

APPROVED

By Jean Gildner at 1:40 pm, Dec 07, 2016

From: [Schneider, Bruce](#)
To: [Lorien Armour](#); [Yao, Michael \(CBER\)](#)
Cc: [Gildner, Jean](#); [Margarita Aguilera](#)
Subject: RE: Request for additional clinical analysis
Date: Friday, October 21, 2016 5:54:07 PM

Thanks very much.

Bruce

Bruce S. Schneider, MD
Division of Clinical Evaluation and Pharmacology/Toxicology
Office of Cellular, Tissue, and Gene Therapies
CBER/FDA

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From: Lorien Armour [<mailto:larmour@vcel.com>]
Sent: Friday, October 21, 2016 2:53 PM
To: Schneider, Bruce; Yao, Michael (CBER)
Cc: Gildner, Jean; Margarita Aguilera
Subject: RE: Request for additional clinical analysis

Dear Dr. Yao and Dr. Schneider,

Please find the response to your information request attached.

We would appreciate if you could confirm receipt of this information.

Kind Regards,

Lorien Armour, RAC
CMC Regulatory Consultant
Vericel Corporation
Office: 919-450-0802
Fax: 734-239-7401

From: Schneider, Bruce [<mailto:Bruce.Schneider@fda.hhs.gov>]
Sent: Tuesday, October 18, 2016 1:07 PM
To: Margarita Aguilera; Yao, Michael (CBER)
Cc: Gildner, Jean; Lorien Armour
Subject: RE: Request for additional clinical analysis

My thanks as well. I wonder if you could also provide the same primary effectiveness results according to arbitrary age quartiles: 18-26, 27-35, 36-44, and 45-54. I am not concerned about the ICH range designations, but just looking to see how the beneficial effect varies with age.

Thanks,

Bruce

Bruce S. Schneider, MD
Division of Clinical Evaluation and Pharmacology/Toxicology
Office of Cellular, Tissue, and Gene Therapies
CBER/FDA

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From: Margarita Aguilera [<mailto:maguilera@vcel.com>]
Sent: Tuesday, October 18, 2016 12:28 PM
To: Yao, Michael (CBER)
Cc: Schneider, Bruce; Gildner, Jean; Lorien Armour
Subject: RE: Request for additional clinical analysis

Dear Dr. Yao,

As a follow up to my email yesterday, please note that we are preparing the subgroup analysis response including output to send to you by Friday. Please note the following:

- Age subgroup analysis: In Section 4.1.1, Table 11 of the ISE, we provided a summary of the primary endpoint for above and below the median age in the study (≤ 35 years and > 35 years of age) because of the narrow age range in the treated population (age range 18 to 54 years old in both treatment groups). We recognize ICH guidelines that provide age cutoffs (< 18 , 18-34, 35-64, 65-75, and > 75); however, 3 of the 5 categories will have 0 patients. Therefore, a re-analysis of the age data will not provide additional information since our data essentially fits within the 2 categories of 18 to 34 and 35 to 64 that would be populated using ICH categories. Please let us know if you disagree with this assessment.
- BMI subgroup analysis: We will provide you with a summary of the primary endpoint for patients with normal BMI (< 25) and those who are overweight (≥ 25) by WHO criteria.

We would appreciate if you can confirm receipt of this information.

With kind regards,
Margarita

Margarita Aguilera, M.Sc.
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From: Yao, Michael (CBER) [<mailto:Michael.Yao@fda.hhs.gov>]
Sent: Monday, October 17, 2016 6:23 PM
To: Margarita Aguilera
Cc: Schneider, Bruce; Gildner, Jean
Subject: RE: Request for additional clinical analysis
Importance: High

Hi Margarita,

Please provide following additional information for us ASAP:

1. Please provide summary of subgroup analysis by ages, which is only for primary endpoint analysis from baseline to 2 years in SUMMIT study;
2. Please provide summary of subgroup analysis by BMI, which is only for primary endpoint analysis from baseline to 2 years in SUMMIT study.

Thanks.

Michael