Supplementary Material

A practical, one-clinic visit protocol for pharmacokinetic profile generation with the ADVATE® myPKFiT® dosing tool in severe hemophilia A subjects

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Supplementary Table 1: Agreements between the washout, 6-sampling time point and the no-washout, single-clinic visit 2 time-point PK protocols for the PK parameter volume of distribution at steady state generated using the ADVATE® myPKFiT® dosing tool and Factor VIII:C levels*.

	PK parameter	One-stage Assay	Chromogenic Assay
		ICC (95% CI)	ICC (95% CI)
All participants (n=35)	Vss (dL/kg)	0.47 (0.17, 0.69)	0.47 (0.17, 0.69)
O Blood Group (n=12)	Vss (dL/kg)	0.50 (-0.07, 0.83)	0.49 (-0.09, 0.82)
Non-O Blood Group (n=20)	Vss (dL/kg)	0.43 (-0.00, 0.73)	0.50 (0.08, 0.77)

Abbreviations: PK, pharmacokinetic; Vss, volume of distribution at steady state.

*Factor VIII:C determinations done in central laboratory

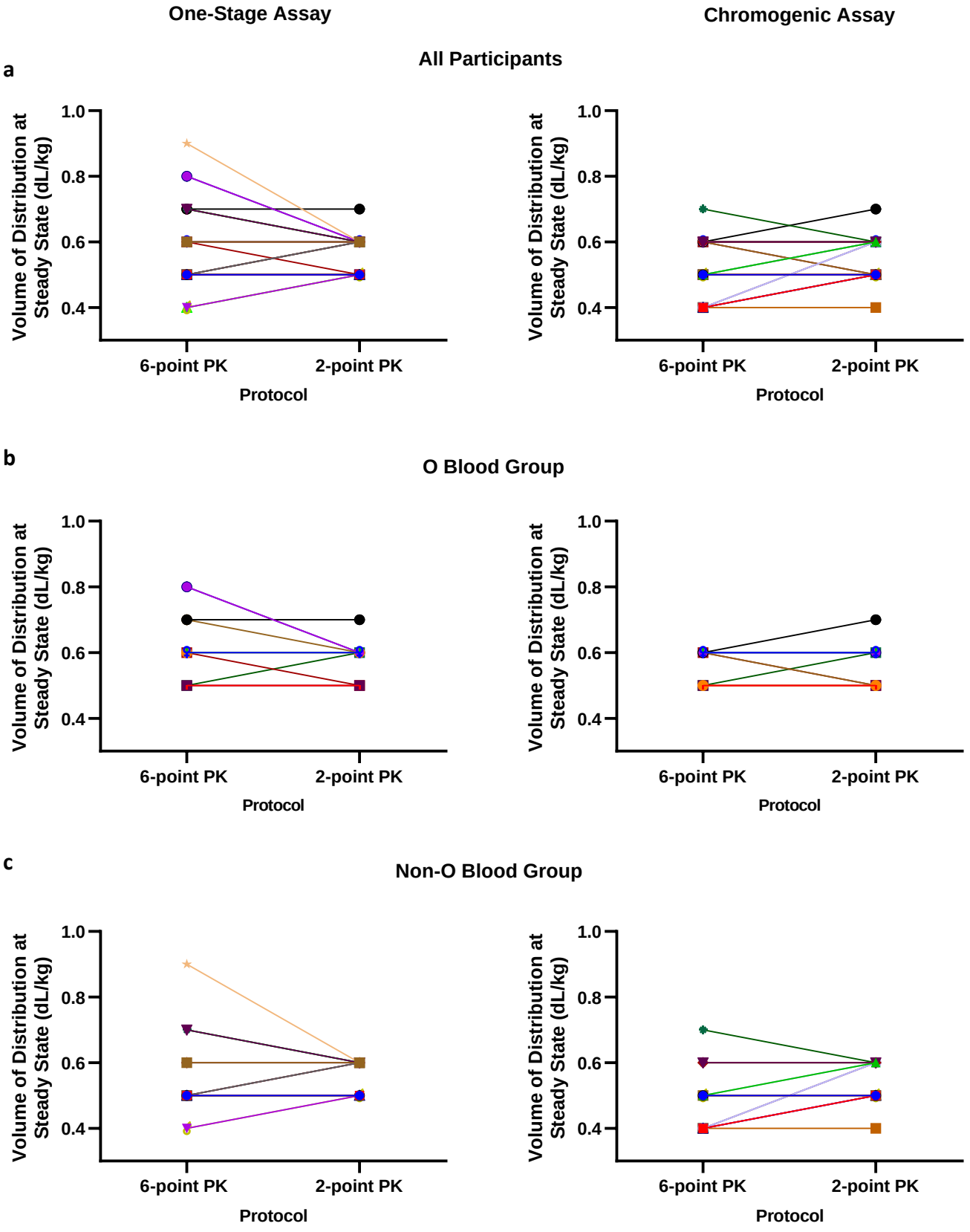
Note: Data for 35/39 subjects were available for analysis: the ADVATE® myPKFiT® application was unable to generate PK parameters for the 2-point PKs of four subjects (2 subjects had doses <10IU/kg which is outside the allowable range of 10-100 IU/kg for the dosing tool), 1 subject had technical issues with the FVIII:C samples and 1 subject did not have adequate documentation of the FVIII infusion prior to the clinic visit for the 2-sampling time point PK study). Blood group status was not available for 3 subjects.

Supplementary Table 2: Agreements between the washout, 6 sampling time point and the no washout, single clinic visit 2 time-point PK protocols for PK parameters generated using the myPKFiT® dosing tool and Factor VIII:C levels measured in the local laboratories.

	PK parameter	One-stage Assay
		ICC (95% CI)
All participants (n=31)	Cl (mL/hr/kg)	0.77 (0.58, 0.88)
	t½ (hrs)	0.91 (0.82, 0.95)
	Vss (dL/kg)	0.49 (0.17, 0.72)
O Group (n=11)	Cl (mL/hr/kg)	0.48 (-0.13, 0.83)
	t½ (hrs)	0.43 (-0.19, 0.81)
	Vss (dL/kg)	0.42 (-0.20, 0.80)
Non-O Group (n=18)	Cl (mL/hr/kg)	0.85 (0.63, 0.94)
	t½ (hrs)	0.95 (0.87, 0.98)
	Vss (dL/kg)	0.46 (0.00, 0.76)

Data for 31/39 subjects were available for analysis: the local results was not provided for 4 patients (3 from the same site), the myPKFiT® application was unable to generate PK parameters for the 2-point PKs of 4 subjects (2 subjects had doses <10IU/kg which is outside the allowable range of 10-100 IU/kg for the dosing tool, 1 subject had technical issues with the FVIII:C samples and 1 subject did not have adequate documentation of the FVIII infusion prior to the clinic visit for the 2 sampling time point PK study). Blood group was not available for 2 subjects.

Supplementary Fig. 1: Spaghetti plots showing, in the same subjects, the PK parameter of volume of distribution at steady state* generated using the myPKFiT® dosing tool and Factor VIII:C levels from the washout, 6-sampling time point and the no-washout, single-clinic visit 2 time-point PK protocols. a, All participants (n=35); b, Subjects with O blood group (n=12); c, Subjects with non-O blood group (n=20).



*For volume of distribution, many of the lines joining the values for the 6- and 2-point PK protocols are superimposed, hence, the fewer apparent lines on these plots.

Supplementary Fig. S2: One-stage and chromogenic assay FVIII:C levels at pre-, and 1hr, 3hr, 9hr, 24hr and 48hr post-infusion from the 6-point PK studies. Data are presented as means ± standard error of the means; *p<0.001 and **p<0.0001.