

Impact of Janus kinase inhibitors on the risk of cardiovascular events in patients with rheumatoid arthritis: systematic review and meta-analysis of randomised controlled trials

We read with great interest the article by Xie and colleagues¹ regarding the impact of Janus kinase inhibitors (Jakinibs) on the risk of cardiovascular events in patients with rheumatoid arthritis (RA). This systematic review and meta-analysis revealed no significant change in cardiovascular risks for Jakinib-treated patients with RA in a short-term perspective study. However, some methodological issues must be addressed. First, Cochran Q is the weighted sum of squares on a standardised scale, and when it is reported with low p values, it indicates heterogeneity.² However, care must be taken when interpreting the χ^2 test results because it has low power in the common situation of a meta-analysis, especially when studies have a small sample size or few cases. While a statistically significant result may indicate a problem with heterogeneity, a non-significant result must not be considered evidence of no heterogeneity. Although no definitive cut-off value has been established at which no data pooling should be performed, a p value of 0.10, rather than the conventional level of 0.05, is usually used to determine statistical significance.² Second, two statistical models can be used for meta-analyses: the fixed-effects model and the random-effects model. The selection of the appropriate model is important to ensure that various statistics are estimated correctly.³ The choice of the meta-analysis method should be explained, and a rationale for choosing the statistical model should also be stated.⁴ The fixed-effects model is generally used in the absence of heterogeneity in a meta-analysis that includes a large number of studies, preferably with large sample sizes. If heterogeneity is a concern, the random-effects model has been advocated for data pooling. A high heterogeneity was detected among the three kinds of Jakinibs for venous thromboembolism events ($I^2=63.5\%$) and all cardiovascular events ($I^2=71.7\%$).¹ Considering the substantial and considerable heterogeneity, the random-effects model would be the more appropriate choice in those cases. A random-effects meta-analysis may be used to incorporate heterogeneity among studies.⁵ However, this is not a substitute for a thorough investigation of heterogeneity.⁴ Exploration of possible causes of heterogeneity is always advisable. Thus, we believe that the

findings of this study should be interpreted with consideration of the aforementioned methodological concerns.

Young Ho Lee , **Gwan Gyu Song**

Department of Rheumatology, Korea University, Seongbuk-gu, Korea (the Republic of)

Correspondence to Professor Young Ho Lee, Rheumatology, Korea University, Seoul 02841, Korea; lyhchg@korea.ac.kr

Correction notice This article has been corrected since it published Online First. The title has been corrected.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.



To cite Lee YH, Song GG. *Ann Rheum Dis* 2020;**79**:e122.

Received 31 May 2019

Accepted 2 June 2019

Published Online First 11 June 2019



► <http://dx.doi.org/10.1136/annrheumdis-2019-215841>

Ann Rheum Dis 2020;**79**:e122. doi:10.1136/annrheumdis-2019-215815

ORCID iD

Young Ho Lee <http://orcid.org/0000-0003-4213-1909>

REFERENCES

- Xie W, Huang Y, Xiao S, et al. Impact of Janus kinase inhibitors on risk of cardiovascular events in patients with rheumatoid arthritis: systematic review and meta-analysis of randomised controlled trials. *Ann Rheum Dis* 2020;**79**:e123.
- Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557–60.
- Borenstein M, Hedges LV, Higgins JPT, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010;**1**:97–111.
- Collaboration C. *Cochrane Handbook for systematic reviews of interventions 5.0. 0: cochrane collaboration*, 2008.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;**7**:177–88.