Genome-wide association study of response to tumour necrosis factor inhibitor therapy in rheumatoid arthritis

Jonathan Massey, PhD1, Darren Plant, PhD2, Kimme Hyrich, FRCP PhD2,3, Ann W Morgan, FRCP PhD4, Anthony G Wilson, FRCP PhD5, Athina Spiliopoulou, PhD6,7, Marco Colombo, PhD6, Paul McKeigue, FRCP PhD6, John Isaacs, FRCP PhD8, Heather Cordell, PhD9, Costantino Pitzalis, FRCP PhD10, BRAGGSS, MATURA Consortium† , Anne Barton, FRCP PhD1,2

Rheumatoid arthritis (RA) is a long-term condition in which inflammation of the joints can cause pain, stiffness and loss of movement in joints. No cure has been found for RA so treatment is based around reducing inflammation. One group of drugs used to reduce inflammation in RA are called tumour necrosis factor alpha inhibitors (TNFi). However, the drugs do not work in all patients and we investigated whether genetic differences exist between those who do and don't benefit from the treatments. We tested hundreds of thousands of genetic markers in just over 1,700 people with differing levels of response to three commonly used TNFi drugs. We showed that there were several genetic markers that may explain some of the reasons why people respond differently. We were also able to show that there may be links between these genetic markers and the genes that increase a person's likelihood of developing RA in the first place; the importance of these links will be investigated in future studies. Additionally, the findings from this study will be put together with other clinical data (such as height, weight, age of disease onset) and other biological data (such as the differing proportions of cells in a person's blood) to see whether a combination of factors can predict who will or won't benefit from a particular treatment. It is hoped that, eventually, this will let patients know how likely they are to improve on a particular medication and, in discussion with their doctors, choose the drug that is most likely to work.