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Guidelines

BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics

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Executive Summary

Scope and purpose

Axial SpA (axSpA) is a chronic inflammatory condition predominantly involving the spine and sacroiliac joints (SIJ), with or without extra-spinal manifestations including peripheral arthritis, enthesitis, iritis, psoriasis and IBD. Individuals with axSpA experience significant pain, stiffness and lack of function that translates into important health care costs and increased mortality.

AxSpA can be classified into two subgroups: radiographic axSpA, commonly referred to as AS, and non-radiographic axSpA (nr-axSpA). The primary difference between these two subgroups is the presence or absence of defined structural changes in the SIJ as detected on plain radiography. Although patients with nr-axSpA do not fulfil the modified New York criteria for AS [1], their burden of disease is similar [2] and they may derive as much benefit from treatment as patients with established AS.

This revision of the 2005 BSR guidelines [3] provides evidence-based guidance for UK clinicians prescribing biologic drugs for adult patients across the spectrum of axSpA. This includes the criteria for starting treatment, the

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NICE has accredited the process used by the BSR to produce its treatment of axial spondyloarthritis with biologics guidance. Accreditation is valid for 5 years from 10 June 2013. More information on accreditation can be viewed at www.nice.org.uk/accreditation. For full details on our accreditation visit: www.nice.org.uk/accreditation.

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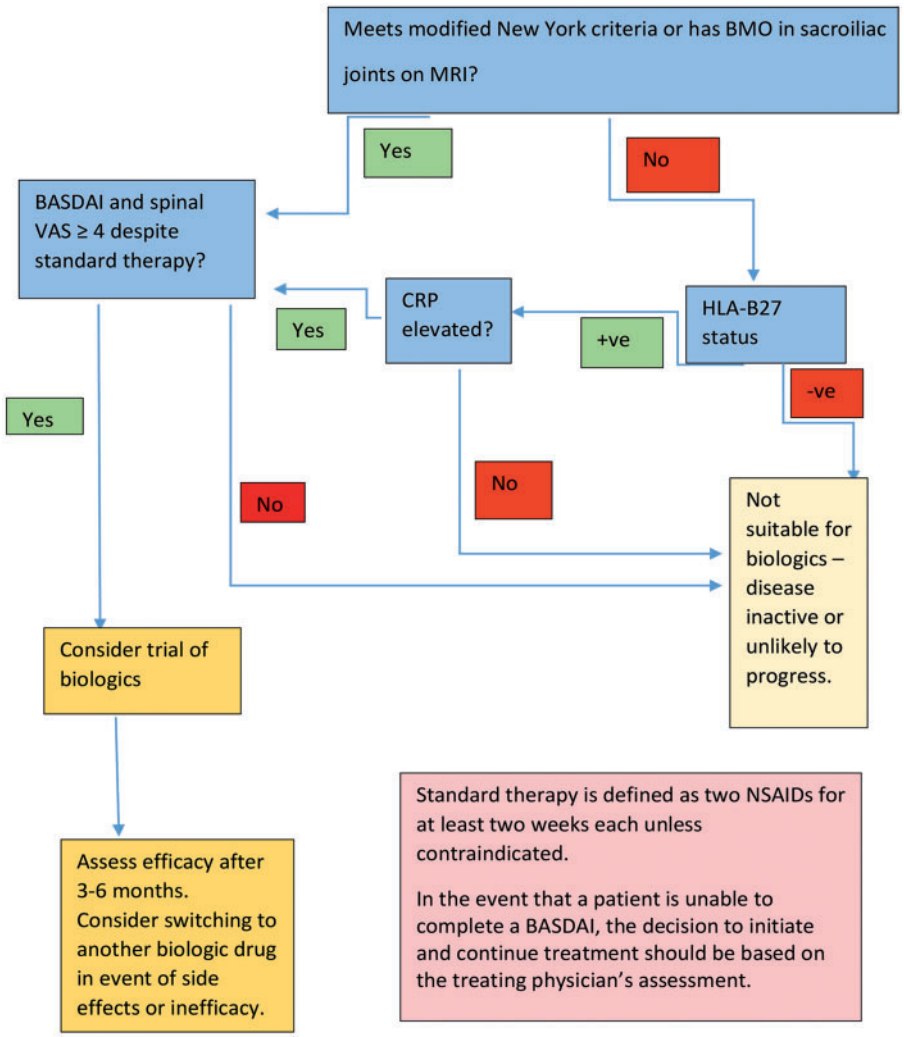
Fig. 1 Treatment algorithm for biologic therapy in axSpA



BMO: bone marrow oedema; VAS: visual analogue scale.

choice of drug and assessing response to treatment. Peripheral spondyloarthritis and juvenile SpA are outside the scope of these guidelines, and readers are referred to the BSR 2012 guidelines for the management of PsA [4].

Key recommendations

These recommendations are summarized in a treatment algorithm (Fig. 1). Accompanying descriptions of evidence and full recommendations are given in the full guideline, provided as supplementary data, available at *Rheumatology* Online.

The effectiveness of biologics in axSpA

(i) Anti-TNF therapy is effective at reducing disease activity and spinal pain in axSpA. While short-term MRI data support the efficacy of anti-TNF therapy in treating inflammatory SIJ and spinal lesions in axSpA, evidence for anti-TNF therapy on radiographic disease progression is currently limited [level of evidence (LOE) 1+; strength of recommendation A; consensus score 9.6].

(ii) Currently there is insufficient evidence to recommend the use of other biologic agents in axSpA (LOE 1+; strength of recommendation B; consensus score 9.3).

Initiating treatment

(i) Patients should be considered for anti-TNF therapy if they have active axSpA (LOE 1+; strength of recommendation B; consensus score 9.6).

(ii) Active disease is defined as a BASDAI and spinal pain visual analogue scale (VAS) score $\geqslant 4$ despite standard therapy (LOE 1+; strength of recommendation B; consensus score 8.5).

(iii) The BASDAI should be measured on two occasions at least 4 weeks apart. Current National Institute for Health and Care Excellence guidelines require patients to have active spinal disease on two separate

occasions 12 weeks apart, with the aim of avoiding the overtreatment of patients with a short-lived flare of disease. However, as flares in AS last for an average of 2–3 weeks [5], an interval of 4 weeks between scores is sufficient and should not delay treatment unduly (LOE 2+; strength of recommendation C; consensus score 7.2).

(iv) Patients with active disease who do not meet modified New York criteria for AS should also have had a positive MRI and/or raised CRP. Prescribers should be confident that worsening symptoms, radiological changes and raised inflammatory markers are due to axSpA and not to other pathology such as malignancy or infection. Discussion with an axSpA specialist should be considered before starting treatment in a patient with nr-axSpA and no SIJ bone marrow oedema on MRI (LOE 1+; strength of recommendation B; consensus score 9.3).

Choice of Drug

(i) Extra-articular manifestations and patient choice should be considered when selecting an anti-TNF agent. In the absence of head-to-head studies, systematic reviews have shown no statistical difference in efficacy between infliximab, golimumab, etanercept and adalimumab in the treatment of AS (certolizumab data were not included in these comparative reviews, but its efficacy has been established in clinical trials). There are insufficient data to comment on relative efficacy in nr-axSpA. However, not all biologics are licensed for or effective in the treatment of extra-articular disease, so drug choice should take into account co-morbidities and the preferred route and frequency of administration (LOE 4; strength of recommendation D; consensus score 8.9).

Assessing Response

(i) Initial efficacy response should be assessed following 3–6 months of therapy and responders should then be reassessed every 6 months (LOE 2+; strength of recommendation D; consensus score 8.6).

(ii) Response is defined as a reduction in the BASDAI and spinal pain VAS of $\geqslant 2$ U from baseline (LOE 1+; strength of recommendation B; consensus score 8.3).

(iii) If, because of cognitive or communication difficulties, the BASDAI cannot be used to monitor disease activity, the decision to initiate and continue therapy should be based on the treating clinician's assessment of disease activity (LOE 4; strength of recommendation D; consensus score 9.9).

Withdrawal of Therapy

(i) In the absence of an initial clinical response by 6 months, or failure to maintain response at two consecutive assessments, withdrawal of that anti-TNF agent should be considered (LOE 4; strength of recommendation D; consensus score 9.4).

(ii) There is no evidence to support the withdrawal of anti-TNF therapy in treatment responders (LOE 2+; strength of recommendation B; consensus score 9).

Switching

(i) In the event of anti-TNF failure due to inefficacy or adverse events, an alternative anti-TNF agent should be offered if clinically appropriate (LOE 2+; strength of recommendation C; consensus score 9.7).

Safety

The safety of anti-TNF therapies in axSpA is comparable to other inflammatory joint diseases such as RA. There is little evidence to suggest that safety issues differ hugely with different disease groups, and the 2010 British Society for Rheumatology (BSR) guidelines on the safety of anti-TNF therapies in RA are applicable in axSpA [6].

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Supplementary data

The full guideline is available at *Rheumatology* Online and an audit tool to assess compliance with these recommendations can be found on the BSR website.

References

1 van der linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.

2 Rudwaleit M, Haibel H, Baraliakos X *et al*. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. Arthritis Rheum 2009;60:717–27.

3 Keat A, Barkham N, Bhalla A *et al*. BSR guidelines for prescribing TNF-alpha blockers in adults with ankylosing spondylitis. Report of a working party of the British Society for Rheumatology. Rheumatology 2005;44:939–47.

4 Coates LC, Tillett W, Chandler D *et al*. The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. Rheumatology 2013;52:1754–7.

5 Cooksey R, Brophy S, Gravenor MB *et al*. Frequency and characteristics of disease flares in ankylosing spondylitis. Rheumatology 2010;49:929–32.

6 Ding T, Ledingham J, Luqmani R *et al*. BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. Rheumatology 2010;49:2217–9.