

Margarita Aguilera

From: Margarita Aguilera
Sent: Monday, April 18, 2016 5:16 PM
To: 'Chamrin, Ronald'; 'Yao, Michael (CBER)'
Cc: 'Schneider, Bruce'
Subject: RE: Request for additional clinical information
Attachments: Site Personnel Guide for CTT Services (IVR) doc (2).pdf; LMH1.pdf

Categories: Red Category

Hi Ron,

As a follow up to my email on Friday, below please find our responses to the additional request for clinical information:

Question1:

Please indicate where we can find information on the randomization procedure, in particular, how the surgeon was informed of the randomization assignment during the arthroscopy procedure.

Response:

The randomization procedure is described in the SUMMIT (MACI00206) Protocol, Section 8.4: Method of Assigning Patients to Treatment. The MACI00206 Protocol can be found in Module 5.3.5.1, Section 16.1.1: Protocol and Amendments. A copy of the IVR Manual is enclosed for reference.

Please also refer to the following Sections of SUMMIT MACI00206 CSR for additional information on the randomization procedure:

- Section 9.1 and Figure 1 Study design that describe how randomization takes place after biopsy collection,
- Section 9.4.1.1.2 that describes how the cartilage biopsy taking place prior to randomization, and
- Section 9.4.3 that describes the randomization procedure that takes place during the arthroscopy procedure.

Question2:

For those subjects with prior surgery to the index knee (prior to screening, please provide information regarding the type of surgery for each subject, along with subject number.

Response:

Attached please find LISTING 16.1.3.2.1 describing prior orthopedic knee surgeries on the Index Knee for all patients screened.

We trust the above answers your questions.

Regards,
Margarita

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From: Margarita Aguilera
Sent: Friday, April 15, 2016 10:13 AM
To: 'Chamrin, Ronald'; Yao, Michael (CBER)
Cc: Schneider, Bruce
Subject: RE: Request for additional clinical information

Hi Ron,

As a follow up to the request for additional clinical information below and after discussion with the team, we do not believe that a Tcon would be necessary at this time.

We will provide responses on Monday. Should the Agency require further discussion or information at this time our team will be available for a Tcon.

Best regards,
Margarita

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From: Chamrin, Ronald [<mailto:Ronald.Chamrin@fda.hhs.gov>]
Sent: Thursday, April 14, 2016 12:29 PM
To: Yao, Michael (CBER); Margarita Aguilera
Cc: Schneider, Bruce
Subject: RE: Request for additional clinical information

Hi Margarita,

In addition to Michael's questions we also have the following questions:

1. Please indicate where we can find information on the randomization procedure, in particular, how the surgeon was informed of the randomization assignment during the arthroscopy procedure.
2. Also, for those subjects with prior surgery to the index knee (prior to screening, please provide information regarding the type of surgery for each subject, along with subject number.

It may be easier to have a tcon for Number One between our clinical team and your clinical experts.

Best,

Ron

Ron Chamrin
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From: Yao, Michael (CBER)
Sent: Thursday, April 14, 2016 11:56 AM
To: 'Margarita Aguilera'
Cc: Schneider, Bruce; Chamrin, Ronald
Subject: RE: Request for additional clinical information
Importance: High

Hi Margarita,

I have more questions for you as listed below:

1. Based upon my review assessments for SUMMIT Extension study, it indicated that the sponsor allowed the subjects who were withdrawn from the SUMMIT study prior to their scheduled Week 104 visit enrolling into the SUMMIT Extension study. Moreover, subjects determined to be treatment failures (per the Independent Treatment Failure Evaluation Committee or Investigator) and/or required surgical re-treatment were not withdrawn from this extension study were included in SUMMIT Extension study. Could you please provide detailed clinical information (# of

subjects, study groups, etc.) regarding subjects enrolled in SUMMIT Extension study, who were withdrawn from the SUMMIT study prior to their scheduled Week 104 visit and subjects determined as treatment failures and/or required surgical re-treatment were not withdrawn from SUMMIT extension study (They were included in SUMMIT Extension study data analysis).

2. Did you provide “risk-benefit considerations” and “risk-benefit summary and assessment” in this BLA? If yes, please help me to locate them. Otherwise, please provide them.

Thanks.

Michael

From: Margarita Aguilera [<mailto:maguilera@vcel.com>]
Sent: Thursday, March 10, 2016 10:16 AM
To: Yao, Michael (CBER)
Cc: Schneider, Bruce; Chamrin, Ronald
Subject: RE: Request for additional clinical information

Dear Dr. Yao,

This is to acknowledge receipt of your request for additional clinical information. We will get back to you as soon as possible.

Sincerely,
Margarita

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From: Yao, Michael (CBER) [<mailto:Michael.Yao@fda.hhs.gov>]
Sent: Thursday, March 10, 2016 9:47 AM
To: Margarita Aguilera
Cc: Schneider, Bruce; Chamrin, Ronald
Subject: Request for additional clinical information
Importance: High

Hi Margarita,

I am a clinical reviewer for BLA 125603. During my review assessment, I could not find detailed summary of subjects (45) who were not randomized to treatment due to screening failures. Please help me to locate such information if these clinical data are already included in this BLA submission. Otherwise, please provide such information, including reasons why each of these subjects did not meet entry criteria.

Thanks.

Michael Yao, MD
Medical officer
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