Clinical Utility of Therapy Selection Informed by Predicted Nonresponse to Tumor Necrosis Factor-α Inhibitors: An Analysis from the Study to Accelerate Information of Molecular Signatures (AIMS) in Rheumatoid Arthritis

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INTRODUCTION

Background

- Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic, symmetrical articular inflammation, pain, and disability
- If left untreated, RA results in progressive joint destruction with subsequent disability and increased mortality
- ACR50 response rates at 24 weeks with TNFi therapy in RA patients with inadequate response to methotrexate range from 27% to 38%
- In the absence of a precision medicine test to inform treatment selection, two-thirds of RA patients fail to achieve ACR50 responses and therefore are unlikely to reach the treat-to-target goal of remission

PrismRA® Test Description

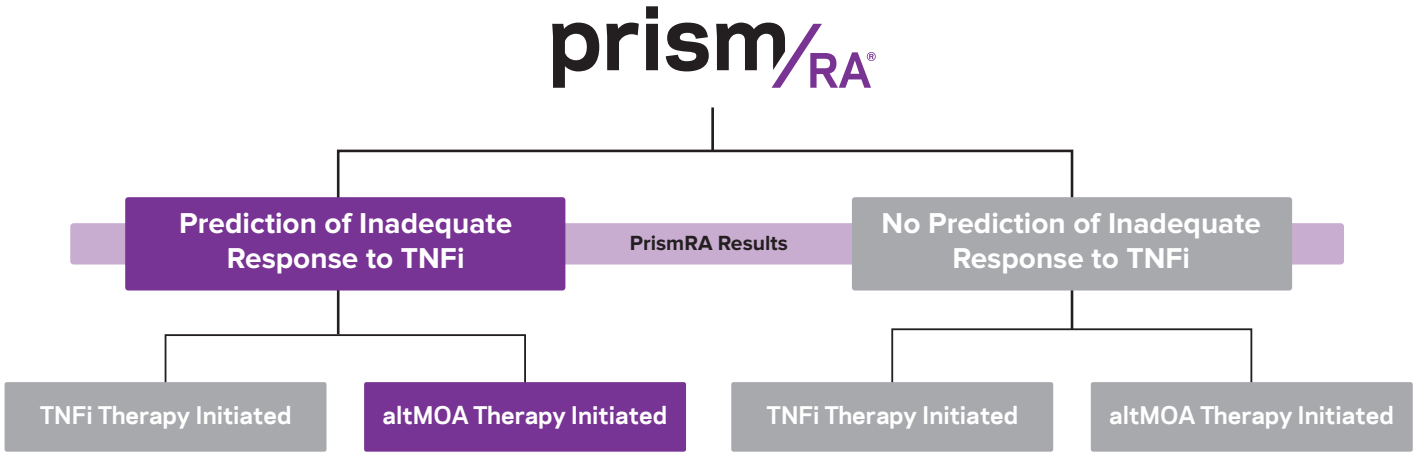
- A blood-based molecular signature response classifier that uses RNA sequencing data combined with clinical factors to predict the likelihood that an individual RA patient will inadequately respond to TNFi therapy

METHODS

- This study reports an interim analysis from the AIMS study, which is a large scale, prospective study to collect longitudinal patient clinical and molecular data to evaluate clinical utility
- 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, with low to high disease activity
- Data was collected at baseline, treatment initiation, and 12- and 24-week follow-up visits
- The primary endpoint of the outcome analysis was therapeutic responsiveness defined by achievement of ACR50 at 24 weeks
- The secondary endpoint evaluated improvement in baseline CDAI scores exceeding MID*

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

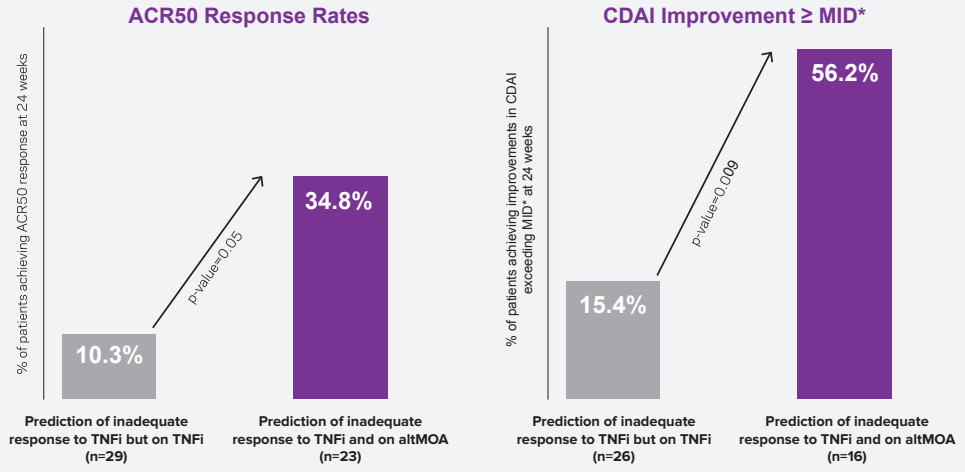
CLINICAL OUTCOMES COHORT



CLINICAL OUTCOMES RESULTS

Therapeutic Responses in Patients with Prediction of Inadequate Response

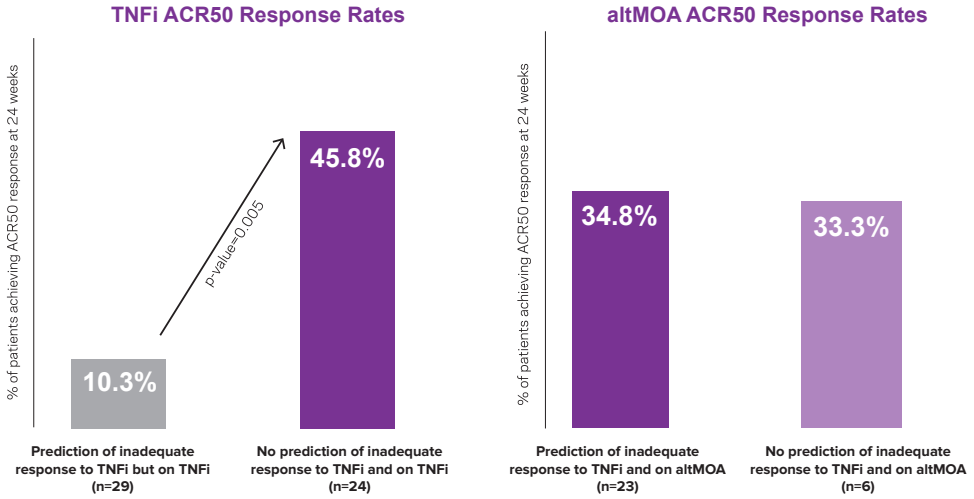
- Patients who were predicted inadequate responders (molecular signature detected) who were prescribed an altMOA instead of a TNFi therapy, experienced significantly improved therapeutic response



* MID: reduction from baseline CDAI by >6 for moderate and >12 for high disease activity

Therapeutic Responses in Patients with Prediction vs. No Prediction of Inadequate Response

- Patients with a molecular signature of inadequate response (predicted inadequate responders to TNFi) had significantly lower therapeutic responses to TNFi therapies when compared with patients lacking the molecular signature
- No significant differences in therapeutic responses between patients with or without a molecular signature who received an altMOA.



CONCLUSION

- This study demonstrated the clinical utility of adopting PrismRA into rheumatology practice; it may reduce inappropriate use of TNFi and increase responses across the RA population
- Patients with a molecular signature of inadequate response 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)
- 90% of patients with a molecular signature of inadequate response according to PrismRA are likely inadequate responders to TNFi therapies and according to a treat-to-target approach should be directed to altMOAs

With PrismRA, providers can evaluate therapy ineffectiveness before a patient presents clinically, thus PrismRA-informed care shows an improvement in clinical outcomes over current care

Strand V, Cohen SB, Curtis JR, et al. Clinical utility of therapy selection informed by predicted nonresponse to tumor necrosis factor-α inhibitors: an analysis from the Study to Accelerate Information of Molecular Signatures (AIMS) in rheumatoid arthritis. *Expert Rev Mol Diagn.* 2022;22(1):101-109. doi:10.1080/14737159.2022.2020648.

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