FIGURES

Fig. 1

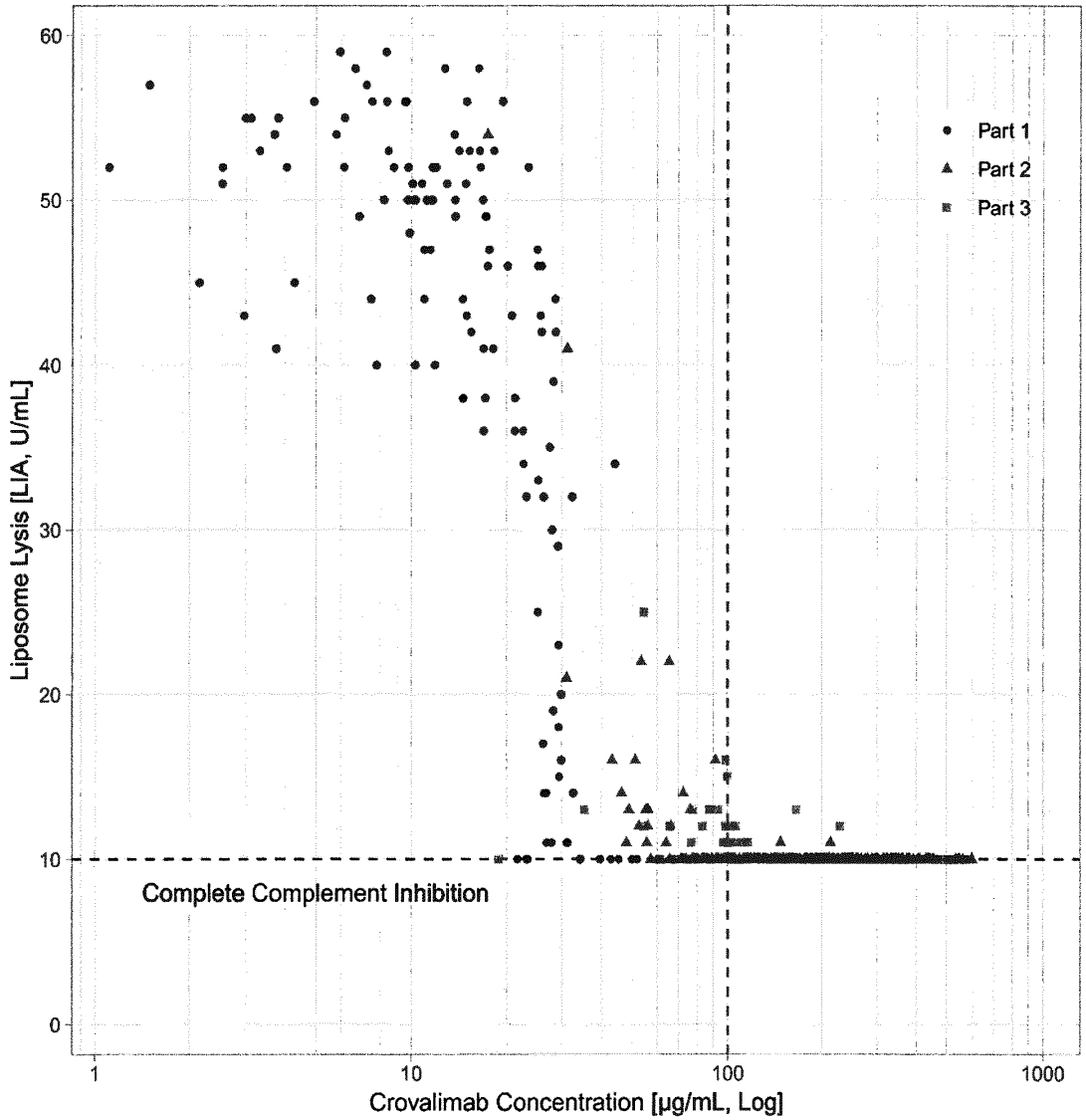


Fig. 2

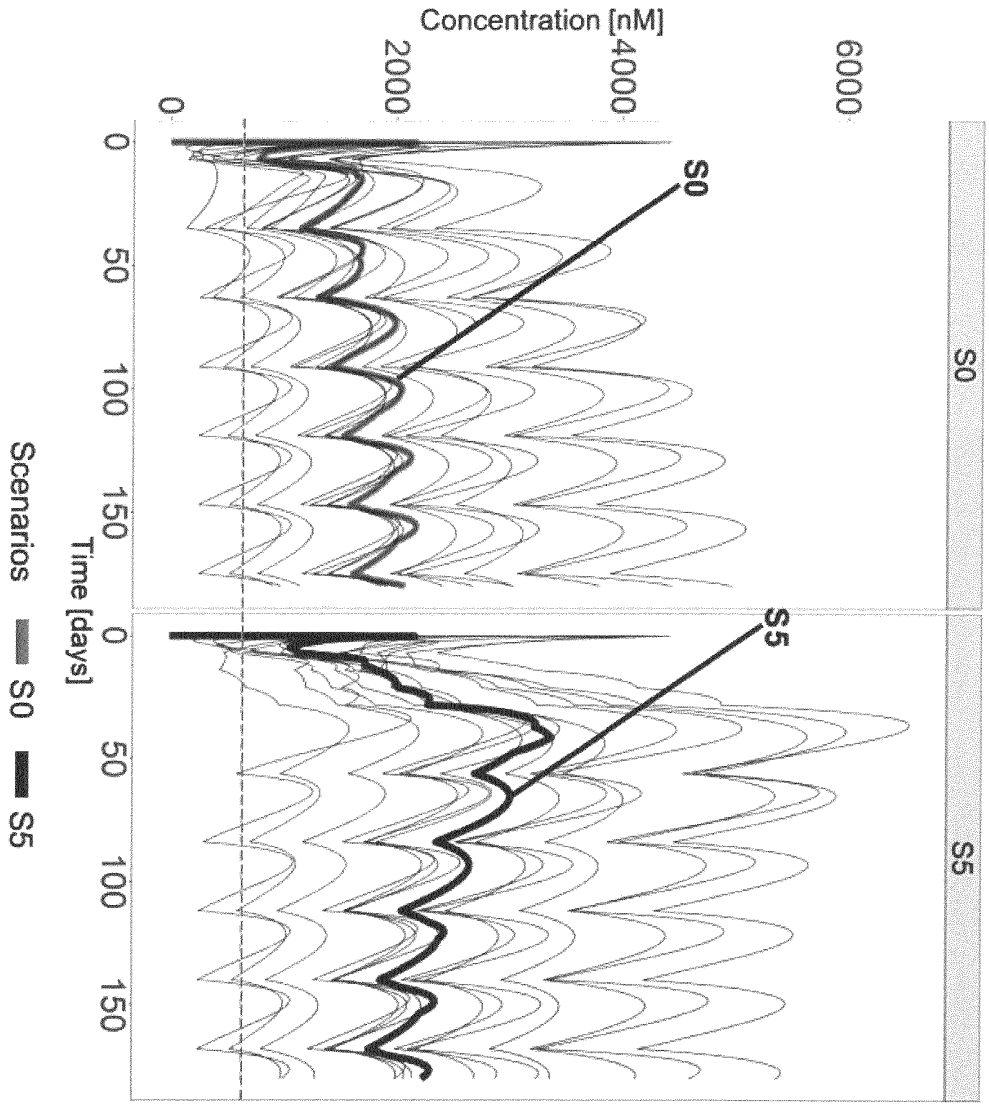

Concentration [nM]
0
2000
4000
6000
S0
S5
Time [days]
0
50
100
150
Scenarios
S0
S5

Fig. 3

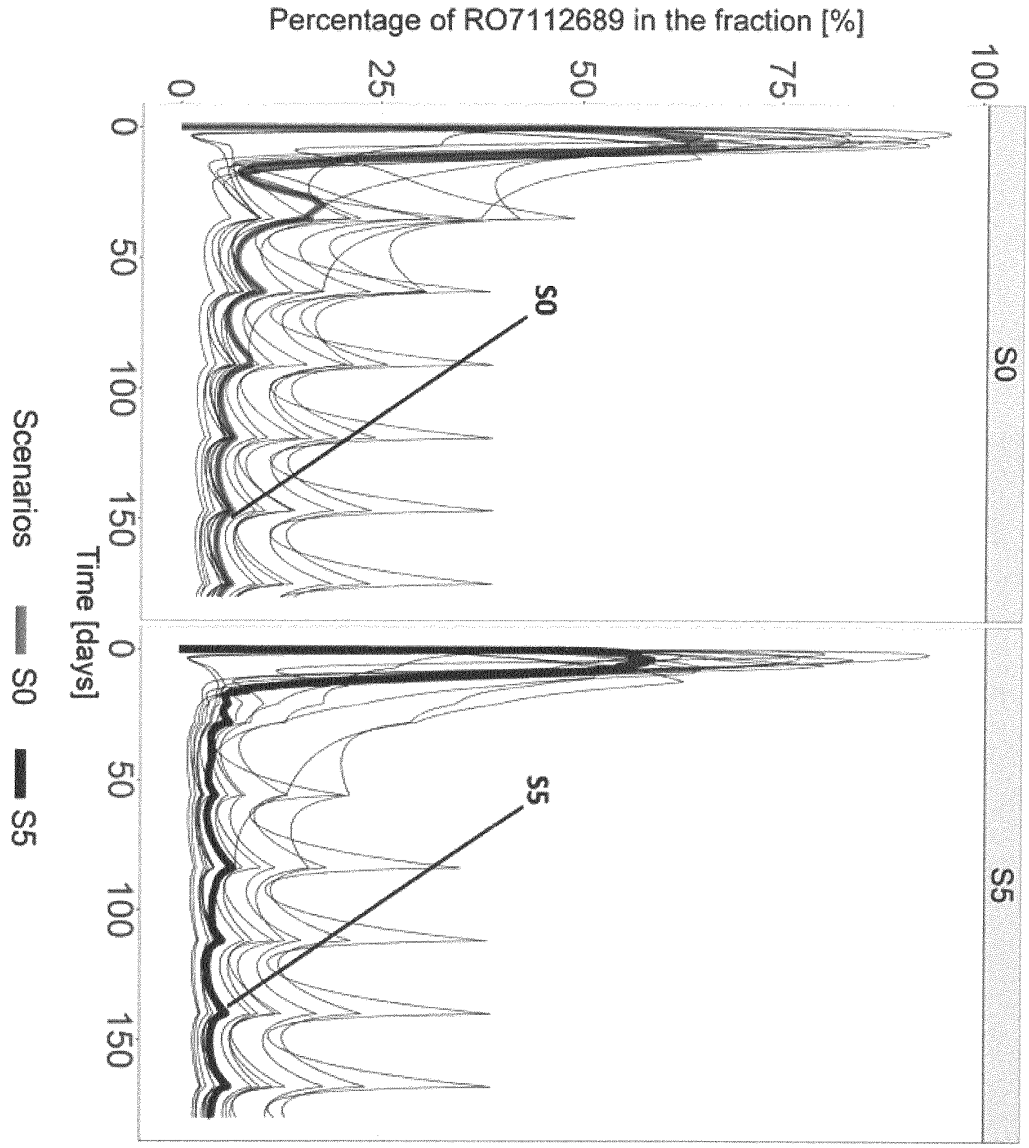

Percentage of RO7112689 in the fraction [%]
0
25
50
75
100
Time [days]
0
50
100
150
S0
S5
Scenarios
S0
S5

Fig. 4

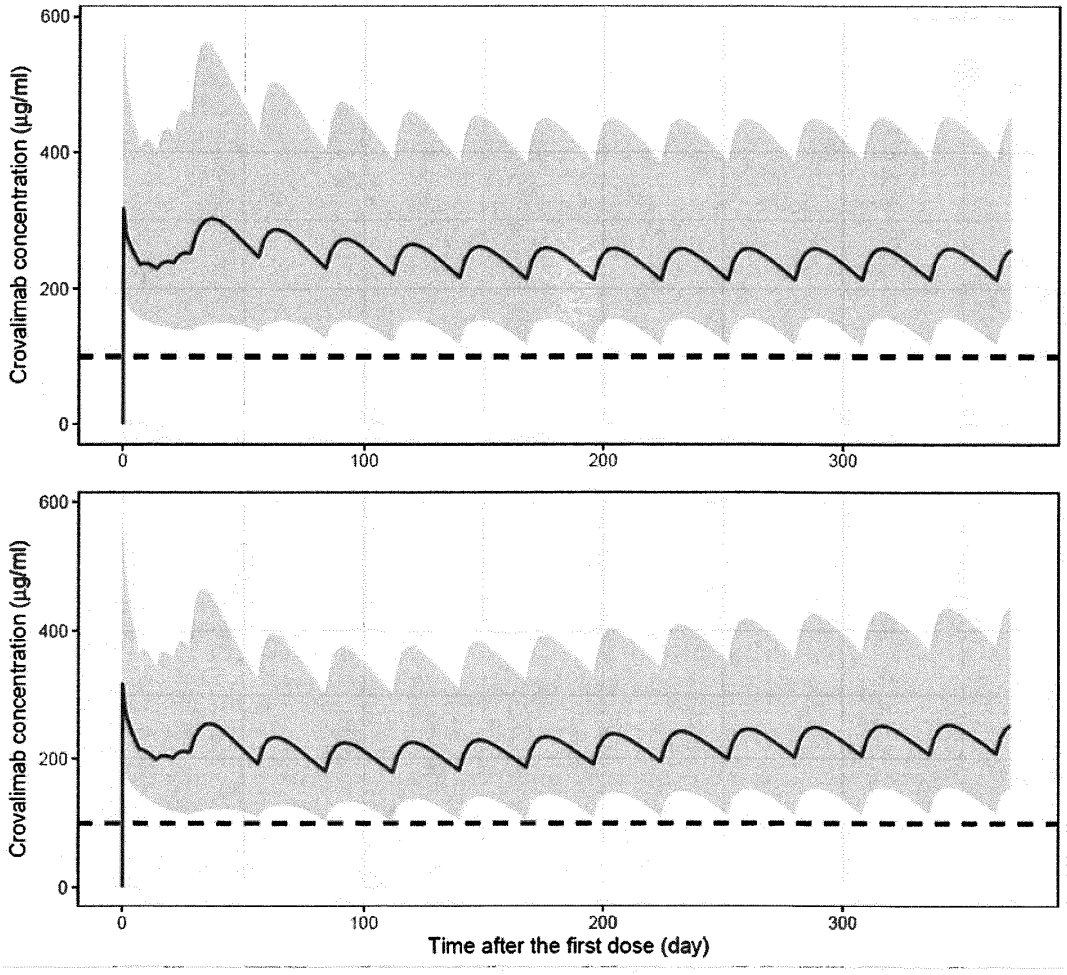

600
400
200
0
Crovalimab concentration (µg/ml)
0
100
200
300
600
400
200
0
Crovalimab concentration (µg/ml)
0
100
200
300
Time after the first dose (day)

Fig. 5

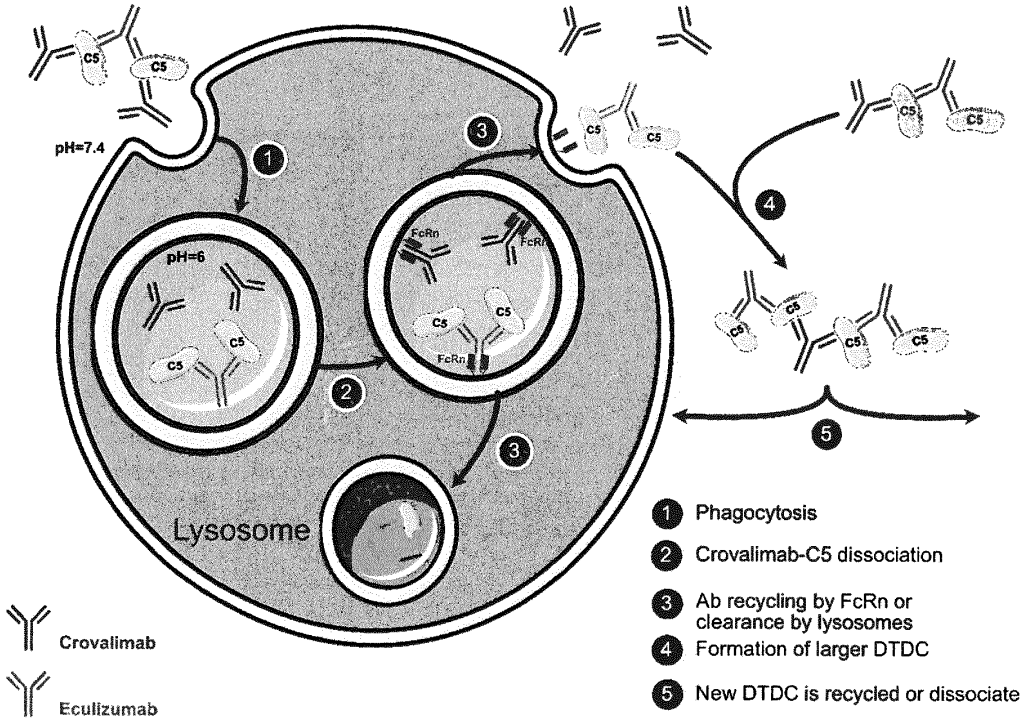

C5
pH=7.4
pH=6
FcRn
Lysosome
Crovalimab
Eculizumab
1 Phagocytosis
2 Crovalimab-C5 dissociation
3 Ab recycling by FcRn or clearance by lysosomes
4 Formation of larger DTDC
5 New DTDC is recycled or dissociate

Fig. 6

Baseline characteristics of patients with PNH in COMPOSER Part 4

Characteristics	Naive (n = 8)	Switched (n = 7)	Total (n = 15)
Median age (range), years	55.5 (42–73)	44.0 (29–57)	51.0 (29–73)
Male, n	6	6	12
Race, n			
Asian	4	2	6
White	3	3	6
Unknown	1	2	3
Median weight (range), kg	80.1 (56.7–100.0)	79.8 (60.4–114.0)	79.8 (56.7–114.0)
History of RBC transfusion[a], n	4	2	6
Median RBC units transfused[a], n, (range)	7.0 (2–198)	3.0 (1–5)	5.5 (1–198)
Median baseline PNH granulocytes clone size (range), %	86.0 (37.0–97.0)	92.3 (17.9–99.6)	88.7 (17.9–99.6)
Median baseline PNH erythrocytes clone size (range), %	17.0 (5.0–58.4)	23.4 (8.7–87.4)	17.0 (5.0–87.4)
History of aplastic anaemia, n	3	2	5
Median baseline normalized LDH x ULN (range)	5.2 (2.3–20.4)	1.1 (0.7–1.3)	2.3 (0.7–20.4)
Median baseline hemoglobin (range), g/L	89.5 (80–121)	105.0 (78–145)	99.0 (78–145)

[a] Transfusion events that occurred within one year prior to randomisation.

LDH, lactate dehydrogenase; RBC, red blood cell; ULN, upper limit of normal

Fig. 7

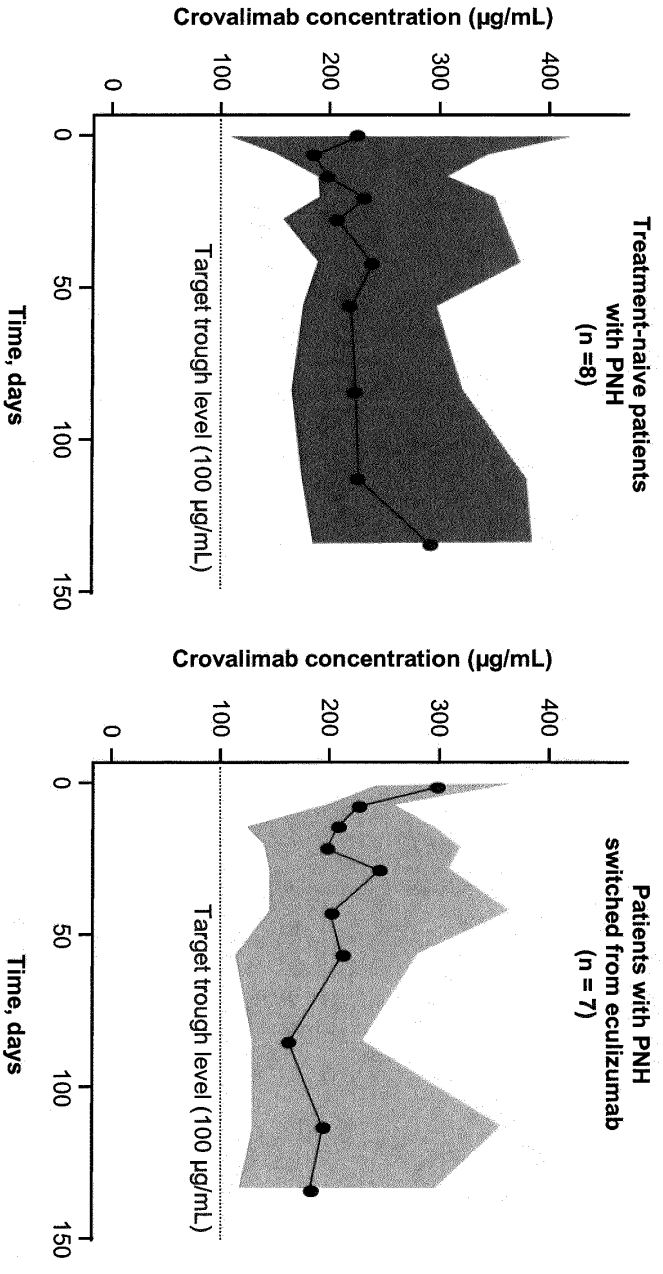

Crovalimab concentration (µg/mL)
0
100
200
300
400
0
50
100
150
Time, days
Target trough level (100 µg/mL)
Treatment-naive patients with PNH (n =8)
Crovalimab concentration (µg/mL)
0
100
200
300
400
0
50
100
150
Time, days
Target trough level (100 µg/mL)
Patients with PNH switched from eculizumab (n = 7)

Fig. 8

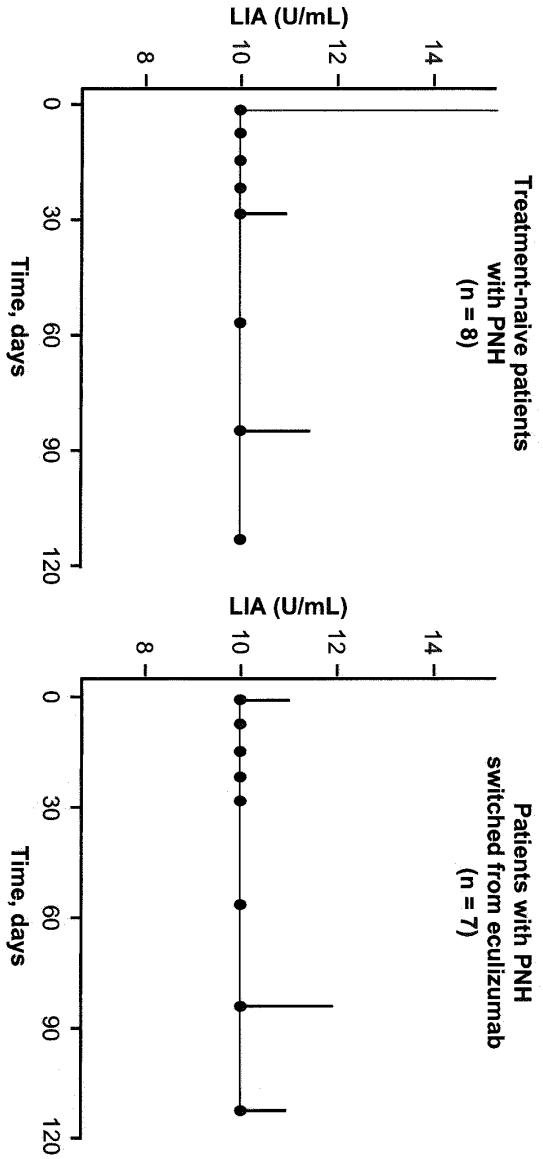

LIA (U/mL)
8
10
12
14
0
30
60
90
120
Time, days
Treatment-naive patients with PNH (n = 8)
LIA (U/mL)
8
10
12
14
0
30
60
90
120
Time, days
Patients with PNH switched from eculizumab (n = 7)

Fig. 9A

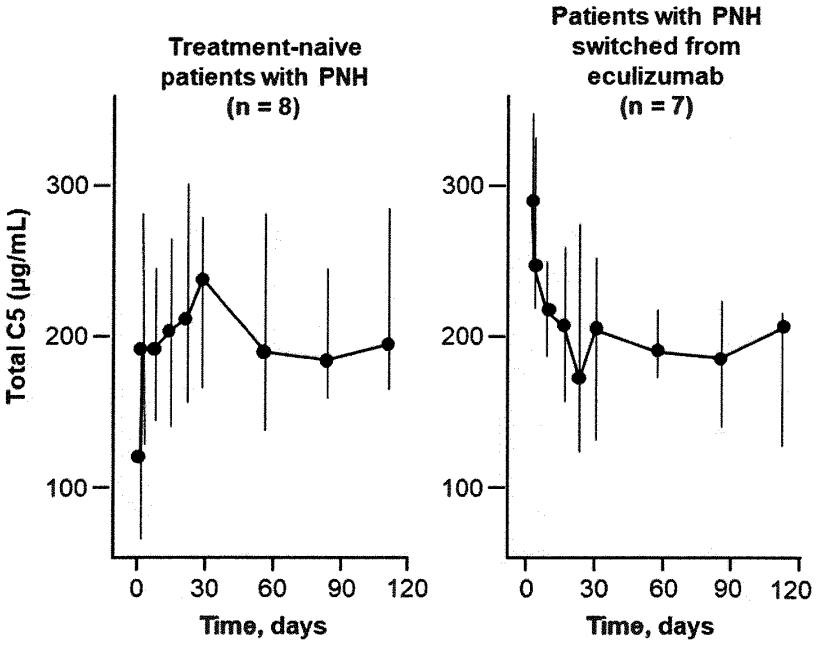

Treatment-naive patients with PNH (n = 8)
Patients with PNH switched from eculizumab (n = 7)
Total C5 (µg/mL)
300
200
100
0
30
60
90
120
Time, days

Fig. 9B

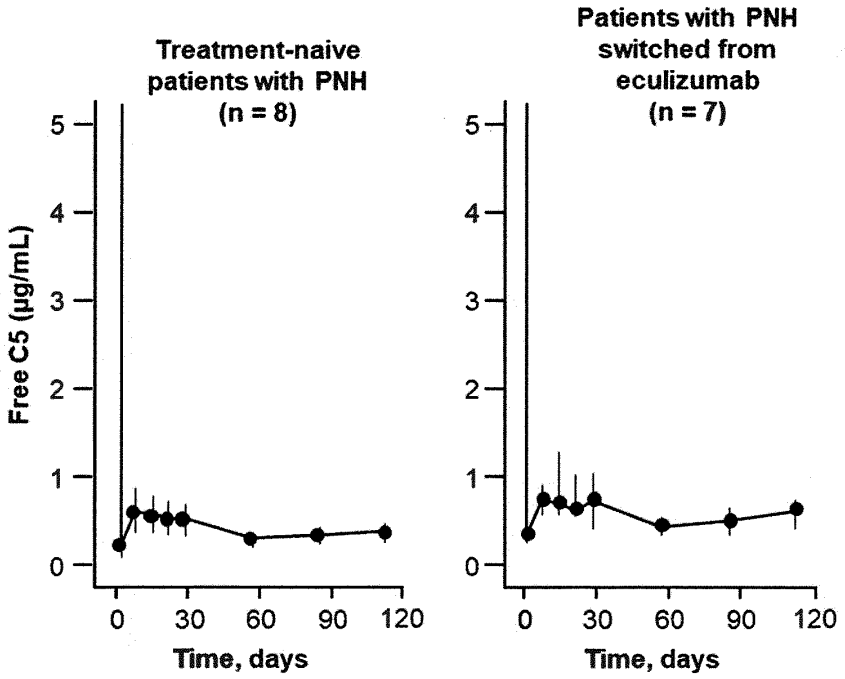

Treatment-naive patients with PNH (n = 8)
Patients with PNH switched from eculizumab (n = 7)
Free C5 (µg/mL)
5
4
3
2
1
0
30
60
90
120
Time, days

Fig. 10

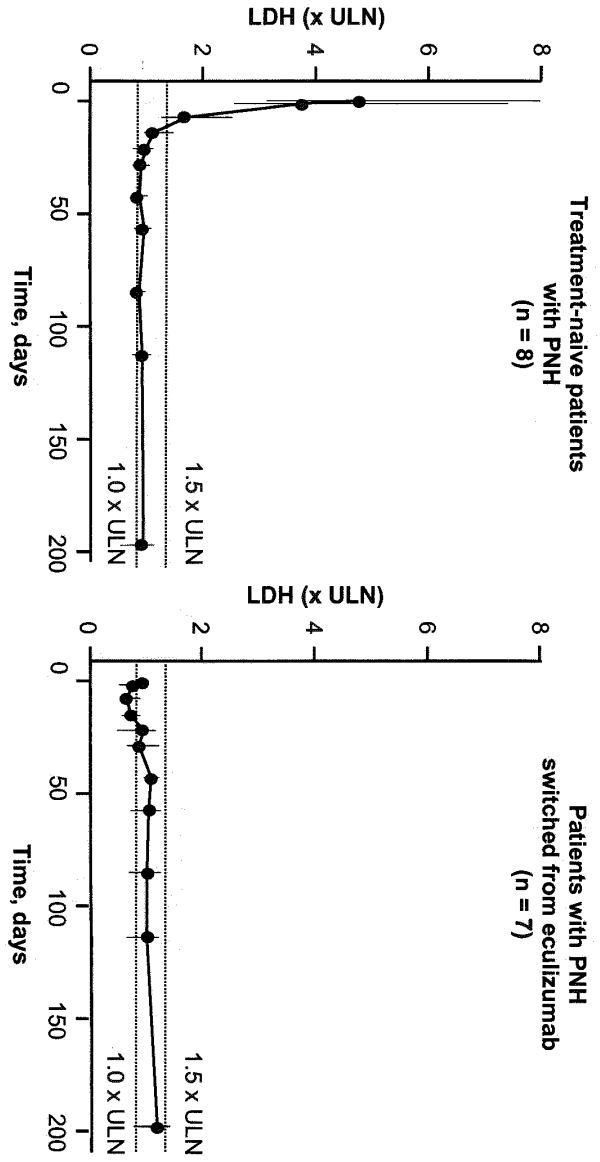

LDH (x ULN)
0
2
4
6
8
0
50
100
150
200
Time, days
1.0 x ULN
1.5 x ULN
Treatment-naive patients with PNH (n = 8)
LDH (x ULN)
0
2
4
6
8
0
50
100
150
200
Time, days
1.0 x ULN
1.5 x ULN
Patients with PNH switched from eculizumab (n = 7)

Fig. 11

Crovalimab was well tolerated and no serious treatment-related adverse events (AEs) were observed

- Overall, 11 patients experienced a total of 56 AEs
  - AEs occurring in > 10% of patients were headache (n = 4), nasopharyngitis (n = 3), peripheral oedema (n = 3), influenza (n = 2), asthenia (n = 2), fatigue (n = 2) and arthralgia (n = 2)
  - There were no AEs leading to withdrawal from treatment
  - There were no AEs leading to dose modification or treatment interruption
  - Treatment-related AEs were fatigue and pruritis in one patient and nasopharyngitis in one patient
  - There was one injection site reaction (injection site pain/discolouration)
- One patient experienced a serious AE of erysipelas, which was assessed by investigators as not related to crovalimab
- There were no deaths
- There were no type III hypersensitivity reactions in patients who switched to Crovalimab from Eculizumab

Fig. 12

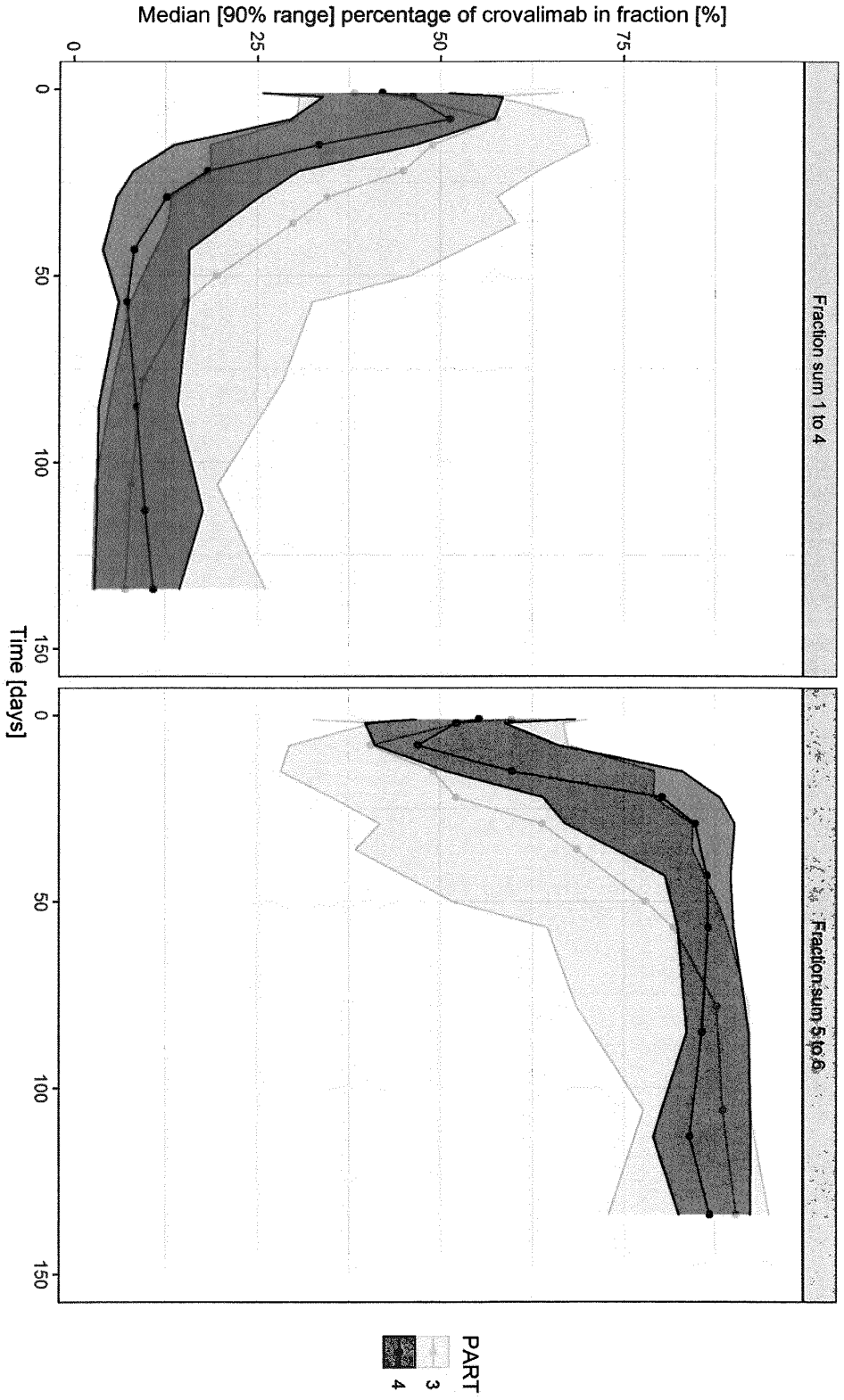

Median [90% range] percentage of crovalimab in fraction [%]
0
25
50
75
Time [days]
0
50
100
150
Fraction sum 1 to 4
Fraction sum 5 to 8
PART
4
3

Fig. 13

Summary of LDH Over Time in Patients with C5 Polymorphism

