From:	Patel, Manisha
To:	Giordano, Erica
Cc:	Riggins, Cindy; Ahmed, Narin
Subject:	RE: BL 125646 Clinical Information Request
Date:	Tuesday, May 09, 2017 8:14:32 PM
Attachments:	image001.png response-fda.pdf
Sensitivity:	Confidential

Dear Erica and Maura,

Please find attached a response to the request for information. A copy will be submitted through the gateway.

Kind regards,
Manisha

From: Patel, Manisha [mailto:manisha.patel@novartis.com]
Sent: Monday, May 08, 2017 2:07 PM
To: Giordano, Erica; Oleary, Maura
Cc: Riggins, Cindy; Ahmed, Narin
Subject: RE: BL 125646 Clinical Information Request
Sensitivity: Confidential

Dear Erica and Maura,

Please find below responses to requests #4 and 5.

FDA request #4
Please provide the UPN identifiers for those subjects who were manufacturing failures on 2202.

Novartis response:
Based on a November 23, 2016 BLA data cut-off date, there was 8 patients who were manufacturing failures on study B2202 (b) (6)). Out of the 8 patients, 7 were manufactured at Morris Plains and 1 (patient (b) (6) was manufactured at Fraunhofer.

Among the 8 patients who experienced manufacturing failure, 1 patient (b) (6) died while the second manufacturing attempt was ongoing and hence was recorded in the CRF as discontinuation due to "Death". The other 7 patients discontinued the study without further manufacturing attempts, and were recorded in the CRF as discontinuation due to "Technical problems (Product not released by manufacturing)".

FDA request #5
Please provide the requested information:
- (b) (6) **% donor chimerism**
- (b) (6) **: CRF: no SCT on some of the forms (not all) but has donor chimerism**
- (b) (6) **what is response status**

- (b) (6) **LP was done in December, and BM in February, was a repeat LP done with the BM in February**

Novartis response

- (b) (6) : % donor chimerism is not reported; patient did not have a prior HSCT.
- (b) (6) : Patient completed screening after the November 23, 2016 BLA data cut-off date. The site has subsequently provided information that the patient had received cord allogenic SCT on February 17, 2016.
- (b) (6) : As of the November 23, 2016 BLA data cut-off date, the response status is complete remission. On January 20, 2016, the patient was removed from the trial due to guardian decision on not being local. The patient only agreed to survival follow-up and did not enter secondary follow-up. As of January 16, 2017 the patient was alive.
- (b) (6) : An LP was not repeated in February. Screening assessments for LP were performed on December 16, 2015 and a BM was performed on February 4, 2016

Kind regards,
Manisha

From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Friday, May 05, 2017 10:37 AM
To: Oleary, Maura <Maura.Oleary@fda.hhs.gov>; Patel, Manisha <manisha.patel@novartis.com>
Cc: Riggins, Cindy <cindy.riggins@novartis.com>; Ahmed, Narin <narin.ahmed@novartis.com>
Subject: RE: BL 125646 Clinical Information Request
Sensitivity: Confidential

You may provide responses by noon on May 10th. If you have any of the information available earlier please send it as you can.

Thanks
Erica

From: Oleary, Maura
Sent: Friday, May 05, 2017 9:33 AM
To: Patel, Manisha; Giordano, Erica
Cc: Riggins, Cindy; Ahmed, Narin
Subject: RE: BL 125646 Clinical Information Request
Sensitivity: Confidential

Question 5 refers to missing data or conflicting data in the CRFs.

Thanks
Maura

Maura O'Leary, MD
Medical Officer, Team Leader
FDA/CBER/OTAT
10903 New Hampshire Avenue
Building 71, Room #4326
Silver Spring, MD 20993-0002
240 402 8338

maura.oleary@fda.hhs.gov

From: Patel, Manisha [mailto:manisha.patel@novartis.com]
Sent: Friday, May 05, 2017 9:25 AM
To: Giordano, Erica
Cc: Riggins, Cindy; Ahmed, Narin
Subject: RE: BL 125646 Clinical Information Request
Sensitivity: Confidential

Dear Erica,

I confirm receive of this request. Can you clarify which study question 5 refers to?

Given the size of this request, would it be acceptable to provide a response by Wed, May 10 instead?

Kind regards,
Manisha

From: Giordano, Erica [mailto:Erica.Giordano@fda.hhs.gov]
Sent: Friday, May 05, 2017 9:01 AM
To: Patel, Manisha <manisha.patel@novartis.com>
Cc: Riggins, Cindy <cindy.riggins@novartis.com>; Ahmed, Narin <narin.ahmed@novartis.com>
Subject: BL 125646 Clinical Information Request
Sensitivity: Confidential

Good morning,

Please see the information request below and provide a response by 11am ET on Monday May 8, 2017 by responding directly to this e-mail and follow-up by submitting

the information as an official amendment to the BLA.

Efficacy and Safety:

1. Please assess ORR (overall remission rate, complete response [CR] or complete response with incomplete hematologic recovery [CRi] and DOR (duration of response) for all subjects who received CTL019 on 2202 (only those manufactured in New Jersey) and 2205J separately and combined using the following parameters:

    - Time from signature of ICD to infusion
    - Time from completion of Screening to infusion
    - +/- Bridging Chemotherapy
    - Donor Chimerism > 90% versus < 90%
    - Use of therapy for CRS Grade 3/4 and/or neurologic toxicity, tocilizumab alone, corticosteroids alone, and tocilizumab plus corticosteroids
    - By overall dose of corticosteroids given to treat adverse events post-treatment.
    - Time from original diagnosis to infusion (0- up to 1 year, 1-3 years, > 3 years)
    - Age at diagnosis (3-6, 2-10, >10)
    - US based subjects versus outside the US

2. Please assess the incidence and Grade of CRS by gender for 2202, 2205J, and 2201J separately and combined.

3. Please provide survival data for subjects in 2202 and 2205J (separately and combined) by reason for off-therapy after treatment:
    - Off therapy in CR or CRi and MRD negative
    - Off therapy in CR or CRi and MRD positive
    - Off therapy, frank relapse

4. Please provide the UPN identifiers for those subjects who were manufacturing failures on 2202.

5. Please provide the requested information:
    - (b) (6) : % donor chimerism
    - (b) (6) : CRF: no SCT on some of the forms (not all) but has donor chimerism
    - (b) (6) : what is response status
    - (b) (6) : LP was done in December, and BM in February, was a repeat LP done with the BM in February

Please confirm receipt of this request.

Thank you,

Erica Giordano

Regulatory Project Manager
Center for Biologics Evaluation and Research
Office of Tissues and Advanced Therapies
U.S. Food and Drug Administration
Tel: 240-402-8298
Erica.Giordano@fda.hhs.gov