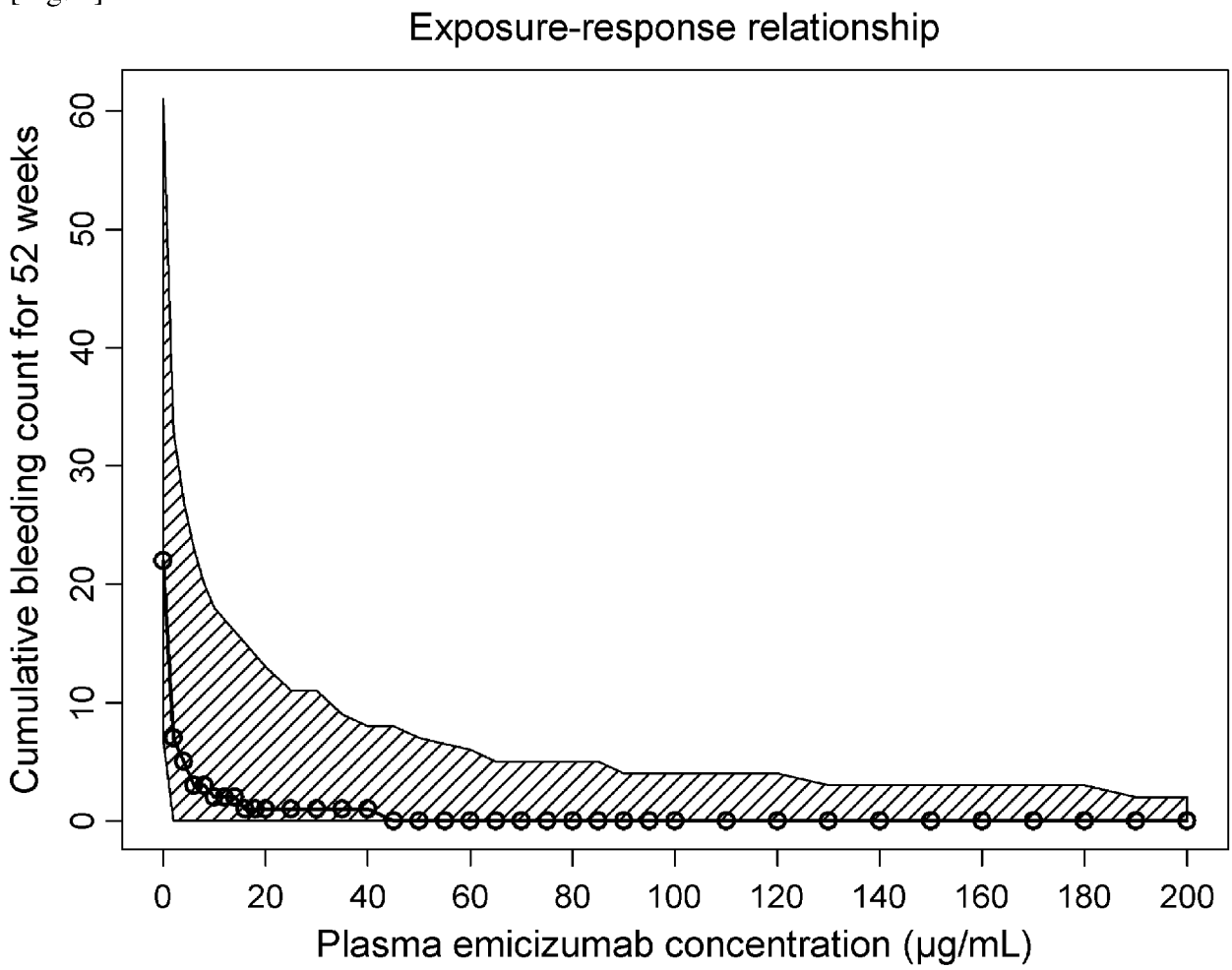
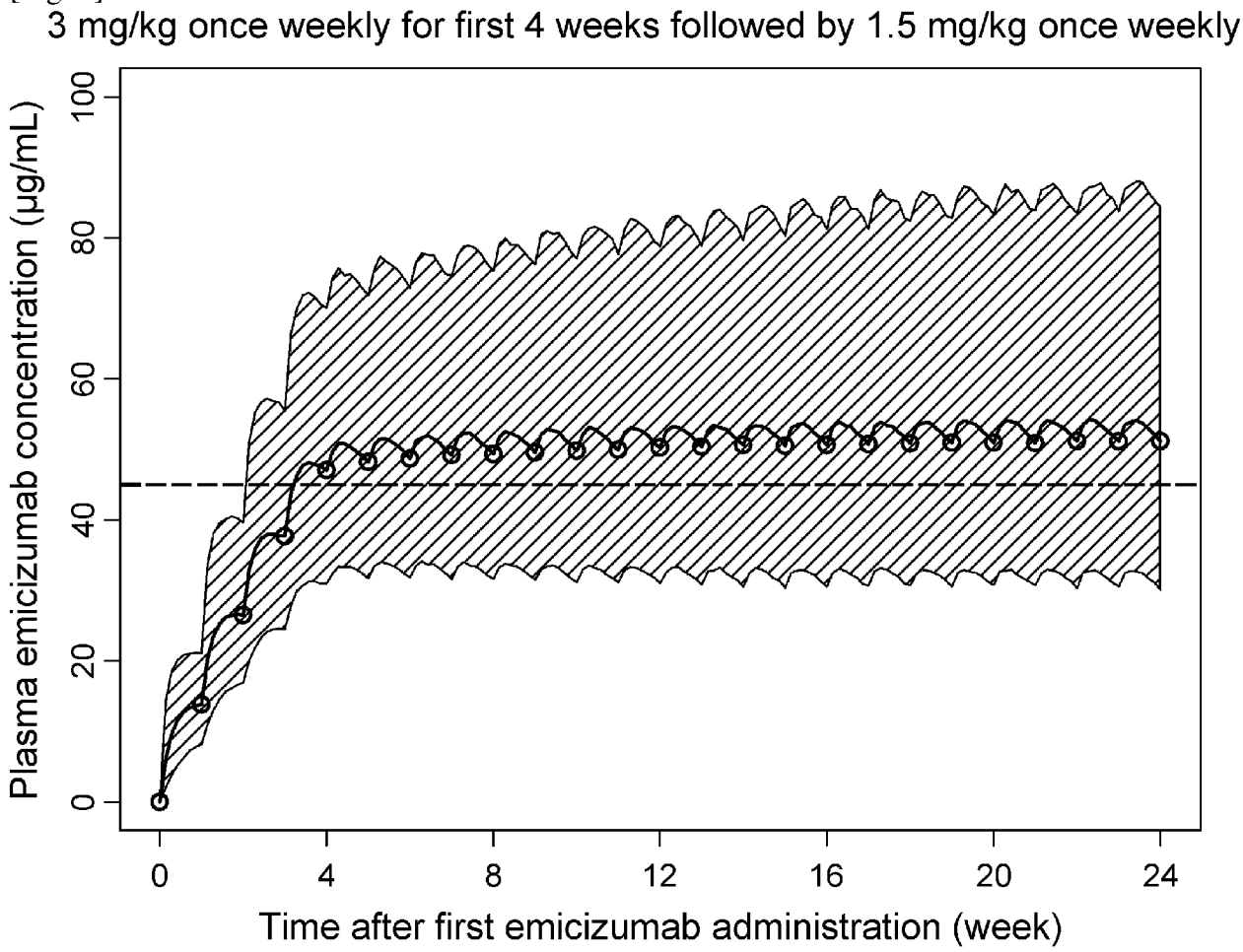
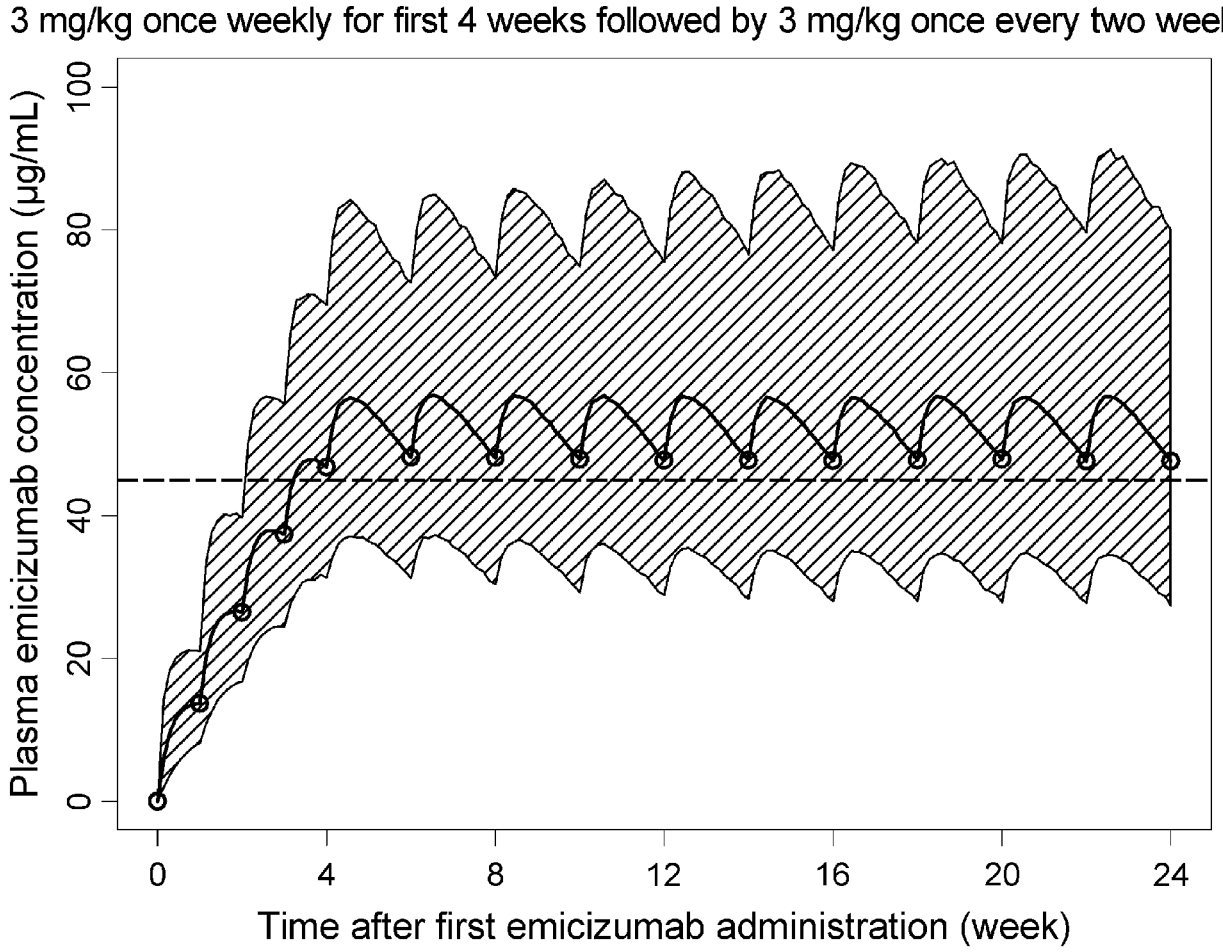
[Fig. 1]


Exposure-response relationship
Cumulative bleeding count for 52 weeks
0
10
20
30
40
50
60
0
20
40
60
80
100
120
140
160
180
200
Plasma emicizumab concentration (μg/mL)

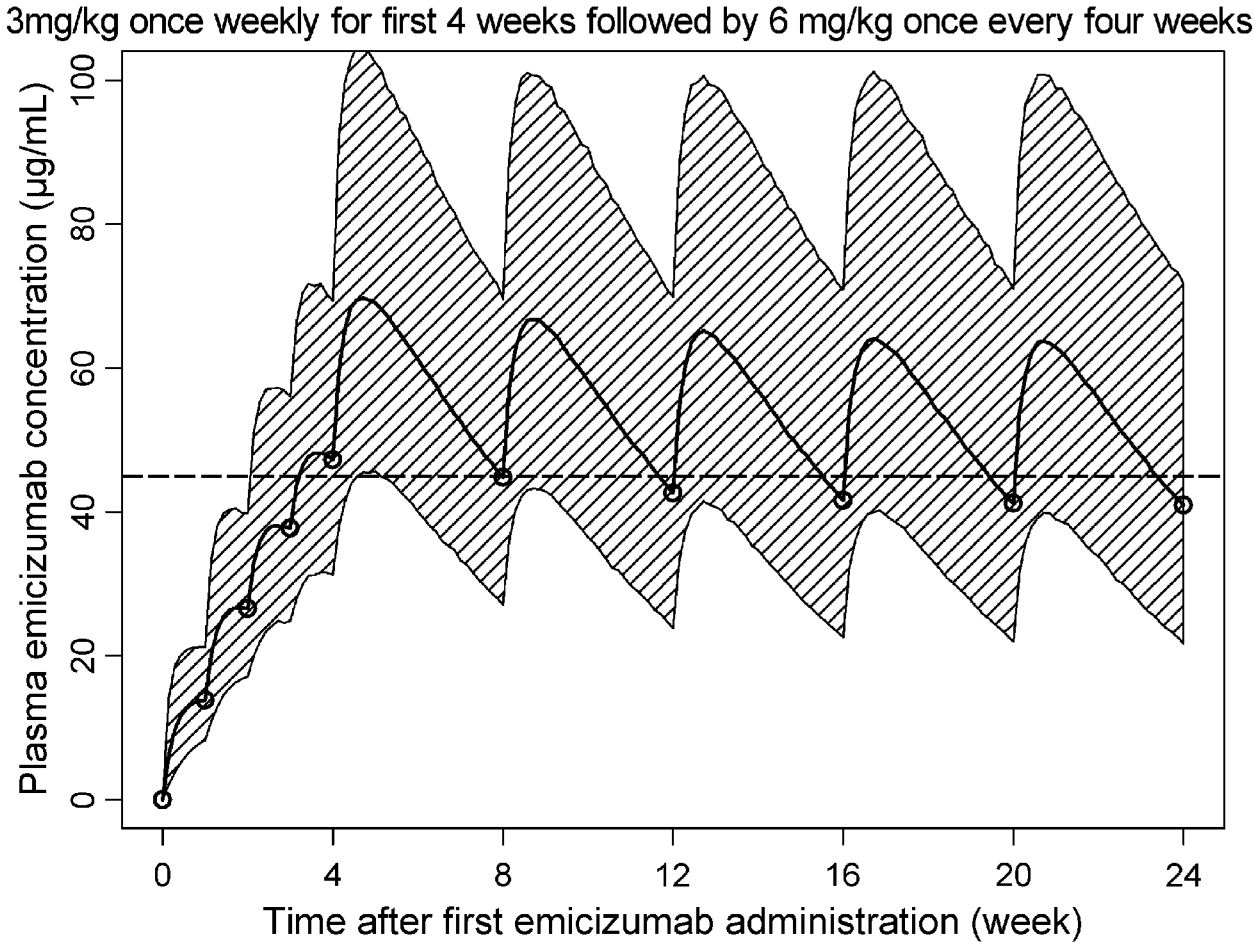
[Fig. 2]


3 mg/kg once weekly for first 4 weeks followed by 1.5 mg/kg once weekly
Plasma emicizumab concentration (μg/mL)
0
20
40
60
80
100
0
4
8
12
16
20
24
Time after first emicizumab administration (week)

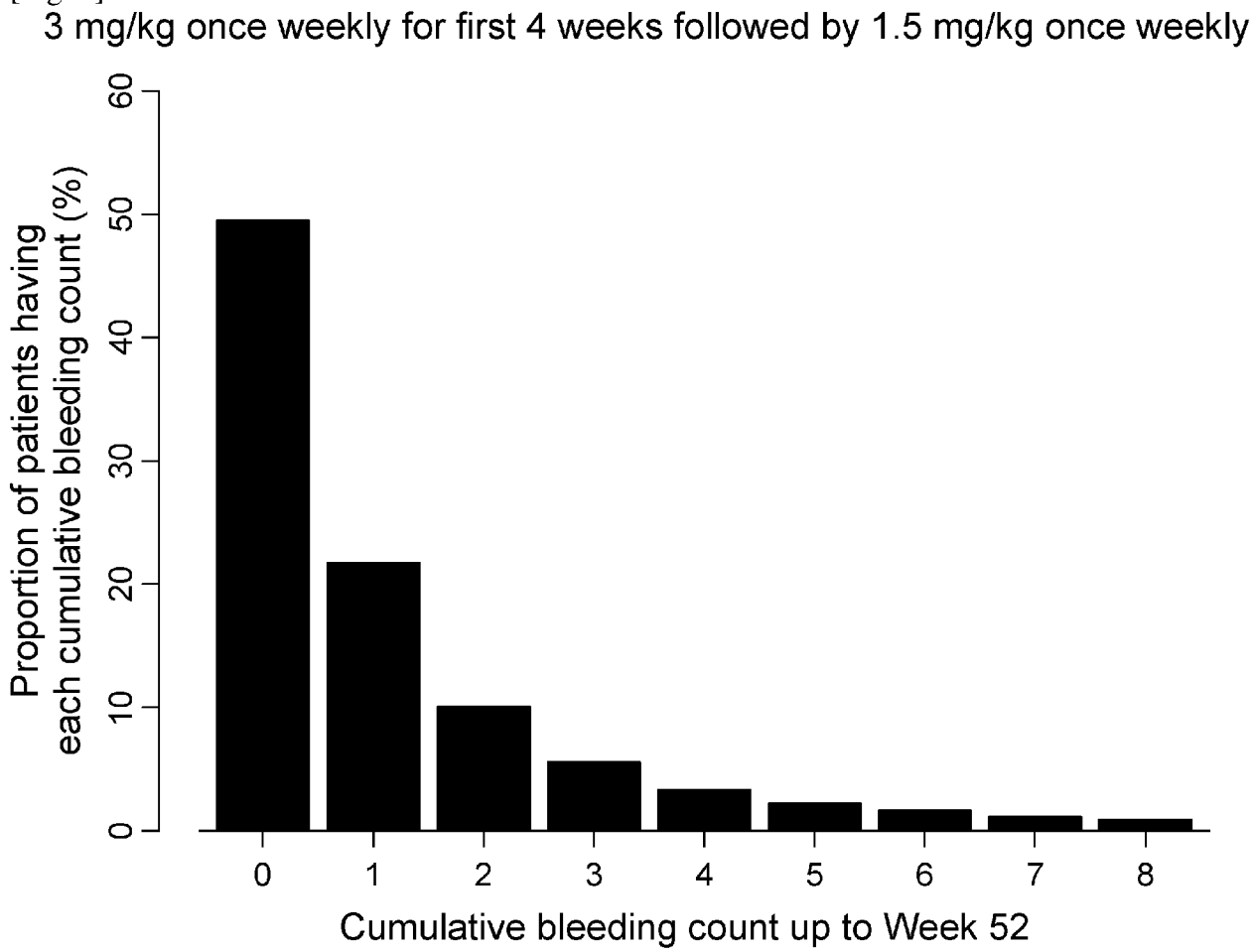
[Fig. 3]


3 mg/kg once weekly for first 4 weeks followed by 3 mg/kg once every two weeks
Plasma emicizumab concentration (μg/mL)
0
20
40
60
80
100
0
4
8
12
16
20
24
Time after first emicizumab administration (week)

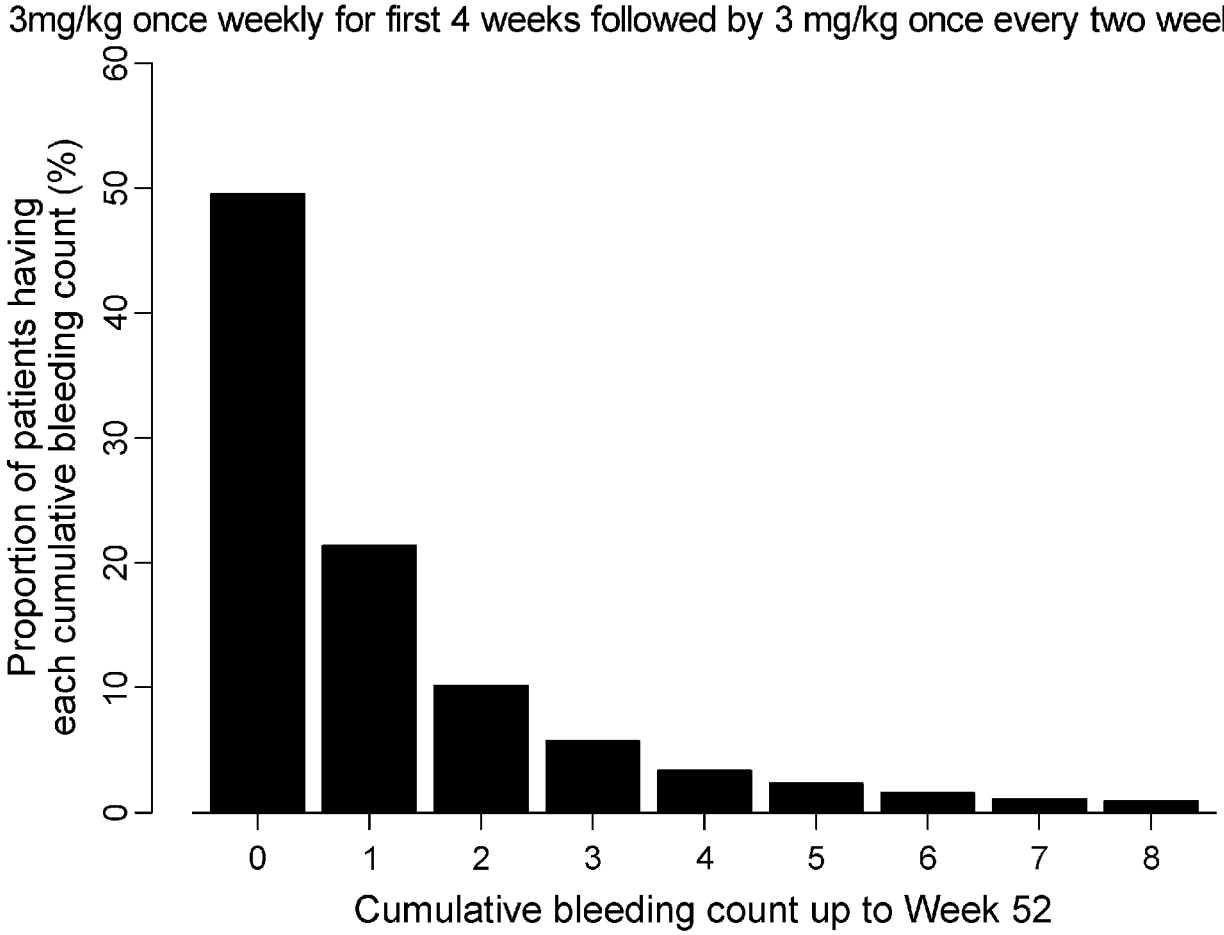
[Fig. 4]


3mg/kg once weekly for first 4 weeks followed by 6 mg/kg once every four weeks
Plasma emicizumab concentration (μg/mL)
0
20
40
60
80
100
0
4
8
12
16
20
24
Time after first emicizumab administration (week)

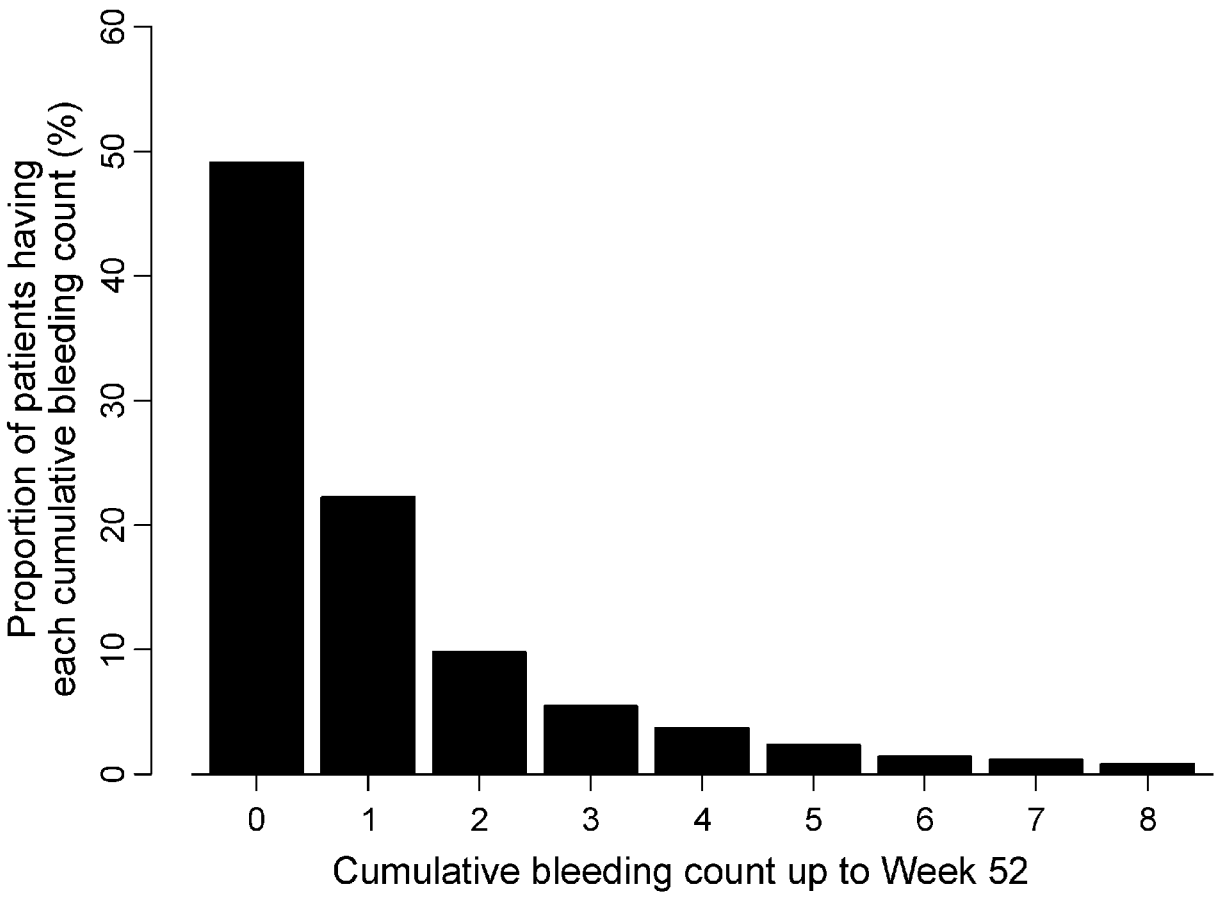
[Fig. 5]


3 mg/kg once weekly for first 4 weeks followed by 1.5 mg/kg once weekly
Proportion of patients having each cumulative bleeding count (%)
0
10
20
30
40
50
60
0
1
2
3
4
5
6
7
8
Cumulative bleeding count up to Week 52

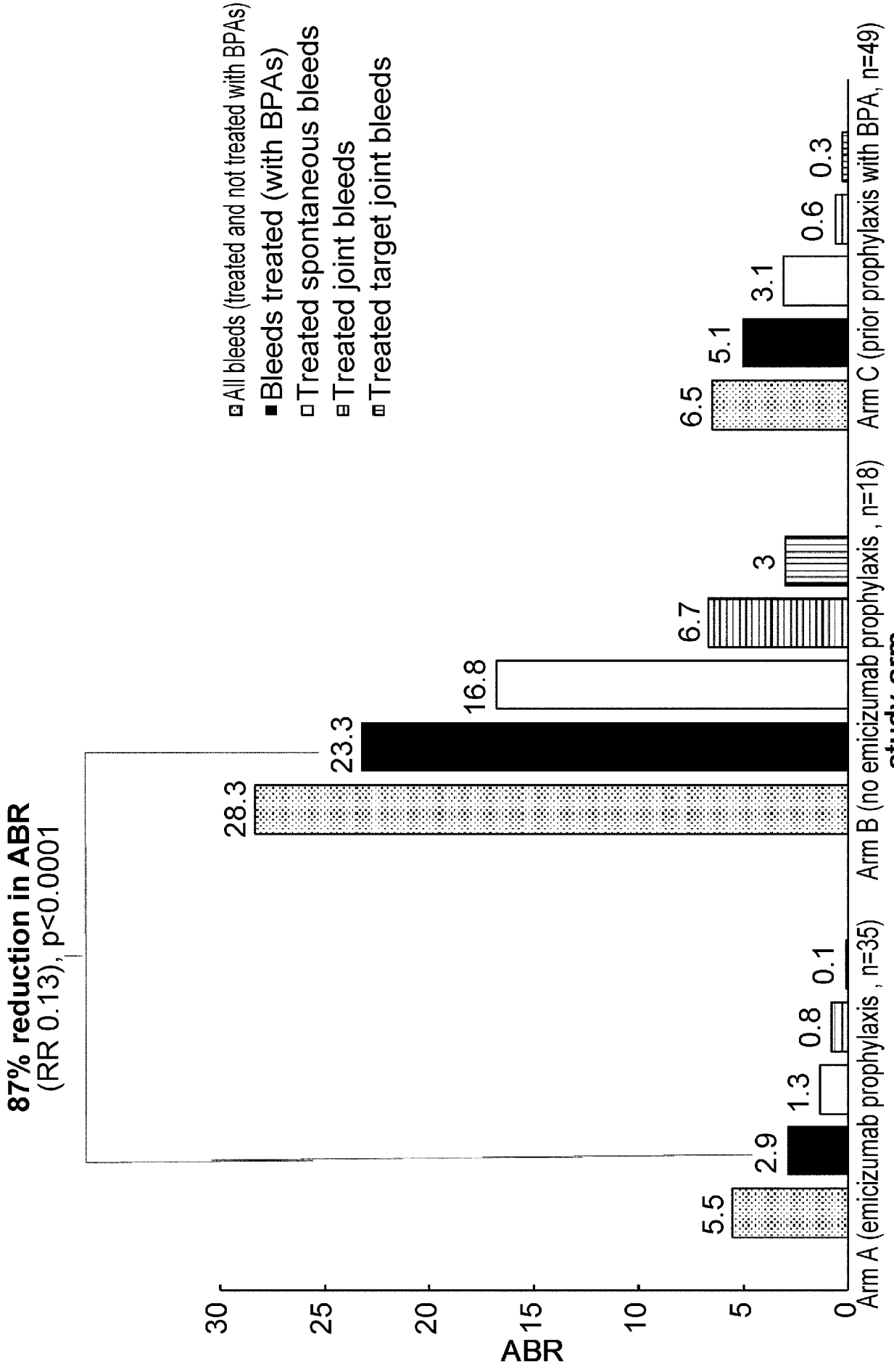
[Fig. 6]


3mg/kg once weekly for first 4 weeks followed by 3 mg/kg once every two weeks
Proportion of patients having each cumulative bleeding count (%)
0
10
20
30
40
50
60
0
1
2
3
4
5
6
7
8
Cumulative bleeding count up to Week 52

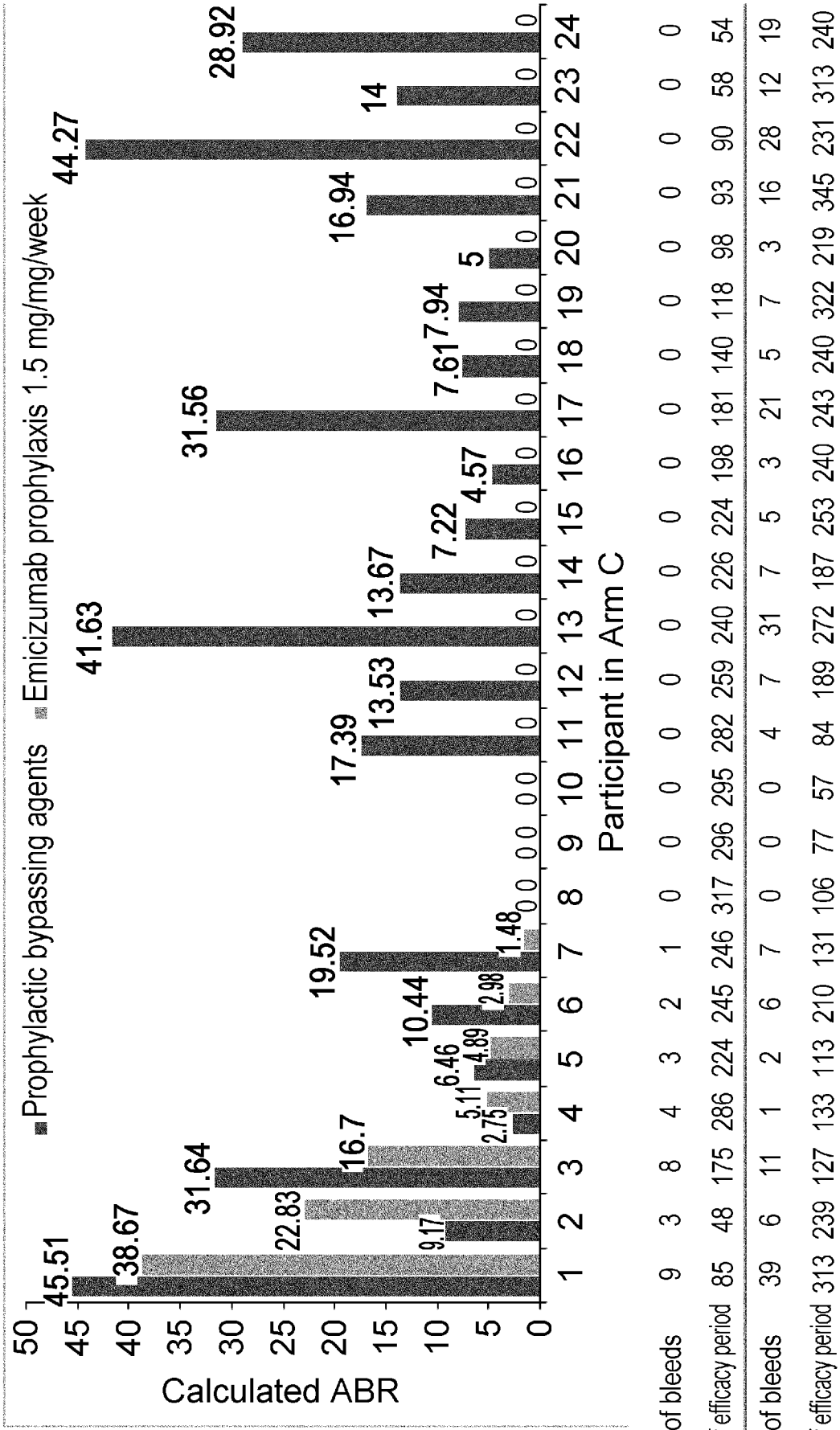
[Fig. 7]


3mg/kg once weekly for first 4 weeks followed by 6 mg/kg once every four weeks
Proportion of patients having each cumulative bleeding count (%)
0
10
20
30
40
50
60
0
1
2
3
4
5
6
7
8
Cumulative bleeding count up to Week 52

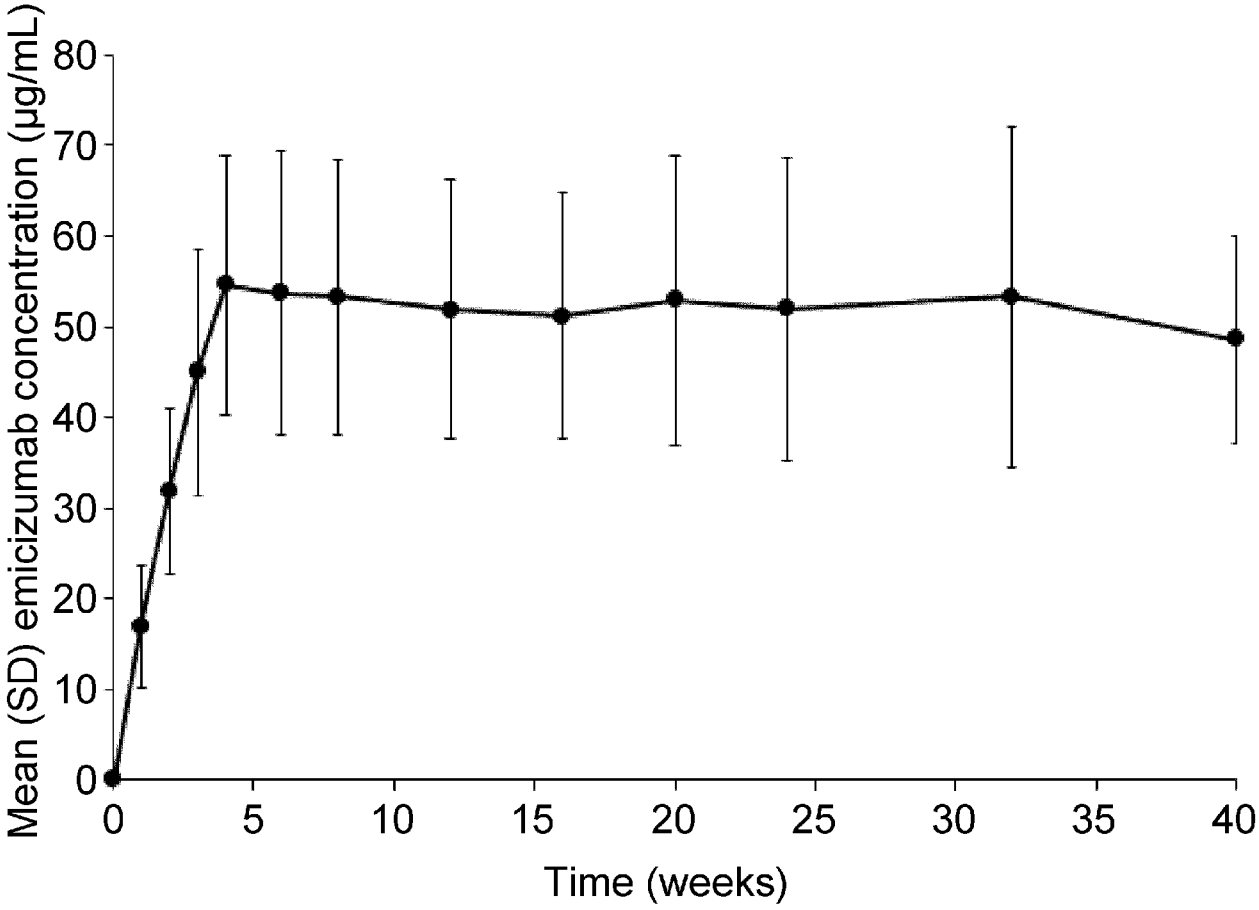
[Fig. 8]


87% reduction in ABR
(RR 0.13), p<0.0001
All bleeds (treated and not treated with BPAs)
Bleeds treated (with BPAs)
Treated spontaneous bleeds
Treated joint bleeds
Treated target joint bleeds
ABR
study arm
Arm A (emicizumab prophylaxis , n=35)
Arm B (no emicizumab prophylaxis , n=18)
Arm C (prior prophylaxis with BPA, n=49)
5.5
2.9
1.3
0.8
0.1
28.3
23.3
16.8
6.7
3
6.5
5.1
3.1
0.6
0.3
0
5
10
15
20
25
30

[Fig. 9]

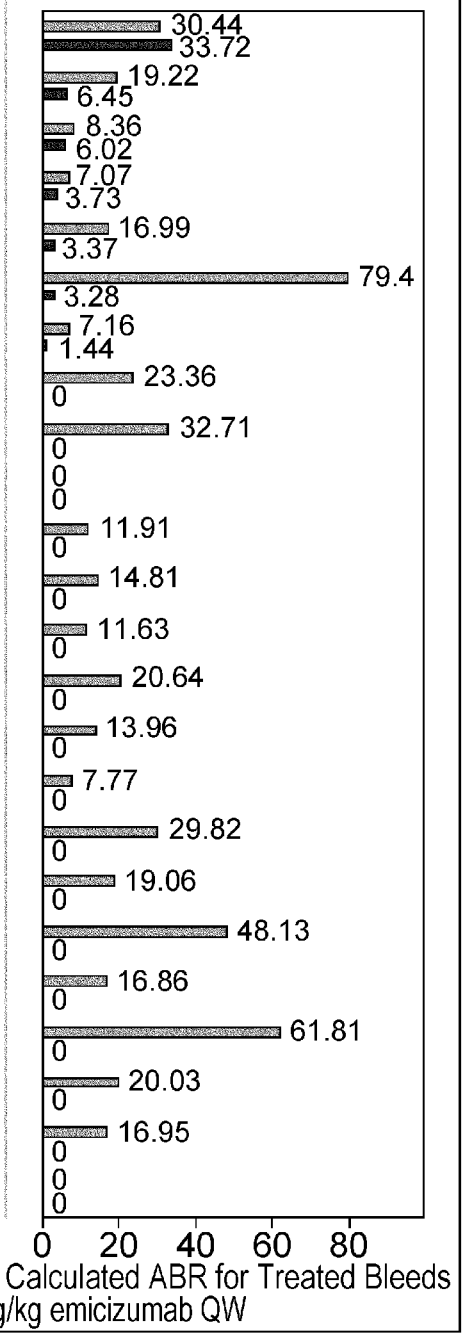

Prophylactic bypassing agents
Emicizumab prophylaxis 1.5 mg/mg/week
Calculated ABR
Participant in Arm C
45.51
38.67
22.83
9.17
31.64
16.7
2.75
5.11
6.46
4.89
10.44
2.98
19.52
1.48
17.39
13.53
41.63
13.67
7.22
4.57
31.56
7.61
7.94
5
16.94
44.27
14
28.92
Emicizumab
Number of bleeds 9 3 8 4 3 2 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
Duration of efficacy period 85 48 175 286 224 245 246 317 296 295 282 259 240 226 224 198 181 140 118 98 93 90 58 54
BPAs
Number of bleeds 39 6 11 1 2 6 7 0 0 0 4 7 31 7 5 3 21 5 7 3 16 28 12 19
Duration of efficacy period 313 239 127 133 113 210 131 106 77 57 84 189 272 187 253 240 243 240 322 219 345 231 313 240

[Fig. 10]

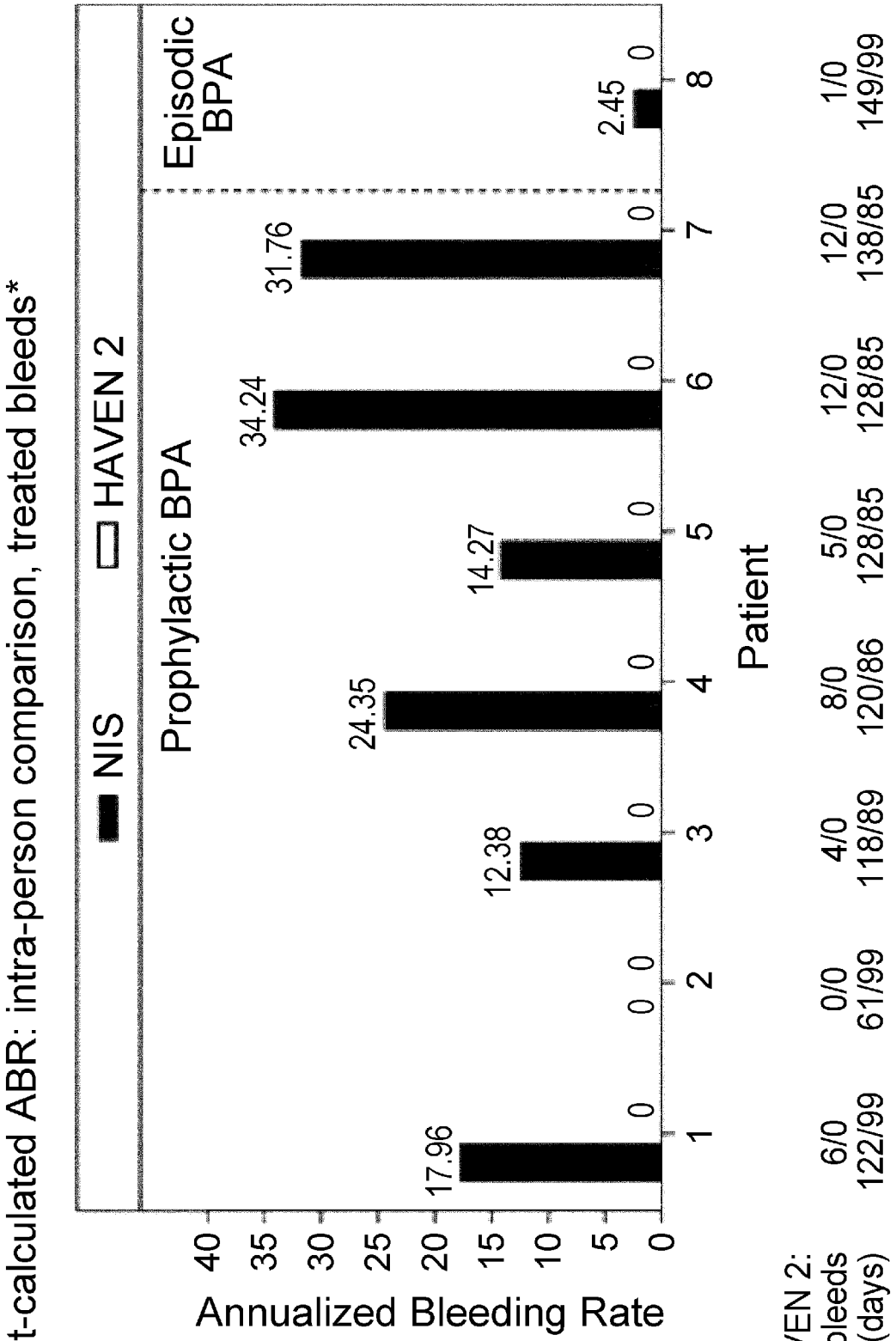

Mean (SD) emicizumab concentration (μg/mL)
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
Time (weeks)

[Fig. 11]

Center/ Patient ID	Episodic bypassing agents: Duration of Efficacy Period	Episodic bypassing agents: Number of treated bleeds	A: 1.5mg/kg emicizumab QW: Duration of Efficacy Period	A: 1.5mg/kg emicizumab QW: Number of treated bleeds
286047/1811	132	11	65	6
287683/1631	190	10	170	3
288148/1572	131	3	182	3
288139/1241	155	3	294	3
288995/1181	172	8	217	2
288990/1034	161	35	223	2
287105/2203	102	2	254	1
287912/1001	172	11	342	0
288139/1242	134	12	294	0
287680/1692	88	0	250	0
288991/1151	92	3	244	0
287105/2205	74	3	237	0
287682/1661	157	5	237	0
289846/1722	177	10	223	0
289846/1725	157	6	217	0
288148/1576	141	3	215	0
289846/1726	196	16	205	0
285344/1331	230	12	204	0
286047/1813	129	17	188	0
286047/1812	130	6	187	0
288993/1212	130	22	184	0
287568/1393	237	13	180	0
287568/1392	237	11	180	0
288148/1573	96	0	1	0



[Fig. 12]

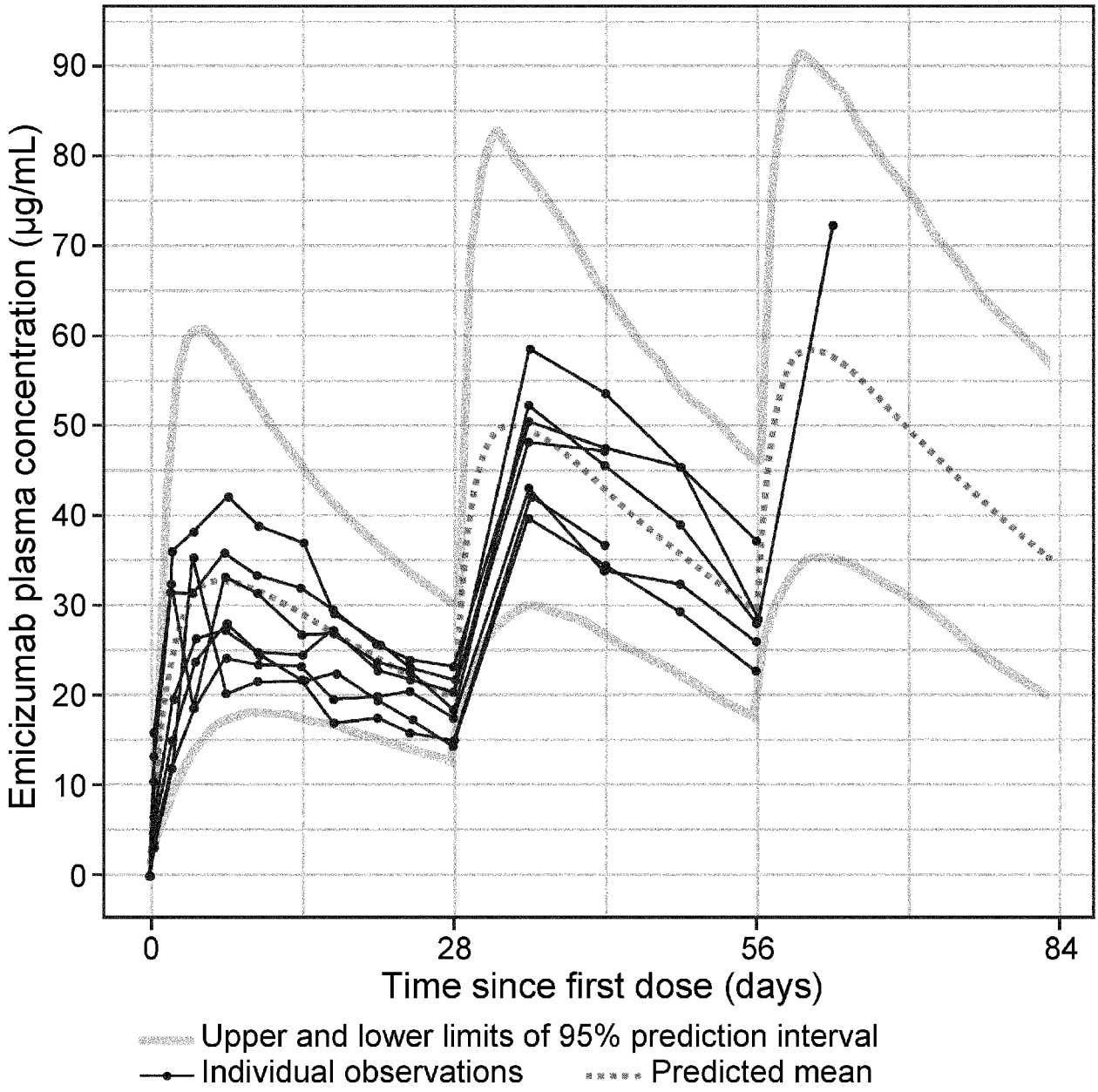


*The intra-participant comparison included patients previously enrolled in the NIS who were enrolled in HAVEN 2 for at least 12 weeks. Seven patients received prophylactic treatment with bypassing agents prior to the study, one received episodic treatment with bypassing agents.

ABR, annualized bleeding rate; BPA, bypassing agent; NIS, non-interventional study.

[Figure. Individual patient-calculated ABR: intra-person comparison, treated bleeds]*

[Fig. 13]


Emicizumab plasma concentration (μg/mL)
0
10
20
30
40
50
60
70
80
90
0
28
56
84
Time since first dose (days)
Upper and lower limits of 95% prediction interval
Individual observations
Predicted mean