

APPROVED

By Jean Gildner at 2:15 pm, Dec 07, 2016

From: [Yao, Michael \(CBER\)](#)
To: [Margarita Aguilera](#)
Cc: [Schneider, Bruce](#); [Gildner, Jean](#); [Riggins, Patrick](#); [David Recker](#)
Subject: RE: Request for additional clinical information
Date: Tuesday, May 24, 2016 10:23:02 AM

Thanks, Margarita.

Michael

From: Margarita Aguilera [mailto:maguilera@vcel.com]
Sent: Monday, May 23, 2016 7:16 PM
To: Yao, Michael (CBER)
Cc: Schneider, Bruce; Gildner, Jean; Riggins, Patrick; David Recker
Subject: RE: Request for additional clinical information

Dear Dr. Yao,

In response to your request for additional clinical information dated 20 May 2016, please find our responses below:

1. Regarding clinical evaluation in SUMMIT study, do you have clinical data (KOOS pain and function) before visit 6 (week 24)? If so, please provide a summary for FDA review.

Per protocol the MACI00206 study did not collect KOOS scores prior to week 24. The rationale behind the 24 week time point was to provide subjects with adequate time to recover from the arthroscopy (microfracture) or the arthrotomy (MACI) procedures, acknowledging that the MACI-treated subjects underwent a more invasive procedure. MACI00206 CSR Section 9.5.2.1. Knee Injury and Osteoarthritis Outcome Score, provides a description of the collection time points for the KOOS efficacy assessments.

2. Please provide subgroup analysis by number of lesions and by subject age, using some reasonable cut-off determine "younger" vs "older."

Section 4 of the Integrated Summary of Efficacy (ISE) included in Module 3.5.5.3, shows a comparison of KOOS pain and function results across subpopulations at year 2. ISE, Table 6 (page 196) shows the results for subjects with 1 or >1 cartilage lesion. ISE, Table 11 (pages 207 and 208) shows the results for subjects based on age. The by age subgroup analysis split the subjects into 2 groups based on the median age of MACI-treated subjects in the MACI00206 study (≤ 35 and > 35). In all subgroups, MACI KOOS pain and function scores were superior to microfracture.

We trust this addresses your questions.

Regards,
Margarita

Margarita Aguilera, M.Sc.
Senior Regulatory Consultant – Vericel Corporation
64 Sidney Street
Cambridge, MA 02139
maguilera@vcel.com;
Telephone: (617) 588-5661
Mobile: (224) 659-2129
Facsimile: (734) 239-7401

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From: Margarita Aguilera
Sent: Sunday, May 22, 2016 10:04 PM
To: 'Yao, Michael (CBER)'
Cc: Schneider, Bruce; Gildner, Jean
Subject: RE: Request for additional clinical information

Dear Dr. Yao,

This is to acknowledge receipt of your request for information. I will get back to you with additional information on Monday.

Regards,
Margarita

Margarita Aguilera, M.Sc.
Senior Regulatory Consultant – Vericel Corporation
64 Sidney Street
Cambridge, MA 02139
maguilera@vcel.com;
Telephone: (617) 588-5661
Mobile: (224) 659-2129
Facsimile: (734) 239-7401

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notify the sender by e-mail or phone.

From: Yao, Michael (CBER) [<mailto:Michael.Yao@fda.hhs.gov>]
Sent: Friday, May 20, 2016 9:02 PM
To: Margarita Aguilera
Cc: Schneider, Bruce; Gildner, Jean
Subject: Request for additional clinical information
Importance: High

Hi Aguilera,

Please provide following information for us:

1. Regarding clinical evaluation in SUMMIT study, do you have clinical data (KOOS pain and function) before visit 6 (week 24)? If so, please provide a summary for FDA review.
2. Please provide subgroup analysis by number of lesions and by subject age, using some reasonable cut-off determine "younger" vs "older."

Thanks.

Michael