Tool to predict response to Etanercept, Tocilizumab, and Rituximab in Rheumatoid Arthritis (RA)

Applications

Personalized Treatment: This tool allows doctors to tailor treatments for rheumatoid arthritis (RA) patients based on their unique genetic profile, increasing the chances of selecting the most effective drug.

Reduced Trial and Error: By predicting how well a patient will respond to specific drugs, the tool minimises the risk of trying ineffective treatments, saving time and reducing discomfort.

Benefits

Improved Drug Selection: Clinicians can use this tool to choose between three biologic drugs (etanercept, tocilizumab, rituximab) for RA patients, based on how likely they are to respond to each one.

Minimally Invasive Testing: The tool requires only a small biopsy from an inflamed joint, making the testing process less invasive and more accessible for patients.

A novel and personalised model which can predict patient treatment response to currently used drugs from a single biopsy, providing clinicians with a tool to select the most efficacious drug, reducing treatment failures, saving time and costs to health systems.

Background

The advent of biological disease modifying anti-rheumatic drugs (b-DMARD) has led to major improvements in the outlook of patients with rheumatoid arthritis (RA). However, not all patients respond successfully to their first line therapy and a proportion of patients are refractory to current medications. Predicting whether a patient will respond to a particular therapeutic agent remains problematic.

The problem

Although biologic therapies have improved the outcomes of patients with RA, approximately 40% of patients do not respond to individual biological therapies. Presently, there are no clinical diagnostic tests which can predict whether a patient with RA will respond successfully to given therapeutic modalities.

Invention: Benefits and application

The invention from Queen Mary, University of London, leverages deep molecular phenotyping and machine learning on synovial fluid samples to enable patient stratification based on their

Contact:
Maria Frolova PhD
Associate Commercialisation Manager
m.frolova@qmul.ac.uk

likely response to specific drugs in clinical practice. Additionally, it can identify patients who are unlikely to respond to b-DMARDs, guiding them toward alternative therapeutic options. The test involves a minimally invasive, ultrasound-guided biopsy from an inflamed joint, followed by gene expression measurement and machine learning analysis. This process accurately estimates response probabilities to etanercept, tocilizumab, and rituximab in 79-85% of patients, with AUC values of 0.765, 0.736, and 0.754, respectively.

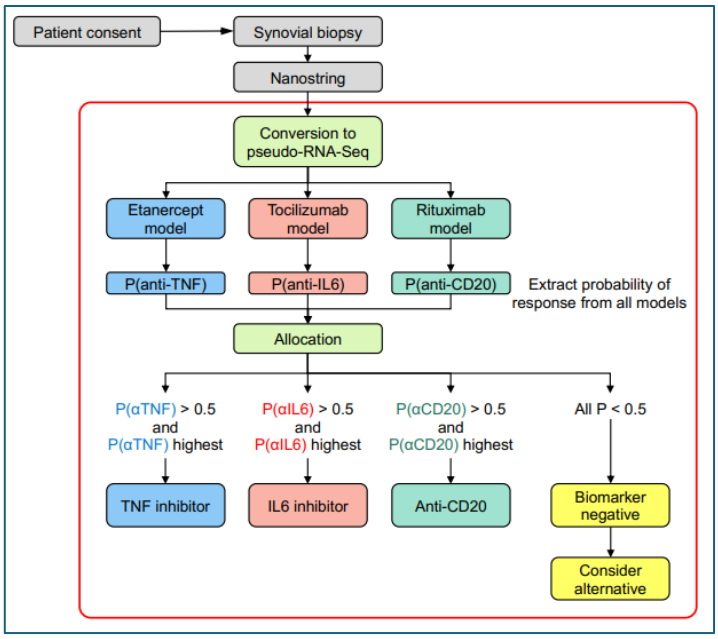

Figure 1. Proposed algorithm for allocation of a new patient to one of three possible biologic therapies categories (TNF inhibitor, IL6 inhibitor or B-cell depleting agent) dependent on whichever gives the highest probability of response. Individuals with low probability (<0.5) of response to all three classes of biologic are categorised as "biomarker negative" and can be offered an alternative class of therapeutic agent.

Patents

A UK patent application has been filed on 12th July 2024.

Lead inventor

Professor Costantino Pitzalis

Versus Arthritis Professor of Rheumatology, Queen Mary University of London

Professor Pitzalis is Deputy Director of the William Harvey Research Institute and Head of the Centre for Experimental Medicine and Rheumatology (EULAR Centre of Excellence in Rheumatology 2023-28), leading a multidisciplinary research team of Clinicians, Scientists, Biostatisticians, Bioinformaticians, Clinical Trial Managers and administrative support staff who strive to deliver best care to patients with Rheumatic Diseases.

Key publications

Lewis MJ, Cubuk C, Sciacca E, Surace A, Goldman K, Giorli G, Fossati-Jimack L, Nerviani A, Rivellese F, Pitzalis C (*In Press*). **Synovial RNA Predicts Response to Three Biologics in Rheumatoid Arthritis**. New England Journal of Medicine.

Contact:
Maria Frolova PhD
Associate Commercialisation Manager
m.frolova@qmul.ac.uk