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Dear Dr Longson

Psoriatic arthritis – etanercept, infliximab and adalimumab

1) The BSR welcomes the opportunity to comment on this Assessment Report. We question the feasibility of pooling the results of trials for all three biologics as it is clear that each trial included patients of different severity, and recommend that it is treated with considerable caution. There are differences in baseline characteristics - particularly previous DMARDs, baseline joint counts and psoriasis severity. We have tabulated the differences between the trials in terms of three important variables: sub-group based on number of joints (the figures differ a little from the report), number of joints involved at baseline, and number of previous DMARDs used. These differences may well have influenced the outcome (ie rates of PsARC response, ACR20 and change in HAQ).

2) There are no head to head trials and using this approach to try to compare the agents may well give misleading results. The effect of the agents on the skin cannot be compared again due to differences in baseline PASI and relatively small numbers involved.

Variable	etanercept		infliximab		adalimumab	
	Mease et al 2000	Mease et al 2004	IMPACT1	IMPACT2	ADEPT	Genovese et al 2007
# previous DMARDs	1.5	2.0	0?	0	1.5	2.1
% polyarticular	?	86	100	100 (in report) 49 (in paper)	64	82
Mean/median swollen joint	-/14	-/?	14/-	14/-	14/-	18/-

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count						
Data compiled by Dr Phillip Helliwell, Leeds Institute of Molecular Medicine						

3) It should be noted that all three trial populations contain patients who are either DMARD naive or have yet to fail 2 or more DMARDs and are therefore not necessarily representative of the true clinical setting. The recommendations from the comparison analysis need to take this into account. For example the etanercept data from 2004 utilise a population where only 20% have failed 2 or more DMARDs (the population NICE are recommending we use these agents in). Comparing HAQ and joint count responses is likely to be different in a population that has already failed 2 or more drugs to one where a drug is being used de novo. This is another example where attempts to compare results from different trials can be fraught with difficulty. It is worth noting that the ACR20 response depends in part on the number of joints involved at outset, so that a person is less likely to achieve ACR20 with fewer joints at onset.

4) There were large areas of text 'hidden' – the reason for this is not made clear to the reader.

5) The estimated rate of progression of HAQ is based on poor quality data from the NOAR database where the diagnosis was unclear and it is likely that the more severe cases were excluded.

6) We also have serious doubts about the elicitation exercise and the assumptions and model parameters used as a result of the exercise. The response rate of experts was poor (5/16) and the reasons for this are not clear. Further, the report is somewhat patronising about the experts, claiming that they did not understand the exercise (despite talking some of the respondents through the process). The results obtained were thought to be unreliable so that the York group chose, as we understand, to dismiss the estimates of progression after discontinuing the drug.

Yours sincerely

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