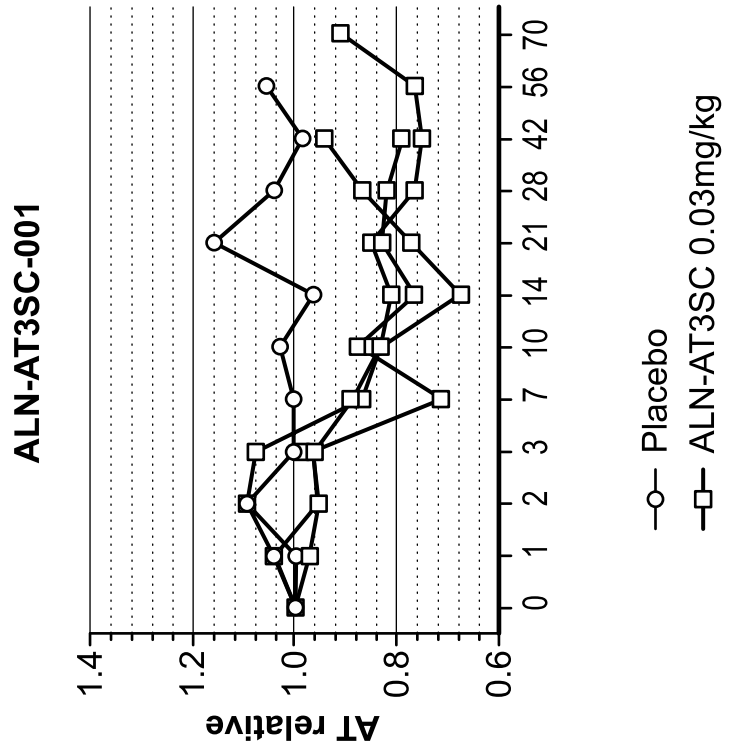


Figure 1A

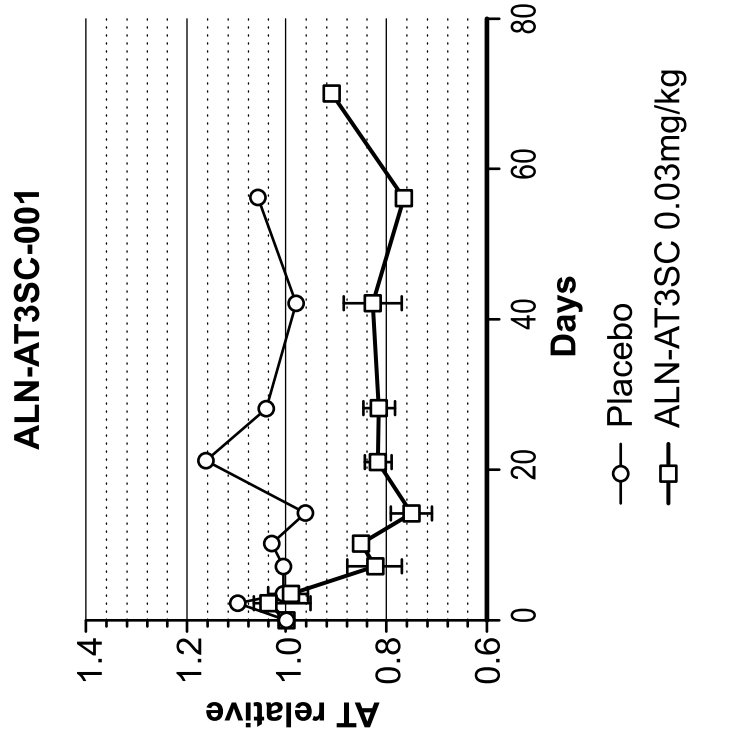


Figure 1B

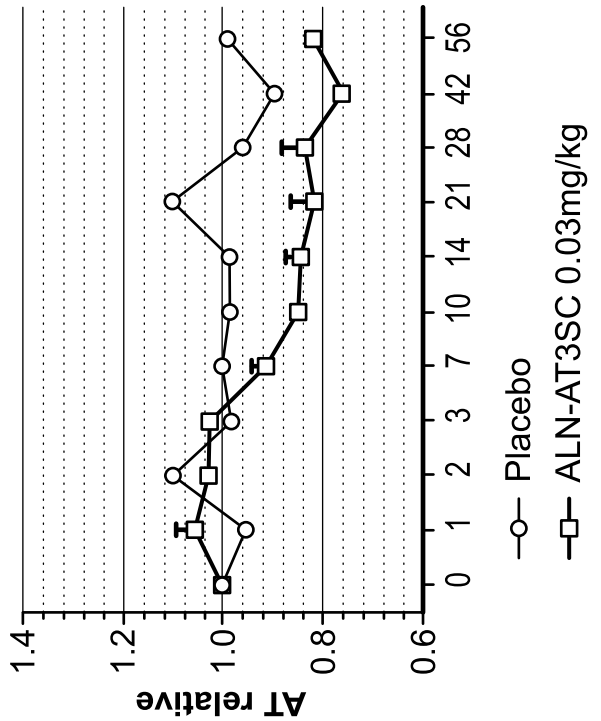


Figure 1D

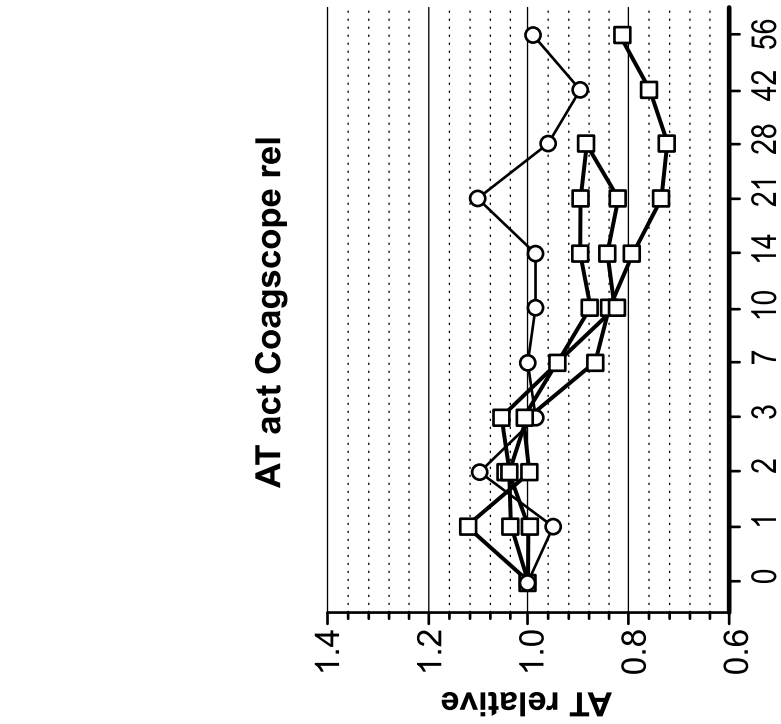


Figure 1C

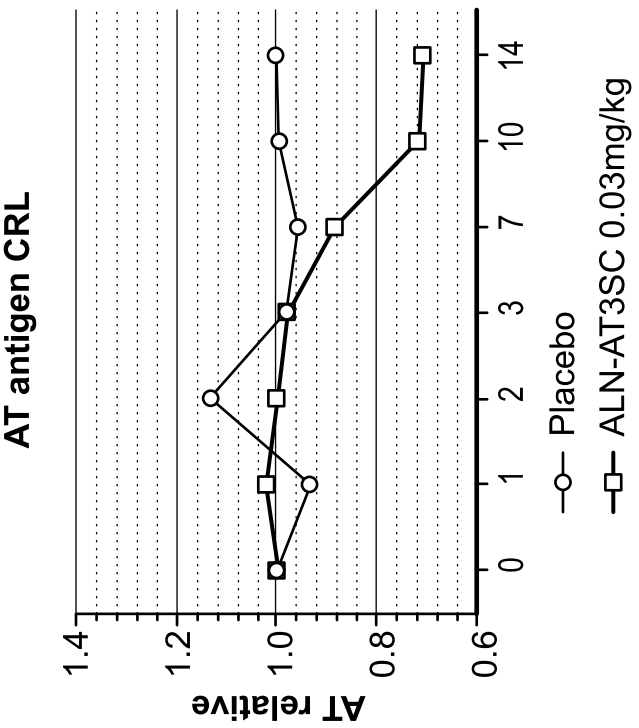


Figure 2B

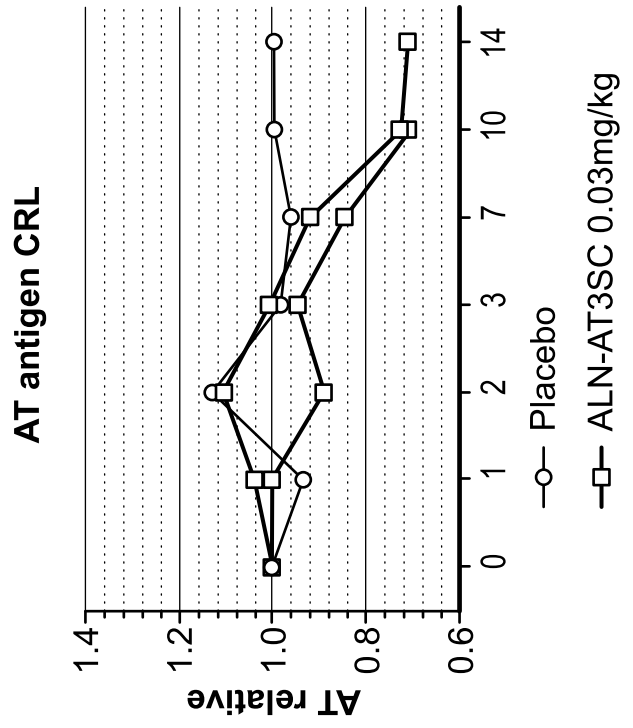


Figure 2A

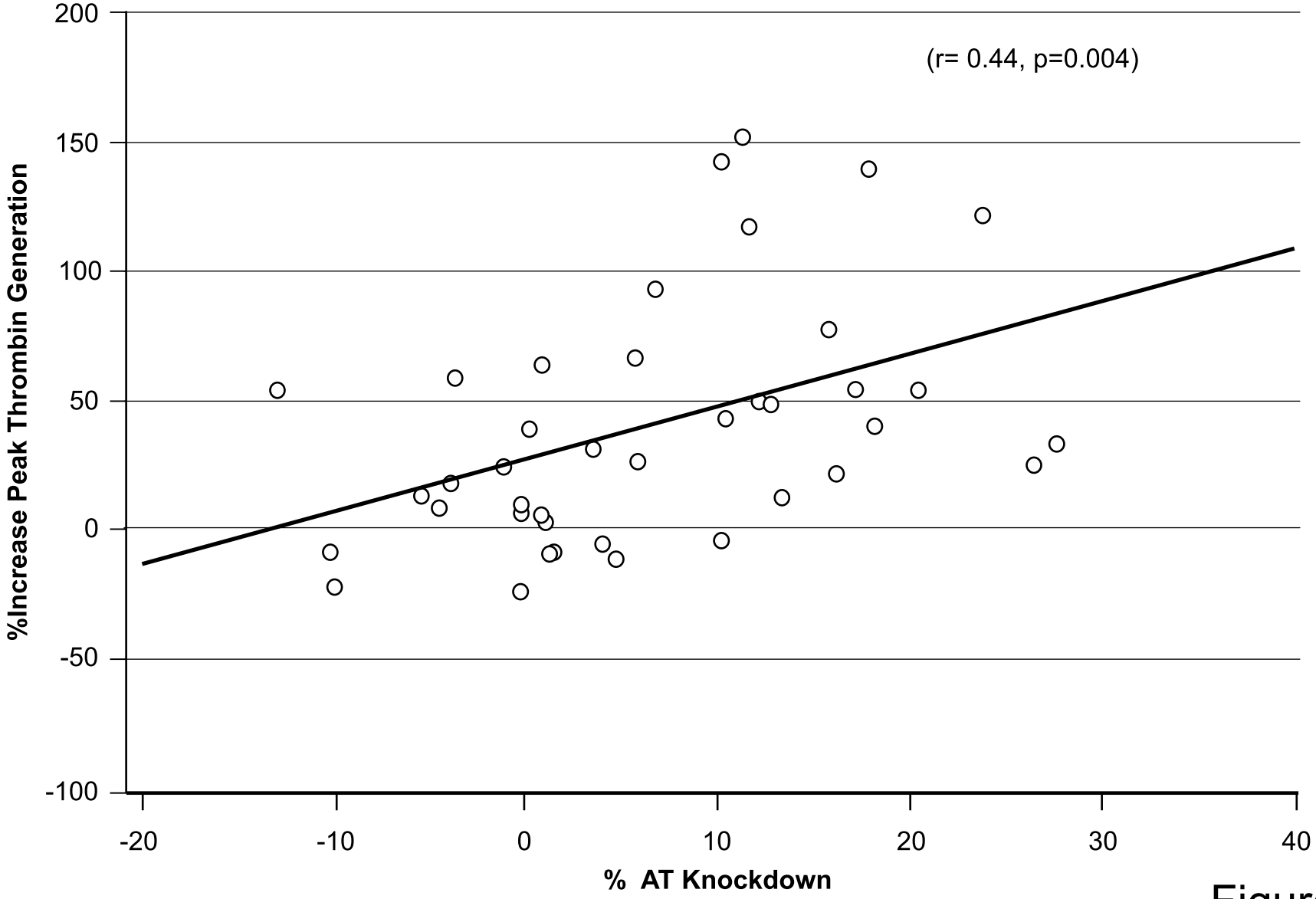

(r= 0.44, p=0.004)
%Increase Peak Thrombin Generation
200
150
100
50
0
-50
-100
-20
-10
0
10
20
30
40
% AT Knockdown

Figure 3

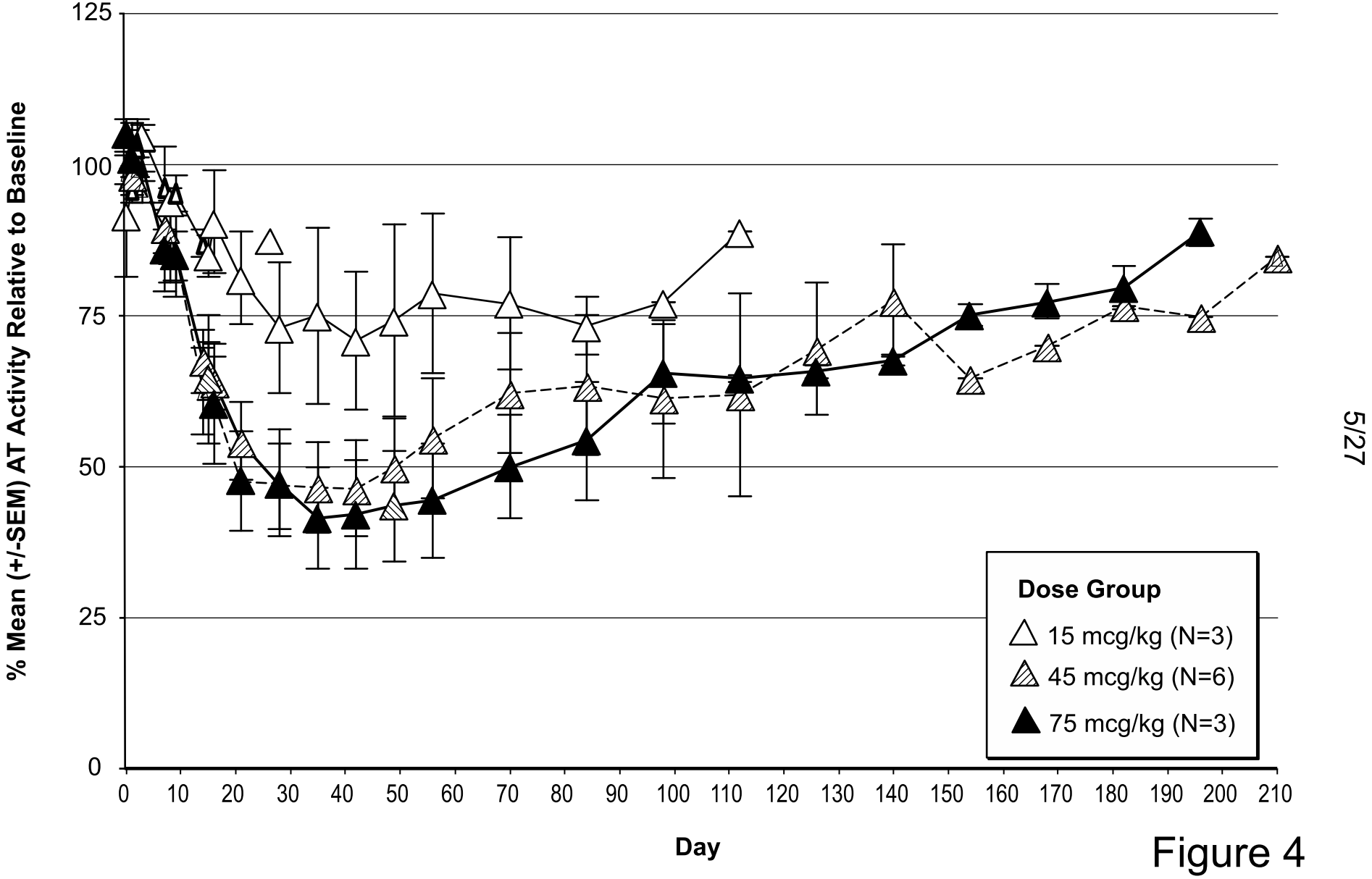

% Mean (+/-SEM) AT Activity Relative to Baseline
125
100
75
50
25
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210
Day
Dose Group
15 mcg/kg (N=3)
45 mcg/kg (N=6)
75 mcg/kg (N=3)

Figure 4

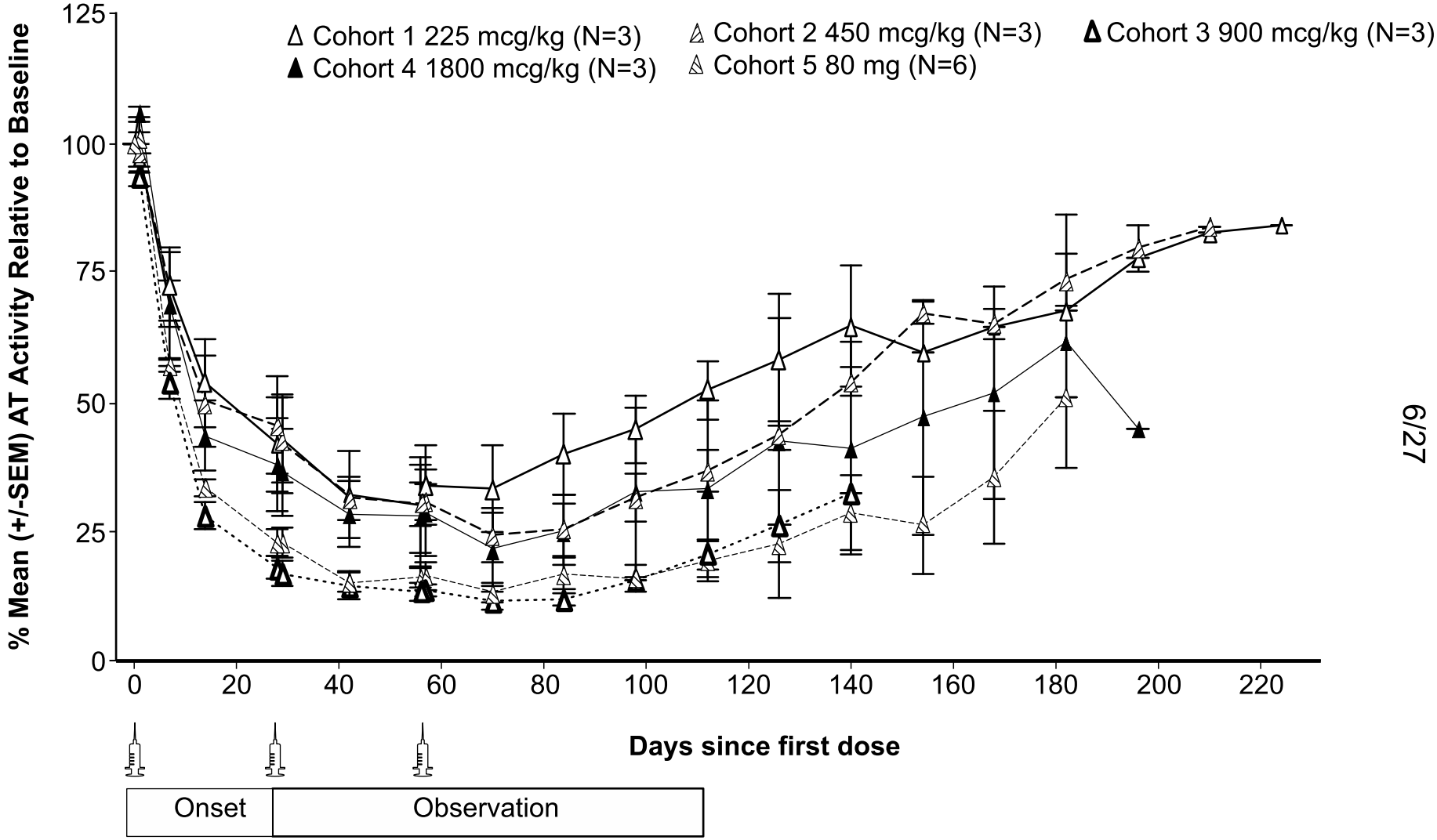

Cohort 1 225 mcg/kg (N=3)
Cohort 2 450 mcg/kg (N=3)
Cohort 3 900 mcg/kg (N=3)
Cohort 4 1800 mcg/kg (N=3)
Cohort 5 80 mg (N=6)
% Mean (+/-SEM) AT Activity Relative to Baseline
125
100
75
50
25
0
0
20
40
60
80
100
120
140
160
180
200
220
Days since first dose
Onset
Observation

Figure 5A

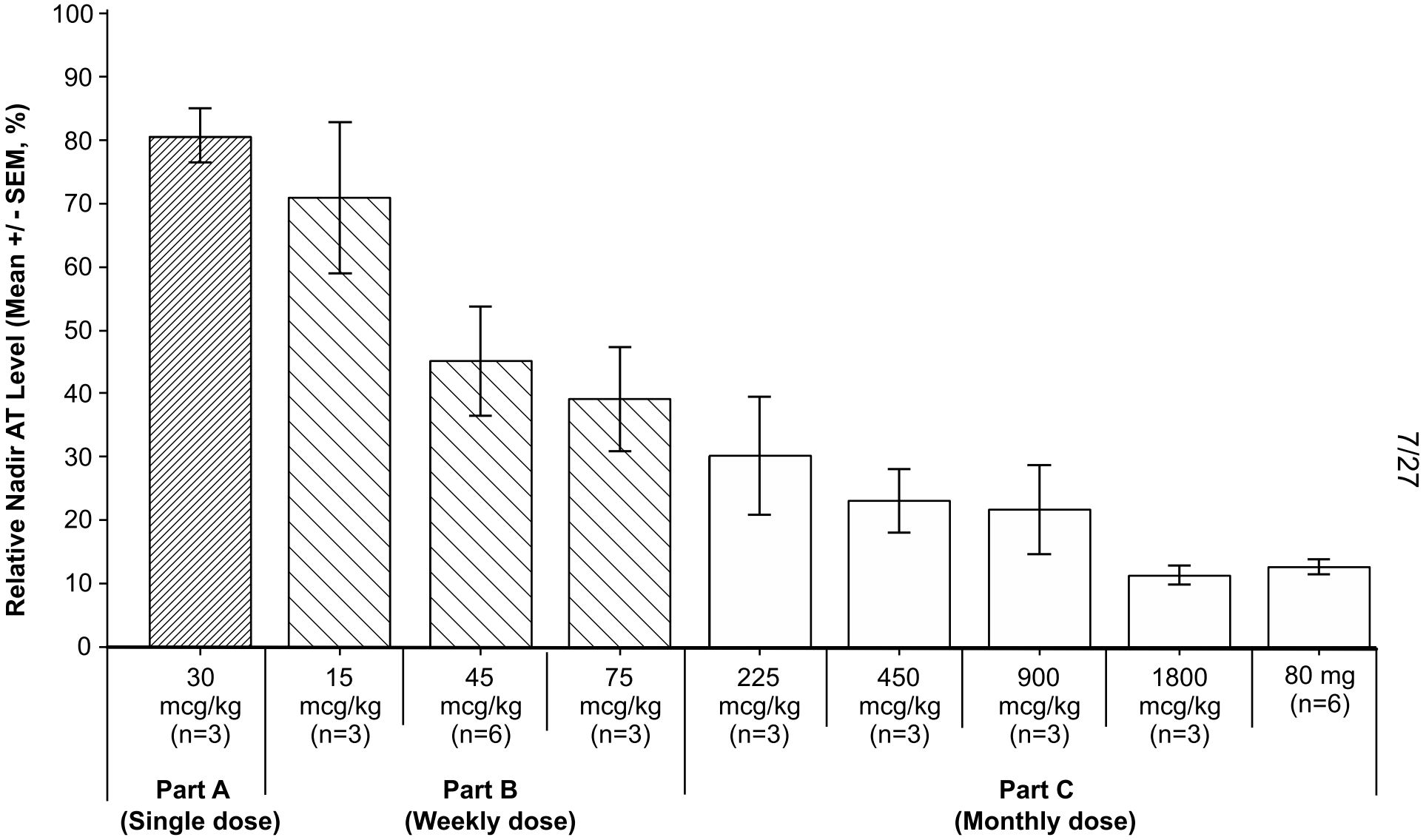

Relative Nadir AT Level (Mean +/- SEM, %)
100
90
80
70
60
50
40
30
20
10
0
30 mcg/kg (n=3)
15 mcg/kg (n=3)
45 mcg/kg (n=6)
75 mcg/kg (n=3)
225 mcg/kg (n=3)
450 mcg/kg (n=3)
900 mcg/kg (n=3)
1800 mcg/kg (n=3)
80 mg (n=6)
Part A (Single dose)
Part B (Weekly dose)
Part C (Monthly dose)

Figure 5B

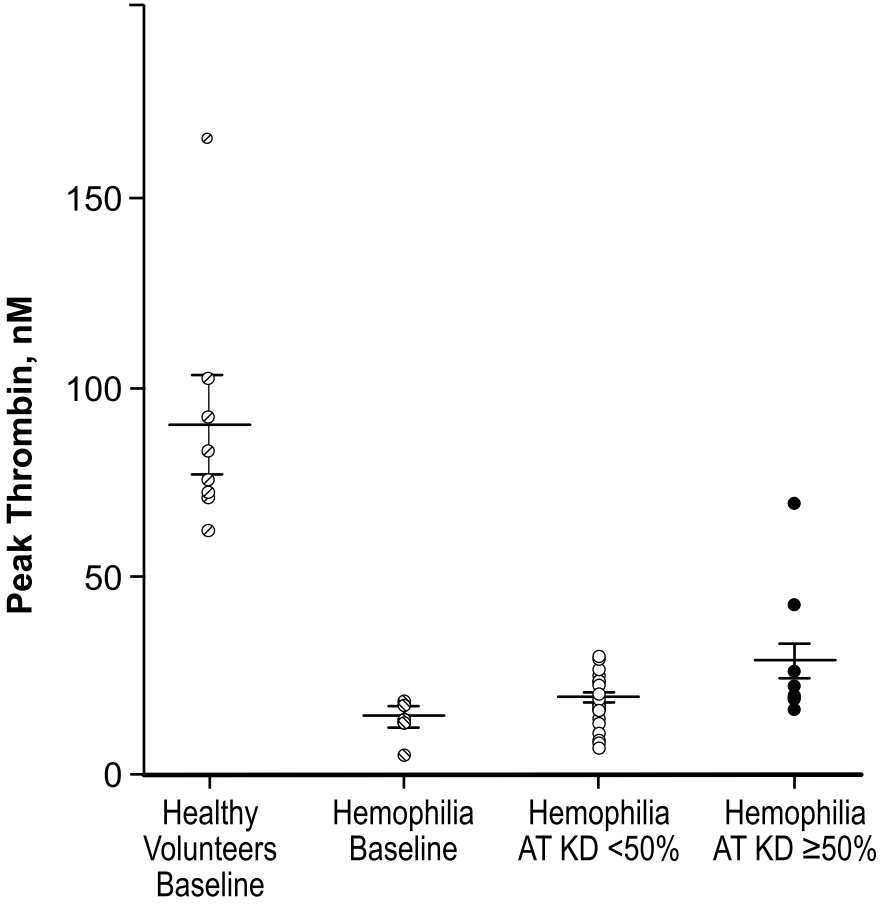


Figure 6A

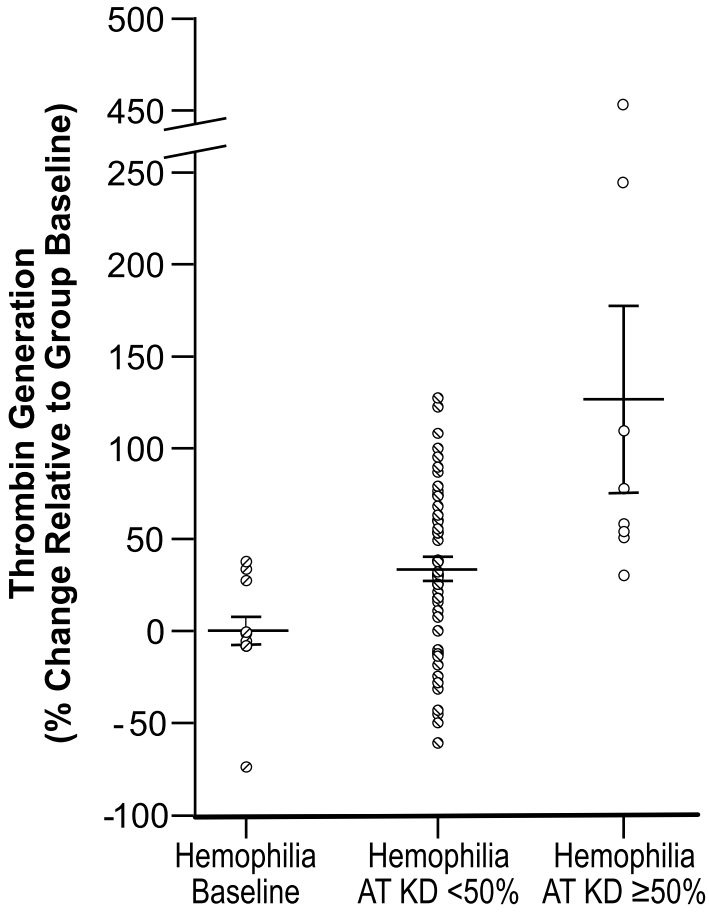


Figure 6B

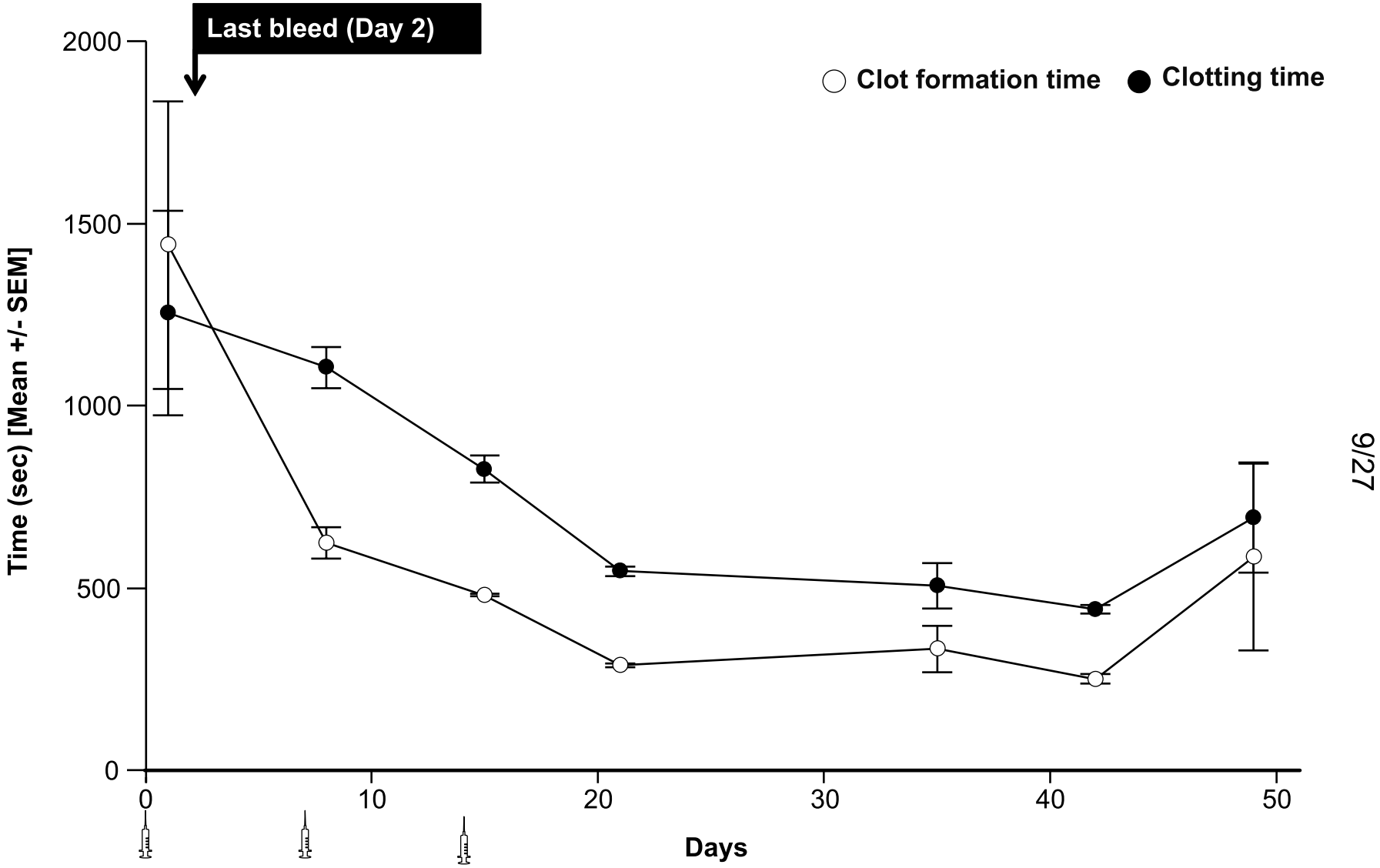

Last bleed (Day 2)
Clot formation time
Clotting time
Time (sec) [Mean +/- SEM]
2000
1500
1000
500
0
0
10
20
30
40
50
Days

Figure 7

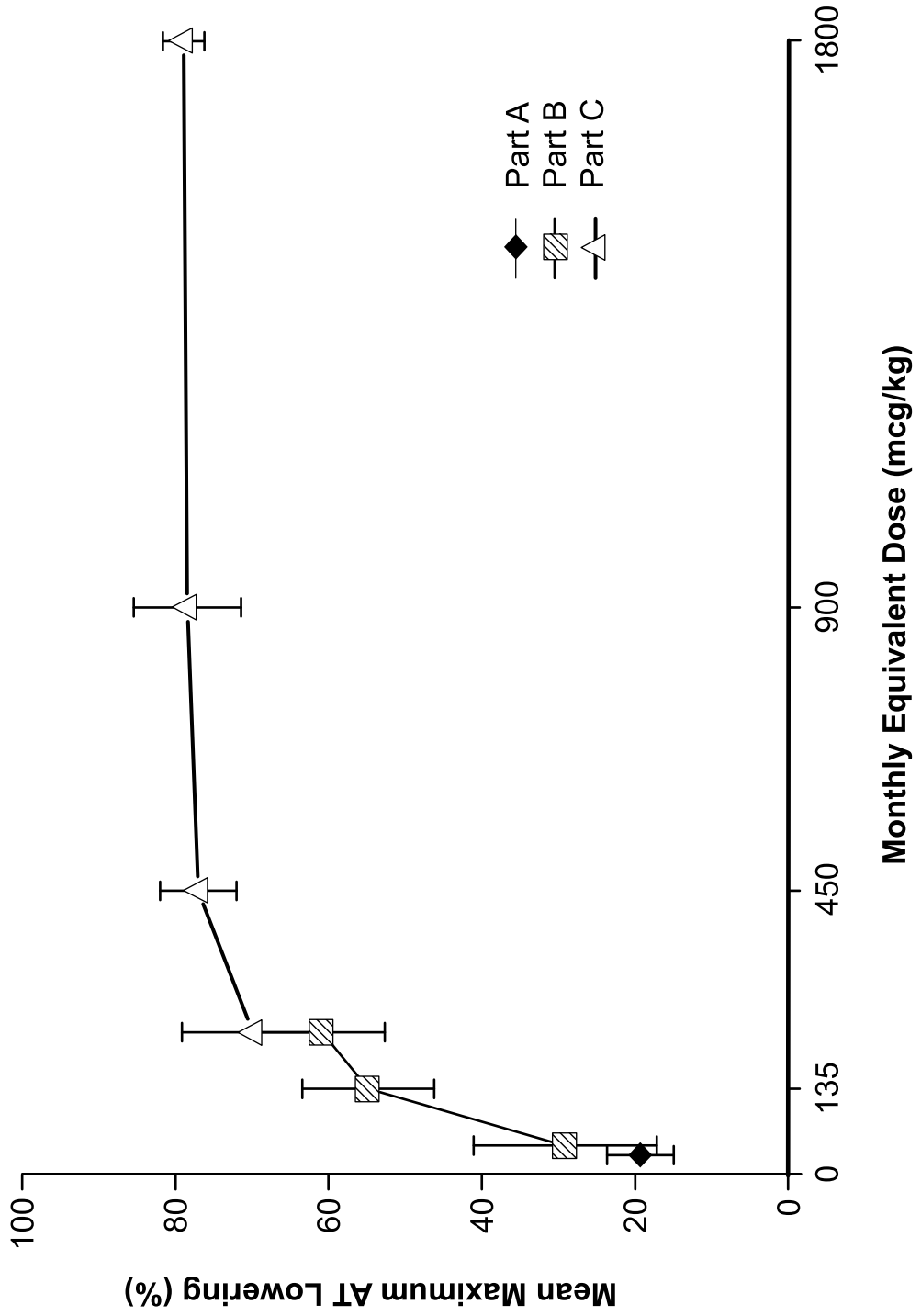
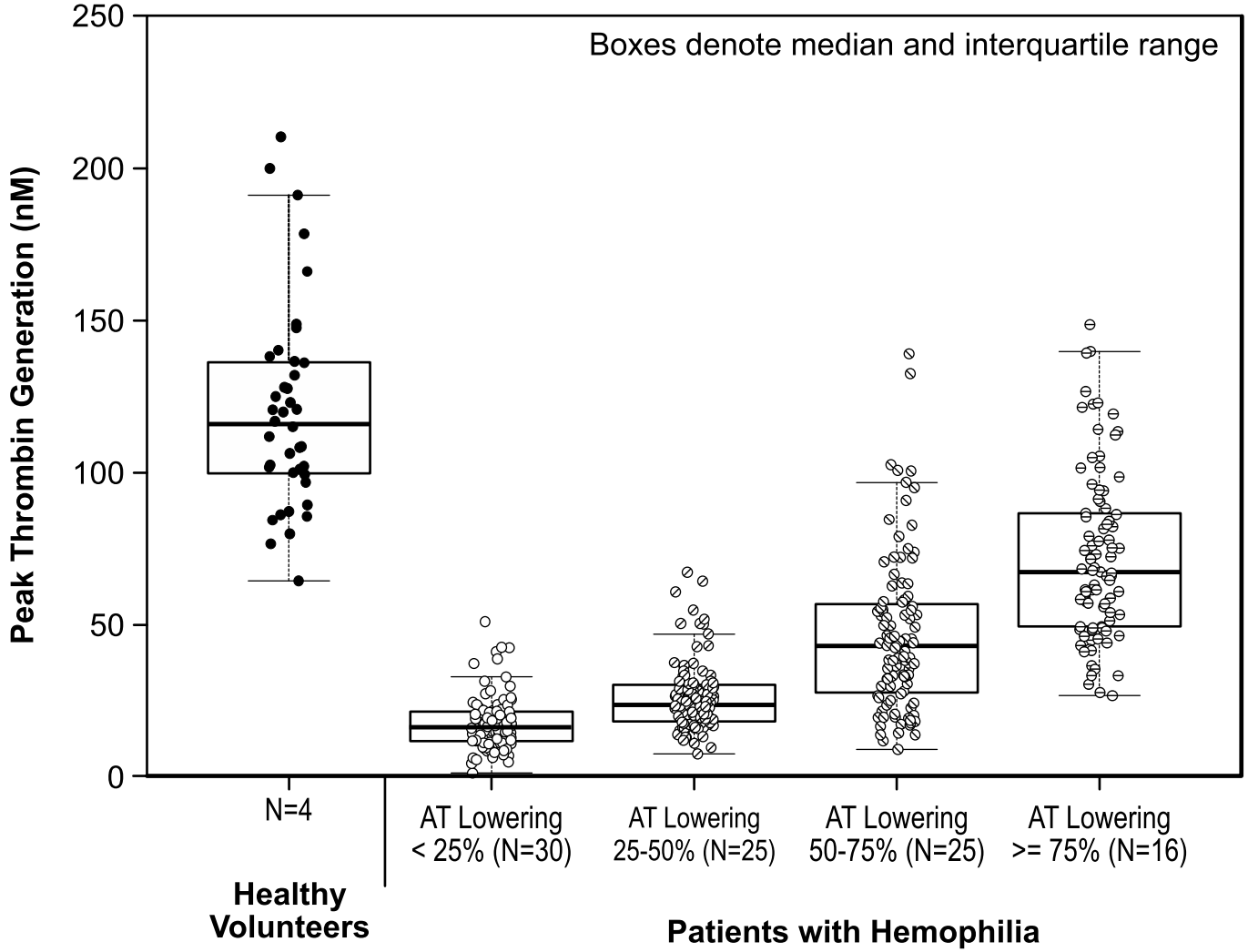

Mean Maximum AT Lowering (%)
100
80
60
40
20
0
0
135
450
900
1800
Monthly Equivalent Dose (mcg/kg)
Part A
Part B
Part C

Figure 8



†%Change in Peak TG: p<0.001 by Mann-Whitney test, when compared with AT3 lowering than <25% group

Figure 9

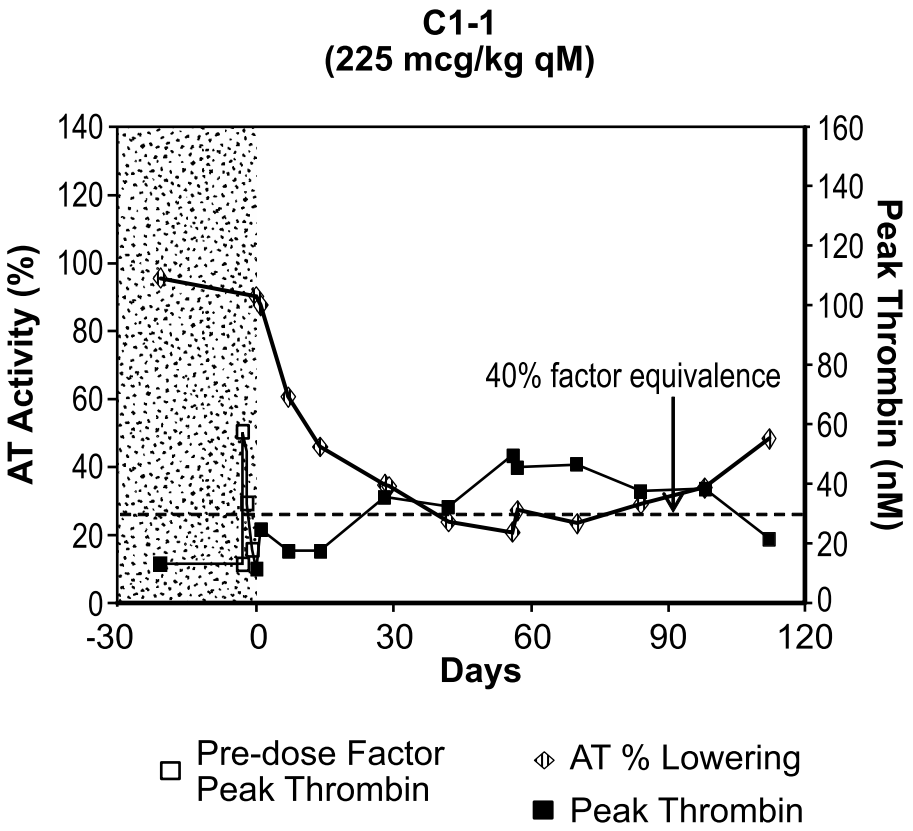


Figure 10A

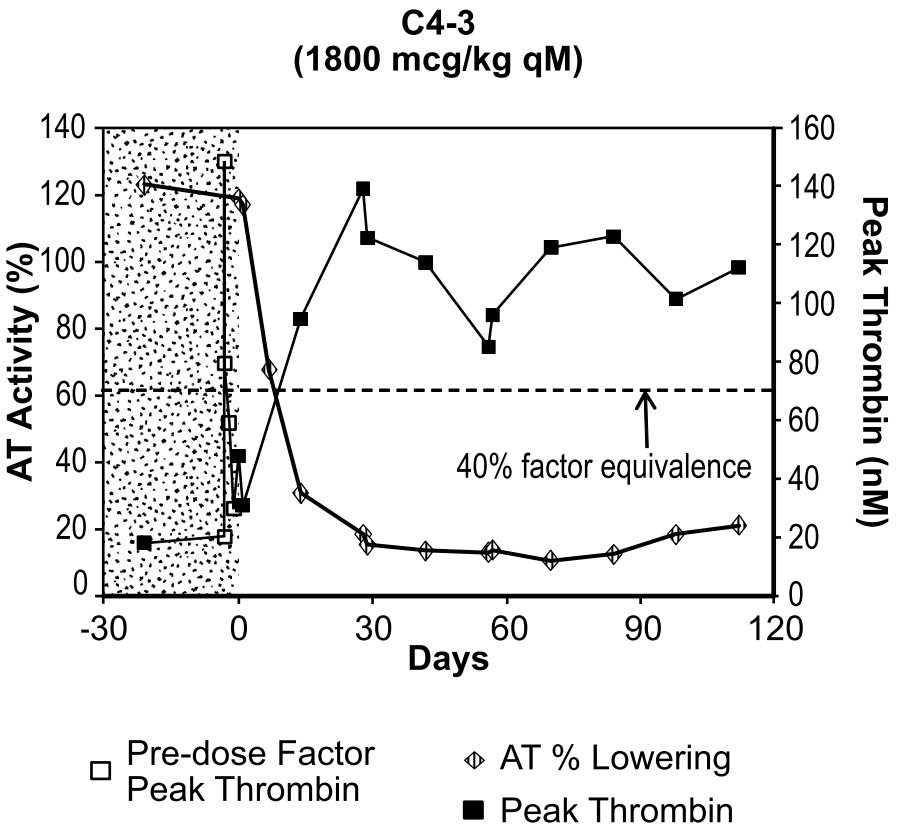


Figure 10B

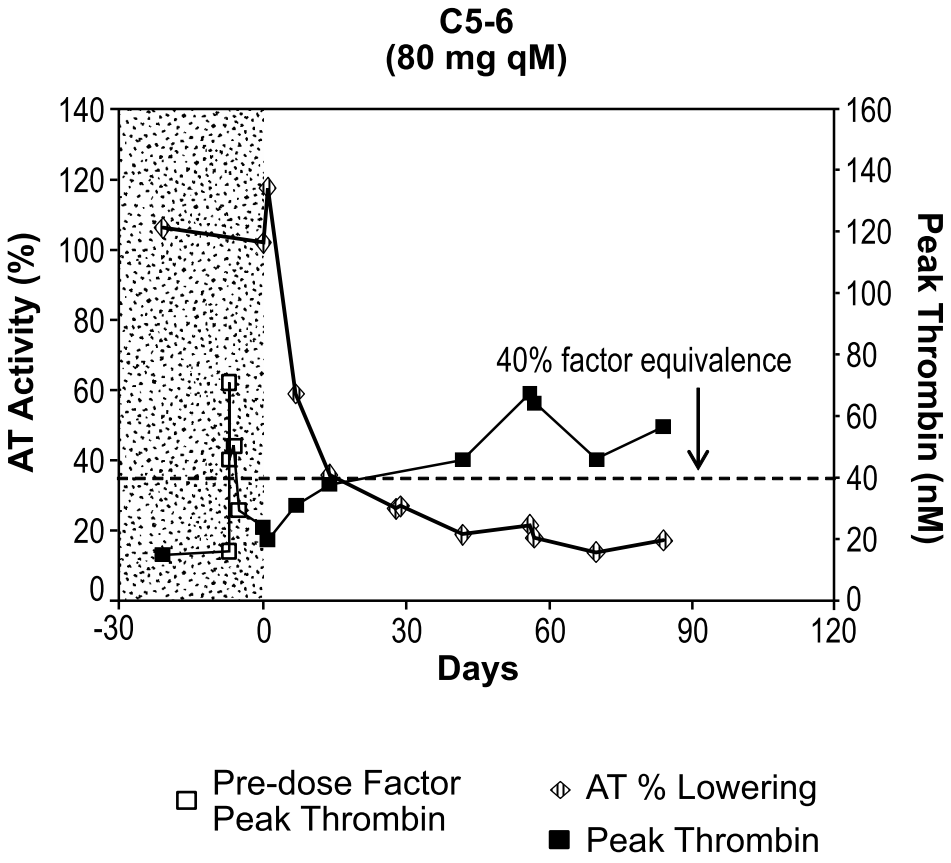
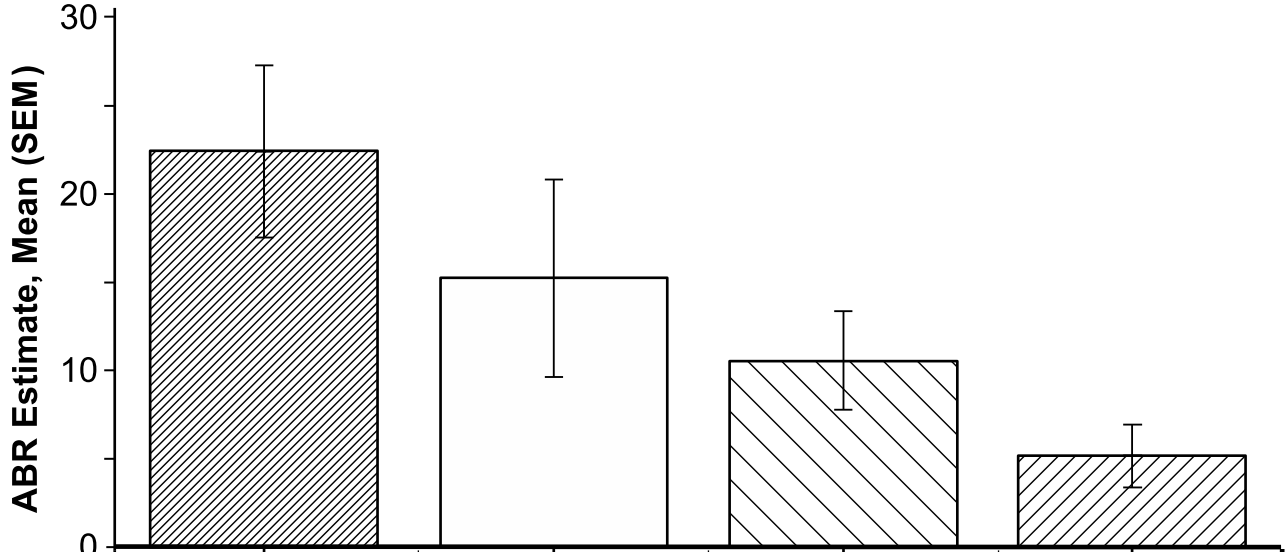

C5-6
(80 mg qM)
AT Activity (%)
Peak Thrombin (nM)
Days
40% factor equivalence
Pre-dose Factor
Peak Thrombin
AT % Lowering
Peak Thrombin

Figure 10C



	AT Lowering <25%	AT Lowering 25-50%	AT Lowering 50-75%	AT Lowering >75%
Patients†	30	27	25	16
Cumulative Days	733	1119	1203	1128
Cumulative Bleeds	47	40	36	11
ABR‡, Mean (SEM)**	22 ± 5	15 ± 6	11 ± 3	5 ± 2
ABR, Median	10	0	6	1

**P-value < 0.05

ABR, annualized bleeding rate; SEM, standard error of the mean
†Number of patients with time spent in quartile;
‡For each patient, the ABR in each quartile is calculated by 365.24*(number of bleed events/number of days in quartile)

Figure 11

Dose	Patient	Prior Tx	Pre-study ABR‡	Onset ABR	Observation Period			
					All Bleeds, n	ABR	Spontaneous Bleeds, n	AsBR
225 mcg/kg	C1-1	PPx	2	13	1	**4**	1	**4**
	C1-2	PPx	0	0	1	**4**	0	**0**
	C1-3	PPx	0	50	4	**17**	0	**0**
450 mcg/kg	C2-1	PPx	4	25	4	**17**	3	**13**
	C2-2	OD	38	13	0	**0**	0	**0**
	C2-3	PPx	4	0	1	**4**	0	**0**
900 mcg/kg	C3-1	PPx	0	0	0	**0**	0	**0**
	C3-2	OD	20	25	3	**13**	0	**0**
	C3-3	OD	32	25	0	**0**	0	**0**
1800 mcg/kg	C4-1	PPx	0	25	0	**0**	0	**0**
	C4-2	OD	24	0	0	**0**	0	**0**
	C4-3	PPx	0	25	0	**0**	0	**0**
80 mg**	C5-1	PPx	12	13	2	**9**	1	**4**
	C5-2	PPx	16	0	0	**0**	0	**0**
	C5-3	PPx	6	13	2	**9**	0	**0**
	C5-5	PPx	6	13	0	**0**	0	**0**
	C5-6	PPx	0	13	0	**0**	0	**0**

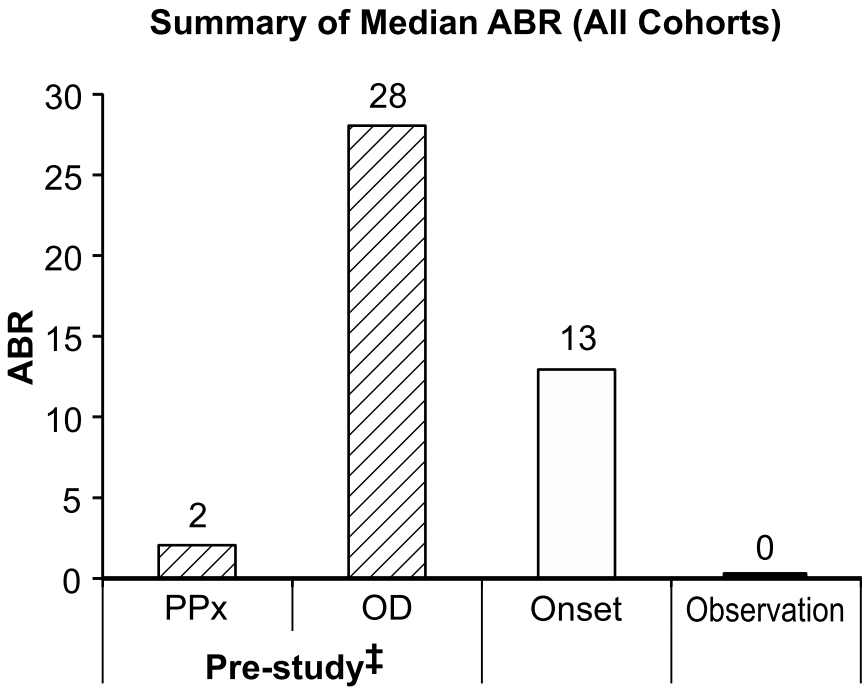
PPx: Prophylaxis, OD: On-Demand; ABR, annualized bleeding rate; AsBR, annualized spontaneous bleeding rate periods

†Post hoc analysis of treated bleed events during Onset (Day 028) and Observation (Day 29 to last study visit or last dose+56 days, whichever is earlier

‡Pre-study ABR derived from medical records.

**Patient C5-4 withdrawn, excluded from analysis

Figure 12



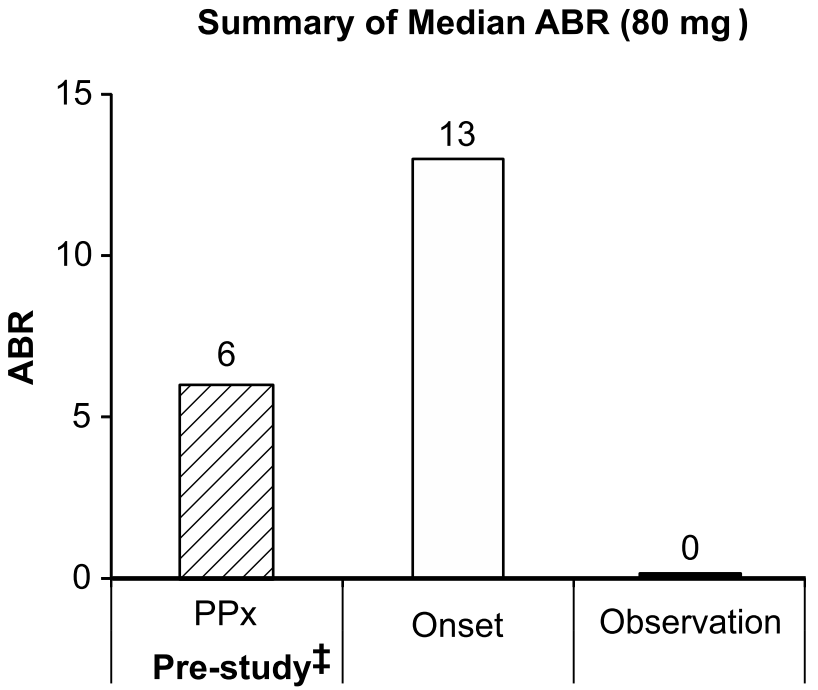
PPx: Prophylaxis, OD: On-Demand; ABR, annualized bleeding rate;

†Post hoc analysis of treated bleed events during Onset (Day 0-28) and Observation periods (Day 29 to last study visit or last dose+56 days, whichever is earlier

‡Pre-study ABR derived from medical records.

**Patient C5-4 withdrawn, excluded from analysis

Figure 13A



PPx: Prophylaxis, OD: On-Demand; ABR, annualized bleeding rate;

†Post hoc analysis of treated bleed events during Onset (Day 0-28) and Observation periods (Day 29 to last study visit or last dose+56 days, whichever is earlier

‡Pre-study ABR derived from medical records.

**Patient C5-4 withdrawn, excluded from analysis

Figure 13B

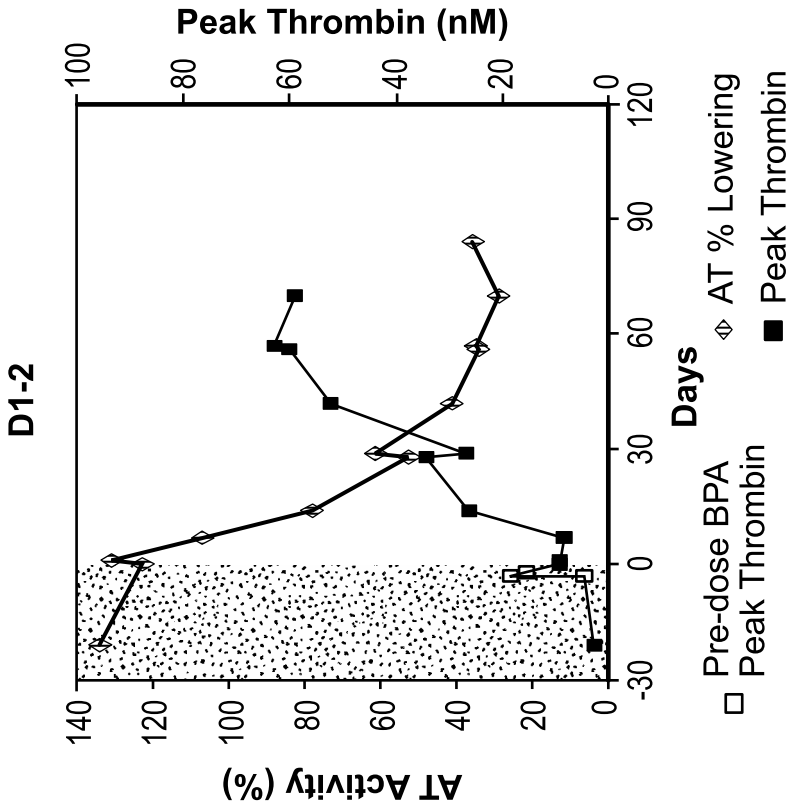


Figure 14B

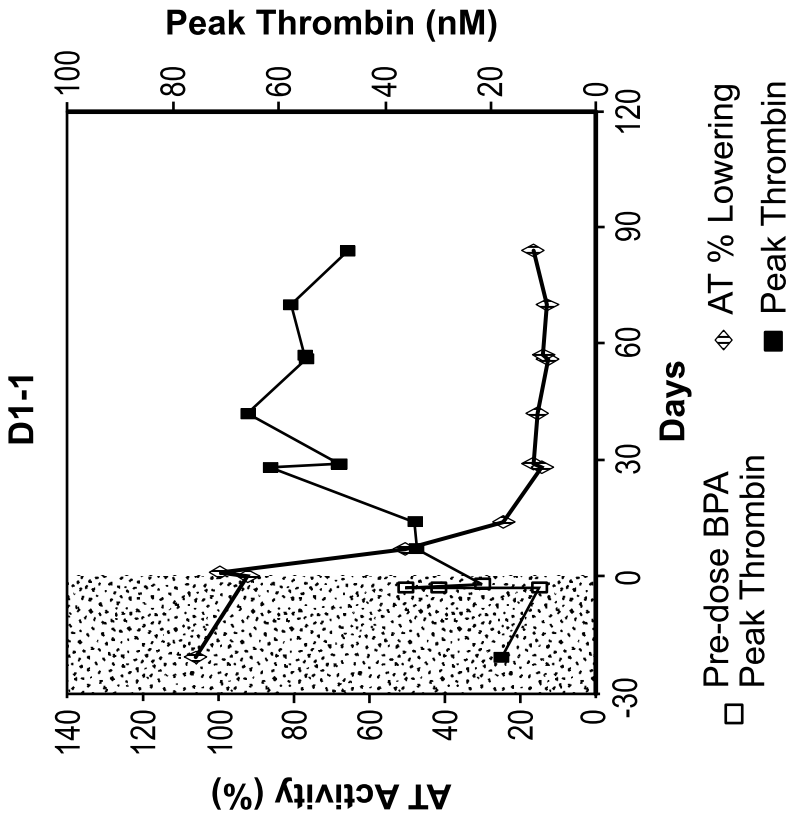


Figure 14A

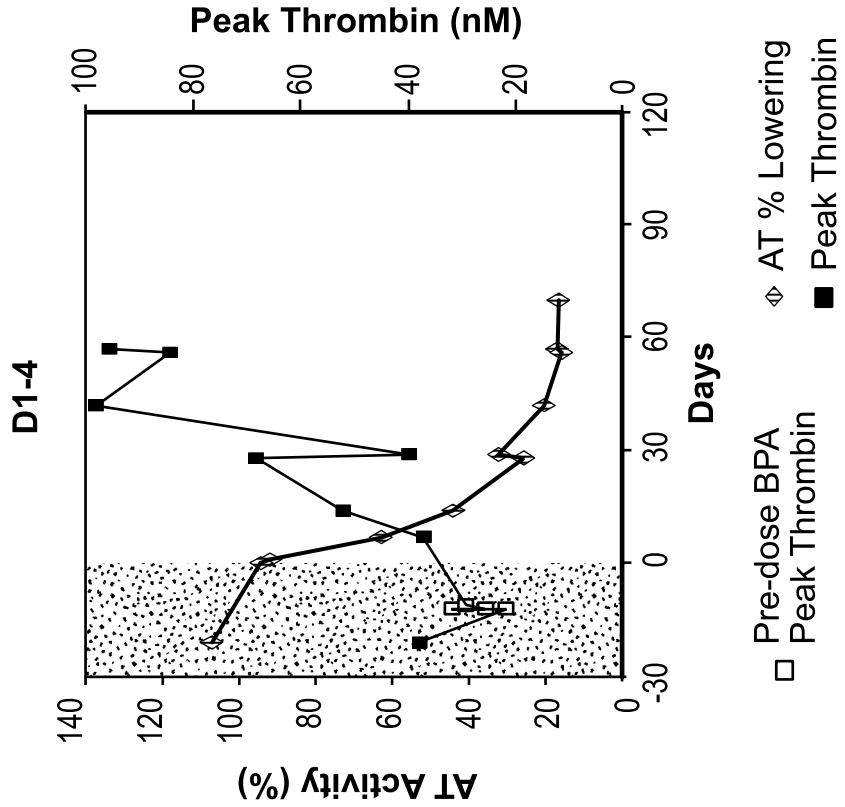


Figure 14D

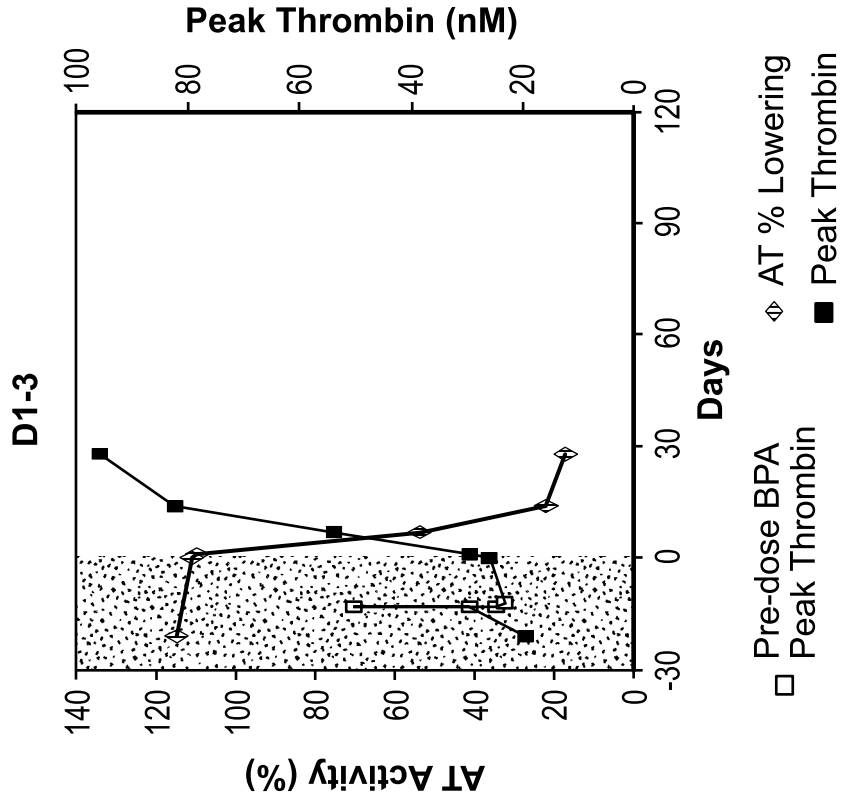


Figure 14C

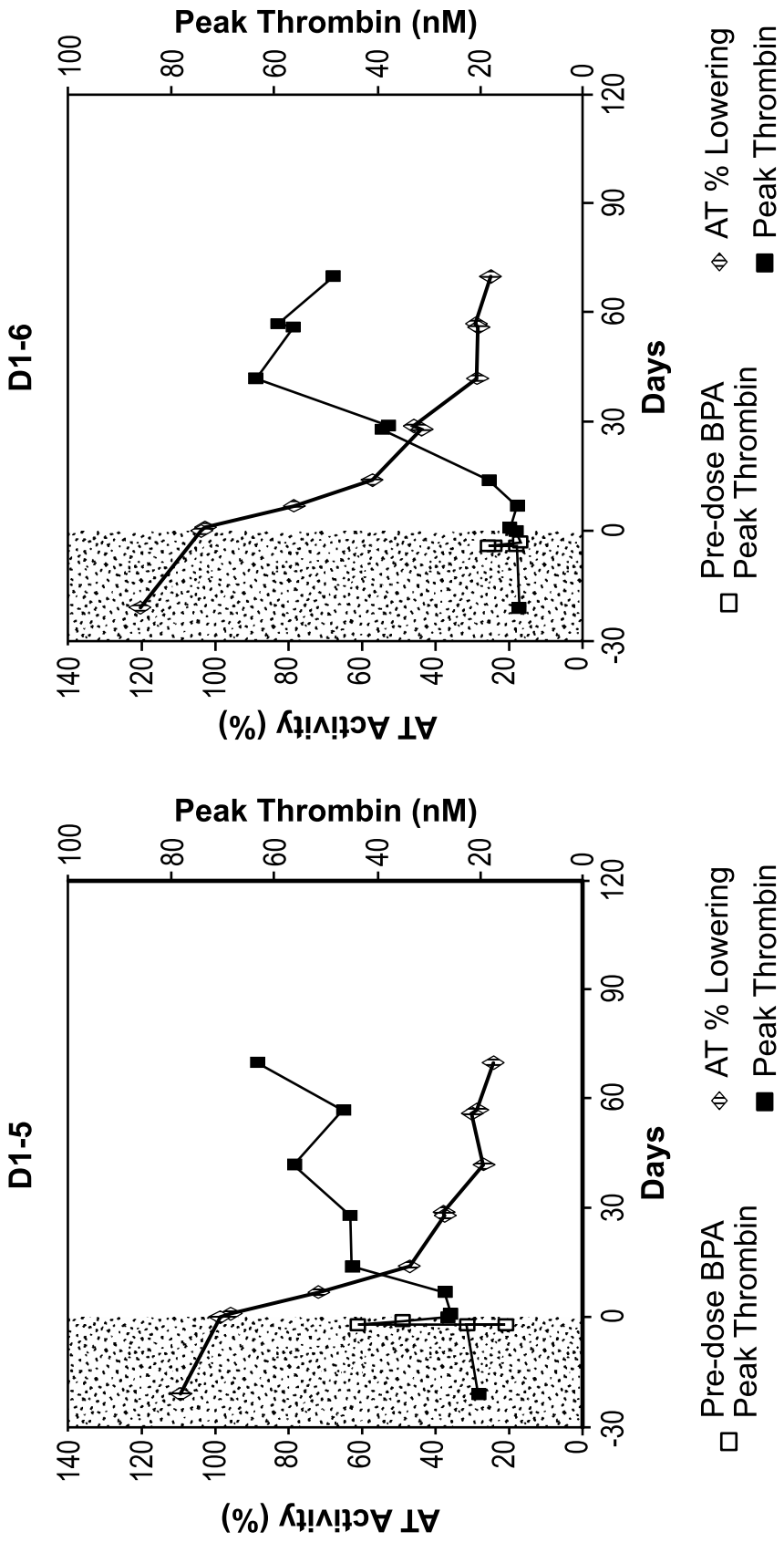


Figure 14F

Figure 14E

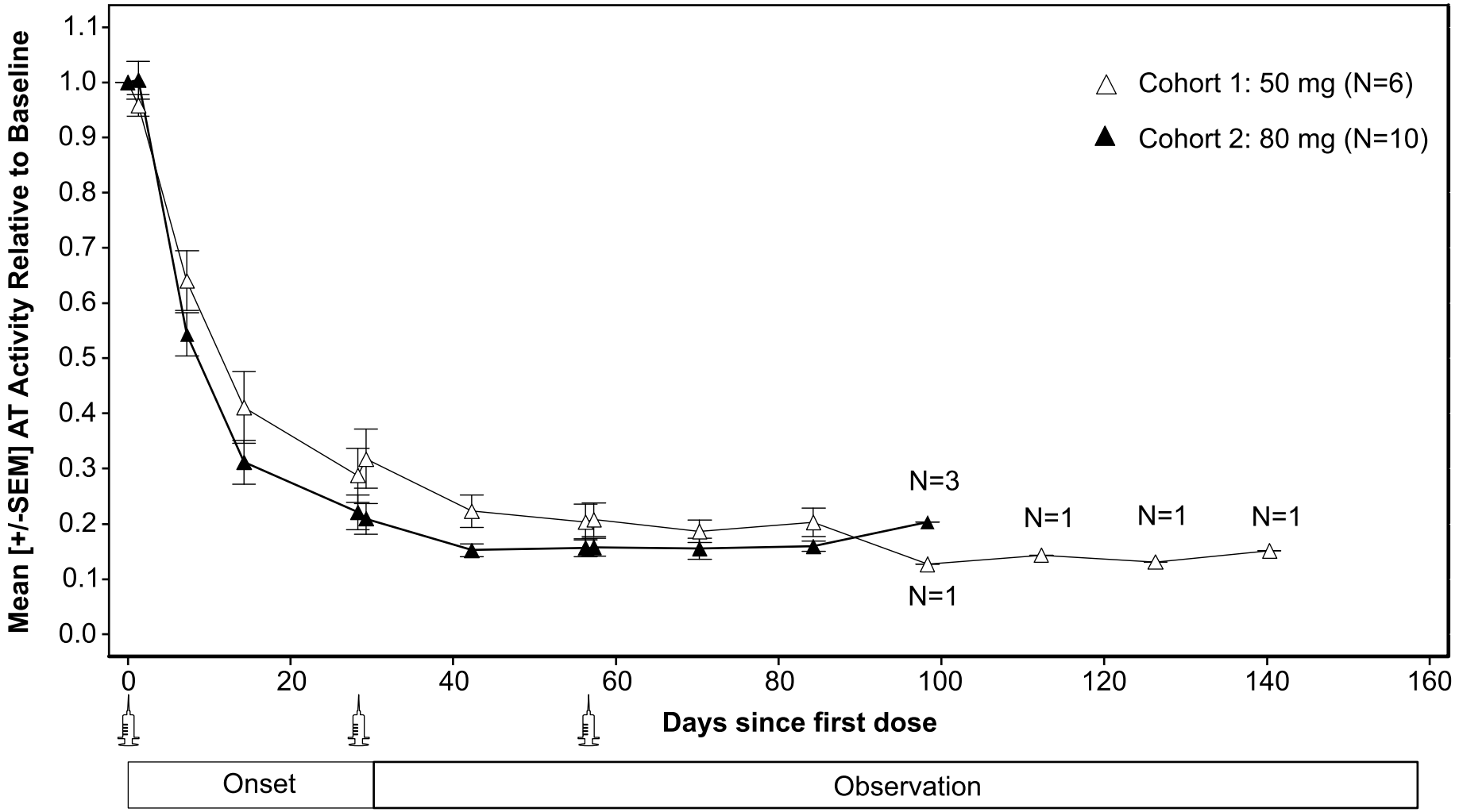

Mean [+/-SEM] AT Activity Relative to Baseline
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Cohort 1: 50 mg (N=6)
Cohort 2: 80 mg (N=10)
N=3
N=1
N=1
N=1
N=1
0
20
40
60
80
100
120
140
160
Days since first dose
Onset
Observation

Figure 15

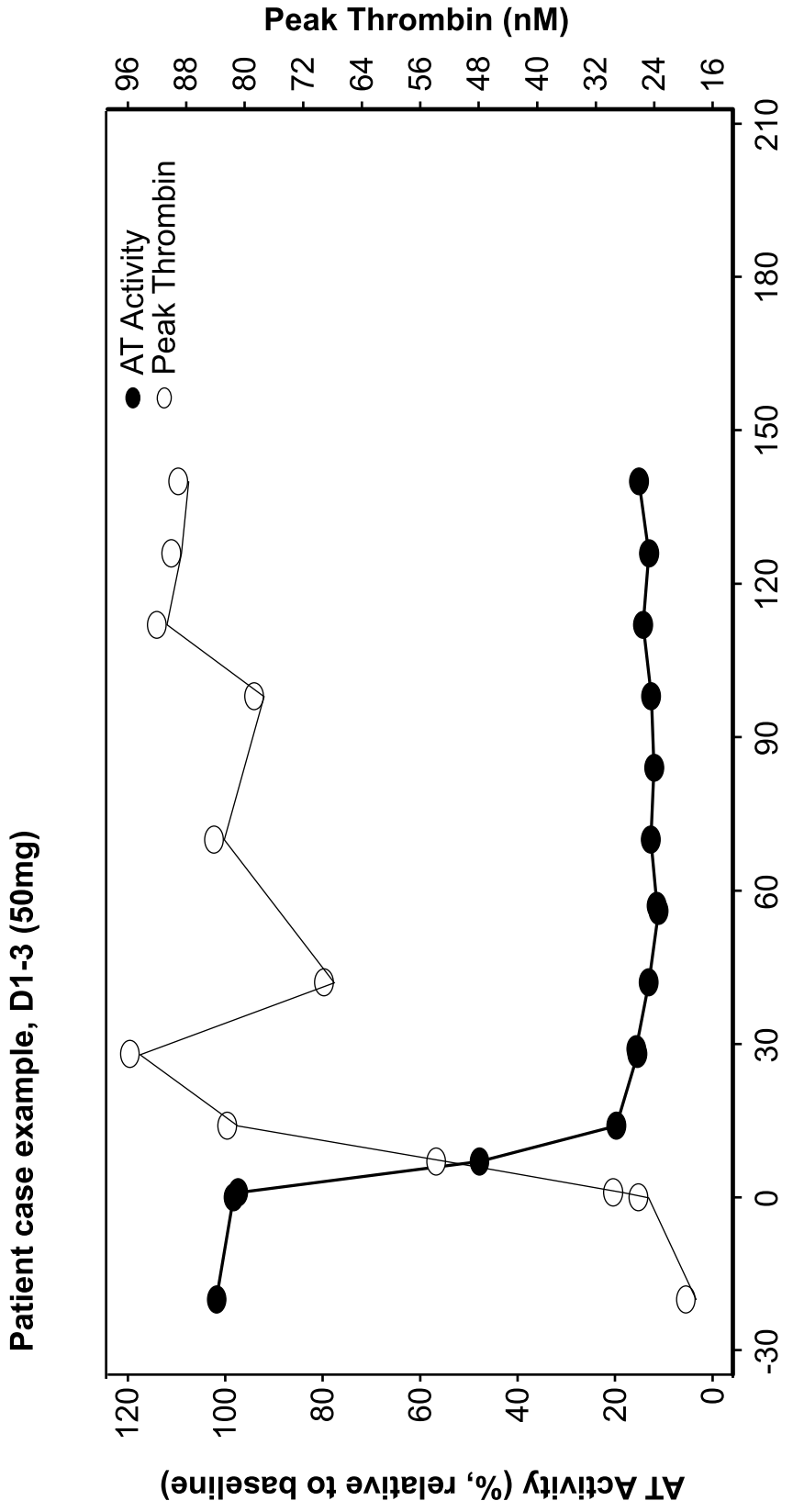

Patient case example, D1-3 (50mg)
AT Activity (%, relative to baseline)
Peak Thrombin (nM)
Days since first dose
AT Activity
Peak Thrombin
120
100
80
60
40
20
0
96
88
80
72
64
56
48
40
32
24
16
-30
0
30
60
90
120
150
180
210

Figure 16

Patient	Dose	Pre-study ABR‡	Onset ABR	Observation Period				
				Days in Obs Period	All Bleeds, n	ABR	Spontaneous Bleeds, n	AsBR
D1-1^	50 mg	40	13	191	3	5.7	2	3.8
D1-2^	50 mg	26	13	180	5	10.1	3	6.1
D1-3	50 mg	0	0	84	0	0	0	0
D1-4^	50 mg	52	38	162	11	25	9	20
D1-5^	50 mg	80	38	160	20	46	12	27
D1-6^	50 mg	16	13	156	0	0	0	0
D2-1	80 mg	48	0	48	1	7.6	0	0
D2-2	80 mg	48	0	41	0	0	0	0
D2-3	80 mg	8	0	72	0	0	0	0
D2-4^	80 mg	48	13	56	0	0	0	0
D2-5	80 mg	36	0	69	0	0	0	0
D2-6	80 mg	20	0	69	1	5.3	0	0
D2-7^	80 mg	14	0	55	0	0	0	0
D2-8	80 mg	20	13	55	2	13.3	2	13.3
D2-9	80 mg	12	0	13	0	0	0	0
D2-10	80 mg	44	0	13	0	0	0	0

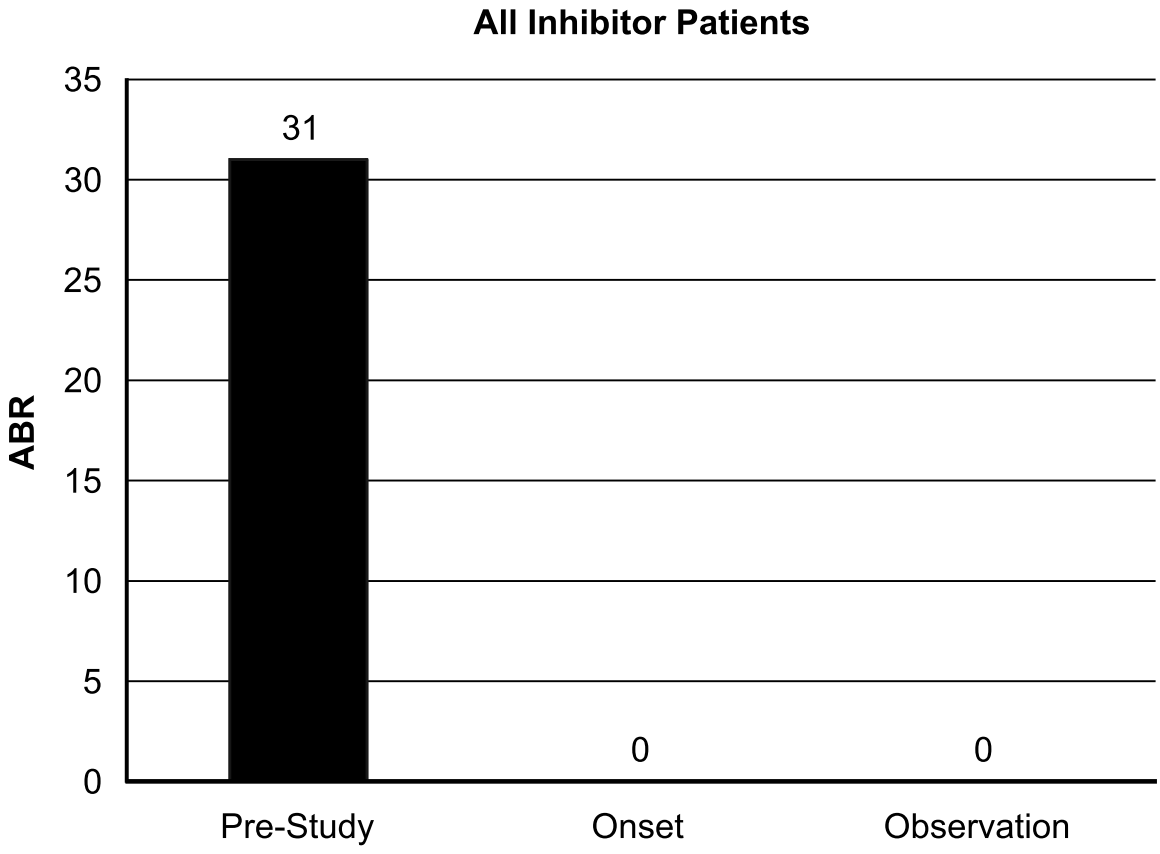
OLE, open-label extension; ABR, annualized bleeding rate; AsBR, annualized spontaneous bleed rate

†Post hoc analysis of treated bleed events during Onset (Day 0-28) and Observation periods (Day 29 to last study visit or last dose +56 days, whichever is earlier);

‡Pre-studu ABR derived from medical records;

^Patients transitioned to Phase 2 OLE as of data cut-off;

Figure 17A



- Median ABR, Pre-study period: 31
- Median ABR, Observation period: 0
  - Patients reporting no bleeds: 9/16 (56%)
  - Patients report no spontaneous bleeds (AsBR= 0): 11/16 (69%)

OLE, open-label extension; ABR, annualized bleeding rate; AsBR, annualized spontaneous bleed rate

Figure 17B

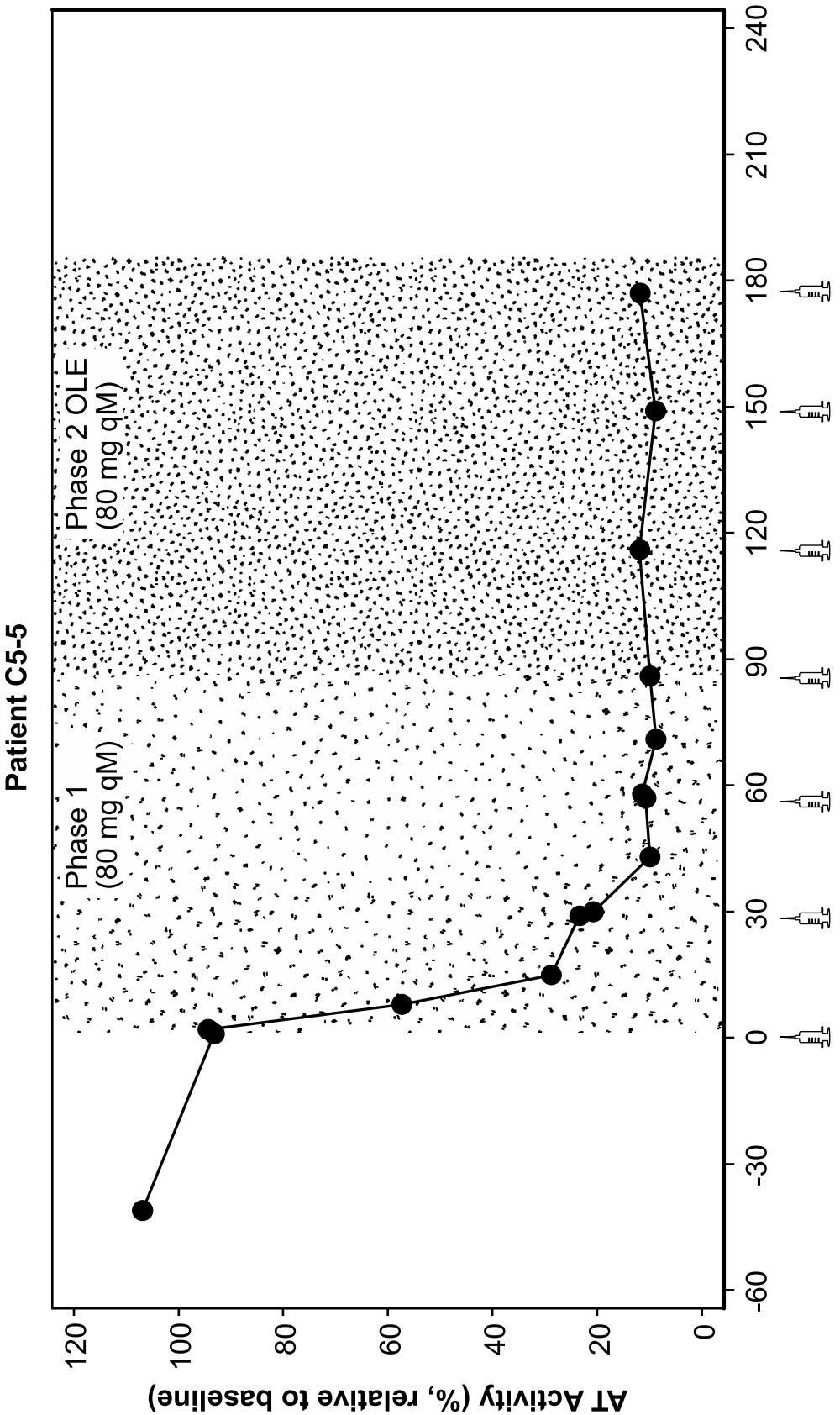

Patient C5-5
AT Activity (%, relative to baseline)
0
20
40
60
80
100
120
-60
-30
0
30
60
90
120
150
180
210
240
Days
Phase 1
(80 mg qM)
Phase 2 OLE
(80 mg qM)

Figure 18

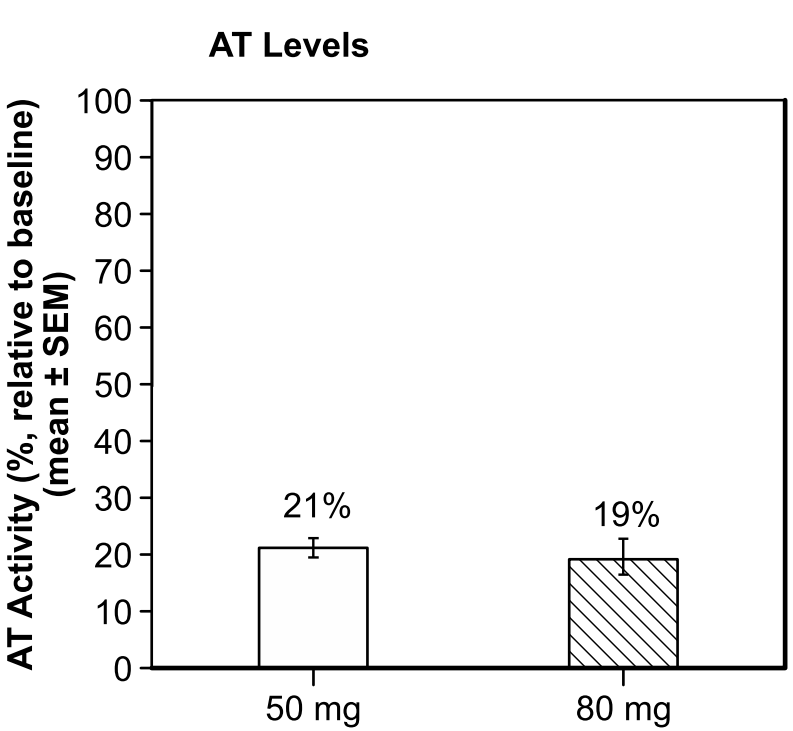


Figure 19A

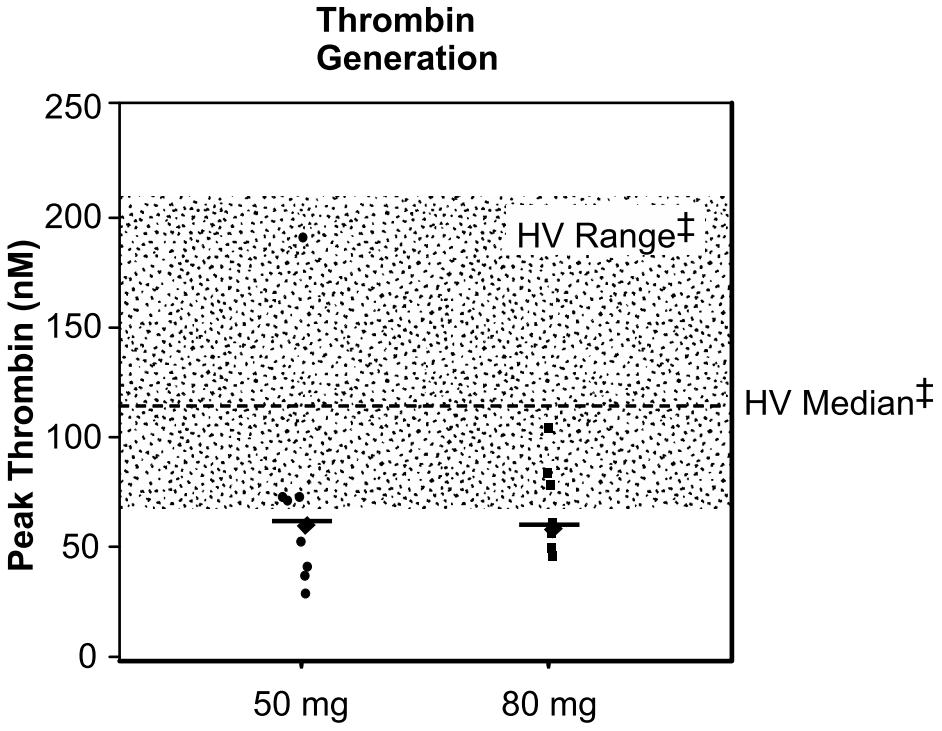
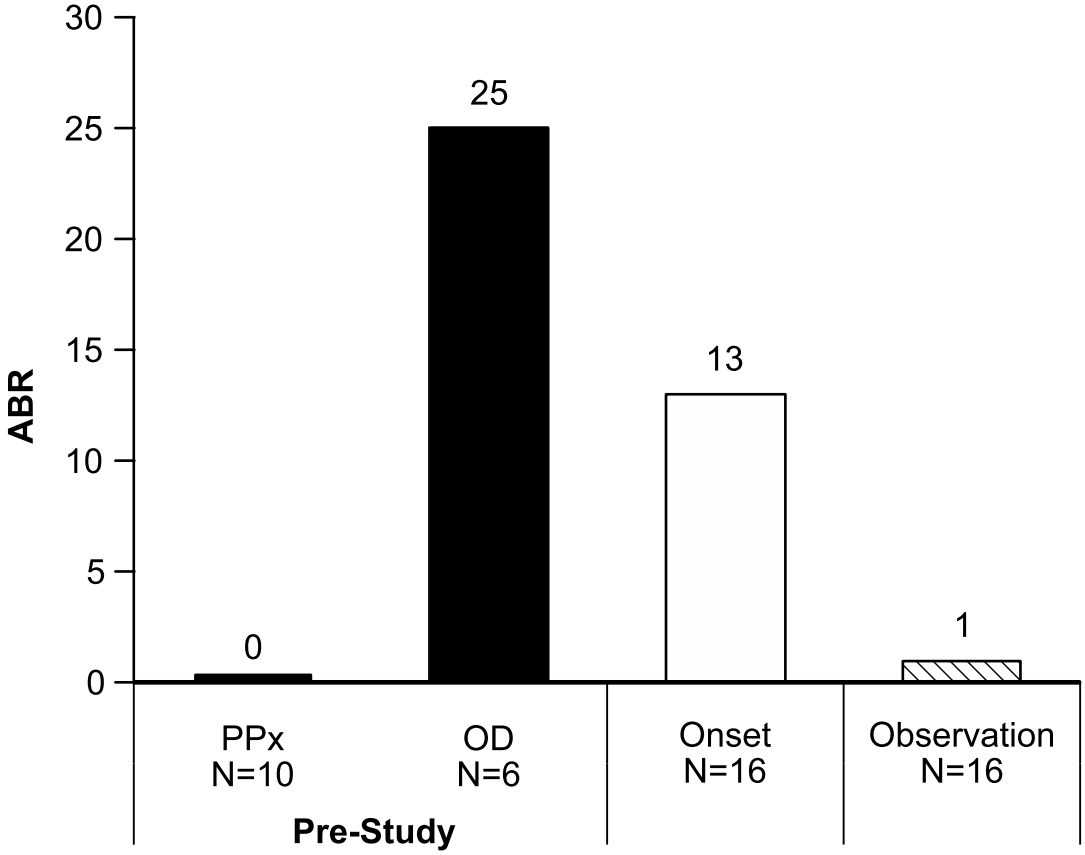


Figure 19B

Patient	Prior Tx	Pre-study ABR‡	Original Phase 1 Dose	Current Dose (qM)	Observation Period				
					Days	All Bleeds, n	ABR	Spontaneous Bleeds, n	AsBR
B2-4	OD	26	45 mcg/kg qW	50 mg	162	4	9.0	2	4.5
B2-5	OD	22	45 mcg/kg qW	50 mg	162	0	0	0	0
B3-1	PPx	4	75 mcg/kg qW	50 mg	63	0	0	0	0
B3-3	PPx	4	75 mcg/kg qW	50 mg	167	0	0	0	0
C1-1	PPx	2	225 mcg/kg qM	50 mg	335	4	4.4	3	3.3
C1-2	PPx	0	225 mcg/kg qM	50 mg	189	1	2.0	0	0
C1-3	PPx	0	225 mcg/kg qM	50 mg	148	2	4.9	0	0
C2-2	OD	38	450 mcg/kg qM	50 mg	174	0	0	0	0
C3-1^	PPx	0	900 mcg/kg qM	80 mg	373	0	0	0	0
C3-2	OD	20	900 mcg/kg qM	80 mg	133	13	35.7	0	0
C3-3	OD	32	900 mcg/kg qM	80 mg	162	0	0	0	0
C4-1^	PPx	0	1800 mcg/kg qM	80 mg	329	0	0	0	0
C4-2	OD	24	1800 mcg/kg qM	80 mg	169	0	0	0	0
C4-3	PPx	0	1800 mcg/kg qM	80 mg	170	1	2.1	1	2.1
C5-5^	PPx	6	80 mg qM	80 mg	261	3	4.2	1	1.4
C5-6^	PPx	0	80 mg qM	80 mg	224	2	3.3	1	1.6
^Patients C3-1, C4-1, C5-5, and C5-6 had no treatment interruption and therefore continuous observation period from Phase 1									

OLE, open-label extension; qW, weekly; qM, monthly; ABR, annualized bleeding rate;
AsBR, annualized spontaneous bleeding rate
†Post hoc analysis of treated bleed events during observation periods (Day 29 to last study visit or last dose +56 days, whichever is earlier);
‡Pre-study ABR derived from medical records

Figure 20A



- Median ABR, Observation period = 1
  - Patients reporting no bleeds: 8/16 (50%)
  - Patients report no spontaneous bleeds (AsBR = 0): 11/16 (69%)
- Median duration in observation period = 170 days (5.7 months)

PPx, prophylaxis; OD, on demand; ABR, annualized bleeding rate; AsBR, annualized spontaneous bleeding rate

Figure 20B