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Abstract Title : Emicizumab for severe von willebrand disease (VWD): The (EmiVWD) study enrollment 2025

Category: Trials In Progress

Review Category: TiP1. Trials in Progress: Classical Hematology

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Abstract Body

Background and Significance: Von Willebrand Disease (VWD) is the most common inherited bleeding disorder affecting up to 0.1-1% of the population, typically characterized by mucocutaneous bleeding. There is increased focus on prophylaxis for VWD with severe bleeding phenotypes, currently limited treatment options, and non-intravenous therapeutics are desired to tailor therapy for patient needs. Emicizumab is a monoclonal, bispecific antibody that demonstrates factor VIII-like activity enhancing thrombin generation, transforming prophylactic therapy for many with hemophilia A. Emicizumab can be administered subcutaneously at a frequency less than that of other currently available therapies for VWD, with a half-life of 27 days. Based on available literature emicizumab has been utilized successfully for VWD prophylaxis, and further investigation is warranted. Our objective is to evaluate the safety and efficacy of emicizumab for prophylaxis in severe VWD compared to the preceding 12-month bleed history.

Study Design and Methods: We initiated a pilot multicenter, prospective open-label study (NCT05500807) to evaluate emicizumab prophylaxis in severe VWD type 3, or VWD with VWF antigen (VWF:Ag), VWF activity (VWF:RCo or VWF:GPIbM), or VWF collagen binding (VWF:CB) ≤20 IU/dl or variant VWD confirmed by genetic mutation or additional VWF activity assays (ie. VWF platelet binding, VWF:FVIII binding, VWF propeptide), or VWD with concomitant hemophilia A defined as VWF:Ag, VWF activity, or VWF:CB < 50 U/dl, and mild, moderate or severe hemophilia A based upon historical medical records, with indication for hemostatic prophylaxis. Targeted enrollment is 40 patients of any age (≥3 kg). Exclusion criteria include patients with non-severe VWD, other bleeding disorders, renal and/or hepatic impairment, emicizumab treatment in the previous 18 months, or previous treatment thromboembolic disease in the past 12 months. Pre-investigation annualized bleed rate and hemostatic therapies are determined by a one-year retrospective chart review, collected at the time of enrollment. Patients then receive Emicizumab, 3mg/kg weekly for 4 consecutive weeks, followed by once weekly dosing of 1.5mg/kg for 52 weeks total therapy. Dose up-titration to 3 mg/kg once weekly will be allowed if suboptimal efficacy. Treatment records are maintained along with bleeding event logs. Patients are closely monitored for safety and tolerability. Breakthrough bleeding events may be treated with the patients usual on-demand products per the investigator's discretion. Central clinical laboratory testing will be completed, in addition to genetic testing. Patient-reported outcomes (PROMIS-29 PROs, SF-36) will be gathered to gain understanding on the impact of treatment on patients. Analysis will be performed through descriptive statistics to determine proof of principle, with patient bleeding evaluated prior to and after emicizumab prophylaxis. End of study is expected to occur 18 months after the last patient's first dose of study drug, to include a 6-month post-emicizumab prophylaxis follow-up. The primary hypothesis is that emicizumab is safe and efficacious for prophylaxis in VWD. Secondary objectives include evaluation of treatment

burden vs VWF concentrate prophylaxis, bleed rate and severity, VWF qualitative defects or genetic mutations that may have impact on emicizumab clinical response. Exploratory objectives include evaluation of health-related quality of life, impact on VWF concentrate use with bleeding events, surgeries, and heavy menstrual bleeding. Total length of the study is expected to be approximately 36 months. Six centers in the United States have currently been enrolling patients. Enrollment is currently ongoing.

Conclusions: This ongoing pilot study is the first prospective investigation of emicizumab in patients with severe VWD. This study will shed light on feasibility, safety and potential efficacy of emicizumab prophylaxis in this patient population.

Keywords: Biological Therapies, Treatment Considerations, Monoclonal Antibody Therapy, VWD, Diseases, Bleeding and Clotting

Disclosure : Jonathan Roberts: Novo Nordisk, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, Pfizer, Consultancy (Includes expert testimony): No, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, Genentech, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: Yes, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, Sanofi, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: Yes, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, Sobi, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, Takeda, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: Yes, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: Yes, May Chien: None declared, Sweta Gupta: None declared, Rebecca Kruse-Jarres: None declared, Erin Cockrell: CSL Behring, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: No, Bayer, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: No, Novo Nordisk, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended employment in the past 24 months: No, Research Funding: No, Divested equity in a private or publicly-traded company in the past 24 months: No, Current equity holder in publicly-traded company: No, Current Employment: No, Current holder of stock options in a privately-held company: No, Current equity holder in private company: No, Honoraria: No, Genentech, Consultancy (Includes expert testimony): Yes, Patents & Royalties: No, Ended

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