

RESPONSE TO CBER COMMUNICATION REGARDING REPORTING OF DEATH OF A PHASE 3 TRIAL PARTICIPANT RECEIVED ON NOVEMBER 27, 2020

The Sponsor acknowledges CBER's communication regarding reporting of death of a phase 3 trial participant.

This document provides the Sponsor's responses to CBER's requests (in **Bold**).

Item 1:

In the safety listing that was submitted in amendment 83 we noted the death of the subject US ID 3432295, 83-year-old male who died on October 2, 2020.

Could you please let us know why an IND safety report was not submitted within the 7-day time frame? Please clarify this discrepancy and let us know the necessary details.

Sponsor Response:

The case in question pertains to an 83 year-old male participant diagnosed with chronic lymphocytic leukemia in 2019 who received investigational product on 26 August 2020 and was hospitalized with a diffuse bullous rash on 17 September 2020 and on 30 September 2020 with fever and acute respiratory failure ultimately resulting in death on 2 October 2020. The participant had radiologic evidence of CLL progression prior to death. This was assessed as unrelated to investigational product by the investigator, and the sponsor also considered that these clinical events would not be uncommon among individuals with CLL. As a result, this case did not meet the reporting requirement for a 7-day SUSAR under § 312.32(c)(1)(i). Subsequently, an autopsy was received on 30 October 2020 noting death due to a systemic inflammatory response syndrome with no pathological evidence of CLL progression. The investigator stated that this new information did not change his assessment that the adverse events were unrelated to investigational product. After receiving this new information, the sponsor reassessed the case, and treatment status was unblinded to the pharmacovigilance function. The participant received placebo, and the event was not reported in an IND safety report within a subsequent 7-day timeframe because there was not a reasonable possibility that the investigational product caused the adverse event. Therefore, this did not meet the requirements of a 7-day SUSAR under § 312.32(c)(1)(i) when initially reported or when an autopsy report was subsequently provided.