

Davidson, Mark

From: Davidson, Mark
Sent: Wednesday, August 16, 2017 10:09 AM
To: 'Rizwana Sproule'
Cc: 'Alex Babayan'; 'Nadia Agopyan'
Subject: Kite Pharma 125643 Clinical IR 8.16.17
Attachments: ktedem.xpt

Dear Dr. Sproule,

We have reviewed your responses submitted July 12, 2017 and August 11, 2017, for our Information Request sent on June 20, 2017, and we have the following comments:

a) In the data file tociadmin.xpt, we identified 147 patients with a cytokine release syndrome (CRS) start date (CRSSTD). Please clarify whether the identification of CRS was taken from a case report form question about CRS, from a report of CRS as an adverse event, or some other derived method.

b) We have identified 83 patients treated with tocilizumab after receiving KTE-C19 on ZUMA-1, ZUMA-2, ZUMA-3 or ZUMA-4 (see variable TOCIYN = Y in data file ktedem.xpt). Please verify that these are the 83 patients that you cited in Table 2.5 of your response document.

c) The current Prescribing Information for tocilizumab provides safety data for a tocilizumab dose of 8 mg/kg (12 mg/kg for patients <30 kg). We identified 15 patients treated with the recommended dose for the first episode of grade 3-4 CRS (variable EFFPOP=Y in datafile ktedem.xpt). Please confirm that these are the 15 patients with grade 3-4 CRS at start of tocilizumab in Table 1.5 of your response document. Variables used:

TOCIDSGP – FDA-derived first toci dose group from tociadmin.xpt

RECDOS – FDA-derived Y if patient received recommended dose (based on weight group > or < 30 kg)

TOCIEP1 – FDA-derived flag for use of tocilizumab for treatment

D1GR- Sponsor's reported grade of CRS at start of toci

d) You indicated in your response to Comment 2(a) that response to tocilizumab was determined by change in modified Lee score. We identified responders as patients whose duration of CRS after the first tocilizumab dose was limited to a specified timeframe using no more than 2 doses of tocilizumab and without additional drugs other than corticosteroids. We identified 3 (20.0%) who responded within 2 days, and 8 (53.3%) who responded within 7 days. Please verify these response rates. Variables used:

NTOCI – FDA-derived number of toci doses given from tociadmin.xpt

OTHRX–FDA-derived variable to identify treatments other than steroids in tociadmin.xpt

INTT1END – FDA-derived interval from first toci dose to end of CRS

TOCISTDT – Sponsor's reported date of first toci dose

CRSENDT- FDA-derived date from Sponsor's CRS start date (CRSSTD) and Sponsor's duration of CRS (CRSDUR) in tociadmin.xpt

e) Please clarify why patients 101-025-005 and 103-002-006 received tocilizumab after resolution of CRS.

Please provide a response by August 17, 2017.

Thank You

Mark L. Davidson, RHIA

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