Pharmacokinetics and Coagulation Biomarkers in Persons with Hemophilia A (PwHA) and FVIII Inhibitors Receiving Emicizumab in the Phase IIIb STASEY Study

Anna Kilalainen,1 Claire Petry,1 Victor Jiménez-Yuste,2 Margarethe Ozelo,3 Oliver Meier,1 Susan Robson,1 Giancarlo Castaman,4 Robert Klamroth,5 Christophe Schmitt6
1F. Hoffmann-La Roche Ltd, Basel, Switzerland; 2Hospital Universitario La Paz, Autonoma University, Madrid, Spain; 3University of Campinas (UNICAMP), Sao Paulo, Brazil; 4Careggi University Hospital, Florence, Italy; 5Comprehensive Care Haemophilia Treatment Centre, Vivantes Klinikum, Berlin, Germany

SUMMARY

- Emicizumab, a novel therapy for prophylaxis of hemophilia A (HA), has demonstrated safety and efficacy in PwHA with and without factor (F)VIII inhibitors in Phase III studies (HAVEN 1-4),1-4 with reduced treatment burden through subcutaneous and less frequent dosing (once every week, 2 weeks, or 4 weeks).5
- While emicizumab mimics FVIII coagulant activity, it has fundamental differences from FVIII in terms of pharmacokinetics (PK) and biochemical and pharmacological properties.6
- STASEY is a single-arm, multicenter Phase IIIb study to further evaluate the safety and efficacy of emicizumab in persons with HA (PwHA) with FVIII inhibitors.7
- The STASEY study demonstrates that the PK and coagulation biomarker profiles of emicizumab in this large population of PwHA with FVIII inhibitors (n=193) are consistent with those reported in other emicizumab studies.8

INTRODUCTION

- HA results from a deficiency of coagulation FVIII, leading to risks of frequent and prolonged bleeds: spontaneously or related to trauma or surgery.9
- Emicizumab is a novel recombinant, humanized, monoclonal antibody that restores the function of missing activated FVIII in PwHA by bridging activated FIX and FX.10
- Emicizumab showed a favorable safety profile and clinically meaningful bleed prevention in PwHA with FVIII inhibitors in the STASEY study (NCT03191799).11
- This analysis aims to present the PK of emicizumab prophylaxis in PwHA with FVIII inhibitors, as well as their biomarkers of coagulation observed during STASEY.12

METHODS

PK and coagulation biomarkers of 193 PwHA with FVIII inhibitors were assessed throughout emicizumab exposure (median 51 weeks) in the STASEY study (Figure 1). Emicizumab levels were measured with a validated ELISA assay. Two PD markers were assessed: FVIII activity (FVIII:C) using a validated chromogenic assay containing human FX and FX (Bayer BPA) and activated partial thromboplastin time (aPTT). Prothrombin time (PT), international normalized ratio (INR) and D-dimer were measured using standard assays. FVIII inhibitor titers were measured using a chromogenic Bethesda assay containing bovine reagents. Emicizumab trough plasma concentrations reached a therapeutic level by Week 5 and were sustained throughout maintenance dosing. • Mean steady-state emicizumab trough plasma concentration reached ~96 µg/mL by Week 5 and were sustained thereafter (data cut-off: 30 May 2019; Figure 2) • The emicizumab levels in the STASEY study are consistent with previous studies of emicizumab in PwHA with FVIII inhibitors.8,9,10

CONCLUSIONS

The PK and coagulation biomarker profiles and PK/pharmacodynamic relationship of emicizumab in the STASEY study were consistent with those from HAVEN 1-4 studies.12

REFERENCES


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Figure 1. STASEY trial design.

Emicizumab is subject to additional safety monitoring requirements in many countries. Healthcare professionals are advised to report any suspected adverse reactions to the regulatory authorities in your country according to your national requirements.