CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761038Orig1s000

STATISTICAL REVIEW(S)

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translation Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION

CLINICAL STUDIES- MEMO

BLA:	761038
Drug Name:	LARTRUVO ® (olaratumab)
Indication:	Advanced soft tissue sarcoma not amenable to curative treatment with surgery or radiotherapy
Applicant:	Eli Lilly
Receipt Date:	February 24, 2016
PDUFA Goal Date:	October 24, 2016
Review Priority:	Priority
Biometrics Division:	Division of Biometrics V
Primary Reviewers:	Huanyu (Jade) Chen, Ph.D.
Concurring Reviewers:	Kun He, Ph.D., Statistical Team Leader
	Rajeshwari Sridhara, Ph.D., Division Director
Medical Division:	Division of Biologic Oncology Products
Clinical Team:	Meredith Chuk, M.D., Clinical Reviewer
	Marc Theoret, M.D., Clinical Review Team Leader
	Patricia Keegan, M.D., Division Director
Project Manager:	Ms. Leah Her

The statistical review is complete and has been added to the Multi-disciplinary Review and Evaluation, which will be uploaded to DARRTS when it is finalized. Refer to the Multi-disciplinary Review and Evaluation for additional details. From a statistical standpoint, the BLA is acceptable to support approval provided that the Applicant and the FDA reach an agreement regarding the labeling language.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HUANYU CHEN
07/29/2016

KUN HE
07/29/2016

RAJESHWARI SRIDHARA
07/29/2016

STATISTICAL REVIEW AND EVALUATION
FILING REVIEW OF AN NDA/BLA

NDA/BLA #:	NDA 761,038	
Related IND #:	121,500	
Product Name:	LARTRUVO (Olaratumab, LY3012207) strength and dosage	
Indication(s):	Patients with advanced soft tissue sarcoma (STS) not amenable to curative treatment with radiotherapy or surgery	
Applicant:	Eli Lilly and company	
Dates:	PDUFA date: October 24, 2016	
Review Priority:	Priority	
Biometrics Division:	V	
Statistical Reviewer:	Huanyu Chen	
Concurring Reviewers:	Kun He	
Medical Division:	OHOP/DOP2	
Clinical Team:	Patricia Keegan	Division Director
	Marc Theoret	CDTL
	Meredith Chuk	Clinical (Efficacy)
	Leslie Doros	Clinical (Safety)
Project Manager:		

1. Summary of Efficacy/Safety Clinical Trials to be Reviewed

Table 1: Summary of Trials to be Assessed in the Statistical Review

Trial ID	Design*	Treatment/ Sample Size	Endpoint/Analysis	Preliminary Findings
JGDG	MC, R, OL Phase I/II	Drug A/66 Control/ 67	Primary: PFS Key Secondary: OS	significant OS improvemen

* MC: multi-center, R: randomized, OL: Open label; Drug A: doxorubicin 75 mg/m2 followed by olaratumab 15 mg/kg on day 1 and olaratumab 15 mg/kg on day 8 of each 21-day cycle; Control: doxorubicin 75 mg/m2 on day 1 of each 21-day cycle

2. Assessment of Protocols and Study Reports

Table 2: Summary of Information Based Upon Review of the Protocol(s) and the Study Report(s)

Content Parameter	Response/Comments
Designs utilized are appropriate for the indications requested.	NO. This is a phase I/II study and not for registration purpose. The two sided type one error is 0.2.
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.	Yes
Interim analyses (if present) were pre-specified in the protocol with appropriate adjustments in significance level. DSMB meeting minutes and data are available.	Yes
Appropriate details and/or references for novel statistical methodology (if present) are included (e.g., codes for simulations).	Yes
Investigation of effect of missing data and discontinued follow-up on statistical analyses appears to be adequate.	Yes

3. Electronic Data Assessment

Table 3: Information Regarding the Data

Content Parameter	Response/Comments
Dataset location	\\cdsesub1\evsprod\BLA761038\0002\m5\datasets\
Were analysis datasets provided?	Yes
Dataset structure (e.g., SDTM or ADaM)	SDTM & ADAM
Are the define files sufficiently detailed?	Yes
List the dataset(s) that contains the primary endpoint(s)	In the OS subfolder adttem; In the PFS subfolder adttem
Are the *analysis datasets* sufficiently structured and defined to permit analysis of the primary endpoint(s) without excess data manipulation? *	Yes
Are there any initial concerns about site(s) that could lead to inspection? If so, list the site(s) that you request to be inspected and the rationale.	Yes
Safety data are organized to permit analyses across clinical trials in the NDA/BLA.	Yes

* This might lead to the need for an information request or be a refuse to file issue depending on the ability to review the data.

4. Filing Issues

N/A

Table 4: Initial Overview of the NDA/BLA for Refuse-to-file (RTF):

Content Parameter	Yes	No	NA	Comments
Index is sufficient to locate necessary reports, tables, data, etc.	X			
ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)	X			
Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated.	X			
Data sets are accessible, sufficiently documented, and of sufficient quality (e.g., no meaningful data errors).	X			
Application is free from any other deficiency that render the application unreviewable, administratively incomplete, or inconsistent with regulatory requirements	X			

IS THE APPLICATION FILEABLE FROM A STATISTICAL PERSPECTIVE? Yes / No

Yes

5. Comments to be Conveyed to the Applicant

N/A

5.1. Refuse-to-File Issues

N/A

5.2. Information Requests/Review Issues

N/A

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

HUANYU CHEN
04/05/2016

KUN HE
04/07/2016