

Patient Outcomes Improve When a Molecular Signature Test Guides Treatment Decision-Making in Rheumatoid Arthritis

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INTRODUCTION

Background

- Rheumatoid arthritis (RA) is a chronic autoimmune disease that can lead to irreversible joint damage with subsequent disability
- Tumor necrosis factor- α inhibitors (TNFi) are most frequently prescribed to RA patients who fail first-line therapy, but only 27% to 38% of TNFi-prescribed patients will reach treat-to-target goals (ACR50 at 6 months)
- Although there are numerous alternative mechanism of action (altMOA) biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARD) to TNFi, they all share similar efficacy and safety profiles

PrismRA[®] Test Description

- A precision medicine molecular signature response classifier validated to predict treatment outcomes in RA patients based on disease biology
- PrismRA analyzes individualized clinical and molecular data to stratify patients by their probability of inadequately responding to TNFi therapy

Methods

- Comparative cohort study that evaluated RA patient outcomes between a PrismRA-tested arm (n=489) and an external control arm (n=761)
- The external control arm was constructed from real-world data derived from a large de-identified US-based EHR database

- Propensity score (PS) analyses were implemented to balance measured baseline characteristics between patients in the PrismRA-tested and the external control arm

Inclusion Criteria

- Clinical diagnosis of RA
- ≥ 18 years of age
- Either b/tsDMARD-naïve, b/tsDMARD-experienced and initiating a new b/tsDMARD, or TNFi-exposed
- Moderate or high RA baseline disease activity (CDAI >10)
- Medication dose adjustments permitted

Primary Endpoints

- The proportion of RA patients achieving CDAI low disease activity or remission (CDAI-LDA/REM), remission alone (CDAI-REM), and minimally important differences in changes in CDAI (CDAI-MID)* at 6 months from baseline

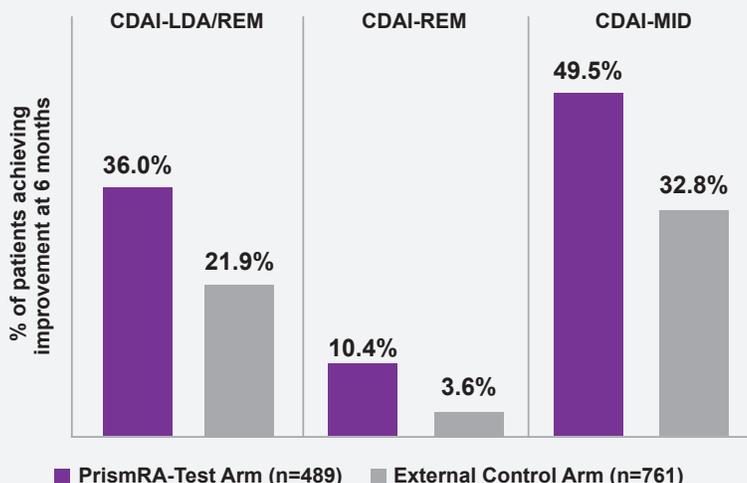
Clinical Validity

- Clinical validity was assessed in patients who received a TNFi therapy after PrismRA testing (n = 369)
- ACR50 criteria at 6 months were used to define response to treatment
- All other inclusion criteria were the same as reported above in the Inclusion Criteria section

*CDAI-MID: minimally important difference defined as a reduction from baseline CDAI scores of >6 for moderate and >12 for high disease activity

CLINICAL UTILITY RESULTS

The PrismRA-tested arm had significantly higher response rates to therapies than the external-control arm



Patients in the PrismRA-tested arm had **2.01 – 3.14x** improved odds of achieving CDAI-LDA/REM, CDAI-REM, and CDAI-MID in response to b/tsDMARD therapy at 6 months compared to external control arm

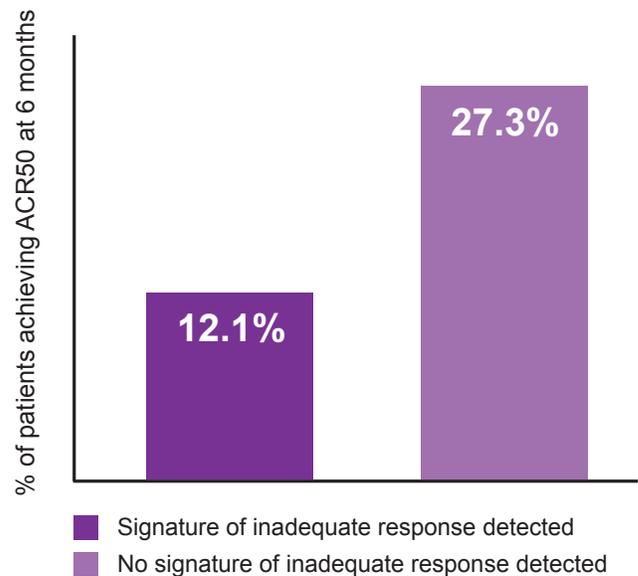
Primary Endpoint	Odds Ratio (95% CI; p-value)
% achieving CDAI-LDA/REM	2.01 (1.55-2.60; p<0.0001)
% achieving CDAI-REM	3.14 (1.94-5.08; p<0.0001)
% achieving CDAI-MID	2.00 (1.58-2.55; p<0.0001)

CLINICAL VALIDITY RESULTS

Clinical validity of PrismRA was evaluated in TNFi-treated patients in the PrismRA-tested arm (n=369)

- Of patients with a signature of inadequate response, 88% did not achieve ACR50 on TNFi (PPV)
- 54% of patients who did not achieve ACR50 had a signature of inadequate response (sensitivity)
- 70% of patients who achieved ACR50 had no signature of inadequate response (specificity)

ACR50 response rates decline when treatment selection is not aligned with PrismRA results



CONCLUSION

- PrismRA identifies patients unlikely to respond to TNFi therapies so rheumatologists may more confidently direct such patients to alternative treatment options sooner
- Despite incomplete adherence (70% of providers prescribed a b/tsDMARD that aligned with test results), patient outcomes resulting from treatment selection guided by PrismRA test results were significantly superior to standard care practices
- Patients in the PrismRA-tested arm were as much as 3x more likely to reach remission than if treatment selection was not guided by PrismRA test results
- Because some patients with a signature of inadequate response were prescribed a therapy that did not align with test results, these results represent a conservative estimate of the benefit of PrismRA
- To date, PrismRA has been validated in more than 500 patients demonstrating that PrismRA is a robust and reliable assay that accurately detects a patient's signature of inadequate response across patient cohorts and different study designs
- Nearly 60% of tested patients had a signature of inadequate response and should not be prescribed a TNFi, thus broad adoption of PrismRA testing could shift RA treatment paradigms and significantly improve clinical outcomes



70% of patients tested with PrismRA were treated with a b/tsDMARD that was aligned with test results

3X

Patients were **3x as likely to achieve remission** on therapies aligned with PrismRA results