Risk of Venous Thromboembolism with Janus Kinase Inhibitors in Rheumatoid Arthritis: A Systemic Review

RWD96

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BACKGROUND

- Janus Kinase inhibitors (JAKi) such as tofacitinib (2012), updacitinib (2020), baricitinib (2018) are the most recent class of medications for rheumatoid arthritis (RA).
- However, increased risk of venous thromboembolism (VTE) was observed for JAKi in through a randomized clinical trial (RCT).[1]
- The US FDA has added a 'black box warning' on all approved JAKi. [2]
- Current systematic reviews on JAKi VTE safety in RA were limited to only evaluating the evidence based on the RCTs.[3,4]
- With the growing use of JAKi for RA, there is a need to systematically examine the post-marketing evidence with JAKi use among patients with RA seen in the real-world.

OBJECTIVE

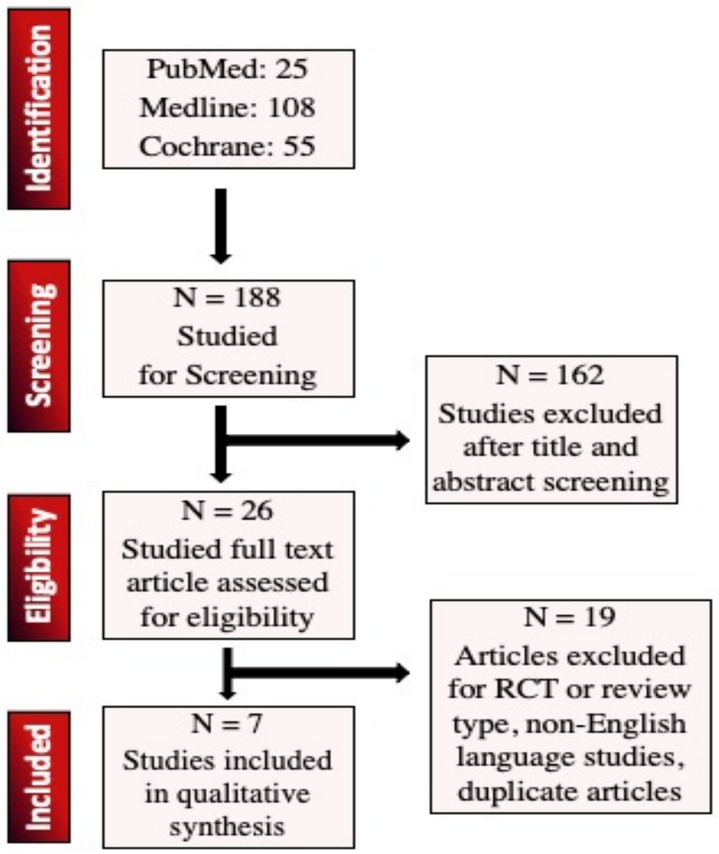
- To examine the risk of VTE with the use of JAKi versus Tumor Necrosis Factor inhibitors (TNFi) in patients with RA using real-world data.

METHODS

- Guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.
- *Searches strategy*: PubMed/MEDLINE, EMBASE & Cochrane/CENTRAL were searched using the search terms: "RA", "JAKi", "TNFi" and "VTE".
- *Study eligibility*: Only English language observational or administrative claim studies comparing the risk of VTE with the use of JAKi or TNFi in RA were included.
- *Data Extraction:* (1) study info: data source & study design; (2) patient characteristics: population & JAKi medication; (3) outcome & association between JAKi and VTE risk.
- *Quality assessment*: the Quality in Prognosis Studies (QUIPS) tool.

RESULTS

- The systemic review identified 188 studies; seven observational studies met the inclusion criteria
- Four studies were conducted in the United States, and the other three were from France, Taiwan, Japan, and Sweden.
- Three studies used administrative claims datasets (Marketscan, Medicare), electronic medical records (EMR), and US registry, and the other four studies used non-US databases.
- Most studies were retrospective cohort studies, and all studies used a new user design.
- The average follow-up period of the studies was 32 months to 7 years
- Of the three studies (N=3) that compared the risk of VTE between JAKi and TNF bDMARDs, two studies found an increased risk of VTE with JAKi use as compared to TNFi and one study reported no association between VTE risk with JAKi.
- Of the four drug-specific studies (N=4), three found no difference in VTE risk between tofacitinib vs TNFi; however, one found there was an increased risk of VTE with baricitinib vs TNFi.



CONCLUSIONS

- The systemic review found mixed evidence regarding the risk of VTE with JAKi as compared to TNFi, and the JAKi class-specific VTE risk as compared to TNFi in RA was also unclear.
- There was also variation in the risk of VTE with individual JAKi vs. TNFi.
- Future studies are needed to evaluate drug-specific VTE risk within the class of JAKi in RA.

KEY REFERENCES

1. Ytterberg, S.R., Bhatt, D.L., Mikuls, T.R., Koch, G.G., Fleischmann, R., Rivas, J.L., Germino, R., Menon, S., Sun, Y., Wang, C. and Shapiro, A.B., 2022. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. New England Journal of Medicine, 386(4), pp.316-326. 2. FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions | FDA. 3. Zhang, J., Li, W., Gong, M., Gu, Y., Zhang, H., Dong, B., Guo, Q., Pang, X., Xiang, Q., He, X. and Cui, Y., 2023. Risk of venous thromboembolism with janus kinase inhibitors in inflammatory immune diseases: a systematic review and meta-analysis. Frontiers in Pharmacology, 14, p.1189389. 4. Maqsood, M.H., Weber, B.N., Haberman, R.H., Lo Sicco, K.I., Bangalore, S. and Garshick, M.S., 2022. Cardiovascular and Venous Thromboembolic Risk With Janus Kinase Inhibitors in Immune-Mediated Inflammatory Diseases: A Systematic Review and Meta-Analysis of Randomized Trials. ACR Open Rheumatology, 4(10), pp.912-922.