

Davidson, Mark

From: Davidson, Mark
Sent: Friday, June 09, 2017 1:45 PM
To: 'Rizwana Sproule'
Cc: 'Nadia Agopyan'; 'Alex Babayan'
Subject: KITE Pharma BLA 125643 Clinical Pharmacology IR on 06/09/2017

Importance: High

Dear Dr. Sproule,

We have the following information request:

Regarding your clinical study ZUMA-1, please provide the following information:

1. In your submission dated on 05/31/2017, you evaluated impact of product characteristics on KTE-C19 expansion. Please also evaluate the effect of product characteristics on in vivo kinetic profiles of the key pharmacodynamics (PD) analytes you identified in your ZUMA-1 study report.
2. Prior to KTE-C19 infusion, subjects had lymphodepletion with conditioning chemotherapy. The baseline levels of cytokine/chemokines may affect KTE-C19 in vivo kinetics. Please conduct quantitative analysis for baseline levels of key PD analytes (e.g. IL-15) and KTE-C19 kinetics.
3. If possible, please explore correlation of product characteristics and PD key biomarkers levels after lymphodepletion with i) disease response, ii) toxicity.
4. You assessed correlation of pharmacokinetic parameters with disease response. Please evaluate KTE-C19 persistence and disease response by plotting mean KTE-C19 blood concentrations vs. time for different disease responses.
5. Interactions between KTE-C19 and cytokines/chemokines play critical roles in exposure-safety/efficacy assessment of KTE-C19. To better understand PK/PD profiles of KTE-C19, including KTE-C19 persistence and perseverance and toxicity, please perform quantitative analysis for:
 - a. KTE-C19 Cmax vs. key PD biomarkers Cmax;
 - b. KTE-C19 AUC vs. key PD biomarkers AUC.
6. In your submission dated on 05/31/2017, you provided additional information of bioanalytical and analytical methods of human studies. However, there are no bioanalytical reports for detection and quantitation of anti-CD19 CART cells in PBMC DNA using (b) (4) for ZUMA-1 and (b) (4) samples. Please submit above information. Please also submit a table of each individual's (b) (4) results at each sampling time point with the corresponding converted anti-CD19 CAR T cell number results.

Please provide your response by 06/23/2017.

Thank You

Mark L. Davidson, RHIA

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