BLA 125661/0 Database Errata Informal Meeting December 19, 2017

FDA Attendees

Bindu George, MD, Hematology Branch Chief
Lin Huo, PhD, Statistical Reviewer
Candace Jarvis, Regulatory Project Manager
Bhanu Kannan, BIMO reviewer
Megha Kaushal, MD, MSHS, Clinical Reviewer
Kay Owosela, MSc, Regulatory Project Manager
Renee Rees, PhD, Statistics Team Leader

Applicant Attendees
Jim Cassaday, Data Management
Monica Maas Enriquez, MD, Clinical Development
Alex Frumin, Data Management
Chi Li, PhD, MBA, Regulatory Affairs
Michelle Meng, PhD, Regulatory Affairs
Lisa Michaels, MD, Clinical Development/Project Management
Susan Radke, Clinical Project Management
Kapil Saxena, MD, Clinical Development
Maria Wang, Clinical Statistics

Agenda:

1) Clarify if CRFs have been updated with the new data
2) Clarification of the impact to the CSR analysis results due to the database errata

Notes

The Applicant presented their slides addressing the agenda.

FDA inquired about current database/datasets and why some content is in the database and others are not. The applicant stated that patients who are in the extension trial will continue to have data being submitted. The applicant stated that those that were in Part A of the study submitted data from the electronic patient diary (EPD) after the data lock. The applicant stated that these new data will have no impact to safety and efficacy. The Applicant also stated that they could not reopen database to enter these additional data.

The applicant confirmed that there were bleeding events that were not added to the total number of bleeds, which may change the mean/median/standard deviation. FDA stated these changes should be updated in the PI and re-analysis of this data should be submitted to the FDA as a separate amendment.

FDA inquired if patients are included in the main database and if a specific patient with outlier data was included. Applicant responded that patients are included in the safety snapshot but not the main database.

FDA inquired if the data collected in EPDs were monitored during the study through sponsor monitoring. The applicant confirmed that the study data were monitored. FDA confirmed with the applicant that events were reported after closure of the database. FDA also confirmed with the applicant, that if a clinical investigator who participated in the study had left the institution, the new investigator would be capable of answering questions arising during the FDA clinical investigator inspection(s).

FDA inquired if applicant had considered how bleeding events had impact on other data. Applicant stated this would be an action item and they would like guidance on what data sets to consider. Applicant also stated that there is an ongoing extension study with additional data.