Annual report

Study Groups

Title of the study group: Eular Synovitis Study Group (ESSG)

Study Group Leader’s name: Doug Veale and Cos Pitzalis
Date of annual report submission: April 2016

Summary of Meetings
ESSG at EWRR Feb 2015, Budapest – Chair Doug Veale
ESSG at eular June 2015, Rome - Co-Chairs Doug Veale & Cos Pitzalis
ESSG/Omeract at ARC Nov 2015, San Francisco - Co-Chairs Doug Veale & Cos Pitzalis
ESSG at EWRR Feb 2016, York – Chair Doug Veale

The ESSG met at the above well-attended meetings to discuss strategic objective and collaborative research. A number of projects were discussed as follows:

1. Investigating the relationship between macroscopic scores of synovitis at arthroscopy, histological findings and serum biomarkers of inflammation.
   Initial data from this study, presented by Carl Orr, Dublin, at the EWRR meeting in Budapest demonstrated significant correlation between histological findings and CRP (n=180). However, over 42% of patients had a normal CRP, but had evidence of macroscopic synovitis at arthroscopy. Further analysis presented at the Rome meeting revealed that most of these patients were ACPA positive. A multicentre study is now proposed to examine the relationship between ACPA and immunohistology of the RA synovial tissue.

2. Cryopreservation of human synovial tissue for biobanking purposes
   Marieke de Vries and Rogier Thurlings presented an assessment of various cryopreservation protocols for human synovial tissue in such a way that it is viable after thawing. Several CPA solutions were tested with a slow freezing protocol and general viability, RNA quality, and cytokine response to inflammatory stimuli were determined. Rogier presented initial survey results at EWRR, York from 20 responses member groups (10 EU, 2 USA and 1 Australian centre) showing that already 95% of the respondents use or considers using cryopreserved synovial tissue, indicating a large interest in the field. The majority of respondents obtain tissue by US guided biopsy from OA, RA or psoriatic arthritis patients for histological and gene expression analysis and 40% use tissue for culture, to derive primary cells and for transplantation experiments.

3. Evaluation / Validation of Synovial Biopsy techniques
   Three studies in this area are coordinated by the Queen Mary University of London (QMUL) and Pavia groups
   (i) Retrospective study of the performance of synovial biopsy techniques (arthroscopic vs US-P&F vs US-NB)
   Steady progress was reported with this study. The study led by Fran Humby (QMUL) includes 4 Centres contributing synovial tissue sections and RNA samples from biopsies obtained using different biopsy techniques (arthroscopic vs US-P&F vs US-NB). Pavia, Italy (US guided- P&F large and small joint biopsies), Birmingham, UK (US guided-P&F large joint), QMUL, UK (US guided-NB large and small joint biopsies) and Adelaide, Australia (arthroscopic large joint biopsies). Quantitative and qualitative analysis
of synovial tissue obtained from each procedure is currently underway at the EMR (QMUL) central laboratory with the plan of reporting the results at the ESSG at eular 2016 London.

(ii) Prospective examination of the performance of US guided NB vs US-P&F vs arthroscopic synovial biopsy in multicentre RCTs

This study led by Fran Humby and Costantino Pitzalis has made exceptionally good progress: 20 sites across Europe are involved in the prospective examination of the performance of US guided NB vs US-P&F vs arthroscopic synovial biopsy in a multicentre NIHR-funded RCT: R4RA, a Randomised, open labelled trial investigating the mechanisms for Response - Resistance to Rituximab versus Tocilizumab in RA anti-TNFa inadequate responder patients (R4-RA) http://www.r4-rihr.whri.qmul.ac.uk
To date over 100 patients (target 124) have been recruited to the R4RA study with 17 sites utilizing US guided-NB to sample synovial tissue, 2 sites utilizing arthroscopy and 2 sites utilizing US guided-P&F. In addition at one site a radiologist (rather than a rheumatologist) performs the biopsy procedures. Quantitative and qualitative analysis of synovial tissue obtained from each procedure is currently underway at the EMR (QMUL) central laboratory with the plan of reporting the results of an interim analysis at the ESSG at eular 2016 London.

(iii) Demonstration of learning curve for US-guided synovial biopsy (needle vs portal and forceps)
Serena Bugatti presented technical data on P&F US-guided synovial biopsy, showing feasibility, safety and tissue quality for both immunohistology and RNA extraction. Data will be shared with QMUL and included in project (ii) above.

4. Training Activities
At the Rome meeting, Stephen Kelly (QMUL) gave an update on the Training activities and outlining the development of a comprehensive training programme to include: a) live demonstration of US-guided biopsy on patients, b) cadaveric hands on training and c) competence examination and certification (See appendix 1).

5. Publications in Progress
In addition to the publications related to the above projects ESSG agreed on the preparation of a Synovial Tissue Research Position Paper.
Joao Fonseca (Lisbon) and Doug Veale (Dublin) gave an update on a state-of-the-art position paper, on methodology of novel techniques of assessment and analysis, to which many members have contributed is ready and a journal has been identified for submission.

6. Publications emerging from recent ESSG activities
1. Evaluation of Minimally Invasive, Ultrasound-guided Synovial Biopsy Techniques by the OMERACT Filter - Determining Validation Requirements.

2. Ultrasound-guided synovial biopsy: a safe, well-tolerated and reliable technique for obtaining high-quality synovial tissue from both large and small joints in early arthritis patients.

3. Use of ultrasound-guided small joint biopsy to evaluate the histopathologic response to rheumatoid arthritis therapy: recommendations for application to clinical trials.