
1. ABSTRACT

- **Title**

Long Term Post Marketing Drug Use Result Survey for Blinatumomab in Japan

- **Keywords**

blinatumomab, prospective, observation study, relapsed or refractory B-precursor acute lymphoblastic leukemia

- **Rationale and Background**

In the Japan new drug application (J-NDA) for blinatumomab, safety and efficacy data on 35 Japanese subjects were presented. The post-marketing surveillance provided descriptive data from the real-world long-term use of blinatumomab in patients in Japan to supplement the data in the J-NDA. Japan Risk Management Plan (J-RMP) included this survey as a part of post-marketing pharmacovigilance activities.

- **Research Question and Objectives**

- **Primary Objective**

The primary objective of the study was to investigate the incidence of CTCAE Grade 3 or higher events of each safety specification of the J-RMP (neurologic events, infections, cytokine release syndrome [CRS], tumor lysis syndrome [TLS], myelosuppression and pancreatitis) in patients receiving long-term administration of blinatumomab.

- **Secondary Objectives**

None

- **Hypotheses/Estimation**

There were no hypotheses to be tested. Instead, descriptive data on real-world long-term use of blinatumomab and adverse event occurrence in patients in Japan were provide in the study.

- **Study Design**

As this study was a non-interventional (observational) study conducted in the post-marketing setting, a comparator arm was not included.

- **Setting**

Study Period: 27 November 2018 to 6 February 2024

(From blinatumomab launch date to when the last case report form (CRF) was finalized.)

Enrollment Period: 29 October 2019 to 12 July 2023

(From the registration of the first patient to when the registration of the last patient needed to reach the target number of patients)

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

The targeted number of patients in the study was set to 40 patients.

- **Data Source and Methods**

The original source of the data used in the study was patient medical records. Data were collected through CRF, which were populated by the investigators. Laboratory test values were measured by each medical site with their own method.

- **Results**

The CRFs were collected from 46 patients, and the 46 patients whose CRFs were finalized were included in the safety analysis population.

The incidences of adverse drug reactions with CTCAE Grade 3 or higher related to neurologic events, infections, CRS, TLS, myelosuppression and pancreatitis defined as safety specifications in this study were 2.17% (1 of 46 patients) in CRS and 8.70% (4 of 46 patients) in myelosuppression. The adverse drug reactions with CTCAE Grade 3 or higher related to neurologic events, infections, TLS and pancreatitis were not observed.

(Note) Adverse drug reactions: Drug-related adverse events included not only events which investigators considered related to the drug, but also events for which the causality was unassessable or unspecified.

The incidences of adverse events with CTCAE Grade 3 or higher related to the safety specifications in the study were 2.17% (1 of 46 patients) in neurologic events, 4.35% (2 of 46 patients) in infections, 2.17% (1 of 46 patients) in CRS and 10.87% (5 of 46 patients) in myelosuppression. The adverse events with CTCAE Grade 3 or higher related to TLS and pancreatitis were not observed.

- **Discussion**

Although there are limitations to the interpretation as the setting, such as the patient background of the patients treated with blinatumomab and the testing systems used, differs between clinical trials and post-marketing, the incidence of adverse events

with CTCAE Grade 3 or higher related to the safety specifications in this study was lower than that in the clinical trials.

The incidence of adverse events with CTCAE Grade 3 or higher in a general drug use-results survey, where the observation period was defined from the initiation of blinatumomab administration to the end of cycle 5 of blinatumomab treatment, was 5.75% (23 of 400 patients) in neurologic events, 8.00% (32 of 400 patients) in infections, 6.00% (24 of 400 patients) in CRS and 0.50% (2 of 400 patients) in pancreatitis, which indicates that the incidence of adverse events did not increase in the long-term use of blinatumomab. Although TLS and myelosuppression were not included as part of the safety specifications in the general drug use-results survey, no adverse events of TLS with CTCAE Grade 3 or higher were observed in this study and the incidence of adverse events of myelosuppression was not found to increase in the long-term use of blinatumomab.

From the results described above, the incidence of adverse events with CTCAE Grade 3 or higher related to neurologic events, infections, CRS, TLS, myelosuppression and pancreatitis defined as safety specifications in the long-term use of blinatumomab in the real-world setting did not tend to be higher than that in clinical trials before the approval of blinatumomab and did not tend to differ from the initiation of blinatumomab administration to the end of cycle 5 of blinatumomab treatment in the real-world setting.

- **Marketing Authorization Holder**

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