Submission from UCB on golimumab ACD and ERG report

Stephanie, living with rheumatoid arthritis

Non inclusion of ACR 70 data from trials

- Detail
  - ACR 70 data has not been included in the model built by S-P and this is used as the justification for not doing the work required by the ERG. The committee has asked for this work to be done
- Issue
  - ACR 70 is effective remission and as such is not a trivial outcome indicator, but central to patient response. The non inclusion of S-P GoForward data – and the data of comparators can favour the relative outcome for golimumab. The incremental QALY gain may be changed if this data is not considered
- UCB comment and request
  - The response of TNFs, whilst similar, is not identical – certolizumab has a more rapid response that other TNFs for example. In order that clinicians understand which TNFs can benefit which patients groups most we need a comprehensive set of comparators. Only having comparators for ACR20 and ACR50 and not ACR70 will prevent a clear understanding of which agents have the best chance of providing remission.

Non inclusion of SF-36 and mapping toEQ-5D

- Detail
  - SF-36 data has been collected as part of the trials and we assume, can be mapped to EQ-5D in order to assess utility in the economic model.
- Issue
  - Relying on the conversion of ACR to HAQ through one algorithm and then to EQ-5D using another algorithm in the model introduces multiple uncertainties into the model.
- UCB comment and request
  - The chosen utility measures in the NICE reference case are quality of life measures such as EQ-5D and SF-36. Many manufacturers have measured these outcomes (Roche and UCB both measured ED-5D as health gain measures in their trials) and where possible this should be the starting point for measuring health gain rather than a mix of HAQ, DAS, ACR, EQ-5D and SF-36 which we currently have.

HAQ progression on palliative care set at 0.09

- Detail
  - Manufacturers have chosen an odd figure for the progression of patients on palliative care. Other submissions (TA130, TA126, TA186) – have used 0.06 as forward deterioration.
- Issue
  - As the measures are incremental if the comparator number for palliative care is set high (i.e 0.09 rather than 0.06) it will exaggerate the treatment effect from the TNF. If the results are marginal it may make the product seem cost effective.
- UCB comment and request
  - The 0.06 progression on palliative care has been a consistent level set through the previous STAs. To use a different measure now – 0.09 – is not logical or consistent and may result in the overestimation of the treatment effect gain from golimumab. We ask that the 0.06 figure for progression on palliative care is used in the model.

Section 3.23 - 30% of the population appear to only have received MTX – so one DMARD

- Detail
  - Section 3.23 of the ACD suggest that the population reflects that of the treatment group. However it appears that only 70% of patients in the GoForward trial have used two DMARDs in previous therapy.
- Issue
  - If only 70% of the population have had two DMARDs then it is likely that the treatment effect of DMARD therapy has not been optimised. If this is the case then the benefit gained by golimumab may be over-estimated.
- UCB comment and request
  - The trial populations in TNF treatments will always have an element of heterogeneity. A common challenge is finding patients who have optimised DMARD treatment. It appears that a proportion of the goliumumab DMARD failure population were not optimised on two DMARDS before TNF therapy. It should be possible to sub-analyse the patients in GoForward to look at the ACR response in the group that has had two DMARDs compared to those who have only had one. We ask that a sub analysis of GoForward is carried out between the one and two DMARD group.

Section 3.26 – CZP trials "stopping at week 12"

- Detail
  - The ERG is making the case that comparing trials in biologics is complex (which it is) and uses the example of certolizumab where there is a high level of ACR response and speculates this is because failures are removed at wk12.
- Issue
  - TNF response is variable. Our phase III trials for certolizumab (RAPID 1and 2) gave a very strong treatment effect, with a low placebo response. The ERG have incorrectly assumed we removed active arm non responders at week 12. This is **not** the case and removal was at week 16, as with the GoForward trial.
- UCB comment and request
  - We need to ensure that this point is well understood. All patients remained in the trial on active, or placebo until week 16, at which point non responders entered into open label active follow up. It is possible to compare the week 14 and week 16 performance of both TNFs

Non inclusion of bone data

- Detail
  - The has been no initial inclusion of bone data in the primary submission. It was provided as an abstract – under commercial in confidence – in follow up questions
- Issue
  - One of the main treatment benefits for the TNF class is the prevention of further joint degradation – particularly as there is a much later use of TNFs here in the UK than in other developed health economies. Others manufacturers have shown this outcome. In addition is seems that the bone benefits can only be gained at a higher dose level – as the published abstract only shows benefit with the higher dose.
- UCB comment and request
  - Prevention of the progression of bone loss under treatment with TNF inhibitors is one of the key benefits of this class. The data redacted from the report is available in other areas and if correct does not show effectiveness in the 50mg dose which is a key issue for the cost effectiveness of golimumab particularly when compared with other treatments. We request that this information is included in the submission and that the cost structure in the model reflects a high use of 100mg dosing in the trials.

Injection site event risk (table 30 on page 93 ERG)

- Detail
  - The ERG report states that the injection site reactions with golimumab are significantly lower than with certolizumab
- Issue
  - The injection site response for certolizumab was essentially similar to placebo. The manufacturer has compared between trials when it should be the response compared to placebo that is considered.
- UCB comment and request
  - We question the analysis carried out on injection site reactions and the statement on page 96 that golimumab had significantly fewer injection site reactions that certolizumab and ask that this is reviewed. We do not believe that it is possible to compare between different trial structures and arrive at this conclusion.

Non inclusion of Kay trial in MTC (ERG pg 121)

- Detail
  - Kay trial was not included in the MTC that provided point estimates for the economic model
- Issue
  - The Kay trial was an early stage trial and provides extra patient outcome evidence for golimumab. It has not been included in the MTC that is used to inform the cost effectiveness model. It may cause increased uncertainty on the outcomes with golimumab if relevant data is not included
- UCB comment and request
  - There are arms of the Kay trial that are the same as the licensed indication and regimen and an MTC that includes a meta-analysis using the Kay data in addition to the GoForward trials will provide additional certainty on the effectiveness of the treatment. We has that an MTC with the relevent Kay data is provided. This approach was taken with certolizumab where we were asked to incude the outcome data from a small early phase III trial.