Effectiveness of targeted disease-modifying antirheumatic drugs for fatigue in rheumatoid arthritis

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INTRODUCTION

Randomized clinical trials established Janus Kinase inhibitors (JAKi) as an efficacious intervention to reduce the disease activity of rheumatoid arthritis (RA), which was also associated with an improvement in fatigue[1].

Results for effectiveness of JAKi to reduce fatigue from real-world patient cohorts is limited to small studies without comparator drugs[2].

AIM

To evaluate the effectiveness of JAKi in reducing RA-associated fatigue compared to tumor necrosis factor inhibitors (TNFi), and interleukin-6 inhibitors (IL-6i).

METHODS

STUDY POPULATION

- 4541 patients observed in the German biologics register RABBIT and treated with:
  - JAKi: 1224
  - TNFi: 2839
  - IL-6i: 478
- Enrolment: 2017 – 2023
- Inclusion criteria: ≥ 1 failure of a disease-modifying anti-rheumatic drug (DMARD)

MEASURES & OUTCOME

- Fatigue, measured on a numerical rating scale (0 - 10)
- Change in fatigue over 180 days after treatment initiation
- Time to follow-up was modelled as a continuous covariate

STATISTICS

- Imbalance between treatment groups: entropy weighting [3]
- Course of fatigue: weighted generalized additive models (wGAM)
- Missing data: 20 imputations
- Differences between treatments: calculation of contrasts, i.e. differences in means

- Sensitivity analysis: population restricted to patients treated with no concomitant methotrexate

RESULTS

BASELINE CHARACTERISTICS

- In unweighted data of this study population minor differences were found between treatments, e.g., regarding age (TNFi: 59.1, JAKi: 59.5, IL-6i: 59.0 years), distribution of sex (females: 74.7%, 74.3%, and 70.4%), disease activity (DAS28-ESR: 4.5, 4.7, 4.8), and fatigue (NRS: 5.0, 5.3, 5.3).
- The application of entropy weighting achieved balanced groups for most patient characteristics (Table)
- Larger differences were found for prior biologic DMARD failures (Table) that could not be eliminated by weighting.

COURSE OF FATIGUE OVER 180 DAYS

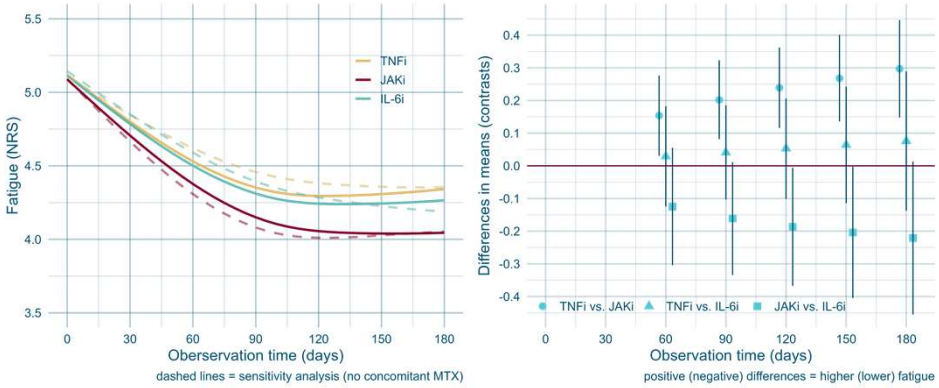

***Table**: Baseline characteristics after entropy weighting[3] and averaged over 20 imputations. For most characteristics imbalance has been reduced; imbalance for prior treatment failure with biologic DMARDs persists.*

Characteristic ‡	JAKi (N=1224)	IL-6i (N=478)	TNFi (N=2839)	SMD	p
Age	59.1 (12.3)	59.1 (12.8)	59.1 (11.3)	<0.01	1.00
Sex	362.2 (29.6)	840.0 (29.6)	141.4 (29.6)	<0.01	1.00
Disease duration	8.1 (7.5)	8.1 (8.4)	8.14 (7.3)	<0.01	1.00
CRP	12.4 (17.8)	12.4 (18.3)	12.40 (18.5)	<0.01	1.00
DAS28-ESR	4.5 (1.3)	4.5 (1.3)	4.5 (1.37)	<0.01	1.00
Physical function	69.7 (22.7)	69.7 (22.2)	69.7 (22.9)	<0.01	1.00
Pain (NRS)	5.6 (2.3)	5.6 (2.3)	5.6 (2.5)	<0.01	1.00
Body-Mass-Index	27.7 (5.6)	27.7 (5.5)	27.7 (5.5)	<0.01	1.00
Fatigue (NRS)	5.0 (2.7)	5.0 (2.7)	5.0 (2.7)	<0.01	1.00
Sleeping difficulties (NRS)	4.8 (3.1)	4.78 (3.1)	4.80 (3.0)	0.01	0.47
Prior bDMARD failures, n (%)				0.43	<0.01
None	847.4 (69.2)	319 (66.7)	2536 (89.3)		
One	209 (17.1)	77.9 (16.3)	219 (7.7)		
Two	82.8 (6.8)	55 (11.5)	53 (1.9)		
Three or more	84.8 (6.9)	26.2 (5.5)	31 (1.1)		

NRS: *numerical rating scale*; SMD: *standardized mean difference*; ‡ due to averaging over 20 imputations decimal end digits may result for discrete characteristics

***Figure**: The left panel shows the model-based course of fatigue over 180 days obtained from the weighted generalized additive model (solid lines = all patients, dashed lines = patients without concomitant methotrexate). The right panel shows differences between treatments groups calculated as contrasts, i.e., differences in means between groups.*

CONCLUSIONS

In this large real-world patient cohort, all targeted therapies reduced fatigue considerably.

Treatment with JAKi resulted in a more rapid and more pronounced reduction in fatigue in comparison to TNFi.

Overall, the average change in fatigue for patients treated with JAKi corresponds to a minimally important difference [4].

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REFERENCES

(1) Tóth L. et al. Janus Kinase Inhibitors Improve Disease Activity and Patient-Reported Outcomes in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis of 24,135 Patients. Int J Mol Sci. 2022;23(3). https://doi.org/10.3390/ijms23031246.

(2) La Barbera L et al. Effectiveness and safety of filgotinib in rheumatoid arthritis: a real-life multicentre experience. Clin Exp Rheumatol. 2024;42(5):991-8. https://doi.org/10.55563/clinexprheumatol/k78ug3.

(3) Hainmueller J. Entropy Balancing for Causal Effects: A Multivariate Reweighting Method to Produce Balanced Samples in Observational Studies. Political Analysis. 2012;20(1):25-46. https://doi.org/10.1093/pan/mpr025.

(4) Khanna D, et al. The Minimally Important Difference for the Fatigue Visual Analog Scale in Patients with Rheumatoid Arthritis Followed in an Academic Clinical Practice. The Journal of Rheumatology. 2008;35(12):2339. https://doi.org/10.3899/jrheum.080375.

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