

SUPPLEMENTAL DATA

Figures S1. CONSORT Flowchart

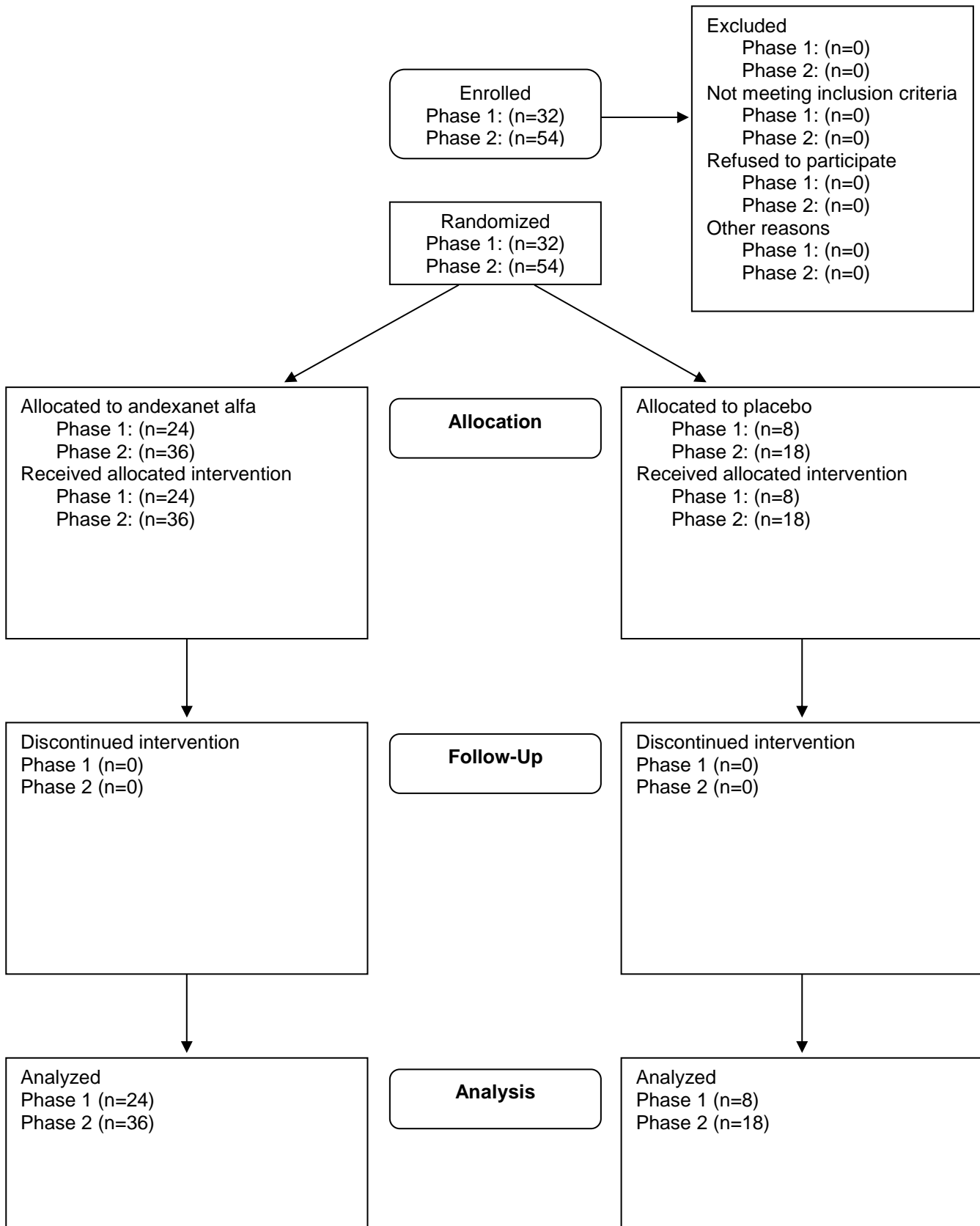


Table S1: Unbound and Total Concentration of Apixaban after Andexanet Administration

Pharmacokinetic Parameters (Mean ± SD)	Andexanet Dose, Mean ± SD (n=6/Cohort)						Placebo* (n=18)
	90 mg bolus (cohort 1)	210 mg bolus (cohort 2)	420 mg bolus (cohort 3)	420/4 x 45 min (cohort 4)	420/180 (cohort 5)	420/4 x 2 hr (cohort 6)	
Unbound Apixaban C _{3.03} ^a (ng/mL)	3.83 ± 1.17	4.53 ± 2.61	2.25 ± 0.918	1.88 ± 0.21	1.10 ± 0.11	1.17 ± 0.31	8.37 ± 1.43 ^b
Total Apixaban C _{3.02} ^a (ng/mL)	176 ± 24.1	286 ± 76.0	326 ± 60.4	398 ± 54.9	439 ± 48.8	361 ± 44.1	133 ± 19.2 ^b

SD, standard deviation

*Pooled placebo group from Cohorts 1 through 6

^aPlasma concentration measured 2 minutes after the end of first andexanet first bolus dose

^bMean ± SD data from C_{3.02} and C_{3.03}

Table S2: Pharmacodynamic Parameters for Andexanet and Apixaban on Day 6.

ACT, activated coagulation time; aPTT, activated partial thromboplastin time; h, hour; m, minute; PTT, partial thrombin time; SD, standard deviation; sec, second;

Assessment, mean (SD)	90mg bolus n=6	210mg bolus n=6	420mg bolus n=6	420mg + 180mg infusion n=6	420mg + 180mg bolus n=6	420mg + 480mg infusion n=6	All active n=36	Vehicle control n=18
ACT, sec^a								
Pre-Apixaban	144 (34.9)	131 (8.9)	133 (7.2)	130 (7.0)	133 (6.6)	148 (18.9)	136 (17.6)	132 (13.8)
Post-Apixaban (3 h)	148 (11.5)	152 (11.0)	149 (5.4)	151 (8.2)	151 (14.6)	164 (14.9)	153 (11.9)	158 (18.2)
Pre-Andexanet (0-2 m)	130 (10.8)	122 (9.7)	113 (9.1)	112 (13.9)	116 (6.4)	112 (11.1)	117 (11.8)	152 (13.7)
Post-Andexanet (15 m)	128 (9.5)	123 (9.2)	119 (5.7)	109 (8.5)	NR	112 (9.7)	118 (10.6)	152 (10.6)
aPTT, sec^b								
Pre-Apixaban	29.8 (2.04)	30.2 (1.72)	29.5 (1.87)	31.3 (2.07)	29.5 (1.52)	31.2 (0.75)	30.3 (1.76)	29.6 (1.65)
Post-Apixaban (3 h)	31.2 (1.72)	31.5 (1.87)	30.8 (1.60)	32.2 (3.31)	30.3 (1.63)	32.3 (0.82)	31.4 (1.96)	30.4 (2.17)
Pre-Andexanet (0-2 m)	30.2 (2.14)	31.2 (0.98)	30.5 (2.66)	31.8 (1.60)	29.7 (2.16)	31.3 (0.82)	30.8 (1.87)	29.5 (2.50)
Post-Andexanet (15 m)	29.5 (1.64)	30.5 (1.38)	30.5 (1.64)	30.8 (1.72)	NR	31.3 (1.37)	30.5 (1.57)	30.1 (1.75)
PTT, sec^c								
Pre-Apixaban	11.2 (0.39)	11.0 (0.41)	11.0 (0.33)	10.9 (0.25)	11.1 (0.31)	11.1 (0.49)	11.1 (0.36)	11.1 (0.42)
Post-Apixaban (3 h)	11.6 (0.44)	11.4 (0.30)	11.2 (0.27)	11.3 (0.39)	11.7 (0.45)	11.3 (0.54)	11.4 (0.41)	11.4 (0.39)
Pre-Andexanet (0-2 m)	11.4 (0.51)	11.2 (0.28)	11.1 (0.35)	11.0 (0.33)	11.2 (0.41)	11.1 (0.47)	11.2 (0.39)	11.5 (0.45)
Post-Andexanet (15 m)	12.1 (1.47)	11.2 (0.26)	11.0 (0.21)	10.9 (0.36)	NR	11.0 (0.47)	11.2 (0.82)	11.4 (0.37)

NR, not reported.

Apixaban 5mg po.

^aRef range 90-150.

^bRef range 23-32.

^cRef range 9.6-11.6.

Figure S2. Dosing and Treatment Regimen for the Phase 2 Trial.

