Improvement in CDAI scores when rheumatoid arthritis treatment selection is informed by a molecular signature test

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;10.1080/14712598.2022.2066972.

Background

- Without timely therapeutic intervention, chronic inflammation causes progressive joint damage leading to deformities, disability, and increased mortality in patients with rheumatoid arthritis (RA)
- 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 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

- The molecular signature response classifier (MSRC) is a blood-based precision medicine test that predicts non-responders to TNFi therapy in RA so that patients with a molecular signature of non-response can be directed to a treatment with an alternative mechanism of action (altMOA)

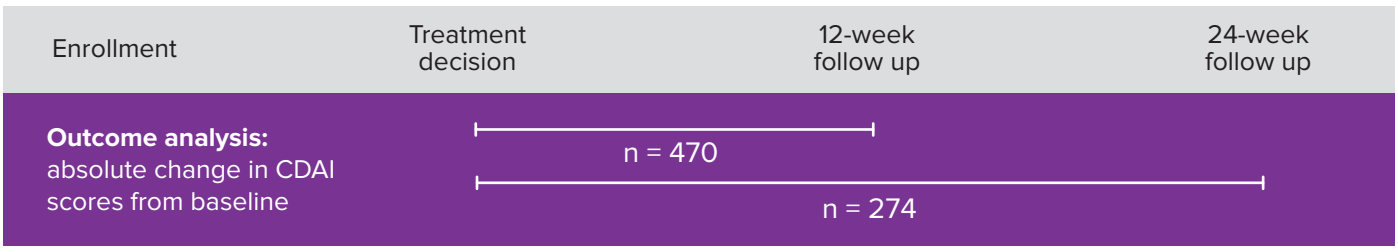
Methods

- 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
- Patients received the PrismRA Test (MSRC) between September 2020 and November 2021
- Absolute changes in clinical disease activity index (CDAI) scores from baseline were evaluated at 12 weeks (n = 470) and 24 weeks (n = 274)

PATIENT COHORT DEMOGRAPHICS & STUDY DESIGN

Inclusion and exclusion criteria:

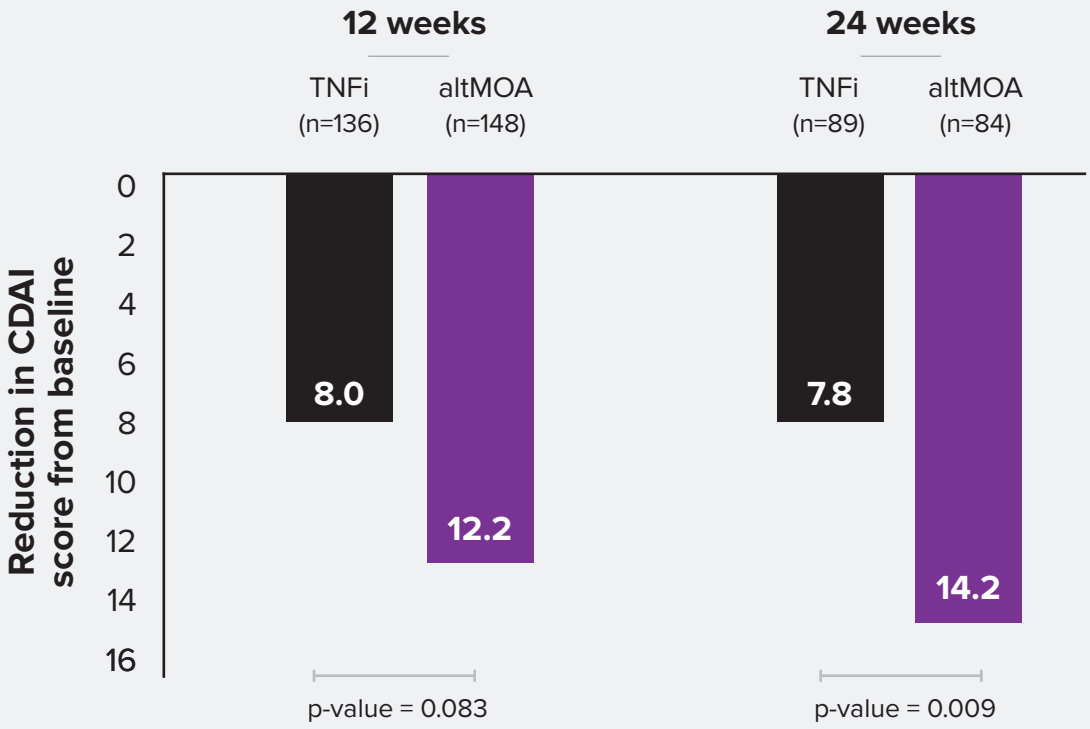
- Age ≥18 years with a clinical diagnosis of RA
- b/tsDMARD-naïve or TNFi-exposed at time of PrismRA (MSRC) testing
- Moderate to high disease activity at baseline (CDAI ≥10)
- b/tsDMARD treatment decision made after MSRC testing
- Data available to calculate CDAI scores



prism/RA®

RESULTS

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



- Patients with a molecular signature of non-response treated with an altMOA experienced a 1.8-fold greater improvement in CDAI scores than patients treated with a TNFi
- Patients without a molecular signature of non-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 a lower disease activity level in response to TNFi compared to 55.7% with non-TNFi b/tsDMARD (43.2% relative improvement)
- A greater proportion of PNR 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)

CONCLUSIONS

- 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 (MSRC) for patients with RA results in a near two-fold greater improvement in CDAI scores for patients with a molecular signature of TNFi non-response treated with non-TNFi b/tsDMARDs
- Data adds to the growing evidence supporting the clinical utility of PrismRA (MSRC) 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 (MSRC) is used to inform treatment selection, outcomes improve in a timely manner

Clinical utility of a molecular signature test in rheumatoid arthritis patients

Strand V, et al. Clinical utility of therapy selection informed by predicted non-response to tumor necrosis factor-α inhibitors: an analysis from the Study to Accelerate Information of Molecular Signatures (AIMS) in Rheumatoid Arthritis. Expert Review of Molecular Diagnostics 2021; https://pubmed.ncbi.nlm.nih.gov/34937469/.

BACKGROUND

- Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic, symmetrical articular inflammation, pain, and disability, and if left untreated, often results in progressive joint destruction with subsequent disability and increased mortality
- ACR50 response rates at 24 weeks with b/tsDMARDs in RA patients with inadequate responses to methotrexate range from 27% to 37%
- In the absence of a precision medicine test, to inform treatment selection, two-thirds of RA patients fail to achieve ACR50 responses regardless of prescribed b/tsDMARDs and therefore are unlikely to reach the treat-to-target goal of remission

PRISMRA® TEST DESCRIPTION

- The molecular signature response classifier (MSRC) is a blood-based precision medicine test that predicts non-responders to TNFi therapy in RA so that patients with a molecular signature of non-response can be directed to a treatment with an alternative mechanism of action (altMOA)

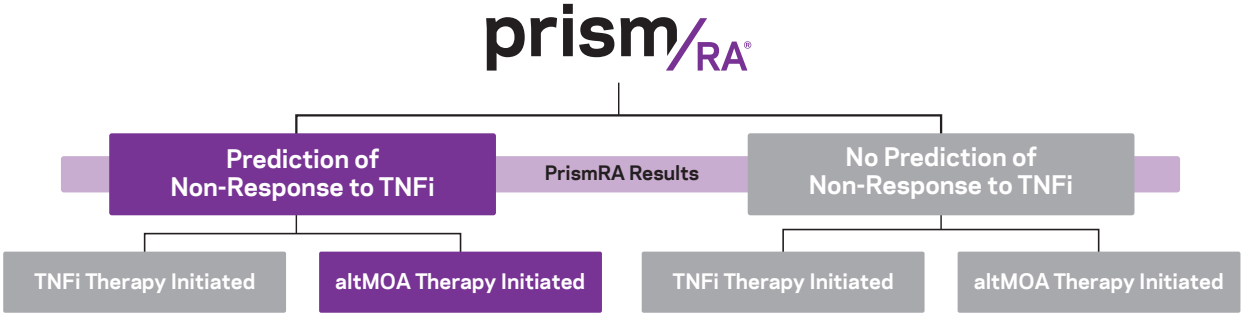
METHODS

- This study reports an interim analysis from the AIMS study, which is a large scale, prospective study to collect longitudinal patient clinical data and molecular data to evaluate clinical utility which includes decision choice and treatment outcomes resulting from PrismRA-informed treatment selection within a real-world cohort
- This was a multicenter study with >70 academic and private rheumatology sites in the US (35 sites were included for this interim analysis)
- Eligibility criteria included age ≥18 years and a clinical diagnosis of RA who initiated a new b/tsDMARD following PrismRA testing
- Data was collected at baseline, treatment initiation, and 12- and 24-week follow-up visits and included PrismRA test results, clinical assessments, RA medical history, routine laboratory testing, and treatment decisions
- The primary endpoint of the outcome analysis was therapeutic responsiveness defined by achievement of ACR50 at 24 weeks
- The secondary endpoint evaluated improvement from baseline in CDAI scores exceeding MID*

* Minimally important difference (MID): reduction from baseline CDAI by >6 for moderate and >12 for severe disease activity

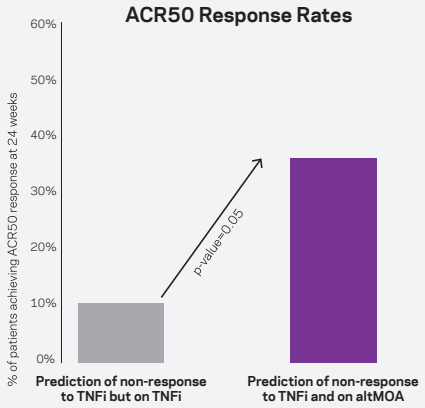
PATIENT OUTCOMES COHORT

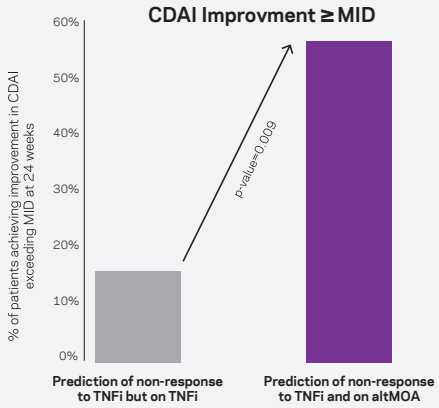
PrismRA test results and b/tsDMARD selection were used to categorize patients into four subsets



RESULTS

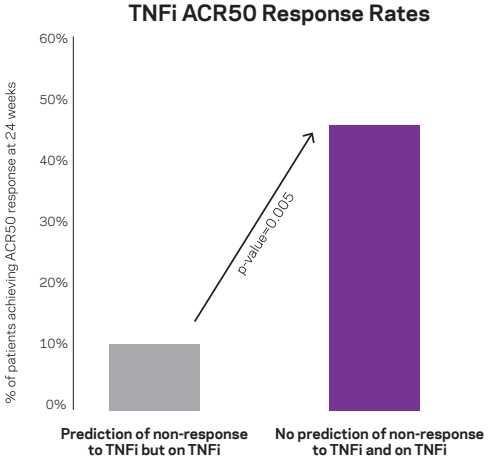
THERAPEUTIC RESPONSES IN AIMS COHORT PATIENT SUBSET

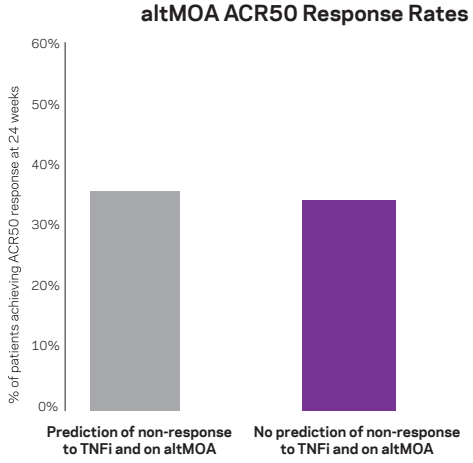




- Patients who were predicted non-responders (molecular signature detected) who were prescribed an altMOA instead of a TNFi therapy, experienced significantly improved therapeutic response
- 34.8% achieved ACR50 on altMOA while 10.3% reached ACR50 on TNFi at 24 weeks (p-value = 0.05)
- 56.2% achieved CDAI ≥ MID on altMOA while 15.4% reached CDAI ≥ MID on TNFi (p-value = 0.009)

TREATMENT IN PATIENTS WITH PREDICTION VS. NO PREDICTION OF NON-RESPONSE





- Patients who were predicted non-responders (molecular signature detected) had significantly lower therapeutic responses to TNFi therapies when compared with patients lacking the molecular signature
- 10.3% with a molecular signature reached ACR50 while 45.8% without a molecular signature reached ACR50 (p-value = 0.005)
- Patients with a molecular signature of non-response prescribed an altMOA had comparable ACR50 responses to those lacking the molecular signature
- 34.8% with a molecular signature reached ACR50 while 33.3% without a molecular signature reached ACR50 (p-value > 0.05)

CONCLUSION

- This study demonstrated the clinical utility of adopting PrismRA into rheumatology practice may reduce inappropriate use of TNFi and increase responses across the RA population
- The comparable ACR50 responses to altMOAs between patients with a molecular signature and patients without indicate PrismRA predicted non-responses specifically to TNFi therapies and did not identify generally refractory patients
- Although PrismRA is not intended to be interpreted as a likely positive response to TNFi therapies, patients who lacked the molecular signature of non-response had mean ACR50 responses to TNFi therapies of 45.8%

Providers can evaluate therapy ineffectiveness before the patient presents clinically, thus PrismRA-informed care shows an improvement in clinical outcomes over standard of care

The PrismRA test is a validated molecular signature response classifier (MSRC) test intended to be used by the treating physician for adults diagnosed with rheumatoid arthritis (RA) who are considering starting or changing targeted therapy.