Gemeinsamer Bundesausschuss

# Resolution

## of the Federal Joint Committee on a Finding in the Procedure of Routine Practice Data Collection and Evaluations according to Section 35a, paragraph 3b SGB V: Autologous Anti-CD19-transduced CD3+ Cells (Relapsed or Refractory Mantle Cell Lymphoma) – Review of Study Protocol and Statistical Analysis Plan and Start of routine practice data collection

of 20 July 2023

At its session on 20 July 2023, the Federal Joint Committee (G-BA) decided the following in the procedure for routine practice data collection and evaluations according to Section 35a, paragraph 3b SGB V for the active ingredient autologous anti-CD19-transduced CD3+ cells (hereinafter referred to as brexucabtagene autoleucel; relapsed or refractory mantle cell lymphoma):

I. It is stated that the implementation of the requirements for routine practice data collection and evaluations in the study protocol and statistical analysis plan prepared by the pharmaceutical company and submitted to the G-BA for review are considered fulfilled under the condition that the pharmaceutical company is obliged to make the following further adjustments to the study protocol (version 2.0, 13 April 2023) and the statistical analysis plan (SAP; version 2.0, 13 April 2023) that are considered necessary:

a) Question according to PICO: Outcome, patient-reported endpoints

Section 2.2.3.1 of the study protocol must conclusively specify the process for increasing the response rate during collection of patient-reported endpoints.

b) Question according to PICO: Outcome, patient-reported endpoints

The changes in the table "Procedure for the Collection of HRQoL using Patient Questionnaires" in section 2.2.3.3 of the study protocol (version 2.0) regarding the tolerance ranges for the time of the respective PRO survey are to be reversed and saved according to Table 2 in version 1.0 of the study protocol.

c) Question according to PICO: Outcome, specific adverse events (AEs)

In the study protocol (table 6 and section 2.2.4.5) and in the SAP (section 8.5.3.1), encephalopathy should be added as a specific AE as part of the neurological events.

The study protocol shall specify that principal investigators are provided with information material that clarify for which of the designated specific AEs specific definitions are available and how CTCAE grades ≥ 3 are defined.

For the specific AEs with information on severity grade, specify in the table in section 2.2.4 of the study protocol that the severity grade is to be determined by the CTCAE grade.

In the case of severe specific AEs, a definition is to be saved in the table in section 2.2.4 of the study protocol and in section 8.5.3.1 of the SAP, which clarifies that a severe specific AE is not defined solely by the criterion "significant impairment of activities of daily living".

d) Study design: Recruitment of the study population

The criteria which are used for the assessment of a sufficiently similar standard of care for the selection of the participating study sites must be made clear in the study protocol. In addition, a justification must be provided in the study protocol for the reasons why study sites collaborating with the EMCL registry are not included in the routine practice data collection with regard to the criteria for a sufficiently similar standard of care.

Before starting the routine practice data collection, the search for suitable study sites must be completed. For the final review of the study protocol and statistical analysis plan, the final participating study sites must therefore be presented in the study protocol.

e) Data source: Confounders

The information on the severity of the morphology confounder within the study protocol and in table 5 of the study protocol should be aligned.

f) Data evaluation: Propensity score method

With regard to the criteria for sufficient balance, it should be clarified in section 8.2.2 of the SAP in the first sentence of the penultimate paragraph that this is the case of multiple imputation and that the median refers to the results of the multiple imputation per confounder and not to the median across all confounders. In the case of a "complete case analysis", the description of the criteria must be supplemented. In addition, an error in section 8.2.2 point 3 needs to be corrected. It should read "Sufficient balance is given by a median of <0.25 for each confounder." not ">0.25".

g) Data evaluation: Dealing with missing data

In SAP, the efforts that are being made to minimise the rate of missing values in the date specification must be added.

It should be added that in the case of restriction to complete case datasets, a comprehensive justification must be provided as to what extent the results are still transferable to the initial population when restricted to the patient population with complete confounder data.

In order to avoid inconsistencies, the pharmaceutical company must check whether the need for changes in the study protocol described here leads to corresponding subsequent changes in the SAP and vice versa.

II. The routine practice data collection starts on 21 August 2023.

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 20 July 2023.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 20 July 2023

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken