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von Willebrand Factor in Pregnancy (VIP) Study: A Multicenter Study of Wilate Use in von Willebrand Disease for Childbirth

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Abstract

Specific guidance is lacking for delivery planning in terms of how high a factor level should be achieved for pregnant women with von Willebrand disease (VWD) who, by the third trimester, do not have von Willebrand factor (VWF) (or factor VIII) levels greater than 50-100%. Specifically, guidance is lacking on whether replacement therapy should target a VWF minimum level in the 100–150% range, i.e., a range closer to the 200–250% levels observed in normal pregnancy.Objectives: The primary objective is to document the rate of primary postpartum hemorrhage (PPH) and thereby the effectiveness of targeting minimum VWF levels of 100–150% for delivery. The secondary objective is to document further effectiveness outcomes and safety. Patient VWF levels will be maintained at 100-150% for the immediate 72-hour postpartum period, and thereafter maintained at 50-100% target VWF levels through days 5-7 postpartum after normal vaginal delivery or days 7–10 postpartum after caesarean section.Methods: This is a prospective, open-label, cohort study of the dosing of Wilate in pregnant patients with VWD to achieve minimum VWF levels of 100–150% for delivery. Outcome parameters will be assessed among patients termed non-correctors and correctors. Patients with a third trimester (gestational week 34–38) VWF level <100% will be enrolled in the non-corrector group. Patients with VWF levels ≥100% at gestational weeks 34–38 will be enrolled in the corrector group. Sample size is based on 65 pregnant VWD non-corrector patients and up to 30 corrector patients. Both correctors and non-correctors will be given tranexamic acid post-partum for 14 days. Inclusion Criteria: includes VWD patients diagnosed prepartum as type 1 per NHLBI criterion of VWF level <30%, or type 2, or type 3. Exclusion Criteria includes age <18 years, presence of other concurrent disorder of hemostasis, platelet dysfunction, or collagen disorders; presence of liver disease or renal disease, clinical suspicion or diagnosis of preeclampsia or eclampsia, HELLP syndrome, TTP, DIC, or other acquired vasculopathy or coagulopathy, or inability to perform local laboratory monitoring. Primary outcome parameter will be the rate of primary PPH, defined as estimated blood loss ≥1000 mL, or severe PPH defined as estimated blood loss >2000 mL within 24 hours postpartum. Other outcomes are secondary PPH, laboratory measures, and safety. Screening will begin in Q3 2019 and end in Q2 2023, with recruitment ending 6 months before (i.e., Q4 2022). Summary: This planned study aims to determine in VWD if VWF levels postpartum should be attained at levels closer to levels achieved physiologically in a normal pregnancy. Conclusions: Results from this study will hopefully lead to reduction of the relatively high rate of PPH in VWD women with levels <50-100% in the third trimester.