Surgical Experience from the Phase III STASEY Trial of Emicizumab Prophylaxis in Persons with Hemophilia A (PwHA) with FVIII Inhibitors: Data from the Second Interim Analysis

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SUMMARY

- The management and outcomes of PwHA who underwent surgical procedures during emicizumab studies are of clinical interest.
- PwHA with FVIII inhibitors receiving emicizumab prophylaxis as part of the Phase II STASEY trial underwent minor and unplanned major surgeries, managed at the investigator’s discretion.
- Overall, minor and major surgeries were safely performed in the STASEY trial with few post-operative bleeds.

INTRODUCTION

- Emicizumab, a subcutaneously administered, bivalent monoclonal antibody, bridges activated factor (FX) and FX replacing the function of missing activated FVIII in PwHA. PwHA receiving emicizumab as study drug were treated in the STASEY trial (Figure 1). The Phase IIb STASEY trial (NCT03191991) assessed the safety and efficacy of emicizumab prophylaxis in PwHA with FVIII inhibitors; an interim analysis revealed that no new signals were identified.
- Here we present the surgical experience in PwHA with FVIII inhibitors enrolled in the STASEY trial.

METHODS

In the STASEY trial (Figure 1), minor and unplanned major surgeries were managed per the investigator’s discretion.

RESULTS

- Surgeries were categorized as minor or major as defined by Santagostino E, et al. (2015).
- Cases of procedures (type and number), use of any additional coagulation factor, adverse events, and management of post-operative bleeds were captured.

As of 20 May 2019, 11 minor and nine major surgeries were performed in 22 and eight participants, respectively.

- Facial (2019, 74.0%): minor surgeries were managed without additional prophylactic coagulation factor; of these, only 3/20 (15.0%) required post-operative treatment for bleeds (Figures 2, Table 1).
- One of 11 (9.1%) minor surgeries managed with additional prophylactic coagulation factor required post-operative treatment for a bleed.
- Case details of a minor arthroscopic knee surgery are shown in Table 2.

- Dental interventions with anti-Ro/SSA were uncomplicated with the exception of one case where an additional dose of 85 µg/kg FVIIIa was added; the combined use of anti-Ro/SSA and FVIIIa led to formation of a hypertrophic clot at the extraction site, which required surgical removal.
- Overall, 8/9 (89%) major surgeries were managed with prophylactic coagulation factor; resulting in four treated post-operative bleeds, two untreated bleeds, and two resulting in no bleeds (Table 3). One major surgery, coronaryography for myocardial ischemia, was managed without prophylactic coagulation factor and did not lead to a post-operative bleed.
- Case details of a total hip replacement are shown in Figure 3.

CONCLUSIONS

- In PwHA with FVIII inhibitors receiving emicizumab prophylaxis, most minor surgical procedures were performed without additional prophylactic coagulation factor and did not result in post-operative treated bleeds.
- Emicizumab alone may provide adequate hemorrhage coverage for patients undergoing certain types of minor surgery.
- Major surgeries were safely performed with additional coagulation prophylaxis.

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REFERENCES

Table 2. Case details and outcomes of major surgery/procedures in PwHA.

Table 3. Case details and outcomes of major surgeries/procedures in PwHA.

PUSHED FOR TIME?

- Emicizumab is subject to additional safety monitoring in early clinical trials. Healthcare providers are asked to be aware of the possible association between emicizumab and thrombotic microangiopathy and to consider intensifying monitoring, including platelet count, in such cases.

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