

IR Request for BLA 125646

Please respond by COB on 6/23/17 if possible. Thanks

Neurotoxicity

1. Please provide the following information on Neuro/Psychiatric (neurotoxicity) toxicity:
 - a. Please provide a table of all B2202 subjects who had neurotoxicity
 - i. Separate lines should be listed for each subject that includes each subcategory that the subject had and that was used to categorize them as neurotoxicity
 - ii. The start and stop day post- tisagenlecleucel of each subcategory
 1. i.e. Start Day 3, stop Day14
 - iii. The Subject ID for each subject
 - iv. Whether or not the subject had cytokine release syndrome and the Grade
 - b. How was the decision made to categorize a subject as Neurotoxicity, was there a minimum amount of subcategories needed.
 - i. i.e. Headache alone or somnolence, headache, agitation
 - ii. Were some subcategories weighted higher than others (i.e. seizure)
2. Please provide a list of all subcategories that were considered for neurotoxicity and how that groups was determined.
3. Who made the judgment on neurotoxicity, the local investigator or was it done centrally based on subcategories.

Cytokine Release Syndrome (CRS):

1. Please provide the following information on CRS toxicity:
 - a. Please provide a table of all B2202 subjects who had CRS
 - i. Separate lines should be listed for each subject that includes each subcategory that the subject had and that was used to categorize them as CRS
 - ii. The start and stop day post- tisagenlecleucel of each subcategory
i.e. Start Day 3, stop Day14
 - iii. The Subject ID for each subject
 - iv. Whether or not the subject had neurotoxicity and the Grade
 - b. How was the decision made to categorize a subject as CRS, was there a minimum amount of subcategories needed.
 - i. i.e. fever, hypotension
 - ii. Were some subcategories weighted higher than others (i.e. fever)
2. Please provide a list of all subcategories that were considered for CRS and how that groups was determined.
3. Who made the judgment on CRS, the local investigator (if they filled out the eCRF for CRS) or was it done centrally based on subcategories regardless of whether or not it was noted by the local investigator.