 5.22]	
			RD	0.3407	[0.2340; 0.4443]	
Day 84	34 / 57 (59.6)	7 / 29 (24.1)	OR	50.45	[11.37; 223.92]	<0.001
	57.1 [45.6; 67.6]	16.5 [7.9; 25.4]	RR	3.46	[2.25; 6.89]	
			RD	0.4064	[0.2809; 0.5237]	
Day 126	33 / 58 (56.9)	6 / 29 (20.7)	OR	36.11	[10.01; 130.27]	<0.001
	58.9 [48.3; 68.9]	20.7 [11.4; 31.0]	RR	2.82	[1.94; 4.98]	
			RD	0.3832	[0.2649; 0.4963]	
Day 140	31 / 58 (53.4)	5 / 28 (17.9)	OR	25.60	[7.75; 84.59]	<0.001
	60.0 [49.5; 69.9]	23.7 [13.5; 34.6]	RR	2.51	[1.78; 4.36]	
			RD	0.3612	[0.2497; 0.4846]	
Day 154	34 / 56 (60.7)	9 / 28 (32.1)	OR	16.16	[4.82; 54.19]	<0.001
	59.4 [48.4; 69.8]	26.6 [15.9; 37.3]	RR	2.22	[1.60; 3.68]	
			RD	0.3250	[0.2098; 0.4617]	
Day 168	37 / 60 (61.7)	9 / 30 (30.0)	OR	9.08	[2.21; 37.30]	0.002
	58.4 [46.6; 69.7]	31.7 [19.6; 43.1]	RR	1.85	[1.34; 2.97]	
			RD	0.2710	[0.1332; 0.4227]	
Day 126 - 168	**62**	**31**	**OR**	**19.19**	**[5.90; 62.42]**	**<0.001**
	59.2 [48.9; 69.0]	**25.6 [15.5; 35.6]**	**RR**	**2.30**	**[1.67; 3.70]**	
			RD	**0.3340**	**[0.2215; 0.4534]**	

Treatment Groups		Comparison			
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
GLMM: Generalized linear mixed model
.....

Analysis methods:
OR, RR and RD from logistic GLMM with random intercept and week as continuous covariate:
Logit(proportion) = treatment + baseline value + treatment * week + baseline value * week + treatment * week * week + baseline value * week * week
Anti-C5 antibody was the reference group for treatment group comparison.
OR with 95% Wald CI and p-value were calculated from model linear predictors, at Day 126 - 168 from a linear function of linear predictors.
Predicted proportions, RR and RD were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group at each visit. Then predicted proportions were averaged over the four visits Day 126 - 168. Then RR and RD were calculated for each visit and for Day 126 - 168. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

Response (improvement) is defined as ≥ 1 step decrease in severity level from baseline.

Cut-off date for analysis: 06-Mar-2023

Table 3-5.4 PGIS responder analysis (improvement defined as ≥ 1 step decrease in severity level from baseline): raw relative risk (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
PGIS					
Day 7					
n / N' (%)	24 / 60 (40.0)	8 / 27 (29.6)	1.35	[0.70; 2.61]	0.372
Day 14					
n / N' (%)	27 / 57 (47.4)	3 / 28 (10.7)	4.42	[1.47; 13.33]	0.008
Day 42					
n / N' (%)	32 / 61 (52.5)	6 / 32 (18.8)	2.80	[1.31; 5.98]	0.008
Day 84					
n / N' (%)	34 / 57 (59.6)	7 / 29 (24.1)	2.47	[1.25; 4.88]	0.009
Day 126					
n / N' (%)	33 / 58 (56.9)	6 / 29 (20.7)	2.75	[1.30; 5.80]	0.008
Day 140					
n / N' (%)	31 / 58 (53.4)	5 / 28 (17.9)	2.99	[1.31; 6.86]	0.010
Day 154					
n / N' (%)	34 / 56 (60.7)	9 / 28 (32.1)	1.89	[1.06; 3.37]	0.031
Day 168					
n / N' (%)	37 / 60 (61.7)	9 / 30 (30.0)	2.06	[1.15; 3.68]	0.015
Day 126 - Day 168					
n / N' (%)	**27 / 62 (43.5)**	**5 / 31 (16.1)**	**2.70**	**[1.15; 6.33]**	**0.022**

N: Number of patients in the analysis set
N': Number of patients with evaluable baseline and post-baseline score at visit
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis methods:
RR was calculated without adjustment with Wald 95% CI and p-value. In case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.
For Day 126 - 168, observed responders per treatment group were derived from change from baseline of the average of the last four visits. Patients with non-missing value at least at baseline and at one of the four visits were included in the calculation.

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

Response (improvement) is defined as ≥ 1 step decrease in severity level from baseline.

Cut-off date for analysis: 06-Mar-2023

4 Safety analyses

Table 4-1 Adverse events overview: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
Any adverse event, n (%)	52 (83.9)	28 (80.0)	OR	1.30	[0.45; 3.79]	0.631
			RR	1.05	[0.86; 1.28]	0.641
			RD	0.0387	[-0.1224; 0.1998]	0.638
Any severe adverse event, n (%)	3 (4.8)	3 (8.6)	OR	0.54	[0.10; 2.84]	0.469
			RR	0.56	[0.12; 2.65]	0.468
			RD	-0.0373	[-0.1444; 0.0697]	0.494
Any serious adverse event, n (%)	6 (9.7)	5 (14.3)	OR	0.64	[0.18; 2.28]	0.494
			RR	0.68	[0.22; 2.06]	0.492
			RD	-0.0461	[-0.1834; 0.0912]	0.511

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table displays TEAE, defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

Cut-off date for analysis: 06-Mar-2023

Table 4-2 Adverse events by SOC and PT: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value
Infections and infestations, n (%)	25 (40.3)	17 (48.6)	OR	0.72	[0.31; 1.65]	0.432
			RR	0.83	[0.53; 1.31]	0.424
			RD	-0.0825	[-0.2882; 0.1232]	0.432
Nasopharyngitis, n (%)	7 (11.3)	3 (8.6)	OR	1.36	[0.33; 5.62]	0.673
			RR	1.32	[0.36; 4.77]	0.675
			RD	0.0272	[-0.0945; 0.1489]	0.661
COVID-19, n (%)	5 (8.1)	9 (25.7)	OR	0.25	[0.08; 0.83]	0.023
			RR	0.31	[0.11; 0.86]	0.025
			RD	-0.1765	[-0.3364; -0.0166]	0.030
Gastrointestinal disorders, n (%)	20 (32.3)	6 (17.1)	OR	2.30	[0.82; 6.43]	0.112
			RR	1.88	[0.83; 4.24]	0.127
			RD	0.1512	[-0.0195; 0.3218]	0.083
Diarrhoea, n (%)	9 (14.5)	2 (5.7)	OR	2.80	[0.57; 13.78]	0.205
			RR	2.54	[0.58; 11.10]	0.215
			RD	0.0880	[-0.0286; 0.2046]	0.139
Nervous system disorders, n (%)	16 (25.8)	1 (2.9)	OR	11.83	[1.49; 93.56]	0.019
			RR	9.03	[1.25; 65.24]	0.029
			RD	0.2295	[0.1074; 0.3516]	<0.001
Headache, n (%)	11 (17.7)	1 (2.9)	OR	7.33	[0.90; 59.44]	0.062
			RR	6.21	[0.84; 46.10]	0.074
			RD	0.1488	[0.0389; 0.2588]	0.008
Investigations, n (%)	12 (19.4)	5 (14.3)	OR	1.44	[0.46; 4.49]	0.530
			RR	1.35	[0.52; 3.53]	0.534
			RD	0.0507	[-0.1013; 0.2027]	0.513
Musculoskeletal and connective tissue disorders, n (%)	12 (19.4)	5 (14.3)	OR	1.44	[0.46; 4.49]	0.530
			RR	1.35	[0.52; 3.53]	0.534
			RD	0.0507	[-0.1013; 0.2027]	0.513
General disorders and administration site conditions, n (%)	10 (16.1)	4 (11.4)	OR	1.49	[0.43; 5.16]	0.529
			RR	1.41	[0.48; 4.17]	0.533
			RD	0.0470	[-0.0926; 0.1866]	0.509
Blood and lymphatic system disorders, n (%)	8 (12.9)	8 (22.9)	OR	0.50	[0.17; 1.48]	0.210
			RR	0.56	[0.23; 1.37]	0.207
			RD	-0.0995	[-0.2618; 0.0627]	0.229
Breakthrough haemolysis, n (%)	2 (3.2)	6 (17.1)	OR	0.16	[0.03; 0.85]	0.031
			RR	0.19	[0.04; 0.88]	0.034
			RD	-0.1392	[-0.2715; -0.0068]	0.039
Renal and urinary disorders, n (%)	7 (11.3)	1 (2.9)	OR	4.33	[0.51; 36.72]	0.179
			RR	3.95	[0.51; 30.82]	0.190

Treatment Groups		Comparison			
Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value
		RD	0.0843	[-0.0119; 0.1805]	0.086

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table displays TEAE that occurred in at least one treatment arm in ≥ 10% of patients. TEAE are defined as events that started during th e on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

MedDRA Version: 25.0

Cut-off date for analysis: 06-Mar-2023

Table 4-3 Severe adverse events by SOC and PT: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
Blood and lymphatic system disorders, n (%)	1 (1.6)	2 (5.7)	OR	0.27	[0.02; 3.10]	0.293
			RR	0.28	[0.03; 3.00]	0.294
			RD	-0.0410	[-0.1241; 0.0420]	0.333
Infections and infestations, n (%)	1 (1.6)	2 (5.7)	OR	0.27	[0.02; 3.10]	0.293
			RR	0.28	[0.03; 3.00]	0.294
			RD	-0.0410	[-0.1241; 0.0420]	0.333

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table displays TEAE that occurred in at least one treatment arm in ≥ 5% of patients. TEAE are defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

MedDRA Version: 25.0

Cut-off date for analysis: 06-Mar-2023

Table 4-4 Serious adverse events by SOC and PT: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
Infections and infestations, n (%)	2 (3.2)	3 (8.6)	OR	0.36	[0.06; 2.24]	0.271
			RR	0.38	[0.07; 2.15]	0.271
			RD	-0.0535	[-0.1561; 0.0492]	0.307
COVID-19, n (%)	1 (1.6)	2 (5.7)	OR	0.27	[0.02; 3.10]	0.293
			RR	0.28	[0.03; 3.00]	0.294
			RD	-0.0410	[-0.1241; 0.0420]	0.333
Blood and lymphatic system disorders, n (%)	0 (0.0)	2 (5.7)	OR	0.11	[<0.01; 2.30]	0.153
			RR	0.11	[<0.01; 2.32]	0.158
			RD	-0.0571	[-0.1340; 0.0198]	0.145

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table displays TEAE that occurred in at least one treatment arm in ≥ 5% of patients. TEAE are defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

MedDRA Version: 25.0

Cut-off date for analysis: 06-Mar-2023

Table 4-5 Adverse events of special interest: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value
Decreased platelets, n (%)	4 (6.5)	0 (0.0)	OR	5.46	[0.29; >99.99]	0.260
			RR	5.14	[0.28; 92.81]	0.267
			RD	0.0645	[0.0034; 0.1257]	0.039
Infections caused by encapsulated bacteria, n (%)	2 (3.2)	1 (2.9)	OR	1.13	[0.10; 12.96]	0.920
			RR	1.13	[0.11; 12.01]	0.920
			RD	0.0037	[-0.0669; 0.0743]	0.918
Severe infections caused by encapsulated bacteria, n (%)	0 (0.0)	1 (2.9)	OR	0.18	[<0.01; 4.64]	0.304
			RR	0.19	[<0.01; 4.55]	0.306
			RD	-0.0286	[-0.0838; 0.0266]	0.310
Serious infections caused by encapsulated bacteria, n (%)	1 (1.6)	1 (2.9)	OR	0.56	[0.03; 9.20]	0.683
			RR	0.56	[0.04; 8.75]	0.683
			RD	-0.0124	[-0.0759; 0.0510]	0.701
PNH Haemolysis and Thrombosis, n (%)	10 (16.1)	10 (28.6)	OR	0.48	[0.18; 1.30]	0.150
			RR	0.56	[0.26; 1.22]	0.147
			RD	-0.1244	[-0.2999; 0.0510]	0.165
Severe pNH Haemolysis and Thrombosis, n (%)	1 (1.6)	3 (8.6)	OR	0.17	[0.02; 1.75]	0.138
			RR	0.19	[0.02; 1.74]	0.141
			RD	-0.0696	[-0.1675; 0.0283]	0.164
Serious pNH Haemolysis and Thrombosis, n (%)	1 (1.6)	3 (8.6)	OR	0.17	[0.02; 1.75]	0.138
			RR	0.19	[0.02; 1.74]	0.141
			RD	-0.0696	[-0.1675; 0.0283]	0.164
Serious or severe infections, n (%)	2 (3.2)	3 (8.6)	OR	0.36	[0.06; 2.24]	0.271
			RR	0.38	[0.07; 2.15]	0.271
			RD	-0.0535	[-0.1561; 0.0492]	0.307
Severe infections, n (%)	1 (1.6)	2 (5.7)	OR	0.27	[0.02; 3.10]	0.293
			RR	0.28	[0.03; 3.00]	0.294
			RD	-0.0410	[-0.1241; 0.0420]	0.333
Serious infections, n (%)	2 (3.2)	3 (8.6)	OR	0.36	[0.06; 2.24]	0.271
			RR	0.38	[0.07; 2.15]	0.271
			RD	-0.0535	[-0.1561; 0.0492]	0.307
Testicular effects, n (%)	1 (1.6)	0 (0.0)	OR	1.73	[0.07; 43.65]	0.739
			RR	1.71	[0.07; 40.99]	0.739
			RD	0.0161	[-0.0152; 0.0475]	0.313
Thyroid changes, n (%)	1 (1.6)	0 (0.0)	OR	1.73	[0.07; 43.65]	0.739
			RR	1.71	[0.07; 40.99]	0.739
			RD	0.0161	[-0.0152; 0.0475]	0.313

Treatment Groups		Comparison			
Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	Para-meter	Esti-mate	[95% CI]	p-value

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table shows all pre-specified AESIs which occurred in at least one patient.

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Table 4-6 Adverse events overview, disease specific events excluded: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
Any adverse event, n (%)	52 (83.9)	27 (77.1)	OR	1.54	[0.54; 4.36]	0.415
			RR	1.09	[0.88; 1.34]	0.437
			RD	0.0673	[-0.0993; 0.2338]	0.428
Any severe adverse event, n (%)	3 (4.8)	2 (5.7)	OR	0.84	[0.13; 5.28]	0.852
			RR	0.85	[0.15; 4.83]	0.851
			RD	-0.0088	[-0.1024; 0.0849]	0.855
Any serious adverse event, n (%)	6 (9.7)	4 (11.4)	OR	0.83	[0.22; 3.17]	0.786
			RR	0.85	[0.26; 2.80]	0.785
			RD	-0.0175	[-0.1461; 0.1110]	0.789

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table displays TEAE, defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

Excluded disease specific events: Preferred Term breakthrough haemolysis or haemoglobinuria.

Cut-off date for analysis: 06-Mar-2023

Table 4-7 Hospitalization: binary analysis (Safety Set)

	Treatment Groups		Comparison			
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**Para-meter**	**Esti-mate**	**[95% CI]**	**p-value**
Any hospitalization, n (%)	5 (8.1)	5 (14.3)	OR	0.53	[0.14; 1.96]	0.339
			RR	0.56	[0.18; 1.82]	0.337
			RD	-0.0622	[-0.1965; 0.0721]	0.364

N: Number of patients in the analysis set
n: Number of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
TEAE: Treatment Emergent Adverse Event
.....

Analysis methods:
OR, RR and RD with Wald 95% CI and p-value. For calculation of OR and RR, in case of zero events in only one treatment arm, one patient with 0.5 events was added to each treatment arm.
Anti-C5 antibody was the reference group for treatment group comparison.

The table considers serious TEAE with hospitalization as reason for seriousness.
TEAE are defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

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Table 4-8 Number of hospitalizations (Safety Set)

	Treatment Groups	
	Iptacopan (N = 62)	**Anti-C5 Antibody (N = 35)**
Number of hospitalizations		
0	57 (91.9)	30 (85.7)
1	3 (4.8)	4 (11.4)
2	2 (3.2)	0 (0.0)
3	0 (0.0)	0 (0.0)
4	0 (0.0)	1 (2.9)

N: Number of patients in the analysis set

.....

The table considers serious TEAE with hospitalization as reason for seriousness. As one hospitalization may by documented by more than one serious adverse events, the number of hospitalizations was determined by medical review based of the patient narratives.
TEAE are defined as events that started during the on-treatment period.
The on-treatment period for Iptacopan is from first dose date until 7 days after the date of last dose administered or the date of the day 168 visit, whichever is earlier.
The on-treatment period for Anti-C5 is from first dose date until one day before the next planned dose or the date of the day 168 visit, whichever is earlier.

N is the denominator for percentage (%) calculation.

Cut-off date for analysis: 06-Mar-2023

5 Subgroup analysis

5-1 Subgroup analysis for efficacy

5-1.1 Hemoglobin levels

Table 5-1.1.1 Increase in hemoglobin levels ≥ 2 g/dL from baseline without requiring pRBC transfusions: logistic model analysis - subgroup analysis (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	RR	[95% CI]	p-value
Increase in hemoglobin levels ≥ 2 g/dL from baseline[a] without requiring pRBC transfusions[b]					
	n / N' (%)	n / N' (%)			
Length of time since diagnosis					
Interaction test	**p = 0.608**				
< 5 years	15 / 18 (83.3)	0 / 11 (0.0)	10.81	[3.78; 27.39]	0.006
≥ 5 years	36 / 42 (85.7)	0 / 24 (0.0)	27.21	[13.47; 61.30]	<0.001
Age categories					
Interaction test	**p = 0.935**				
< 45 years	20 / 23 (87.0)	0 / 16 (0.0)	11.66	[5.24; 20.61]	0.001
≥ 45 years	31 / 37 (83.8)	0 / 19 (0.0)	29.44	[9.76; 64.11]	<0.001
Sex					
Interaction test	**p = 0.486**				
Male	15 / 19 (78.9)	0 / 11 (0.0)	8.85	[2.74; 52.75]	0.038
Female	36 / 41 (87.8)	0 / 24 (0.0)	23.15	[10.66; 43.82]	<0.001
Baseline hemoglobin					
Interaction test	**p = 0.618**				
< 9 g/dL	24 / 31 (77.4)	0 / 18 (0.0)	23.19	[12.99; 45.97]	<0.001
≥ 9 g/dL	27 / 29 (93.1)	0 / 17 (0.0)	18.51	[9.13; 43.14]	<0.001
History of MAVE prior to screening					
Interaction test	**p = 0.566**				
No	39 / 48 (81.3)	0 / 25 (0.0)	28.97	[14.59; 59.17]	<0.001
Yes	12 / 12 (100.0)	0 / 10 (0.0)	6.73	[3.72; 9.65]	0.033
Anti-C5 medication history 6 months prior to randomization					
Interaction test	**p = 0.786**				
Eculizumab	33 / 38 (86.8)	0 / 23 (0.0)	27.20	[14.11; 52.06]	<0.001
Ravulizumab	18 / 22 (81.8)	0 / 12 (0.0)	26.95	[5.31; 59.63]	0.013
Transfusion in the last 6 months prior to randomization					
Interaction test	**p = 0.846**				
No	24 / 27 (88.9)	0 / 14 (0.0)	19.20	[6.08; 44.84]	0.006
Yes	27 / 33 (81.8)	0 / 21 (0.0)	21.97	[11.31; 38.61]	<0.001

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**
Number of transfusions in the last 6 months prior to randomization					
Interaction test	**p = 0.873**				
< 2	31 / 37 (83.8)	0 / 21 (0.0)	25.36	[12.69; 50.04]	<0.001
≥ 2	20 / 23 (87.0)	0 / 14 (0.0)	12.85	[5.28; 26.46]	0.002
Duration of anti-C5 treatment					
Interaction test	**p = 0.476**				
< 12 months	9 / 11 (81.8)	0 / 6 (0.0)	3.91	[0.96; 20.96]	0.063
≥ 12 months	42 / 49 (85.7)	0 / 29 (0.0)	33.52	[17.82; 72.03]	<0.001

N: Number of patients in the analysis set
N': Number of patients included in the analysis
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis method for interaction test:
Logistic regression model using Firth's penalized maximum likelihood estimation:
Logit(proportion) = treatment + subgroup factor + treatment * subgroup factor + baseline hemoglobin (indicator of hemoglobin ≥ 9 g/dL) + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Covariates baseline hemoglobin, transfusion history, prior anti-C5-treatment, sex and age were excluded from the model equation if they were connected to the subgroup factor.
The interaction test p-value is the type III p-value for the interaction treatment * subgroup factor.

Analysis methods for within-subgroup analysis:
RR and p-value from logistic regression model using Firth's penalized maximum likelihood estimation:
Logit(proportion) = treatment + baseline hemoglobin (indicator of hemoglobin ≥ 9 g/dL) + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Covariates baseline hemoglobin, transfusion history, prior anti-C5-treatment, sex and age were excluded from the model equation if they were connected to the subgroup factor.
Anti-C5 antibody was the reference group for treatment group comparison.
p-value from test on model linear predictor of treatment.
Predicted proportions and RR were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group. Then RR was calculated from predicted proportions. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

a: between Day 126 and Day 168 (at least 3 out of 4 scheduled assessments)
b: between Day 14 and Day 168

Cut-off date for analysis: 06-Mar-2023

Table 5-1.1.2 Hemoglobin levels ≥ 12 g/dL without requiring pRBC transfusions: logistic model analysis - subgroup analysis (Full Analysis Set)

	Treatment Groups		Comparison		
	Iptacopan (N = 62)	Anti-C5 antibody (N = 35)	RR	[95% CI]	p-value
Hemoglobin levels ≥ 12 g/dL[a] without requiring pRBC transfusions[b]					
	n / N' (%)	n / N' (%)			
Length of time since diagnosis					
Interaction test	**p = 0.677**				
< 5 years	12 / 18 (66.7)	0 / 11 (0.0)	10.97	[2.51; 45.96]	0.031
≥ 5 years	30 / 42 (71.4)	0 / 24 (0.0)	28.76	[13.66; 65.41]	<0.001
Age categories					
Interaction test	**p = 0.871**				
< 45 years	16 / 23 (69.6)	0 / 16 (0.0)	14.59	[4.52; 30.94]	0.004
≥ 45 years	26 / 37 (70.3)	0 / 19 (0.0)	19.95	[7.09; 41.14]	0.001
Sex					
Interaction test	**p = 0.587**				
Male	12 / 19 (63.2)	0 / 11 (0.0)	6.97	[2.38; 23.84]	0.014
Female	30 / 41 (73.2)	0 / 24 (0.0)	24.28	[9.98; 61.09]	<0.001
Baseline hemoglobin					
Interaction test	**p = 0.196**				
< 9 g/dL	15 / 31 (48.4)	0 / 18 (0.0)	12.27	[5.85; 25.49]	0.020
≥ 9 g/dL	27 / 29 (93.1)	0 / 17 (0.0)	18.51	[9.13; 43.14]	<0.001
History of MAVE prior to screening					
Interaction test	**p = 0.906**				
No	32 / 48 (66.7)	0 / 25 (0.0)	36.52	[13.69; 98.94]	<0.001
Yes	10 / 12 (83.3)	0 / 10 (0.0)	5.98	[2.08; 12.68]	0.048
Anti-C5 medication history 6 months prior to randomization					
Interaction test	**p = 0.964**				
Eculizumab	27 / 38 (71.1)	0 / 23 (0.0)	23.36	[9.39; 47.11]	<0.001
Ravulizumab	15 / 22 (68.2)	0 / 12 (0.0)	16.35	[3.83; 54.20]	0.018
Transfusion in the last 6 months prior to randomization					
Interaction test	**p = 0.477**				
No	23 / 27 (85.2)	0 / 14 (0.0)	17.30	[5.51; 43.22]	0.004
Yes	19 / 33 (57.6)	0 / 21 (0.0)	15.09	[5.74; 32.40]	0.003
Number of transfusions in the last 6 months prior to randomization					
Interaction test	**p = 0.526**				
< 2	28 / 37 (75.7)	0 / 21 (0.0)	24.87	[11.78; 50.37]	<0.001
≥ 2	14 / 23 (60.9)	0 / 14 (0.0)	12.57	[3.42; 45.04]	0.009
Duration of anti-C5 treatment					
Interaction test	**p = 0.532**				
< 12 months	6 / 11 (54.5)	0 / 6 (0.0)	3.54	[0.70; 17.96]	0.147
≥ 12 months	36 / 49 (73.5)	0 / 29 (0.0)	30.16	[15.14; 60.18]	<0.001

Treatment Groups		Comparison		
Iptacopan (N = 62)	**Anti-C5 antibody (N = 35)**	**RR**	**[95% CI]**	**p-value**

N: Number of patients in the analysis set
N': Number of patients included in the analysis
n: Number of patients with response
CI: Confidence interval
RR: Relative risk
.....

Analysis method for interaction test:
Logistic regression model using Firth's penalized maximum likelihood estimation:
Logit(proportion) = treatment + subgroup factor + treatment * subgroup factor + baseline hemoglobin (indicator of hemoglobin ≥ 9 g/dL) + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Covariates baseline hemoglobin, transfusion history, prior anti-C5-treatment, sex and age were excluded from the model equation if they were connected to the subgroup factor.
The interaction test p-value is the type III p-value for the interaction treatment * subgroup factor.

Analysis methods for within-subgroup analysis:
RR and p-value from logistic regression model using Firth's penalized maximum likelihood estimation:
Logit(proportion) = treatment + baseline hemoglobin (indicator of hemoglobin ≥ 9 g/dL) + transfusion history + prior anti-C5-treatment + sex + age (indicator of age ≥ 45 years)
Covariates baseline hemoglobin, transfusion history, prior anti-C5-treatment, sex and age were excluded from the model equation if they were connected to the subgroup factor.
Anti-C5 antibody was the reference group for treatment group comparison.
p-value from test on model linear predictor of treatment.
Predicted proportions and RR were calculated by marginal standardization from predicted values. First, predicted proportions were calculated by marginal standardization for each treatment group. Then RR was calculated from predicted proportions. Estimates and 95% CI were constructed by median and 2.5% and 97.5% percentiles from 1000 bootstrap samples.

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

a: between Day 126 and Day 168 (at least 3 out of 4 scheduled assessments)
b: between Day 14 and Day 168

Cut-off date for analysis: 06-Mar-2023