Author's response to reviews

Title: Th1/Th2 cytokine profile in relapsing-remitting multiple sclerosis patients treated with glatiramer acetate or natalizumab

Authors:

Celia Oreja-Guevara (orejacbn@gmail.com)
Jaime Ramos-Cejudo (jaime.ramosc@gmail.com)
Luis Stark Aroeira (lstark.hlpr@salud.madrid.org)
Beatriz Chamorro (beatrizlapaz2@gmail.com)
Exuperio Diez-Tejedor (ediez.hulp@salud.madrid.org)

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Author's response to reviews: see over
Dear Dr. Scott,

Please, find enclosed the revised version of our original manuscript "TH1/TH2 CYTOKINE PROFILE IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS TREATED WITH GLATIRAMER ACETATE OR NATALIZUMAB" by Dra. Oreja and cols. (Manuscript ID: 1756613734710443).

We thank the reviewers for their detailed and useful review of our manuscript. We appreciate the positive feedback as well as the constructive suggestions to further improvement of our manuscript, and we are glad to answer to each of the valuable reviewers’ comments.

We have carefully revised the original manuscript and have modified it according to the reviewer’s comments. The changes in the revised manuscript are highlighted with tracked changes in order to easily identify them. In addition, detailed responses to all comments requested by the reviewers are provided below. We report the reviewer’s concern in black, and our replies in blue.

We would be grateful if you reconsidered the revised manuscript for publication in BMC Neurology.

All of the listed authors have read the article and agree with the content of the revised version of the manuscript. I am the corresponding author, and I will be responsible for communicating with the other authors about revisions and final approval of the proofs.

We thank you for your kind consideration and we are looking forward to hearing from you.

Sincerely,

Dra. Celia Oreja-Guevara
Responses to the reviewers’ comments:

Reviewer 1: Oliver Neuhaus

Reviewer’s comments:

In this study, the authors measured serum levels of several Th1- and Th2-associated cytokines in 23 patients with relapsing-remitting multiple sclerosis treated for one year either with glatiramer acetate (GA) or with natalizumab (NAT). The authors observed several differences between the two groups confirming previous data on a Th2 shift in GA-treated patients. According to the putative mechanism of action of NAT, the authors observed a Th1 bias in the serum of NAT-treated patients.

As the authors state correctly, this study is limited by its small sample size and the cross-sectional study design with only one time point. The value of this study could be increased by adding data from untreated MS patients, ideally longitudinally from the same patients before and during treatment.

Response:

We agree with the reviewer that the results of the study could have been enriched by adding data from untreated patients. However, it is difficult to compare our data on cytokine levels after one year of treatment with those from RRMS untreated patients given that nearly all RRMS patients are under treatment nowadays and the only untreated patients that could be found are those with low risk clinically isolated syndrome (CIS), although these patients are not comparable as they do not fulfil MS criteria. We also concur with the reviewer that a longitudinal collection of data from the same patients before and during treatment would be an ideal design to provide an additional value to the study. However, we have not available data on Th1/Th2 cytokine levels before the initiation of treatment with GA or NAT since this study was conceived as a cross-sectional study to compare the Th1/Th2 cytokine profile of relapsing-remitting multiple sclerosis (RRMS) patients after one year of treatment with GA or NAT. Nevertheless, despite our primary aim was the comparison of cytokine profile between GA and NAT patients, we appreciate your valuable suggestion for the design of a subsequent study.

Reviewer 2: Thomas F Scott

Reviewer’s comments:

There are too few studies such as this, examining T cell functions in actual MS patients rather than in EAE. The 2 drug comparator paradigm works well, and the findings are largely confirmatory of previous work, but remain important. The authors should list the n for each group in the abstract.

Response:

We agree with the reviewer that information regarding the sample size (n) of each group should be included in the Abstract section. We are glad to have the chance to properly complete the content of our manuscript and we have now included this information in the
Abstract as follows: “Eleven patients under treatment with NAT and 12 patients treated with GA were evaluated“.