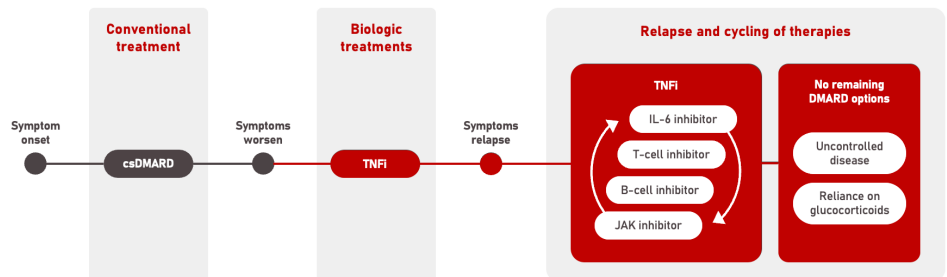


Rheumatoid Arthritis Treatment Selection Product



Background

Rheumatoid arthritis (RA) is estimated to affect approximately 1 percent of the population and to be twice as common in women compared with men. Targeted treatments for RA have significantly improved disease management by controlling symptoms and slowing progression. Despite these advances, a substantial proportion of patients exhibit suboptimal responses to specific biologic and targeted synthetic DMARDs (b/ts DMARDs), often cycling through multiple treatments before achieving disease control. This variability in therapeutic response underscores a critical gap in treatment selection and the pressing need for a precision medicine approach.



A predictive test to identify responders to specific b/ts DMARDs would support more informed and effective treatment decisions, improving patient outcomes and cost-effectiveness. Aqtual has conducted the PRIMA-102 study to support development and validation of a novel blood-based assay leveraging cell-free DNA derived from regulatory-active chromatin (cfDNA_{ac}) to predict response to multiple DMARD classes.

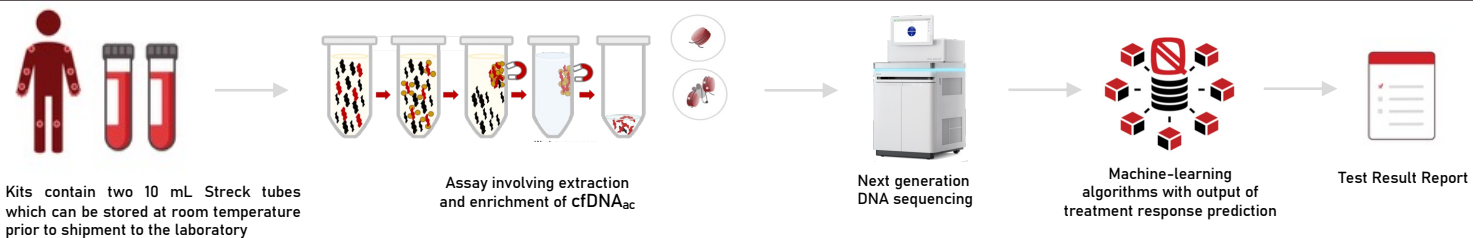
Intended use, indications for use, and test performance targets

The product, a blood-based test that analyzes molecular biomarkers in cell-free DNA, is intended for the qualitative prediction of response to tumor necrosis factor- α inhibitor (TNFi), janus kinase inhibitor (JAKi), and T-Cell co-stimulation blocker drug classes, enabling clinicians to make better treatment decisions for rheumatoid arthritis patients.

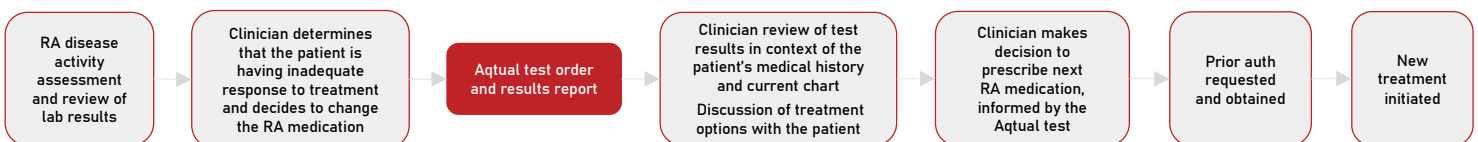
The test is indicated for adults who have RA with moderate to high disease activity who are initiating a new or alternative b/ts DMARD after inadequate response, contraindication, intolerance, or insurance denial to another cs/b/ts DMARD.

The target positive predictive value is 80% (to be determined during the clinical validation analysis), with sensitivity and specificity metrics sufficient to support adoption by clinicians. Performance may vary by b/ts DMARD class and whether patients are naïve or experienced with DMARD treatment.

Blood collection, assay, sequencing, and test result reporting, with target turnaround time of < 14 days



Incorporation of Aqtual's treatment selection test into the clinical workflow



The RA Treatment Selection Test could inform clinician & patient decision-making, support prior authorization requests, and improve patient outcomes.

Accumulation of data & samples supporting R&D and product launch

> 400 evaluable participants and samples utilized for biomarker discovery and model training to support initial launch of test predicting the likelihood of response to 3 b/ts DMARD classes: TNFi, JAKi, T-Cell co-stimulation blocker (abatacept)

> 350 evaluable participants and samples available for analytical and clinical validation in the first 3 drug classes, supporting review and approval by regulatory authorities and payors

> 100 Anti IL-6R participant samples and data available for model training to support version 2 of a product that may predict response to 4 drug classes

~ 1,500,000 clinical and sample data points captured

Medications captured in study supporting product development

TNFi	JAKi
Adalimumab (Humira)	Baricitinib (Olumiant)
Adalimumab-aaty (Yuflyma)	Tofacitinib (Xeljanz)
Adalimumab-adaz (Hyrimoz)	Upadacitinib (Rinvoq)
Adalimumab-adbm (Cyltezo)	
Adalimumab-bwmd (Hadlima)	T-Cell co-stimulation blocker
Certolizumab pegol (Cimzia)	Abatacept (Orencia)
Etanercept (Enbrel)	
Gotimumab (Simponi, Simponi Aria)	Anti IL-6 R
Infliximab (Remicade)	Sarilumab (Kevzara)
Infliximab-abda (Renflexis)	Tocilizumab (Actemra)
Infliximab-axxq (Axsola)	Tocilizumab-aazg (Tyenne)
Infliximab-dyyb (Inflectra)	
	Anti B-Cell
	Rituximab (Rituxan)
	Rituximab-abbs (Truxima)
	Rituximab-pvvr (Ruxience)

Regulatory approval, coverage, and product adoption pathway

The product will be marketed as a laboratory developed test (LDT) with CLIA and CAP accreditation, as well as New York State CLEP approval.

Clinical utility has been established, and coverage determination has been previously granted, for a test that predicts non-response to TNFi.

Payer dossiers, advocacy efforts, and preparation for guideline submissions are underway to secure coverage post-launch and accelerate adoption at launch, ensuring a strong market entry.