Comparison of Ideal vs. Actual Weight Base Factor Dosing

Background

Hypothesis: Factor dosing based on ideal body weight will result in hemostatic factor levels (recovery of at least 66% and a 6 hour half life)

[BDC will make distinctions for A/B; yield will be primary endpoint, half-life at different time points will be secondary endpoint]

Trial Design

This is a randomized, prospective, multicenter, open-label, cross-over study comparing the pharmacokinetics (PK) of ideal vs. actual body weight dosing of factor concentrate in patients with hemophilia.

The study will be conducted at the Washington Center for Bleeding Disorders (WCBD), Oregon Health & Science University (OHSU), Seattle Children's Hospital (SCH) and Sacred Heart Hospital (SH). Ethics approval will be obtained at all locations before trial enrollment.

Inclusion Criteria

- At least 2 years of age [primary endpoint will be patients 12 and over. Will likely not be able to have enough sample size to determine statistically significant differences in patients under 12 years of age, but may enroll these patients as a secondary endpoint]
- Hemophilia A or B
- Male gender
- Able and willing to comply with PK testing schedule
- Either overweight body weight (BMI 25 - <30) or obese (BMI > or equal to 30)

Exclusion Criteria

- Inhibitor of > 0.6 BU twice in the past
- Known other bleeding disorder
- Known other prolongation in aPTT (lupus anticoagulant, FXII deficiency)
- Female gender

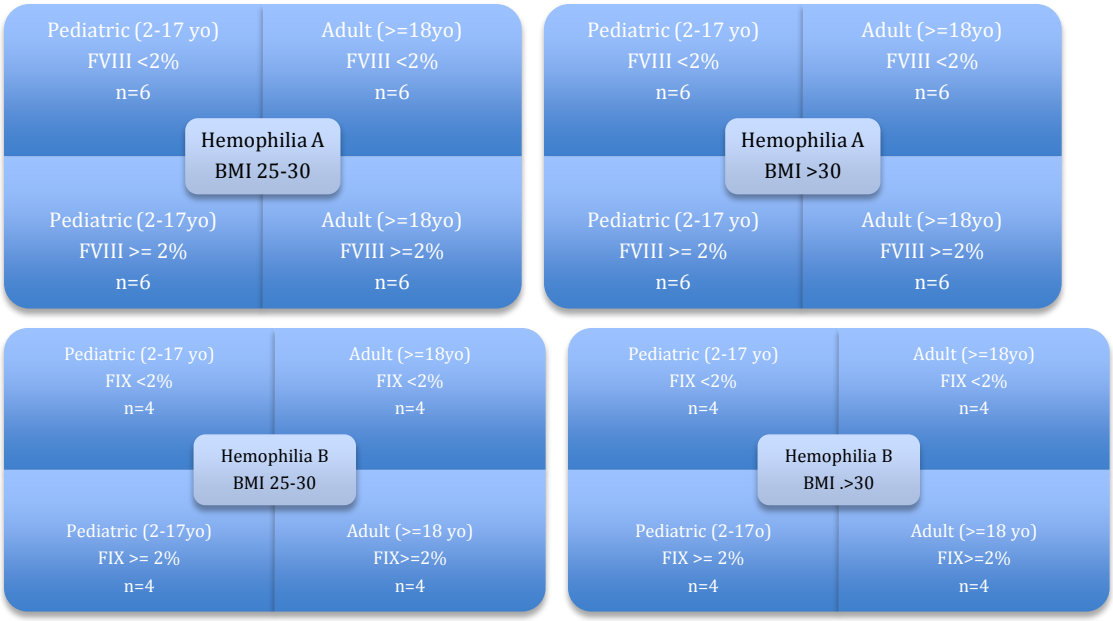
<u>Recruitment</u>

Patients will be recruited through the participating centers.

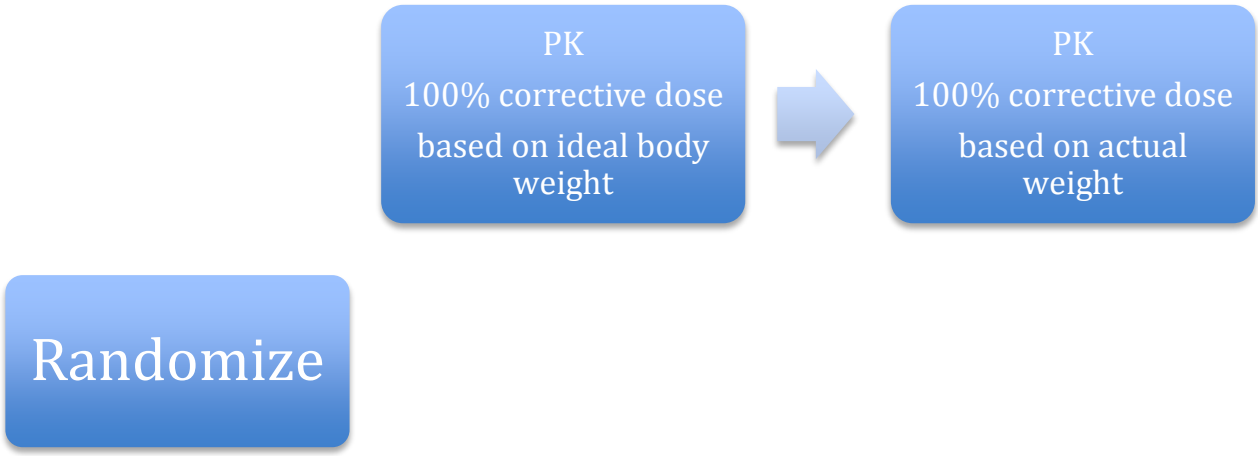
Sample size

Do we want to differentiate between overweight and obese?

What is a feasible n? [will contact biostatistician regarding appropriate n]



[will adjust these based on estimated sample size]
Study Procedure:
How do we want to randomize?



[washout period will be dependent upon product used; second phase will be done within 2 months of completion of first phase]

PK protocol:

PK studies will be measure in response to one 100% corrective dose of the patient's current product. All patients will undergo PK testing twice: One with a 100% corrective dose (50U/kg for hemophilia A and 100U/kg for hemophilia B) base on ideal body weight and once based on actual body weight.

Ideal body weight will be calculated as follows:

50 + 2.3 (height in inc. – 60)

Hemophilia A – regular half-life product

Baseline – 30 min to 60 min – 5 to 7 hours – 20 to 26 hours – 44 to 50 hours

Hemophilia A – extended half-life factor

Baseline – 30 min to 60 min – 5 to 7 hours – 20 to 26 hours – 44 to 50 hours – 69 to 75 hours – 93 to 99 hours

Hemophilia B – regular half-life product

Baseline – 30 min to 60 min – 5 to 7 hours – 20 to 26 hours – 44 to 50 hours – 69 to 75 hours

Hemophilia B – extended half-life factor

Baseline – 30 min to 60 min – 5 to 7 hours – 20 to 26 hours – 44 to 50 hours – 69 to 75 hours – 93 to 99 hours – 117 to 123 hours

[Yield must be done in the same lab. Half-life is not feasible all in the same lab. BDC will develop criteria to determine if local labs are reasonable for inclusion in study. BDC will develop criteria on when to accept historical fall-off (PK) from outside the study.]