2. ABSTRACT

Study KT-EU-472-5966
Kite Pharma Inc.
2400 Broadway
Santa Monica, CA 90404
United States of America

Study title: Tecartus Survey: Quantitative Testing of Health Care Professional Knowledge About Tecartus® Risk Minimisation Measures

Keywords *(Maximum of 10)*: **Tecartus, risk minimisation measures, adverse reactions, healthcare provider survey**

Rationale and background: Tecartus® (brexucabtagene autoleucel) is a gene therapy medicinal product containing autologous T cells CCI [redacted] It was launched in Europe on 14 December 2020 for the treatment of adult patients with relapsed/refractory mantle cell lymphoma after ≥ 2 lines of systemic therapy, including a Bruton's tyrosine kinase inhibitor. To ensure safe and effective use, Tecartus was authorised with additional risk minimisation measures (aRMMs) in Europe. These aRMMs include educational material targeted for both health care professionals (HCPs) and patients (via the patient alert card [PAC]). The primary aim was to inform HCPs and patients about the important risks associated with Tecartus, including cytokine release syndrome (CRS) and serious neurologic adverse reactions, and how to correctly handle and administer Tecartus to ensure product viability. Use of Tecartus is restricted to physicians experienced in the treatment of haematological cancers who have been trained on the aRMMs during the site qualification process or annual retraining, if applicable. Another key risk mitigation measure is to ensure hospitals or clinics treating patients with Tecartus have immediate access on-site to tocilizumab to manage the risk of CRS.

The rationale of conducting the survey was to measure the effectiveness of the aRMMs for Tecartus, as described in the Risk Management Plan (RMP), version 1.0, dated 09 October 2020; specifically, to conduct a survey to measure knowledge and understanding of the key messages in the HCP-directed aRMMs and Summary of Product Characteristics (SmPC) for Tecartus, including how to mitigate the risks of CRS and serious neurologic adverse events (AEs) and how to correctly handle and administer Tecartus to ensure product viability.

The survey was administered to HCPs who work at hospitals and associated clinics who have received training on the aRMMs and prescribe, handle, dispense, or administer Tecartus or manage patients experiencing Tecartus-related adverse drug reactions. The survey assessed HCPs knowledge of the risks of Tecartus and its mitigation strategies, as outlined in the aRMMs.

Research objectives: The primary objective of the study was to measure the awareness and knowledge of aRMMs for Tecartus, as described in the RMP; specifically, to conduct a survey to measure knowledge and understanding of the key messages in the HCP-directed aRMMs and SmPC for Tecartus, including how to mitigate the risks of CRS and serious neurologic AEs, and appropriately handle and administer Tecartus.

To meet this objective, the HCP survey:

- Measured HCPs' knowledge of known important identified risks associated with Tecartus
- Assessed whether HCPs understand how to identify and treat CRS or serious neurologic AEs
- Assessed whether the relevant HCPs understand the correct way of handling and method of administration of Tecartus to maintain product viability
- Assessed whether HCPs are aware of the PAC, distribute the PAC, and inform patients about the PAC's content

Setting: The survey was conducted in countries where Tecartus was launched, including the Czech Republic, France, Germany, Great Britain, Italy, Portugal, and Sweden.

Inclusion Criteria

Respondents who met the following inclusion criteria were eligible to participate in the survey.

- Is an HCP who has received training on the educational materials and prescribes, dispenses, handles, or administers Tecartus or manages patients experiencing Tecartus-related AEs.

Exclusion Criteria

Respondents were considered as non-eligible for participation if they fulfilled any of the following criteria.

- Is an HCP who has participated in qualitative pretesting of the Tecartus survey
- Is an HCP who has confirmed that they or any of their immediate family members have ever directly worked for Kite, Gilead, ICON plc, or the EMA

Subgroups

- Country: Czech Republic, France, Germany, Great Britain, Italy, Portugal, and Sweden
- Primary medical/clinical specialty: Haematologist and/or oncologist; Intensive or Critical Care Physician; Neurologist; Physician (other); Haematology/Oncology Nurse; Intensive or Critical Care Nurse; Nurse (other); Pharmacist; Personnel in charge of receipt/handling product

Study design: This was a non-interventional, cross-sectional survey of HCPs from 7 European countries who prescribed, dispensed, handled, or administered Tecartus, or managed patients experiencing Tecartus-related ADRs.

Survey data were collected in each local language through self-administered internet-based surveys.

Study size: This survey aimed to collect a minimum of 100 completed HCP surveys. With a minimum of 100 responders and the observed value of HCPs knowledge of 80%, the true value is estimated to lie within the margin of 72.1% to 87.9%.

With 111 HCPs having ultimately completed all survey questions, precision was higher than what was originally calculated for the study.

Data sources: The data source for the survey were HCPs who received training on the aRMMs during the site qualification process or retraining and who agreed to participate in the survey.
Variables: Information on survey administration and eligibility was collected. HCP demographic variables included medical specialty and country. The primary effectiveness endpoints were the knowledge levels corresponding to the key/essential questions in the survey. Data on individual patients treated with Tecartus, or patient-specific outcomes, were not collected.
Statistical methods: Responses to questions for all completed surveys were analyzed using descriptive statistics. HCPs' knowledge was evaluated and expressed as number, percentages, and 95% CIs overall, and stratified by subgroups. Survey responses were aggregated and summarized overall in table format. No formal hypothesis testing was conducted, and no adjustments for multiple comparisons were made. An 80% threshold for acceptable level of knowledge for key questions within the survey was used. Key questions within the survey were identified as being essential to measure HCP knowledge of the aRMMs.

Results: The primary effectiveness endpoints were the knowledge levels corresponding to 22 key questions covering 2 domains essential to measure HCPs' knowledge of the Tecartus aRMMs.

The knowledge levels for the individual 22 key questions grouped by domain are summarized below:

- One key question evaluated on how often the HCP provided patients with a copy of the PAC. Most of the HCPs (74.2%, n=46/62) reported always providing patients with a copy of the PAC.
- There were 6 key questions regarding the correct dispensing, handling, and administration of Tecartus. Overall, of the 6 questions, knowledge levels from the 97 HCPs reached or surpassed the 80% threshold for 4 of them. Only the questions pertaining to use of leukodepleting filter and stability and thawing of Tecartus had knowledge levels below 80%.
- There were 16 key questions about prescribing Tecartus and managing AEs related to Tecartus. Of the 16 questions asked of the 88 HCPs who reported prescribing Tecartus and managing AEs, 4 questions demonstrated (overall) a complete understanding, registering a 100% threshold. These questions were about knowledge of CRS and neurological toxicities. Furthermore, for 7 of the 16 questions, overall knowledge levels exceeded 90%, and 2 more questions surpassed the 80% threshold. Only 1 question, overall, that assessed knowledge about what symptoms of neurological adverse reactions should prompt patients to contact their treating physician or get emergency help was below the 70% threshold (65.9%, n=58/88).

Discussion: Across all 22 key questions, HCPs achieved > 80% knowledge levels for 17 questions suggesting that overall, HCPs had strong knowledge of the key information about managing identified adverse events associated with Tecartus as well as the knowledge of correct dispensing, handling, and administration of Tecartus. Knowledge levels for the remaining 5 questions ranged from 65.9 % to 78.4%.

For the key question where the knowledge level was 65.9% (n=58/88), the response involved multiple answers. The correct answers for the question, "Patients contact their treating physician or get emergency help immediately if which of these symptoms of neurological adverse reactions occur?", were "Confusion," "Dizziness," and "Difficulty speaking and/or understanding speech." Since this question required multiple answers, it may have been misread or HCPs answered it too quickly only selecting one correct answer leading to an overall incorrect response.

The other 4 questions with knowledge levels <80% had a range from 68.0%-78.4%. Two of the questions pertained to HCPs who dispense, handle or administer Tecartus, and the other 2 questions applied to HCPs who prescribed Tecartus or managed patients who experience adverse events related to Tecartus. Specifically, 70.1% of HCPs (n=68/97) understood that a leukodepleting filter should not be used when administering Tecartus and 68.0% of HCPs (n=66/97) were aware of the stability of Tecartus at room temperature after being thawed. The remainder of the 2 questions that did not meet the knowledge threshold were related to the HCPs monitoring of adverse events occurring in patients who have received Tecartus. Specifically, 78.4% of HCPs (n=69/88) had knowledge that patients with Grade 2 or higher neurologic events should be monitored with continuous cardiac telemetry and pulse oximetry while 75.0% of HCPs (n=66/88) understood an echocardiogram to assess cardiac function should be considered if a patient experiences severe CRS.

Conclusion: The objective of the survey was to assess the relevant HCPs' knowledge of the aRMMs and how to mitigate the risks of CRS and serious neurologic AEs, and appropriately administer, handle, and manage Tecartus, and inform patients of the PAC. Results from the study indicate that overall, HCPs' knowledge levels of key information were high. Specifically, for 17 of the 22 key questions, the threshold for the knowledge level was met. Furthermore, HCPs' awareness of the PAC and disseminating of the PAC to patients was high.

Some knowledge levels were however below the 80% target threshold and were mainly in the domain related to preparation and thawing procedures of Tecartus, the negative impact of using leukodepleting filters, and the management of certain adverse events.

The lower knowledge levels observed for some questions do not negatively impact the safe use of Tecartus and therefore the existing recommendations to minimize these risks are considered adequate.