# Minutes of the MATURA Patient Advisory Group (MPAG) – Fourth meeting

**Room:** B02/B03, Heart Centre, Charterhouse Square (Basement seminar room)

**Date and Time: Wednesday** 14th September 2016, 1pm – 3pm

**Attendees:**
Zoe Ide (ZI), MPAG Chair
Professor Anne Barton (AB), MATURA Co-Lead
Dr Frances Humby (FH), Consultant Rheumatologist
Hannah Maltby (HM), Lay member of MPAG
Sonia Jeevanason (SJ), Lay member of MPAG
Eleanor Goddard (EG), Lay member of MPAG
Caroline Wallis (CW), Lay member of MPAG
Lesley Cooke (LC), Lay member of MPAG
Simon Stones (SS), Lay member of MPAG
Caroline Vass (CV), Research Fellow
Gaye Hadfield (GH) MATURA Project Manager WorkStream 1
Laura White (LW) EMR Clinical Trials Centre Manager

**Apologies:**
Professor Costantino Pitzalis, MATURA Lead
John Game (JG), Lay member of MPAG
Deborah Maskell, MATURA Project Manager WorkStream 2
Chris Wills, Lay member of MPAG
Cameron Neil, Lay member of MPAG
Philip Bell (PB), Lay member of MPAG
Elin Rees (ER) STRAP Clinical Trial Manager

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1. **Welcome:**

   Zoe welcomed everyone to the fourth MATURA Patient Advisory Group (MPAG) meeting and thanked them for attending. Apologies were noted.

## 2. MATURA Updates:

Work Stream 1 is based at Queen Marys and is investigating synovial tissue biomarkers within the STRAP clinical trial, whilst Work Stream 2 is based in Manchester and is investigating biomarkers in blood.

### 2.1 Work Stream 2 Update- Prof Anne Barton

Anne is the lead for Work Stream 2 (WS2) and is based at the University of Manchester she presented an update on the work which is taking place at seven universities across the UK with support from MATURA industry partners.

She explained that stratified medicine is about tailoring the approach to medication by identifying sub-groups, or strata, in the RA population who respond to different medicines in different ways.

This includes investigating genes and their activity to help try and develop a test that detects whether a patient with RA is likely to respond to a particular drug.

Anne used the analogy of a book to explain genetics:
Book = genome
23 chapters = 23 chromosomes
Sentences = genes
Letters = bases

A change in one letter of a sentence can complete change its meaning. For example, changing a 'c' to a 't' changes the sense of this sentence:

She caught a thief
She taught a thief

There are gaps between the groups of bases in the genes, much as there are spaces and punctuation in sentences, they are known as introns and for many years were considered to be of little importance but we now know that they regulate the activity of the genes and are also very important.

In genetics, changing one of the bases can change how a gene works. These are known as single nucleotide polymorphisms (SNPs, pronounced 'snips') and they are like spelling mistakes. Genotyping is used to identify if any SNPs are more common in patients with a particular disease than those who don't have the disease (controls). These are known as case-controlled studies.

WS2 are undertaking genetic analysis of existing samples and datasets. This includes analysing the whole genome in samples from approximately 1,000 patients treated with methotrexate and 1,800 treated with an anti-TNF. For rituximab, a specific part of the genome the FCGR genes are being analysed in over 800 samples.

All the data is uploaded to TranSMART where analysis also performed and data can be shared across the consortium. MATURA is being used as a pilot to trial and showcase this TranSMART platform and there will be a demonstration of how it works at the next MPAG.

The aim is to find predictors (e.g. genetic factors, measurements of gene expression, measurements of

DNA methylation) that predict response to treatment (e.g. change in DAS28, change in CRP, change in ESR).
Methods are being used that allow researchers to look at one variable at a time and to test whether the variable is a good predictor of response or advanced analysis techniques can be used that allow researchers to model the effects of multiple predictor variables simultaneously.

Epigenetic patterns are chemical changes (methylation) to DNA structure but not sequence, these affect whether a gene can be turned on or off and can be caused by environmental factors e.g. smoking. We know that smoking is detrimental for RA patients and epigenetic changes may be one of the reasons for this.

Differences in methylation (epigenetics) between 36 excellent responders and 36 non-responders to methotrexate (MTX) at baseline and after 4 weeks of therapy have been analysed. Twelve genetic regions that may be associated with response to MTX have been identified and researchers are now checking to see if these results can be confirmed in other patient samples.

At the moment researchers are concentrating on finding a marker that predicts response, how it works would be another project.

Decisions on drug therapy depend on being able to measure disease activity that in turn predict long-term joint damage. WS2 are also trying to find better outcome measures. DAS28 is weighted towards swollen joint count but researchers have early evidence that tender joint count and blood tests (ESR or CRP) are the best measures of synovitis and progression of joint damage.

**2.2 MATURA Discrete Choice Experiment: Caroline Vass**

Anne introduced Caroline, a research fellow from the department of economics in Manchester. She reminded the group of the qualitative work undertaken by Kanta Kumar that MPAG was involved in to identify the factors influencing five areas:

(1) Perceptions surrounding the use of synovial biopsy and blood tests
(2) Perceptions surrounding the use of synovial biopsy vs blood test
(3) Utility of test to manage expectations: positives and negatives of accuracy
(4) The stages of illness on decision making for predictive testing
(5) Understanding the predictive tests in clinic: the importance of information

Kanta has now submitted a paper for publication.

The next step is the development of the discreet choice questionnaire (DCE) which will be used to survey the preferences of a large number of RA patients, public and healthcare professionals on the application of stratified medicines.

Caroline is leading the DCE project which is part of a larger programme of work called 'Mind the risk'. What the research aims to determine is:

*"What is the required predictive ability of a 'biologic calculator' (prescribing algorithm) to target the selection of a first-line biologic and associated dosage?"*

The DCE asks people to make choices about predictive tests so that we can better understand what their preferences are. This is a way of quantifying (putting into numbers) what the preferences are. It is used widely to determine preferences for healthcare and has been used in RA and stratified medicines for other diseases, this will be the first DCE on stratified medicines for RA.

The survey will be available online, links to the survey will be sent to clinicians, people with RA, and the general public in both the UK and Sweden (n≈900). They will be identified through an internet panel provider.

The survey will be interactive and include:

- Training materials
- The choice sets
- Background questions on the respondent

Caroline asked for feedback:

Lesley felt the online format would exclude many people from participating. The use of ipads in waiting areas of clinics or infusion clinics was suggested.

Caroline confirmed the survey would take about 20mins, it was noted that people who are not feeling well have time on their hands and are more likely to complete this. The challenge may be getting those who are currently well, the public and consultants to participate.

Anne prosed that a mixed sampling method should be considered.

Sonia suggested using social media to promote the survey but the ethics committee have refused this as it won't be possible to remunerate people for their time.

Timescales for the survey are: software available October, pilot and then translate into Swedish.

**Action: CV will send the survey attributes and background questions to MPAG for review and comment**

### 2.3 The STRAP clinical study – Gaye Hadfield

Gaye reported that there are now 11 sites are open and 39 patients have been recruited:

| Site Name | Greenlight | 1st Randomisation | Jun-15 | Jul-15 | Aug-15 | Sep-15 | Oct-15 | Nov-15 | Dec-15 | Jan-16 | Feb-16 | Mar-16 | Apr-16 | May-16 | Jun-16 | Jul-16 | Aug-16 | Sep-16 | Total by site |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Barts Health, Dr Kelly | 05/06/2015 | 17/06/2015 | 1 | 1 | | 1 | | 1 | | 4 | 3 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 19 |
| Glasgow, Prof McInnes | 03/11/2015 | 07/12/2015 | | | | | | | 1 | 1 | | 1 | 1 | | 1 | | | | 5 |
| UCLH, Dr Ehrenstein | 04/11/2015 | | | | | | | | | | | | | | | | | | |
| Cardiff, Prof Choy | 19/01/2016 | 15/07/2016 | | | | | | | | | | | | | | 1 | 2 | | 3 |
| Newcastle, Dr Pratt | 11/02/2016 | 09/03/2016 | | | | | | | | | | 3 | | 1 | | | 1 | | 5 |
| Oxford, Prof Taylor | 25/02/2016 | 23/03/2016 | | | | | | | | | | 1 | | 2 | | 1 | | | 4 |
| Birmingham, Dr Filer | 30/03/2016 | 12/07/2016 | | | | | | | | | | | | | | 1 | 1 | | 2 |
| Southampton, Prof Edwards | 20/04/2016 | | | | | | | | | | | | | | | | | | |
| Leeds, Dr Buch | 23/05/2016 | 19/07/2016 | | | | | | | | | | | | | | 1 | | | 1 |
| Manchester, Dr Ho | 26/05/2016 | | | | | | | | | | | | | | | | | | |
| Salisbury, Dr Smith | 23/08/2016 | | | | | | | | | | | | | | | | | | |
| Total | | | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 5 | 3 | 6 | 2 | 4 | 2 | 6 | 5 | 1 | 39 |

Whilst 39 is a significant achievement for a complex study such as STRAP which requires synovial biopsy expertise, recruitment is behind target. More sites are in the process of being opened (Southend, Homerton, Guys and Baslidon) and we are looking for new sites to replace some that are no longer able to do the trial.

Actions taken or underway to improve recruitment are:

For sites:

- Reminded that medicines in STRAP are free-of-charge, giving a cost saving of ~£8,500 per patient.
- Trial poster for outpatient clinics is with ethics
- A video for healthcare professionals on consenting a patient for biopsy is underway.
- Sharing best practice for recruitment/identifying patients.
- Targets and prizes for good recruiters.
- Providing professionally produced eligibility reminder cards for sites to circulate within the clinic team.
- Monitors are engaging sites re: recruitment and screening strategies at 6-monthly on-site visits.
- Implemented an enhanced biopsy training programme for new rheumatologists

For patients

- Patient video discussing the biopsy procedure (Birmingham are also producing one)
- Information sheets translated into Hindi, Bengali & Urdu

General awareness of Stratified Medicine at the STRAP sites and other initiatives

- Organising stratified medicine talks/presentations in sites, at conferences and publicising the STRAP trial online, these include:
    1. NRAS – 15th August, Zoe and Gaye met Clare Jacklin to discuss how she can help raise awareness of stratified medicine (she will use MATURA slides in presentations, we will provide leaflets and there will be an article in the December magazine, the deadline for this is end of October)
    2. Oxford – NRAS meeting 15th September, MATURA/STRAP will be included.
    3. Leeds – PPI meetings 22nd September, lunchtime & evening session on MATURA
    4. Manchester – RUG, 30th September, to get feedback on best way of disseminating information locally.
    5. Newcastle – 20th October, MATURA/STRAP will be included
    6. Glasgow – NRAS event 27th Oct on MATURA

The questions for the video of a consultant talking to a patient about having a biopsy have been sent to research ethics committee:

- How did you feel when you were asked to take part in a study that required a biopsy?
- Did you have any concerns about the biopsy?

- Please describe what the procedure was like.
- Do you have any advice for patients who are asked to take part in a research trial involving a biopsy?

Lesley suggested that we also make a video of a patient talking to a patient. She has had a biopsy and was asked by a patient in the waiting room about research. The group agreed that this was a very good idea.

**Action: GH/ER to take patient-patient video forward**
**Action: GH to include discussion on patient ambassadors at next meeting**

It was suggested that we look to GPs to recruit to STRAP, Fran advised that patients going onto biologic treatment are all under specialist care at hospitals so motivation of the clinical teams is key.

Zoe reminded MPAG that our role is to advise and to raise awareness of Stratified Medicine and research in general terms with the patient population.

**3.0 Arthritis Research UK grant update**

An application to ARUK was made in July to fund the MPAG and patient engagement activities, this includes some funding to remunerate MPAG members for their time, this would be done with vouchers as we would be unable to give money. The total budget is £19,000 and we expect to hear any day now as whether we have been successful in securing ring-fenced funding.

**4.0 Review of MPAG website**

No further feedback received, needs a general update

**Action: GH /DM to update**

**4.0 General discussion, feedback and Q&A session: Zoe Ide**

4.1 The Terms of Reference (TOR) were reviewed.

The following amendments were agreed:

1. ~~Although~~ We hope that all members will be involved for ~~approximately~~ at least one year, you are free to withdraw at any time
2. ~~Members who miss 3 meetings in a row will be contacted by the chair of the group with the option of withdrawing membership or continuing.~~

4.2 It was agreed that it would be useful to extend the group by 2/3 to cover for absences and it was suggested that we advertise specifically for a representative from Wales and someone with PR experience.

**Action: Gaye to identify places to advertise for additional members e.g. INVOLVE/NRAS**

4.3 In reviewing drafts of printed materials MPAG has identified that the images we have available are out-dated and do not depict RA for patients. Zoe asked that everyone looks out for images that

they would like to see used.

**5.0 AOB**

5.1 Sonia asked about vagal nerve stimulation for RA. Fran believes that more research is needed to check the efficacy and safety.

5.2 The next Scientific Symposium will be held at Queen Mary's on Friday the 27th of January 2017. MPAG members will soon receive an invitation and are very welcome to attend but were advised that the presentations are for a scientific audience. Those who attended last year felt it had been a useful and interesting day and recommended to the group.

**Next meeting:** now confirmed for 1-3 pm 8th February 2017