Golimumab for Treating Non-Radiographic Axial Spondyloarthritis: A Fast Track Appraisal

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advisor stated that "active" is generally understood to mean a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of 4 or more. They also advised that golimumab and the comparator technologies would be considered alternatives in the same patients at the same point in the treatment pathway.

1.1 Summary of clinical effectiveness evidence submitted by the company

The key clinical effectiveness evidence in the CS[2] for golimumab was based on one randomised controlled trial (RCT): the GO-AHEAD trial.[6] This RCT investigated subcutaneous (SC) golimumab 50mg every 4 weeks versus placebo in patients ages ≥18 years to ≤45years who had active nr-axSpA according to the Assessment of SpondyloArthritis international Society (ASAS) criteria for ≤5 years since symptom onset (Company's clarification response,[4] A10), high disease activity, and an inadequate response to or intolerance of NSAIDs. The inclusion criterion of ≤5 years since symptom onset was based on the fact that long-standing disease is more likely to have radiographic changes not consistent with diagnosis of nr-axSpA (Company's clarification response,[4] question A10) and the inclusion criteria of age ≤45 years at enrolment was selected because it is the ASAS criteria for axial spondyloarthritis (Company's clarification response,[4] question A11).

Patients were recruited from 52 centres in 13 countries (Czech Republic, Denmark, Finland, Germany, Greece, Ireland, Italy, Russia, Slovakia, Spain, Turkey, UK, and US, see CS, p.30).[2] Ninety-eight patients were randomised (97 treated) to the golimumab arm and 100 patients were randomised to the placebo arm, of which 4/97 (4%) and 5/100 (5%) respectively were from the UK (Company's clarification response,[4] question A13). Ninety-three (95%) and 97 (97%) patients respectively completed the 16-week follow-up. GO-AHEAD[6] was a two-part study. After 16 weeks, placebo patients switched to golimumab for a pre-planned 44-week, open-label extension to evaluate long-term treatment effectiveness and safety. In response to the clarification letter (Company's clarification response,[4] question A1), the company stated that assessment of clinical response at 16 weeks was consistent with patients receiving a fourth dose of treatment at 12 weeks and the monthly schedule of study visits. The company also stated in the clarification letter[4] (question A1) that performing the assessment at week 16, at a time of trough (i.e. lowest) levels of golimumab, was conservative relative to assessment at week 14 when levels would have been higher.

In the double-blind phase of the GO-AHEAD[6] study, for the primary endpoint of 20% improvement in the Assessment of SpondyloArthritis International Society score (ASAS20) at 16 weeks, the between-group difference was statistically significant in favour of golimumab compared with placebo (p<0.0001). A statistically significant difference in favour of golimumab was also observed in the OSI population (MRI positive sacroiliac [SI] or CRP >upper limit of normal [ULN]) (p<0.001).

axSpA who were inadequate responders to or intolerant of NSAIDs for ASAS20, ASAS40, BASDAI50, change from baseline in BASFI and change from baseline in BASDAI and BASMI, adverse events (AEs), serious AEs (SAEs), and infections. The outcome time point was 12 weeks for all studies except for safety data and change from baseline BASMI from GO-AHEAD,[6] which was only reported at 16 weeks (CS, p.54).[2] In response to the clarification letter (Company's clarification response,[4] question A5) the company stated that they were unable to rerun the NMA for the SF-36 MCS and PCS outcomes including the GO-AHEAD[6] trial data at the time of responding to the clarification request.

The comparator studies in the NMA were as follows. ABILITY-1[7] evaluated adalimumab 40mg every other week versus placebo in 185 (94 placebo and 91 adalimumab) adult patients with nr-axSpA. The primary endpoint was the percentage of patients achieving ASAS40 at week 12. Haibel *et al.*[8] also evaluated adalimumab 40mg every other week versus placebo in 46 (24 placebo and 22 adalimumab) adult patients with nr-axSpA. The primary endpoint was also the percentage of patients achieving ASAS40 at week 12. The RAPID-axSpA[9] study evaluated certolizumab pegol 200mg every other week or 400mg every four weeks versus placebo in 325 (107 placebo, 111 certolizumab pegol 200mg and 107 certolizumab pegol 400mg) adult patients with AS (n=178) or nr-axSpA (n=147). The CS includes only the population with nr-axSpA, of which 50 were prescribed placebo, 46 certolizumab pegol 200mg and 51 certolizumab pegol 400mg. The primary endpoint was the percentage of patients achieving ASAS20 at week 12. The EMBARK[10] study evaluated etanercept 50mg every other week versus placebo in 215 (109 placebo and 106 etanercept) adult patients with nr-axSpA. The primary endpoint was the percentage of patients achieving ASAS40 at week 12.

1.2 Summary of the ERG's critique of clinical effectiveness evidence submitted

The literature searches in the AG report for TA383 were conducted in July 2014. Searches in the company submission were conducted in April 2017. The GO-AHEAD[6] study was identified in the searches for TA383 but it was excluded because golimumab was excluded from the scope of TA383 for this indication. The ERG considers the searches for clinical effectiveness evidence reported in the CS[2] to be adequate, and believes that the included RCT of golimumab to be relevant to the decision problem.

The eligibility criteria applied in the selection of evidence for clinical effectiveness were considered by the ERG to be reasonable and consistent with the decision problem outlined in the final NICE scope. The studies included in the NMA are consistent with those considered in the AG report for TA383 except that the GO-AHEAD[6] study has been added to the NMA and the infliximab study by Barkham *et al*.[11] has been removed, which is consistent with the scope of this FTA.[1, 12] The quality of

certolizumab pegol included patients with longer disease duration (up to 24 years[8] and up to 41.5 years,[9] respectively). The ABILITY-1[7] study reported a disease duration of approximately 10 years, whereas the GO-AHEAD[6] study reported a median disease duration of 0.5 years. The proportions of patients who were MRI and/or CRP positive ranged from 48% for adalimumab[6] to 88% for etanercept[10] but were not reported for certolizumab pegol.[9] The proportion of patients who were HLA-B27 positive was reasonably comparable across studies (82%,[6] 78%,[7] 67%,[8] 71%,[10] 75%[9]). All studies reporting the prior treatments of patients indicated that patients were biologic-naïve, except for RAPID-axSpA[9] where 10.9% of patients were not biologic naïve.