Abstract

Supported in partnership with Arthritis Research UK, the Maximising Therapeutic Utility for Rheumatoid Arthritis (MATURA) consortium, led by Queen Mary, University of London, and the University of Manchester, aims to enable early, effective treatment and to improve the cost-effectiveness of care for approximately 500,000 people in the U.K. who suffer from the painful inflammatory condition rheumatoid arthritis.

Mission

MATURA has two parallel work streams (WSs); one is investigating synovial tissue within the clinical trial (STRAP), the second is investigating peripheral blood, and both will identify biomarkers of response. The two WSs are fully integrated through the “multi-omic” approaches that constitute cross-cutting themes that will converge in a large analytical and modeling package driven by experts in bioinformatics and statistics.

WS1 will help identify synovial tissue–driven biomarkers for rheumatoid arthritis and its correlates to
blood serum, which will include two time points, zero and six months. This will be the largest global synovial tissue biobank of this type and includes an array of datasets, involving more than 200 patients.

In addition, the prospective randomized clinical trial STRAP will test the hypothesis that discrete cellular and molecular signatures in the synovial tissue (pathotypes) will enrich the response to existing biological therapies. This will be achieved by demonstrating that Rituximab (RTX) therapy is mainly effective in patients with B cell rich synovial pathotypes, so that in patients with the B cell poor synovium, RTX is inferior to anti-TNF (tumor necrosis factor) or Tocilizumab.

WS2 will take advantage of large, observational cohorts of patient samples that have either already been collected or that will be collected to undertake a comprehensive analysis to identify genetic, genomic, transcriptomic, proteomic, or, more likely a combination of these factors that will reliably identify responders/nonresponders to each of the drugs. These collections include biological samples from more than 3,000 anti-TNF, 1500 MTX, 1200 RTX and 200 TOC treated subjects.

At present there is no genetic information that can reliably predict which patients will respond to therapies. Finding genetic predictors has been difficult, and at present there are only two accepted genetic regions: CD84 and PDE3A-SLCO1C1. For this reason, MATURA is now beginning to look at epigenetic factors — inheritable modifications that are not caused by sequence variation. It is particularly looking at methylation modifications of cytosine residues that are located in CpG sites (next to guanine residues). It is also looking at the differences in the levels of gene expression between patient groups with good response to therapy and those with a poor response. These data will then be integrated with existing genetic data to improve algorithms that will eventually enable patients to be stratified into treatment streams early in disease course.

Consortium History

December 2014: MATURA launch meeting

Financing

MATURA is co-funded by a £1 million grant from Arthritis Research UK. The project combines 12 academic groups with nine industry partners.
Patent Engagement

MATURA is very keen to engage and involve patients and the public along this very important journey. A MATURA Patient Advisory Group (MPAG) has been formed, whose main aim is to assess the direction and strategy of MATURA development to ensure the research remains meaningful.

MPAG is also involved in disseminating information and research findings to the wider community and policymakers through newsletters, lay summaries, and press releases as well as contributing to a patient information area on the website and participating in medical conferences.

Links/Social Media Feed

Homepage http://www.matura.whri.qmul.ac.uk/

Sponsors & Partners

Constantino Pitzalis
Work Stream 1 Lead
e-mail: c.pitzalis@qmul.ac.uk

Jennifer Helen Barrett
Work Stream 2 Lead
e-mail: j.h.barrett@leeds.ac.uk

Michelle Korda
Project Manager
phone: 0207 882 3497
e-mail: m.korda@qmul.ac.uk

Deborah Maskell
Project Manager
phone: 0161 275 5046
e-mail: deborah.maskell@manchester.ac.uk
Abbvie
Amgen
Arthritis Research UK
Avacta Life Sciences
Eli Lilly
Genentech
Janssen
Johnson & Johnson
Medical Research Council
MedImmune
Pfizer
Pharmatics, Ltd.
Protagen Diagnostics
Qiagen
QMUL
Queen Mary, University of London
Roche
University of Manchester

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