

News Release

Sequential disease activity assessment for predicting future treatment trajectories in patients with rheumatoid arthritis treated with JAK inhibitors: a group-based trajectory and landmark analysis

Key Points

- A multicenter study of 843 patients with rheumatoid arthritis identified four distinct 52-week disease activity patterns during treatment with Janus kinase (JAK) inhibitors.
- Incorporating disease activity measured at weeks 4 and 12 substantially improved the prediction of patients' long-term treatment trajectories compared with baseline information alone.
- Sequential assessment of disease activity at weeks 4 and 12 substantially improved prediction of long-term treatment trajectories.

Summary

A research team led by Kenya Terabe, Clinical Associate Professor, Shuji Asai, Associate Professor, and Shiro Imagama, Professor, of the Department of Orthopaedic Surgery and Rheumatology, Nagoya University Graduate School of Medicine, analyzed data from the Tsurumai Biologics Communication Registry (TBCR), a multicenter rheumatoid arthritis registry involving Nagoya University and affiliated institutions.

The study included 843 patients with rheumatoid arthritis treated with JAK inhibitors and examined changes in disease activity over 52 weeks. Using group-based trajectory modeling, we identified four distinct patterns of treatment response: rapid responders with sustained low disease activity, partial responders with persistent residual disease activity, patients with high disease activity at baseline who subsequently showed marked improvement, and persistent nonresponders.

We then examined whether information obtained during treatment could improve prediction of these long-term trajectories. When CDAI measured at week 4 was added to baseline clinical information, the area under the receiver operating characteristic curve (AUC) increased from 0.799 to 0.917. At week 12, the AUC increased from 0.814 to 0.948 after incorporating the week-12 CDAI. In contrast, adding the rate of CDAI change provided little additional improvement.

These findings suggest that long-term treatment response should not be estimated from pretreatment characteristics alone. Instead, sequential

assessment of disease activity during the first 12 weeks of treatment may allow clinicians to progressively update the expected long-term course of individual patients.

The study provides real-world evidence supporting the Treat-to-Target approach in rheumatoid arthritis, in which disease activity is repeatedly assessed and treatment strategies are adjusted according to the patient's response.

Research Background

Rheumatoid arthritis (RA) is a chronic immune-mediated disease characterized by inflammation of the joints. Without adequate treatment, persistent inflammation can lead to joint destruction, impaired physical function, and reduced quality of life.

In recent years, the treatment of RA has advanced substantially, and several effective therapies, including JAK inhibitors, are now available. However, treatment response varies considerably between patients. Some patients improve rapidly after starting a JAK inhibitor, whereas others show only partial improvement or continue to have high disease activity.

Previous studies have attempted to predict treatment outcomes using information available before treatment, including age, baseline disease activity, radiographic joint damage, and previous treatment history. However, patients with similar clinical characteristics at treatment initiation may subsequently follow very different clinical courses. Therefore, baseline information alone may not adequately predict long-term treatment response.

In current RA management, disease activity is repeatedly assessed after treatment initiation under the Treat-to-Target (T2T) strategy, and treatment is adjusted according to the patient's response. Against this background, we first aimed to identify distinct long-term disease activity patterns during JAK inhibitor treatment. We then investigated whether these long-term trajectories could be predicted more accurately by sequentially incorporating disease activity information obtained at weeks 4 and 12 after treatment initiation.

Research Results

1. Four distinct long-term disease activity trajectories were identified during JAK inhibitor treatment

We analyzed CDAI measurements over 52 weeks in 843 patients with RA treated with JAK inhibitors. Group-based trajectory modeling identified four distinct patterns of disease activity. The largest group, accounting for 64.9% of patients, consisted of rapid responders who quickly achieved and maintained

low disease activity. Another 18.1% showed partial improvement but had persistent residual disease activity. A third group, comprising 12.7%, had high disease activity at baseline but showed marked improvement after treatment. The remaining 4.3% had persistently high disease activity throughout follow-up. Importantly, patients with high disease activity at baseline did not necessarily have poor long-term outcomes. Although two groups started treatment with similarly high disease activity, one improved markedly whereas the other remained highly active. This finding indicates that the long-term treatment course cannot always be determined from baseline disease activity alone.

2. The four trajectories were associated with markedly different clinical outcomes

At week 52, 96.0% of rapid responders had achieved low disease activity and 47.7% had achieved remission. Among patients with high baseline disease activity who subsequently improved, 92.5% achieved low disease activity and 41.1% achieved remission.

By contrast, remission rates were only 5.2% among partial responders with persistent residual disease activity and 0% among persistent nonresponders. Differences were also observed in treatment continuation and glucocorticoid reduction. Based on these clinical outcomes, the rapid-response and high-baseline-activity responder groups were classified as favorable trajectories, whereas the other two groups were classified as unfavorable trajectories for subsequent prediction analyses.

3. Disease activity at weeks 4 and 12 substantially improved prediction of long-term treatment trajectories

We next compared prediction based on baseline clinical information alone with models that incorporated disease activity measured during treatment. At week 4, the AUC for predicting a favorable long-term trajectory increased from 0.799 to 0.917 after adding the week-4 CDAI. At week 12, the AUC increased from 0.814 to 0.948 after adding the week-12 CDAI.

The CDAI thresholds associated with a favorable long-term trajectory were 12.0 at week 4 and 9.3 at week 12. These findings suggest that some residual disease activity may still be compatible with a favorable long-term course early after treatment initiation, whereas tighter disease control becomes increasingly important by week 12.

Research Summary and Future Perspective

This study showed that patients with RA treated with JAK inhibitors follow distinct long-term disease activity trajectories and that sequential assessment at weeks 4 and 12 improves prediction of these trajectories.

Patients with high disease activity at baseline may still achieve favorable long-term outcomes if they respond early. The identified CDAI thresholds may provide useful time-specific reference points for treatment assessment.

Future studies should validate these findings in independent populations and explore whether additional clinical information or biomarkers can further improve prediction.

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