Potential impact of European Medicines Agency measures to minimize risk of serious side effects on JAKi prescribing and utilization in the UK

Zixing Tian, Lianne Kearsley-Fleet, James Galloway, Kath Watson, BSRBR-RA Contributors Group, Mark Lunt, Kimme L Hyrich

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What was already known?

JAK inhibitors are the newest type (or class) of advanced Rheumatoid Arthritis (RA) treatment and have been available since 2017. Four JAK inhibitors have been approved by the EMA which evaluates and supervises medicine use in the European Union. These include: Jyseleca, Olumiant, Xeljanz and Rinvoq.

In 2023, the EMA limited the use of JAK inhibitors to certain high-risk patients unless no other suitable treatments are available, due to evidence suggesting that JAK inhibitors increase the risk of cardiovascular disease or cancer compared to TNF inhibitors (another advanced RA treatment). This advisory change was also adopted by the UK Medicines and Healthcare Products Regulatory Agency (MHRA). The four at-risk patient groups include:

- age 65 years or above,
- increased risk of major cardiovascular problems,
- current or past smokers,
- increased risk of cancer.

What was discovered?

We wanted to investigate how many RA patients using JAK inhibitors in the UK do not fit the new safety guidelines from the EMA. This will help to understand how these changes might affect JAK inhibitor prescriptions now and in the future.

We used data from the BSRBR-RA study, which is a national cohort study, established in 2001, of over 30,000 patients with RA on biological therapies (otherwise known as Biologic Disease Modifying Anti-Rheumatic Drugs or bDMARDs) and JAK inhibitors. This cohort study has been recruiting RA patients using JAK inhibitors since 2017. The four other classes of targeted therapies (bDMARDs) have been available for much longer than the JAK inhibitors and the BSRBR-RA has captured extensive long-term data showing the safety and effectiveness of the bDMARDs.

We found that among 1,341 RA patients who had started the JAK inhibitors before EMA advisory change, 80% (1,075 patients) met at least one EMA risk criterion. Of these high-risk patients:

- 49% (529 patients) used JAKi as their first or second treatment type. Suitable alternatives might likely have existed for them, and re-evaluation of the suitability of their treatment

may be needed.

- 28% (299 patients) had already tried at least three out of four other advanced RA treatment types. For these patients, options for alternative therapies would be very limited.

Why is this important/what is the benefit to patients?

These treatments are so new and this is just the start of the JAK inhibitor analysis in the BSRBR-RA data; once more data has been collected the following will be looked at:

- Analysis of treatment data collected after January 2023 will help understand the impact of licensing recommendations and shifts in the practical use of JAK inhibitors.
- Comparing the risk of cardiovascular disease and cancer between JAK inhibitors and the other four types of advanced RA treatments.

Should you wish to read this scientific paper in full, the text can be found online here:
https://academic.oup.com/rheumatology/advance-article/doi/10.1093/rheumatology/keae279/7674871