NICE Multiple Technology Appraisal

TNF alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis spondylitis (including a review of technology appraisal 143 and technology appraisal 233)

Introduction

The British Society for Rheumatology (BSR) exists to promote excellence in the care of people with rheumatic and musculoskeletal disorders (RMDs) and to support those delivering it. Its membership is drawn from wide range of healthcare professionals involved in the care of people with RMDs, including rheumatologists, nurses, allied health professionals, GPs and academics. BSR aims to improve standards of care in rheumatology and secure a high priority for rheumatology services across the UK.

Response

The BSR welcomes the appraisal consultation document (ACD) – TNF alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis (including a review of TA143 and TA 233). We agree with the majority of the conclusions, however we are extremely concerned that the ACD does not recommend treatment with another anti-TNF for people whose disease has not responded to treatment with the first anti-TNF, or those who had an initial response which was then lost. We have outlined our response under 4 headings;

1. Patients in England and Wales may be disadvantaged

At present, Ankylosing Spondylitis (AS) patients in the UK are only allowed access to one anti-TNF, unless they experience an adverse event within 12 weeks of initiating therapy[1]. The new proposed guidance has not changed this position. In our opinion, this severely limits the therapeutic options for patients, particularly in comparison to Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) where many more biologic treatment options exist. This means that AS patients are placed at a significant disadvantage relative to other patients with inflammatory arthritis. NICE has published a commissioning algorithm for patients with RA which includes guidance on the sequential use of biologics, much of which does not have an evidence base[2]. No restriction has been placed on switching anti-TNF therapy in the psoriatic arthritis guidelines[3]. This has set a precedent for other patients with inflammatory arthritis. As TA199 is silent on the issue of switching in the absence of RCT evidence, the axial spondyloarthritis (axSpA) guidelines should also remain silent on this issue. At an International level, The Scottish Medicines Consortium, European League Against Rheumatism and the Assessment of Spondyloarthritis International Society have not advised against or placed any restriction on sequential anti-TNF therapy in axSpA[4,5]. These documents specifically state “switching to a second TNF blocker might be beneficial especially in patients with loss of response”. This is being interpreted by rheumatologists as an opportunity to switch selected patients to an alternative TNF inhibitor in their respective countries.

2. Axial SpA is a complex disease requiring an option to switch TNF agents

Axial SpA is a complex disease with a variety of phenotypic manifestations which may evolve and change over time. The biology of inflammatory arthritis and TNF therapies is also

complex. We know that TNF inhibitors work via a number of different mechanisms; monoclonal antibodies, receptor blockade etc. For example, if a patient being treated with a TNF inhibitor developed colitis or uveitis, it may be clinically appropriate to change to a different TNF inhibitor. Similarly, in patients who develop human anti-chimeric antibodies (HACAs), it may be clinically appropriate to switch to another agent. Under proposed guidance, if the choice of initial drug proves to be incorrect or inappropriate, patients will not have access to an alternative effective treatment. Clinicians and patients are being placed under unreasonable pressure to select one and one-only TNF inhibitor.

3. Published data on switching

We accept that there are limited published data on the sequential use of TNF-inhibitors and no RCTs exist, and it is unlikely that these studies will ever be undertaken. On p19 of the ACD, the committee included the DANBIO data in a table[6], and stated: "The Assessment Group concluded that, despite a decrease in response rate, sequential treatment with TNF-alpha inhibitors can be beneficial for people with ankylosing spondylitis". In addition to the DANBIO data, there are 2 controlled studies (NOR-DMARD, ATTRA)[7,8]. In NOR-DMARD, 77 of 514 TNF-treated AS patients switched (30 because of inefficacy representing <6% of the total TNF treated population. One-third of these "switch" patients demonstrated a good clinical response. In ATTRA, the response rates of 163 "switch" patients were compared to 1012 patients treated with a first TNF inhibitor. More than 50% of "switch" patients achieved a major clinical response or partial remission. In both studies, the numbers of patients who needed to switch because of inefficacy was extremely small and there were no difference in outcomes between those switching due to adverse events or inefficacy. Denying this group of patients the opportunity to access sequential therapy would in our opinion place them at a significant clinical disadvantage as there is no alternative effective treatment pathway available. No studies have specifically examined switching in non-radiographic axSpA, however there is no reason to assume that outcomes would be significantly different in this group.

4. Implications of a "no switch" policy

If there is no "switch" option patients may remain on sub therapeutic treatment (for example a patient who had an initial excellent response and deteriorates over time yet still by definition meets the response criteria may be better served by an alternative agent.

Conclusion

In our opinion, patients should be allowed to switch to alternative anti-TNF drugs at any point during treatment, whether for reasons of inefficacy or adverse events. We urge the committee to reconsider their position on sequential TNF inhibitors in axial SpA.

[redacted] [redacted]

on behalf of the British Society for Rheumatology

References

1. NICE TA143
2. NICE CG79
3. NICE TA199
4. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with ankylosing spondylitis. J Braun, J Davis, M Dougados et al. ARD 2006;65(3): 316-20
5. Update of the literature review on treatment with biologics as a basis for the first update of the ASAS/EULAR management recommendations of Ankylosing Spondylitis. X Baraliakos; R van den Berg; J Braun; D van der Heijde. Rheumatology. 2012;51(8):1378-1387.
6. Clinical response, drug survival and predictors thereof in 432 ankylosing spondylitis patients after switching tumour necrosis factor alpha inhibitor therapy: results from the Danish nationwide DANBIO registry. Glintborg B, Ostergard M, et al. ARD 2013;72(7): 1149-55.
7. Effectiveness of switching between TNF inhibitors in ankylosing spondylitis: data from the NOR-DMARD register. E Li, D van der Heijde et al. ARD 2011;70: 157-63
8. Efficacy of the first and subsequent courses of anti-TNF therapy in patients with ankylosing spondylitis – results from the Czech National Register ATTRA. Rheumatologia 2012; 50(4): 294-306