1. ABSTRACT

- **Title**

An Observational Study to Assess the Effectiveness of the Neulasta® Patient Alert Card and to Measure Medication Errors Related to the Use of the Neulasta® On-Body Injector.

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Name and affiliation of main author: [redacted], (Center for Observational Research, Amgen, 4 Uxbridge Business Park, Sanderson Road Uxbridge UB8 1DH, UK)

- **Keywords**

Neulasta, On-body Injector (OBI), Patient Alert Card (PAC), safety messages, awareness, device issues

- **Rationale and Background**

Neulasta (pegfilgrastim) is approved in the European Union (EU) for reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes). It is administered at least 24 hours after cytotoxic chemotherapy and often requires the patient to return to the health care facility for this purpose. The Neulasta Onpro Kit, consisting of 1 prefilled syringe with Neulasta and an OBI delivery system eliminates this return visit. Approval of the OBI by the European Medicines Agency was received in February 2018. An additional risk minimisation measure (aRMM) in the form of a PAC was developed to support patients in the safe and appropriate use of the OBI. In line with regulatory guidance, this study evaluates the aRMM for the OBI.

- **Research Question and Objectives**

The main aim of the study was to investigate the level of respondent awareness of key safety messages and behavioural intent to implement recommended actions as described in the PAC (primary objective). The key secondary objective was to determine if respondents received the PAC, with a further secondary objective to estimate the proportion of OBI administrations associated with medication error.

- **Study Design**

In this observational, cross-sectional study, respondents (patients or their main caregivers) who met the inclusion criteria and provided their consent to participate in the study, completed questionnaire approximately 27 to 72 hours after each OBI device application by their health care provider (HCP). The respondents' HCPs also completed a HCP questionnaire at the time of each of their participating respondents' on-study OBI application.

- **Setting**

The study was conducted at 8 sites in 3 EU countries: Belgium (1 site), Germany (5 sites), and Slovakia (2 sites).

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

This study included patients who were prescribed the OBI for Neulasta delivery for their current chemotherapy cycle.

Respondents (ie, patients or caregivers primarily responsible for monitoring the OBI) of age ≥18 years, who provided informed consent to participate in the study, and could read and understand the language in which the study was conducted were enrolled in the study.

A total of 86 eligible respondents were enrolled into the study: 12 respondents in Belgium, 51 respondents in Germany, and 23 respondents in Slovakia. Of the 86 respondents enrolled, 78 respondents were evaluable for the study; 8 respondents were not evaluable as they had missing questionnaires. A total of 230 OBI administrations were reported (Belgium: 29; Germany: 130, and Slovakia: 71) in the study. Therefore, this final analysis of the study encompasses 78 respondents, who received 230 OBI administrations across 8 study sites.

- **Data Source(s) and Methods**

The data sources for this study were the HCP and respondent questionnaires. Variables collected from the HCP captured details on their experience, practice setting, knowledge of where to obtain the PAC, eligibility of the patient receiving the OBI application, details on the OBI application itself (date, time), and observations on the functioning of the OBI device at the time of application. The respondent questionnaire for the first on-study OBI application captured variables to determine respondent demographics, receipt of the PAC, and assessed the respondents' knowledge of key safety messages in the PAC. In addition, respondent-reported functioning of the OBI device, symptoms experienced, and actions taken by the respondents and their HCPs were captured. For each subsequent OBI application, respondents completed a shortened version of the questionnaire, which did not re-assess their awareness of safety messages or variables relating to receipt of the PAC.

- **Results**

– Eligibility criteria for the study as assessed by HCPs were fulfilled for 86 respondents. For 8 of these respondents the initial (comprehensive) questionnaires were lost in the post resulting in a final study sample of 78 respondents, for whom 230 on-study OBI administrations were included. A further 16 initial respondent questionnaires were partially completed by the respondents. Thus, the final analysis for the primary and key secondary endpoints focused on 62 respondents who had completed all relevant sections of the questionnaire.

– The primary objective of the study was to assess respondent awareness of key safety messages and behavioural intent to carry out recommended actions as described in the PAC. The primary endpoint was a composite score for the study measure, based on the proportion of all awareness and behavioural intent questions with correct responses. Success was defined as a median composite score of at least 70.0% for the study. The median value for the composite score in this study was 75.0% (IQR: 57.1 to 92.9).

– The key secondary objective of this study was to determine if the respondent received the PAC. The key secondary endpoint was receipt of the PAC, as reported by the respondent, with success defined as a point estimate of at least 70.0% of respondents who provided an affirmative response to the key question regarding receipt of the PAC. A total of 81.0% (n = 47) respondents reported receiving the PAC from their HCP at the time of their first on-study OBI application (95% CI, 68.6 to 90.1).

- An additional secondary objective was to estimate the proportion of OBI administrations associated with medication error. The study questionnaire was found to be unfit for purpose to assess medication errors. Respondent-reported device related observations (referred to as 'device issues' in the report) were instead summarised to address this objective. A total of 230 OBI administrations across 78 respondents were included in the final analysis. The proportions of observations reported for each individual device issue were low.

- **Discussion**

The final analysis for the primary and key secondary endpoint focused on respondents who completed all relevant sections of the questionnaire (n = 62). For these respondents, the median composite score for awareness of key safety messages and behavioural intent to carry out recommended actions was 75.0%, demonstrating that the PAC was successful per the predefined cut-off level (70.0%). A total of 81.0% of respondents received the PAC at their first on-study OBI administration, hence, the threshold for successful distribution of the PAC (70.0%) was also exceeded Medication errors were not captured due to a poorly designed data collection tool. Instead, respondent-reported device related observations were summarised and occurred at low frequencies.

- **Conclusion**

- The study met the primary endpoint, demonstrating that the PAC is effective in educating patients about the key safety messages for the OBI and recommended actions for OBI-related issues.
- The study also met the key secondary endpoint, demonstrating that the PAC was frequently distributed to patients receiving the OBI in clinical practice.
- For most OBI administrations, there were no reported device issues. The data collection tool was not fit-for-purpose to estimate proportions of medication errors due to the questionnaire design, and cannot be relied upon to quantify the occurrence of medication errors with the OBI device in clinical practice.
- In summary, the final analysis of this observational multi-centre study suggests successful respondent awareness of key safety messages and behavioural intent to carry out recommended actions as described in the PAC, as well as successful distribution of the PAC. The study does not raise any new safety concerns for the OBI.

- **Marketing Authorisation Holder(s)**

Amgen Europe B.V.

Minervum 7061,

4817 ZK Breda,

The Netherlands

- **Names and Affiliations of Principal Investigators**

A total of 8 investigators participated in the study. These investigators oversaw data collection at their respective sites. This study does not have one overarching principal investigator.