Author's response to reviews

Title: Impact of Efalizumab on Patient-Reported Outcomes in High-Need Psoriasis Patients: Results of the International, Randomized, Placebo-Controlled Phase III Clinical Experience Acquired with Raptiva (CLEAR) Trial [IMP24011]

Authors:

Jean-Paul Ortonne (ortonne@unice.fr)
Neil Shear (Neil.Shear@sw.ca)
Stephen Shumack (sshumack@bigpond.com)
Eric Henninger (eric.henninger@serono.com)

Version: 2 Date: 2 December 2005

Author's response to reviews: see over
2 December 2005

The Editors  
*BMC Dermatology* 
BioMed Central Ltd 
Middlesex House 
34-42 Cleveland Street 
London W1T 4LB 
UK

Dear *BMC Dermatology* Editors,

I am resubmitting on behalf of the CLEAR Multinational Study Group to *BMC Dermatology* the revised Manuscript 2100003737615190: “Impact of Efalizumab on Patient-Reported Outcomes in High-Need Psoriasis Patients: Results of the International, Randomized, Placebo-Controlled Phase III Clinical Experience Acquired with Raptiva (CLEAR) Trial [IMP24011].” A point-by-point response to the referees accompanies this letter (pages 2 – 4).

Please note that the CLEAR Study has been registered with the ClinicalTrials.gov Protocol Registration System and has been assigned the identifier: NCT00256139.

The submitted manuscript file has been titled “MS 2100003737615190 Ortonne CLEAR QOL text revised” and was prepared using Microsoft Word 2003 running on a Windows XP operating system.

Thank you very much for considering this manuscript for publication. I look forward to receiving your response and the comments of the reviewers.

Best regards,

Eric Henninger, MSc
Reviewer comments are present in normal text; responses are indicated in italics.

Reviewer: Jennifer Cather

General:
Try to shorten the paper. The data are similar to that of the large clinical trials.
Response: Thank you for your time and review of this manuscript.

The paper was initially shortened by removing redundant information regarding the patient population and study design. However, with the addition of a paragraph qualifying DLQI (per second reviewer’s request; please see below), the overall length of the paper has not been reduced. While 2 of the previous reports of clinical trials have addressed QOL of efalizumab-treated patients [1,2], the focus of this manuscript is on the QOL of the “High Need” patients, which has not been reported previously. It was not possible to remove additional information without compromising the presentation of the results.

Reviewer: Dan J Pearce

Thank you for your time and comments which are specifically addressed below.

Major Compulsory revisions:
1. Need to briefly mention the limitations of the DLQI and other measures. Also, we really don’t have a firm understanding on what is a meaningful improvement in the DLQI, i.e. a Minimally Important Difference or MID. Statistical significance is great, but if the change is not clinically meaningful then the message is convoluted.
Response: Indeed, an understanding of the relationship between the DLQI and clinically important differences is necessary. The use of SF-36 and DLQI as QOL measures has recently been critically reviewed and a reference indicating this information has been added. Information regarding the relationship of such measures to the clinical efficacy of efalizumab (as previously presented), has also been added for clarification (lines 339 to 354).

2. I would like to see any statistical significance attained with the adverse events even though this study is not powered necessarily to detect this.
Response: The assessment of safety and efficacy for the CLEAR study is reported in more detail separately (manuscript submitted to the British Journal of Dermatology); the purpose of the present manuscript is to describe the impact of efalizumab on patient-reported outcomes. While the statistical significance for safety has not been analyzed, the cumulative information collected and reported previously support the safety and tolerability of efalizumab [3-7] (Papp et al., Int J Dermatol, in press.), and is referenced in the manuscript (lines 376-379).
3. There is a relatively high degree of subjectivity in the determination of the high need cohort that needs to be recognized. For example

Response: The manuscript has been modified to acknowledge this point by the addition of “subjectively” at line 91 in materials and methods and “but subjectively” at line 302 in the discussion.

4. Psoriasis is typically a chronic disease and considering 36 month safety data “long” term is inappropriate since one major concern is an increased risk of malignancy in the future. Furthermore, aplastic anemia seems to be more prominent with longer courses of treatment.

Response: The manuscript has been modified by the removal of the term “long-term” and replacement with “extended” (line 382) and “Three-year” (line 382).

Minor Essential Revisions:
The figures are mislabeled; the legend uses 1a, 1b, 2a, 2b and they are labeled 1 – 4.

Response: Thank you for this information. The mislabeling must have occurred during the upload process of the individual figures. To circumvent this problem, the figures have been saved in pairs (e.g. 1a, 1b and 2a, 2b) and uploaded as two files instead of four.

Discretionary Revisions:
In the abstract “regardless of disease severity” is mentioned in the abstract as far as the efficacy. I think this should be stressed again in the discussion.

Response: The last paragraph of the discussion has been amended to stress this point.

Reference List


