Reviewer's report

Title: Approaches to discontinuing efalizumab: an open-label study of therapies for managing inflammatory recurrence

Version: 1 Date: 23 June 2006

Reviewer: Dan J Pearce

Reviewer's report:

General

Manuscript attempting to provide data for a relatively uncommon but significant clinical scenario. Certainly worthy of publication as this information may aid many dermatologists in dealing with this scenario. Furthermore, this type of information improves care and may enhance access to effective treatments such as efalizumab. There are several changes that may increase the strength of the manuscript.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. One problem with systemic psoriasis therapies is the difficulty in applying clinical trial paradigms to practice. Several references to "rebound" are made without clear definition of the term. Either providing a full explanation of terms such as recurrence, rebound and relapse or speaking more generally will help avoid confusion. Furthermore, these formal terms are defined in PASI terms and PGA was used in this study. --it would also be interesting to comment on the evolution of these terms as a possible consequence of study design with the pivotal efalizumab studies. Ref: J Am Acad Dermatol. 2006 Apr;54(4 Suppl 1):S171-81.

2. The definitions of psoriasis morphologies are not clear to me. Certainly pustular and erythrodermic flares are of concern with d/c of efalizumb. this needs to be emphasized; possibly presentation of these to types together a rebound group would be clinically useful. this may help to make one of the main points of the paper. I found the morphology data, in particular table 3 difficult and time consuming to understand. Also, I am not familiar with the "inflammatory" variant.

3. I think important to flaring after discontinuing efalizumab is the reason that the therapy was discontinued. Is this data available? Also, was treatment allowed during the 2 months?

4. The PGA data is difficult to understand, particularly table 2. I wasn't sure what was meant by first and last treatment. Better perhaps is to analyze according to either the first OR the last treatment and present graphically (this gets back to the intent to treat question).

5. 

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. BACKGROUND--All cases of psoriasis are not chronic.

2. METHODS--the inclusion criteria are not clear. how was it determined "natural progression" versus related to efalizumab?
---given that the physician could switch between therapies during the 12 week treatment interval, was an "intent to treat" approach used?
---i assume that the only retinoid was acitretin. also, there is a major difference in the dosing range allowed for acitretin and corticosteroids (which steroids were used by the way??); a comment in the discussion is appropriate to address these points.
---again, can you define "inflammatory" psoriasis
---is recurrence the appropriate term in the last para of the methods?

RESULTS--be consistent with spelling out numbers and listing them in numerical form.
---limitation that only 3 were treated with acitretin???
---p8, 1st para "incidence" is used incorrectly
---p9, 2nd para was "recurrence" the intended term
DISCUSSION--another limitation was retrospective nature of a portion.
TABLES-table 2 could be clarified as mentioned above.
---Table 3 is confusing and dilutes the message that pustular and erythrodermic flares post d/c of efalizumab were successfully treated with mtx, cys; also missing is the acitretin patients; did they d/c b/c of AEs?? dose related???

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
while a psoriasis research fellow my department received support from all biologic manufactures relevant to dermatology as well as Connetics. formerly consultant for Biogen Idec.