Improvement in Clinical Disease Activity Index (CDAI) When Treatment Selection Is Informed by the Tumor Necrosis Factor-α Inhibitor Molecular Signature Response Classifier: Analysis from the Study to Accelerate Information of Molecular Signatures (AIMS) in Rheumatoid Arthritis

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INTRODUCTION

Background

- Without timely therapeutic intervention, chronic inflammation causes progressive joint damage leading to deformities, disability, and increased mortality in patients with rheumatoid arthritis (RA)
- Biologic and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARD) have become integral to the treat-to-target paradigm designed to gain low disease activity or remission
- 27 - 38% of patients with RA who inadequately respond to methotrexate achieve ACR50 responses at 6 months on tumor necrosis factor-α inhibitor (TNFi) therapies
- Near equivalent efficacy and safety profiles between b/tsDMARD, a lack of clinically validated biomarkers for patient stratification, and an inability to prioritize b/tsDMARD selection by clinical guidelines have led to a preponderance of trial-and-error treatment selection

PrismRA® Test Description

- A blood-based molecular signature response classifier analytically and clinically validated to identify patients with RA who are likely to be inadequate responders to TNFi therapies

Methods

- AIMS is a clinical database of real-world longitudinal data from patients with RA across a network of 72 private and academic rheumatology practices in the US
- This study reports an interim analysis of data collected from patients who received PrismRA testing between September 2020 and November 2021
- The primary and secondary endpoints of the clinical outcomes analysis were changes from baseline in absolute CDAI scores at 24 weeks (n=274) and 12 weeks (n=470), respectively

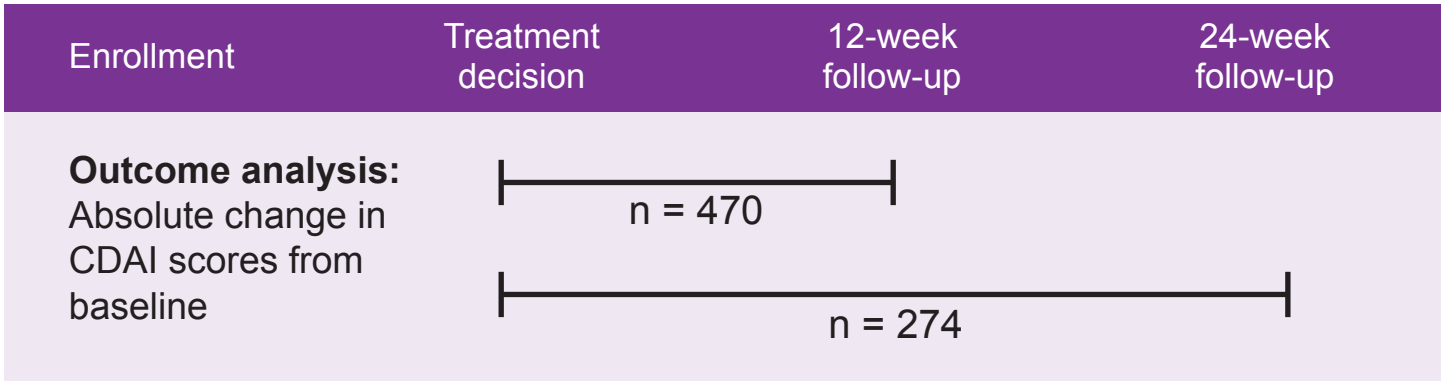
PATIENT COHORT DEMOGRAPHICS & STUDY DESIGN

Inclusion criteria:

- Age ≥18 years with a clinical diagnosis of RA
- b/tsDMARD-naïve or TNFi-exposed at time of PrismRA testing
- Moderate or high disease activity at baseline (CDAI >10)
- Data to calculate CDAI were available at baseline and at least one follow-up visit
- Changes in doses of concomitant medications permitted

Exclusion criteria:

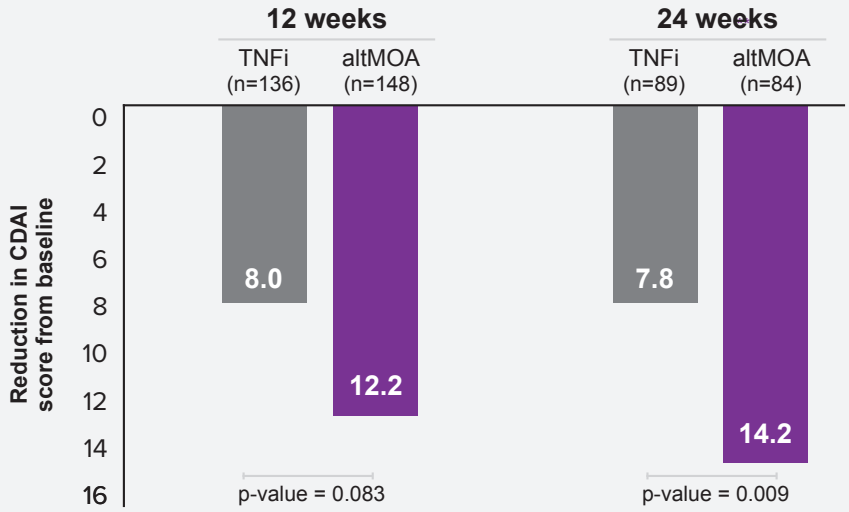
- Treated w/ a b/tsDMARD other than TNFi at time of PrismRA testing
- b/tsDMARD changed between initial treatment and first follow-up visit



RESULTS

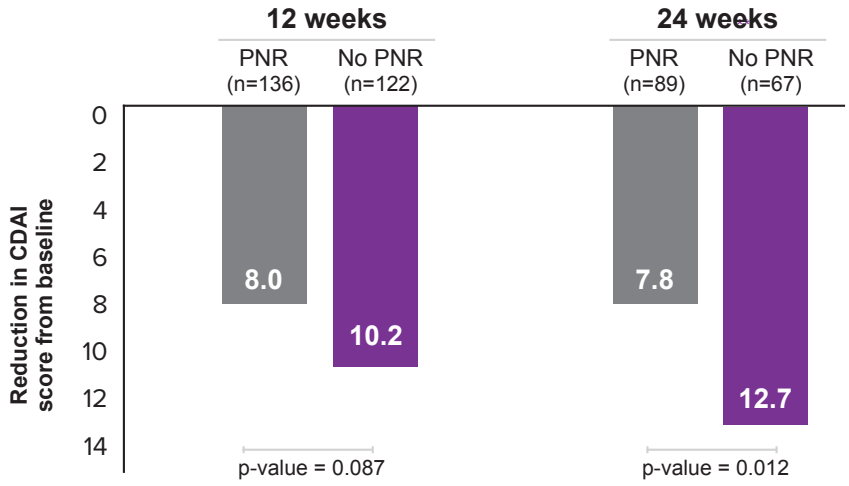
Absolute Change in CDAI for Predicted Non-Responders (PNR)

Patients with a molecular signature of inadequate response treated with an altMOA experienced a **1.8-fold greater improvement** in CDAI scores than patients treated with a TNFi at 24 weeks



Absolute Change in CDAI for Patients on TNFi Therapy

Patients without a molecular signature of inadequate response treated with a TNFi experienced a **1.6-fold greater improvement** in CDAI scores than patients with a molecular signature at 24 weeks



- In patients with baseline high disease activity (HDA), 38.9% of patients achieved lower than moderate disease activity in response to TNFi compared to 55.7% with altMOA therapy (43.2% relative improvement)
- A greater proportion of predicted non-responders experienced worsening CDAI scores when treated with a TNFi compared with an altMOA therapy (baseline HDA: 27.8% in PNR-TNFi vs. 17.1% in PNR-altMOA)

CONCLUSION

- A trial-and-error approach to treatment selection in RA has thus far been a necessity given the paucity of evidence supporting pairing of individual patient disease biology to specific b/tsDMARD options
- Treatment selection informed by PrismRA for patients with RA results in a near 2-fold greater improvement in CDAI scores for patients with a molecular signature of TNFi inadequate response treated with non-TNFi b/tsDMARD
- Data adds to the growing evidence supporting the clinical utility of PrismRA and shows that integration into RA management results in improved clinical outcomes
- Most of the improvements in CDAI scores were evident by the 12-week follow-up visit, indicating that when PrismRA is used to inform treatment selection, outcomes improve in a timely manner

Strand V, Zhang L, Arnaud A, Connolly-Strong E, Asgarian S, Withers JB. Improvement in clinical disease activity index when treatment selection is informed by the tumor necrosis factor-α inhibitor molecular signature response classifier: analysis from the study to accelerate information of molecular signatures in rheumatoid arthritis. *Expert Opin Biol Ther.* 2022;22(6):801-807. doi:10.1080/14712598.2022.2066972.

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