Author’s response to reviews

Title: A randomized placebo-controlled trial of delayed-release dimethyl fumarate in patients with relapsing-remitting multiple sclerosis from East Asia and other countries

Authors:

Takahiko Saida (saida_takahiko@maia.eonet.ne.jp)
Takashi Yamamura (yamamura@ncnp.go.jp)
Takayuki Kondo (takakon78@hotmail.com)
Jang Yun (jang.yun@biogen.com)
Minhua Yang (minhua.yang@biogen.com)
Jie Li (ieli97@yahoo.com)
Lalitha Mahadavan (lalitha.mahadavan@biogen.com)
Bing Zhu (bing.zhu@biogen.com)
Sarah Sheikh (sarah.sheikh@biogen.com)

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Author’s response to reviews:

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Benjamin Ragen
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Title: A randomized placebo-controlled trial of delayed-release dimethyl fumarate in patients with relapsing-remitting multiple sclerosis from East Asia and other countries
Dear Dr. Ragen,

Thank you for the thorough review. The editor’s suggestions have been addressed as detailed below.

We verify that the references included in the manuscript are accurate.

Please let me know if we missed anything or if you have any additional queries.

Thank you for considering our submission. We look forward to your response.

Yours sincerely,

Takahiko Saida

Takahiko Saida, MD, PhD
Kansai Multiple Scleroses Centre
Kyoto Min-iren Central Hospital
Nishinokyo-Kasuga-cho 16-44-409
Nakakyo-ku, Kyoto 604-8453, Japan
Phone: 81-(0)75-468-8642
Fax: 81-(0)75-802-2380
E-mail: saida_takahiko@maia.eonet.ne.jp

Editor Comments

1) We note that the current submission contains some textual overlap with other previously published works, in particular: "Japanese guidelines for dimethyl fumarate" (2018) Clinical and Experimental Neuroimmunology. https://doi.org/10.1111/cen3.12477. Overlap exists in your abstract results section. While we understand that you may wish to express some of the
same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. Please re-phrase these sections to minimise overlap.

a) Authors’ response: Thank you for letting us know. The results section of the manuscript abstract have been revised (pg 3) and is shown below with edits highlighted.

Results: A total of 213 patients (95.1%) completed the study. From weeks 12 – 24, Compared with placebo, DMF reduced the total number of new gadolinium-enhancing (Gd+) lesions was reduced by from weeks 12–24 (primary endpoint) by 84% (p < 0.0001) in DMF compared with placebo. For the secondary endpoint, from baseline to Week 24, for, the total number of new Gd+ lesions from baseline to week 24 (secondary endpoint) was reduced by 75%, and the mean number of new/newly enlarging T2 hyperintense lesions at week 24 compared with baseline (secondary endpoint) was reduced by 63% (both all p < 0.0001). Flushing and flushing-related symptoms, and gastrointestinal events were adverse events related to DMF treatment included flushing and related symptoms, and gastrointestinal tolerability events. Efficacy and safety results in the Japanese subgroup and the East Asian subgroup (which included patients from Japan, Taiwan, and South Korea) were consistent with the overall study population.

2) Please add a “Conclusions” section after the “Discussion” section. This should state clearly the main conclusions of the research article and give a clear explanation of their importance and relevance.

a) Authors’ response: A Conclusions section has been added after the Discussion section.

3) Please include a statement in your Funding section describing the role of the funding body in the design of the study, the collection, analysis, and interpretation of data and in writing the manuscript.

a) Authors’ response: The funding section has been updated as follows.

This study was sponsored Biogen (Cambridge, MA, USA). Biogen provided funding for study design development, data collection, analysis, interpretation of the data, and medical writing support in the development of this paper. Biogen reviewed and provided feedback on the paper to the authors.

4) Please remove the response to reviewers document from the end of your manuscript file as this is no longer needed in the publication process.
a) Authors’ response: The response to reviewers has been removed as suggested.

5) Please upload your finale, revised version as a single, clean file.

a) Authors’ response: A clean, revised manuscript has been uploaded.