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Personally identifiable information (PII) within this document is either removed or redacted (i.e., specific content is masked irreversibly from view with a black bar) to protect personal privacy. Personally identifiable information includes:

- All named persons associated with the study
- Patient identifiers within text, tables, or figures
- By-patient data listings

Anonymized patient data may be made available subject to an approved research proposal submitted. Information which is considered intellectual property or company confidential was also redacted.

1.0 ABSTRACT

Title

241302 - Post-Marketing Non-Interventional Safety Evaluation of Obizur in the Treatment of Bleeding Episodes for Patients with Acquired Hemophilia A

Keywords

Acquired Hemophilia A; Antihemophilic Factor (recombinant), Porcine Sequence; Post-marketing safety; Obizur

Rationale and Background

Acquired hemophilia A (AHA) is a rare autoimmune disorder in which non-hemophilic persons develop auto-antibodies directed against circulating blood coagulation factor VIII (FVIII). Patients with AHA often experience serious bleeding episodes where the mortality rate due to bleeding or other underlying conditions can be as high as 22%. Recommended treatments include hemostatic agents such as bypassing agents and porcine, human plasma-derived, or human recombinant FVIII products. While bypassing agents have been shown to be effective, they carry thrombogenicity risk and are unable to be measured. An alternative to bypassing agents for the treatment of AHA is Obizur®, a novel highly purified antihemophilic recombinant porcine FVIII (rpFVIII) therapy, which was approved on 23 Oct 2014 by the Food and Drug Administration. Obizur temporarily replaces inhibited human FVIII with an rpFVIII as it is less susceptible to inactivation by circulating human FVIII antibodies. Clinical trial data on Obizur demonstrated a positive safety and efficacy profile of rpFVIII in patients with AHA after 90 days of post-treatment follow-up, however additional data are needed to evaluate the long-term safety and effectiveness of Obizur in the real-world setting.

Research Question and Objectives

This study was designed to assess safety and to describe factors related to the safety, utilization and effectiveness of Obizur in real-world clinical practice.

The primary objective is to determine the incidence of therapy related serious adverse events (SAEs) in patients with AHA who are prescribed and treated with Obizur in routine clinical practice.
Secondary objectives include:

- To describe hemostatic effectiveness of Obizur in the treatment of bleeding episodes.
- To describe the frequency, total dose, and total number of infusions of Obizur required to control bleeding episodes.
- To describe concomitant medication use.
- To describe the clinical setting in which patients first present with symptoms of AHA,

patient comorbidities, time from presentation of symptoms to a positive diagnosis, and time from a positive diagnosis to first treatment with Obizur.

- To describe the immunogenicity of Obizur during the course of treatment.

Study Design

This study was a multicenter, uncontrolled, open-label, non-interventional, prospective and retrospective post-marketing safety surveillance study. Data were collected for each patient over a period of approximately 180 days from the time of Obizur treatment. Patient prospective and retrospective status was based on site initiation date and Obizur treatment date.

Setting

Study participants were enrolled in an inpatient hospital setting, primarily from hematology departments. The study enrollment and data collection period lasted from 30 Dec 2015 to 04 June 2019.

Subjects and Study Size, Including Dropouts

Patients with AHA were eligible for participation in this study if they were treated with Obizur in a hospital setting. All patients were required to be prescribed Obizur by a physician, prior to the decision to enroll in the study. Overall, 53 patients were enrolled in this study, among whom, 29 completed the study.

Variables and Data Sources

Data were extracted from existing patient medical charts. Data elements collected included: patient demographics, disease and medical history, Obizur treatment information, concomitant medication use, laboratory data, safety events, and bleeding event characteristics.

Results

Six patients experienced 7 therapy related SAEs equating to an incidence of 12.00 (95% Confidence Interval [CI]: 4.53, 24.31) SAEs. The only commonly reported SAE, ie, ≥5%, was FVIII inhibition (incidence: 8.00, 95% CI: 2.22, 19.23). Further, 7 thrombotic events were observed during this study, however, only 1 (with multiple confounding factors) was classified as possibly related to Obizur treatment. Approximately 80% of all bleeds treated with Obizur resolved, and when used as first line treatment for initial bleeds, an even higher effectiveness was observed (85.0% of treated bleeds resolved). Median total dose infused for resolved bleeds equaled 450.0 U/kg.

Discussion

The results from this observational study found that Obizur is a novel option for the treatment of bleeding events among patients with AHA. A favorable effectiveness and safety profile was

demonstrated despite physician reports that resolved bleeds frequently required substantially lower total doses infused than observed in previous trials. As such, this study revealed that real-world dosing patterns vary widely possibly indicating a need for individualized treatment regimens. These results can be leveraged to provide a benefit-risk assessment in the real-world and better inform patient and provider treatment decisions.

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