1. ABSTRACT

- **Title**

A Cross-sectional Study of Patients With Immune Thrombocytopenic Purpura and Caregivers to Estimate the Proportion Who Administer Romiplostim Correctly After Receipt of Home Administration Training Materials

Abstract date: 04 April 2016

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- **Keywords**

Nplate®, immune thrombocytopenic purpura (ITP), Home Administration Training (HAT), non-interventional, self-administration

- **Rationale and Background**

A variation to the romiplostim (Nplate) Marketing Authorisation and Product Information was approved in the European Union (EU) in December 2012 to allow for the possibility of administering romiplostim by patients or their caregivers. To mitigate risks of medication errors from self-administration, a HAT pack was designed to support the training of physicians and patients. This study was conducted to measure the effectiveness of this additional risk minimization activity.

The Nplate EU Summary of Product Characteristics (SmPC), Section 4.2 Method of Administration, provided the following approved instructions for self-administration:

> "Patients who have a stable platelet count ≥ 50 x 10^9/L for at least 4 weeks without dose adjustment may, at the discretion of the supervising physician, self-administer Nplate solution for injection. Patients eligible for self-administration of Nplate should be trained in these procedures.
>
> After the first 4 weeks of self-administration, the patient should again be supervised while reconstituting and administering Nplate. Only patients who demonstrate the ability to reconstitute and self-administer Nplate are allowed to continue doing so."

- **Research Question and Objectives**

The primary objective of this study was to estimate the proportion of adult subjects and caregivers who administered romiplostim correctly after being trained with the HAT pack.

The secondary objectives of the study were to:

- estimate the proportion of subjects and caregivers who reconstituted romiplostim correctly;
- estimate the subjects' and caregivers' accuracy in administering the prescribed dose of romiplostim; and
- estimate the proportion of subjects and caregivers who injected romiplostim successfully.

- **Study Design**

This cross-sectional study involved direct observation by a healthcare professional (HCP) of a series of subjects and caregivers in the act of administering romiplostim at their first standard-of-care visit 4 weeks after training with the HAT pack. Further observations, if requested by the HCP, were also recorded in the study (if made within 16 weeks of enrollment). Additionally, data was collected from the subjects' self-administration diary at the first standard-of-care 4-week visit to ensure there were no problems with administration while not at the clinic.

- **Setting**

The study was conducted at 12 study centers in Austria, Belgium, France, Germany, Greece, The Netherlands, Spain, and The United Kingdom. The recruitment period began on 07 July 2014. The last subject last visit was on 20 November 2015 and the database lock was on 20 January 2016.

- **Subjects and Study Size, Including Dropouts**

Subjects were eligible if they met the following criteria: (1) adult ITP patient, treated per EU SmPC, or caregiver new (or at least a 3-month gap) to romiplostim administration; (2) received HAT pack training; (3) available at standard-of-care medical visit 4 weeks (range 2 to 8 weeks) after HAT pack training; and (4) provided informed consent. A total of 41 subjects or caregivers who were provided with HAT pack training were enrolled into the study. One subject failed study eligibility criteria as the first standard-of-care visit occurred 1 week post-HAT pack training; therefore, 40 subjects or caregivers were included in the Full Analysis Set. No subjects were lost to follow-up.

- **Variables and Data Sources**

Variables for data collection included subject demographics, expected and observed injection volume per syringe, appropriate use of alcohol wipe at injection site, clinically appropriate handling of syringe to avoid contamination, and clinically appropriate technique of subcutaneous injection. In this non-interventional study the data collected were derived from routine clinical care. HCPs completed a standardized data collection form to record their direct observation of subject or caregiver administration.

The primary endpoint in this study was defined as a yes/no indicator for whether the subject or caregiver administered romiplostim correctly at the standard-of-care 4-week visit.

The secondary endpoints in this study were defined as:

- a yes/no indicator for whether the subject or caregiver reconstituted romiplostim correctly at the standard-of-care 4-week visit / at follow-up visits
- for accuracy in administering the prescribed dose of romiplostim, the difference between the prescribed and self-administered dose of romiplostim, expressed as a %
- a yes/no indicator for whether the subject or caregiver injected romiplostim successfully at the standard-of-care 4-week visit / at follow-up visits
- a yes/no indicator for whether the subject or caregiver administered romiplostim correctly at follow-up visits.

- **Results**

For the primary endpoint, at the first standard-of-care visit 4 weeks after training with the HAT pack, 35 subjects or caregivers (87.5%) administered romiplostim correctly (ie, reconstituted romiplostim correctly, administered the prescribed dose accurately, and successfully injected romiplostim without any HCP intervention). A HCP intervened in 5 instances to correct the administration of romiplostim by 3 subjects and 2 caregivers. Two of these 5 subjects or caregivers had a follow-up visit and did administer romiplostim correctly at that visit.

For the secondary endpoints, 1 subject (2.5%) did not reconstitute romiplostim correctly because the subject did not ensure all of the romiplostim was dissolved. All 40 subjects or caregivers injected romiplostim successfully and the difference between the prescribed and administered dose of romiplostim was within the 10% margin error for dose.

Subsequent voluntary visits (if requested by the HCP) were recorded for 6 subjects or caregivers (15%) and all administered romiplostim correctly at these visits.

No adverse drug reactions (ADRs) were reported.

- **Discussion**

This study was conducted to measure the effectiveness of the HAT pack training in mitigating the risk of medication errors from self-administration. Most subjects or caregivers (87.5%) were able to administer romiplostim correctly without any HCP intervention after HAT pack training. The types of issues observed in this study were associated with addressable factors which can be managed by training with the current HAT pack materials. The physician guide in selecting and treating patients for home administration lists the eligibility criteria for the patient to be an appropriate candidate for self-administration. The patient training materials include specific instructions (paper and video formats) indicating steps where care needs to be taken to avoid the risk of medication error, the importance of checking that romiplostim has been reconstituted correctly, the importance of receiving the correct dose, and the consequences of dosing errors.

The results of this study highlight the importance of supervising the patient or caregiver again after the first 4 weeks of self-administration (as required by the EU SmPC and the HAT pack training materials), patient selection by the physician, and the HAT pack training in helping to mitigate the risk of medication errors during self-administration.

- **Marketing Authorization Holder(s)**

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