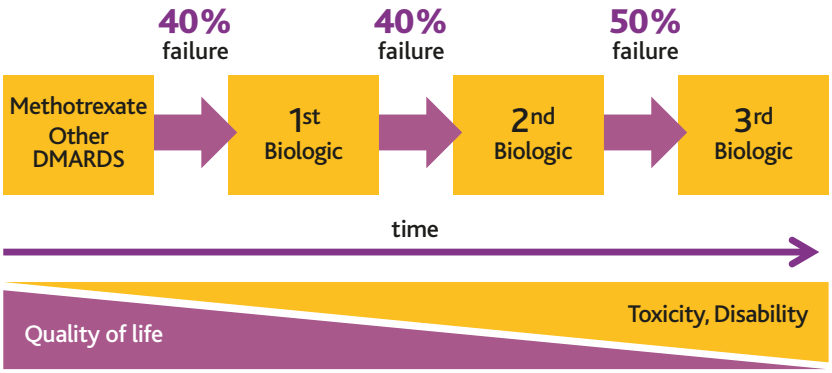
The potential of personalised/stratified medicines

for rheumatoid arthritis (RA)

By Debbie Maskell, Gaye Hadfield & Zoë Ide

Just imagine if a blood test and/or a simple biopsy of the tissue in one of your joints could tell your clinician what RA medication would most likely work best for you as an individual. This is the dream of personalised or stratified medicine for rheumatoid arthritis and could transform the way that patients are currently treated.

Standard Treatment Pathway



Put simply, personalised or stratified medicine as it is also known, means providing the right medicine to the right patient, at the right dose at the right time.

As we know, there have been many advances in the treatment of RA over the last 20 years, including aggressive treatment at the early stages after diagnosis and the introduction of effective new drugs called biologics.

However, the major problem is, we still can't predict who will respond to which treatment: with 40% of patients experiencing no real benefit from each drug that is used, it can take years of trying different drugs before a suitable one is found. It also means exposing patients to the potential side effects of drugs that aren't working for them and often leaves them to cope with the severe symptoms of uncontrolled RA, including unnecessary joint damage. There are also major economic costs to consider with a bill for the NHS approaching £50 million a year - £16-20 million (30-40%) where many savings could be made if patients were treated more effectively.

Currently the standard NICE(National Institute for Health & Clinical Excellence) guideline treatment pathway for RA tells us that patients should be treated with at least two disease modifying anti rheumatic drugs (DMARDs such as methotrexate) first, followed by up to three biologic drugs. Unless an effective treatment is selected early on, as you can see by the diagram, there is a significant risk that patients can be left with increased disability and decreased quality of life.

MATURA (**MA**ximising **T**herapeutic **U**tility for **R**heumatoid **A**rthritis) is an international consortium of academics, clinicians and industry partners who are working together to try and make stratified medicine a reality for patients by developing a test that identifies those genes and biomarkers in a patient's biological make up which can predict with quite a high level of accuracy who will respond better to which type of drug. This test would also help us understand if any drugs should be avoided, or used at a lower dose, because of the risk of side effects.

The MATURA team are currently running two specific projects nationally that involve patients in their work to help them achieve this goal.

One is a clinical trial which concentrates on patients who are ready to be treated by a biological drug and is currently taking place in 15 hospitals. It is called **STRAP** (**S**tratification of Biologic **T**herapies for **RA** by **P**athobiology) and is investigating whether the most effective choice of drug may be guided by the examination of the tissue in a swollen joint (synovial tissue) and whether particular immune cells (B cells) in the tissue can predict a response to treatment.

In parallel, blood samples are being collected in over 45 hospitals through the **BRAGGSS** (**B**iologics in **RA** **G**enetics & **G**enomics **S**tudy **S**yndicate) study to test whether changes in genes, antibodies, inflammatory markers, cells or other factors can be used to predict future response to treatments.

The MATURA consortium have set up, with the help of NRAS, a nationwide group of patients with different experiences and backgrounds who are at different points on their journey with RA. As part of their role they help the project understand more about the treatment pathway from a patient's perspective and the frustrations often involved. They also make sure that the investigators are asking the right questions and concentrating on the right areas in the research undertaken. The group is called MPAG (MATURA Patient Advisory Group).

Some personal statements from patients about what Stratified Medicine could mean for them…

"Having tried two biologics with no results before finding one that works for me, I am all too keenly aware of the years of uncertainty that could possibly have been avoided while I waited hopefully for each medicine to start working."

Hannah Maltby

"If stratified medicine had been available when I was growing up with juvenile idiopathic arthritis, it might have meant that I would have needed fewer medicines on a 'trial and error' basis, before finding one that worked well for me."

Simon Stones

"I am really looking forward to the day a biopsy and/or blood investigation helps me and my consultant choose the best treatment for my RA rather than 'Professor pathway NICE' and 'Dr High hurdle DAS' who really aren't very good at all for me."

Zoe Ide

"Stratified medicine could increase the chance of successful treatment sooner for RA patients than I experienced myself, hopefully eliminating the painful wait for the right treatment."

Caroline Wallis

"If the stress and anxiety associated with failed RA treatment could be reduced with a targeted solution, my quality of life would have improved significantly."

Chris Wills

We hope this article has stimulated your interest in stratified medicines and has highlighted the potential of this approach to revolutionise future care for RA patients. If you are interested in being part of the patient advisory group, you can contact one of the project managers to find out more details on this or any aspect of the studies:

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MATURA
Maximising Therapeutic Utility for Rheumatoid Arthritis

For more information about these research studies and to find out which hospitals are taking part please visit:

for STRAP: **www.matura-mrc.whri.qmul.ac.uk/**

for BRAGGS: **http://research.bmh.manchester.ac.uk/Musculoskeletal/research/CfGG/pharmacogenetics/braggss/**

If you are interested in participating please discuss this with your rheumatologist.