RHEUMATOLOGY ADVANCES IN PRACTICE

# Letter to the Editor (matters arising from published papers)

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## Comment on: Tumour necrosis factor inhibitor survival and predictors of response in axial spondyloarthritis—findings from a United Kingdom cohort

Sir, We read with interest the report by Yahya *et al.* [1] on tumour necrosis factor inhibitor (TNFi) survival and predictors of response in axial spondyloarthritis (axSpA) patients treated in a real-life setting in the UK, where no sex differences were identified impacting these outcomes. Data over the last decade suggest sex-attributable differences in disease features, clinical outcomes and treatment response in axSpA, with a longer diagnostic delay [2], older age at disease onset [3] and higher number of affected first-degree relatives [4] in females. These findings suggest that a higher genetic load is needed in order to develop the disease in females than in males [5]. Furthermore, women appear to have a higher burden of disease [3], reduced response to TNFi [6, 7] and higher switching rate [8]. Characterization of these differences is essential for a better understanding of the disease trajectory in order to deliver optimal personalized medical management. Here, we report our experience from a single tertiary centre in a large teaching hospital, exploring the role of sex in treatment response, drug survival and switching rate in a cohort of biologic-treated axSpA patients.

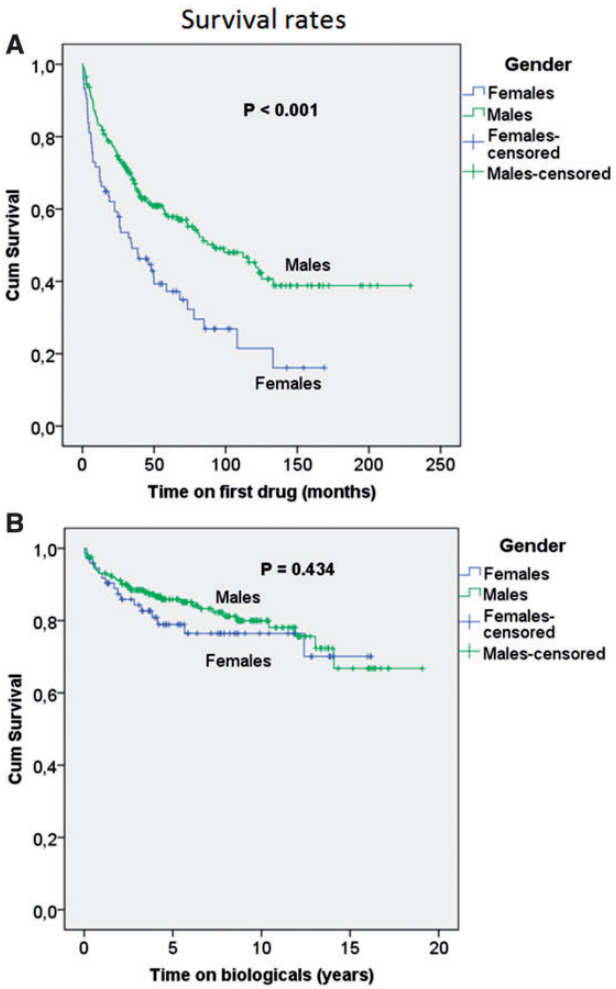
As part of service development and to comply with mandatory audit according to National Health Service governance systems, we conducted a retrospective evaluation of anonymized data using the Leeds Spondyloarthritis Service database. Subjects were eligible if they had a physician-verified diagnosis of radiographic axSpA fulfilling the modified New York criteria (mNYC) for AS and if they received the first TNFi between 1999 and 2017. Exclusion criteria included being prescribed the first TNFi for a diagnosis other than AS, not having TNFi as the first biological (switch to another biological class was allowed), having a follow-up $<12$ months or participating in the placebo arm of a clinical trial. In compliance with National Institute for Health and Care Excellence guidance, all subjects had a BASDAI $\geq 4$ at initiation of the first TNFi. Information on disease characteristics, patient-reported outcomes for disease activity (BASDAI), function (BASFI) and pain (visual analog scale) were available at baseline. Treatment response was evaluated by the improvement of 50% in BASDAI (BASDAI50) after 3–6 months (first evaluation) and 1–1.5 years (second evaluation) of treatment. Kaplan–Meier curves were calculated to describe drug survival, and the log-rank test was used to test for differences between the sexes. Discontinuation was classified as attributable to non-response, intolerance (including adverse events) or other reasons (patient decision, death, finished a trial), and the frequency of switching between biologicals was calculated by sex for each drug. All statistical analyses were done in SPSS software (SPSS Statistics, version 21).

Data from 280 patients (75 females and 205 males) were available for analysis (Supplementary Table S1, available at *Rheumatology Advances in Practice* online). Significant differences between the sexes were observed, with females having a higher prevalence of IBD at the baseline (21.3 *vs* 9.8%; $P = 0.010$) and family history of SpA (61.4 *vs* 41.8%; $P = 0.013$) than males. No other sex differences were observed with regard to age at diagnosis, disease onset, delay in diagnosis, symptom duration, patient-reported outcomes or baseline CRP. At the first evaluation, more females reached BASDAI50, but this was not sustained at the second evaluation (Supplementary Tables S2 and S3, available at *Rheumatology Advances in Practice* online). In contrast to the findings of Yahya *et al.* [1], females showed a significantly shorter drug survival for the first drug compared with males (median, 34.4 *vs* 91.6 months; $P < 0.001$), but this difference was not significant for the total number of biological drugs (Fig. 1). More females than males discontinued treatment owing to intolerance (Supplementary Figure S1, available at *Rheumatology Advances in Practice* online), which includes adverse events (81.3 *vs* 48.6%). A total of 40.4% of patients switched to a second drug, with more females than males (53.3 *vs* 35.6%) mainly because of non-response. Our cohort comprises solely AS patients, with a switching rate similar to the DANBIO registry [8] but higher than that reported by Yahya *et al*. [1], probably reflecting locally agreed commissioning pathways.

There are a number of limitations to our report, such as the retrospective design, small sample size and missing BASDAI data, which lead to a low statistical power; however, these data provide one of the longest observational reports to date, with some patients being followed up for 19 years.

In conclusion, in our cohort there was no difference in disease burden between sexes at the time of TNFi initiation, although females had a higher prevalence of IBD and more relatives with SpA, as shown by other groups. Although no sex difference in treatment response was seen, a higher switching rate and shorter drug survival of the first TNFi was seen in females compared with

Fig. 1 Survival rates of first TNFi and all biologicals stratified by gender




(**A**) First TNFi. (**B**) All biologicals.

males. The majority of patients, of both sexes, remained on biological treatment (81.1%) for a median treatment duration of 6.3 years. These data add to the body of evidence of real-life response to TNFi in radiographic axSpA.

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## Supplementary data

Supplementary data are available at *Rheumatology* online.

**Wala Al Arashi[1,2,3], Carlota Iñiguez Ubiaga[1,2], Elizabeth M. Hensor[1,2], Katie Gaffney[2], Jane Freeston[1,2], Claire Vandevelde[1,2], Andrew Barr[1,2], Irene van der Horst-Bruinsma[3] and Helena Marzo-Ortega[1,2]**

*[1]Department of Rheumatology, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, [2]Department of Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK and [3]Department of Rheumatology, Amsterdam Rheumatology and immunology Centre/VU University Medical Centre, Amsterdam, The Netherlands*
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Correspondence to: Helena Marzo-Ortega, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Second floor, Chapel Allerton Hospital, Chapeltown Road, Leeds LS7 4SA, UK.
E-mail: medhmo@leeds.ac.uk

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