TIMES

Issue 27

www.cambridge-arthritis.org.uk

2017

SUPPORTING PATIENT CARE AND RESEARCH IN RHEUMATIC DISEASES

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FAREWELL TO DR ANDREW OSTOR

We were sorry to say goodbye to Dr Ostor as he left Addenbrooke's and the Rheumatology Clinical Research Unit, to return to Australia in July 2016.

Andrew came to Addenbrooke's as Clinical Fellow many years ago. He was supposed to return to Australia the following year but stayed with us and became a Consultant. When Dr Hazleman retired he then became Director of the Rheumatology Clinical Research Unit. Andrew will be missed by both his patients and his colleagues. He may return to Addenbrooke's in 4 years' time so watch this space.

CLINICAL RESEARCH ON E6

Dr Deepak Jadon took over as Director of the Rheumatology Clinical Research Unit (RCRU) in July 2016. Dr Jadon is a consultant rheumatologist at Addenbrooke's Hospital, and his interests include: rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and utilisation of ultrasound to detect / monitor arthritis. Dr Jadon is leading on a number of studies in these areas. The 'STRAP study' aims to improve our ability to predict which patients with RA will respond to the multitude of biologic agents available to them; through blood tests and ultrasound-guided joint biopsy. The 'EARLY study' is investigating a novel oral tablet that inhibits an intracellular molecule called JAK, that may be useful to treat RA in its early stages. The 'AMORE study' is an observational study assessing the impact of a 'patient support programme' on the quality of life of patients with PsA and AS treated with the anti-TNF drug Humira. The 'APIPPRA study' is investigating if the use of a medication called abatacept can halt RA in its very early stages,

before joints become swollen. Two other studies are in set-up phase, and will investigate the effectiveness of JAK and interleukin-17 inhibitors for PsA. The 'British Society of Rheumatology Biologics Registry' for AS continues to enrol patients as part of a monitoring exercise to assess the safety of anti-TNF medications for AS.

Later this year, Dr Jadon will be leading on a study in PsA. The 'MONITOR' study is an observational study of patients newly presenting with PsA, that will monitor progression and predictors thereof in terms of clinical characteristics and biomarkers (blood, urine and stool). Two sub-studies will evaluate the use of NSAIDs-only in patients with mild PsA (POISE study), and the early use of anti-TNF in patients with more severe PsA (SPEED study).

Dr Jadon has established a weekly dedicated clinic for patients with PsA, and a monthly psoriatic multi-disciplinary team meeting with colleagues in dermatology to ensure a unified approach to managing patients with complex PsA and skin psoriasis. The same is planned for patients with inflammatory bowel disease (IBD) by working with colleagues in gastroenterology.

Another new initiative is a 6-monthly 'Education Evening for Patients with PsA and / or Psoriasis'. The events at Addenbrooke's in September 2016 and April 2017 were each attended by 80-100 patients and their family. The next meeting will be in September 2017, and once again is only possible through the support of CARE.

Drs Jadon, Negoescu, Rees and Shenker have set up a musculoskeletal ultrasound service for patients under the care of rheumatology. This has also served as an opportunity to train our specialist registrars in this very important skill.

If you would like to be involved in any of these studies or initiatives, please do not hesitate to contact the Rheumatology Research Unit (RRU).

PAIN RESEARCH

The study of Pain continues to be supported by CARE and given that it is the most common and important symptom associated with musculoskeletal diseases, any advance in this field would be most welcome. Fatigue and pain are intimately related and Dr Maliha Shaikh, Prof Daniel Wolpert and Dr Ben Seymour are working with Dr Shenker having received a grant from Arthritis Research UK to examine whether patients with RA who have pain and fatigue have unique 'brain signatures' when these are studied in a functional MRI. This strand of work complements the projects already supported by CamPAIN and led by Dr Mike Lee, Dr Ben Seymour, Prof Geoff Woods and Prof David Menon who are examining both the genetics and the neurophysiology of chronic pain states. Hopefully this work will continue to bear fruit and Dr Maliha Shaikh, who is currently supported by CARE, is contributing to a number of these projects. Clinical trials continue to be a focus and the unblinding from the LIPS study (intravenous immunoglobulin therapy for patients with CRPS) has been revealed and patients who participated in this trial will know whether they received the

placebo or treatment. There is currently a drive to recruit to the CRPS-UK Registry and should you have CRPS, then you may have been approached. This Registry (the second largest in the world now with more than 300 patients) provides the foundation for research groups to ask patients with existing symptoms of CRPS to take part in their research and several UK studies have accessed this repository already. Thank you for your time in reading this and should you wish to take part in any Pain research, then please do not hesitate in making contact with the Rheumatology Clinical Research Unit.

TRACTISS: TRIAL OF RITUXIMAB IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

The clinical trial of Rituximab versus placebo in primary Sjogren's Syndrome is completed and the data have been analysed in Leeds. I am expecting the paper to be published soon, and we will then be able to share the outcome data. Thank you again to all our local patients who participated.

TRACTISS: T cell substudy

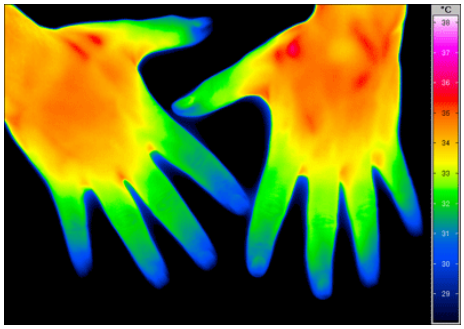
During the main study, we also collected samples for the T cell substudy. Samples of blood, and minor salivary gland biopsies, have been collected pre- and post- treatment with Rituximab (or Placebo). Dr Paul Lyons (Cambridge) and his team have separated different types of T cells from the blood samples. Analysing the sequence of the RNA in particular groups of cells is a way of finding out which genes the cell is expressing (using) at that time. This can be different in disease states, compared to in health and can be different after treatment, compared with baseline. The next step is to compare the set of genes being used by T cells before and after use of Rituximab and to look for correlations between disease patterns and gene use.

Dr Michele Bombardieri (QMUL) has been preparing sections and cells from salivary gland biopsies, before and after Rituximab. His group are now looking for correlations between the cells they see in the biopsy and patterns of disease, and also for response to treatment.

SYSTEMIC SCLEROSIS RESEARCH

ESOS: The European Observational Study in Scleroderma,

which followed patients with recent-onset diffuse systemic sclerosis allowed clinicians to choose the medication which they believed to be most suitable for the patient. Data were then gathered on skin thickness, lung involvement, occurrence of digital ulcers and a host of other outcomes. This study is now complete and a manuscript has been submitted for publication, so we should be able to share this information soon.



VALIDS: A comparison of laser speckle contrast imaging and thermography in patients with Raynaud's phenomenon secondary to systemic sclerosis

Several of you will remember this study for the unusual request to put on gloves and dip your hands in buckets of cold water! The point of this was to find measurements which could be used as robust outcome measures in clinical trials of drugs, or other interventions, for severe Raynaud's or digital ulcer disease in systemic sclerosis. The results are now being presented at conferences and I hope this will also be published soon.

We have recently started recruiting to **STRATUS, a clinical trial of an antibody treatment called Abituzumab in patients with systemic sclerosis and lung disease.** The antibody is made by Merck and it blocks a pathway which leads to fibrosis. We think this is particularly relevant to systemic sclerosis, and especially for lung disease in this context, because fibrosis is dominant feature in many tissues affected by systemic sclerosis. The study will randomise patients to receive either mycophenolate mofetil and placebo or mycophenolate mofetil and abituzumab. This design is important because recent trials have shown that mycophenolate mofetil has some beneficial effect on lung disease in systemic sclerosis and this is currently our "standard of care" (or best available treatment). So all patients will be on the best "standard" treatment for the condition, and 60% will also be on abituzumab.

We are also expecting to start recruiting soon for **RECITAL a clinical trial of the B cell depleting antibody, Rituximab, versus the potent immunosuppressive agent, Cyclophosphamide**. This study is also recruiting patients with connective tissue disease (including systemic sclerosis) and lung disease. Again, importantly, both arms of the study are active treatments. Clinical trials in systemic sclerosis, over the last couple of years, have shown that cyclophosphamide (like mycophenolate mofetil) has a modest beneficial effect. The trial has been designed to assess if Rituximab can improve on this.

IMMUNOLOGY RESEARCH IN THE DEPARTMENT OF RHEUMATOLOGY

Whilst there have been very encouraging advances in the treatments available for

rheumatoid arthritis and related conditions – most obviously the anti-TNF drugs – we still need to do better to produce long-term control of disease for the vast majority of patients. The best of our treatments produce useful benefit for about 2/3rd patients but complete freedom from symptoms and joint damage in less than a quarter. Dr. Carmel Stober, supported by CARE, has been looking at the cells of the immune system which end up in the inflamed joint, and comparing them with the ones which are found in the blood in patients, and also in the blood of people with no arthritis. She has looked at both rheumatoid arthritis and psoriatic arthritis. The cells in the joint make much more of a potent inflammation-inducing substance, called GM-CSF; there is an antibody drug which targets GM-CSF and looks promising in early clinical trials. The question we would like to answer is what turns cells on to make so much GM-CSF. To do this we can use very powerful technologies, firstly to identify all the different kinds of cell that make GM-CSF, and the ones which seem to be most prominent in the joint. We can then look at the genes which are turned on in these cells, especially those which might control whether or not the cell makes GM-CSF. If we know that, we might be able to turn off those genes with drugs that would be simpler to make and take than antibodies, which are expensive and need to be given by injection. Currently applications to funding bodies to support this line of research are underway. This is in line with CARE's strategy of sponsoring the early stages of a research project. This allows the initial experiments to be done, and data collected to convince a large funding organization (like Wellcome Trust or MRC) to take on support of a full experimental programme.

ORTHOPAEDIC

The Division of Trauma and Orthopaedic Surgery seeks to deliver excellence in research, teaching and training as it relates to the surgery of bones, joints and other structures relevant to movement. We adopt a translational approach, meaning that we seek advances in fundamental musculoskeletal sciences that apply to patient care in the operating theatre and clinic.

Over the last twelve months we have had a significant expansion of staff numbers within the University department. Mr Stephen McDonnell and Mr Wasim Khan are University lecturers and honorary consultant orthopaedic surgeons. Mr Ben Davies has been appointed at clinical lecturer level and started in February. Mr Matt Seah has been appointed as an ACF as has Mr Andrew Hotchin.

There are a number of studies and clinical trials undertaken within the department. These have been split into trauma, elective and cell therapies. The trauma lead is Mr Peter Hull. He has received an NIHR grant for the KFORT study. This is a study for a knee fix or replace trial. A feasibility study comparing fixation versus replacement in patients sustaining distal femoral fractures. We are also a site for the HEALTH study which is hemi arthroplasty versus total hip replacement in patients sustaining intra-capsular fractured neck of femurs.

For elective surgery we have a study looking at patient specific instrumentation in total knee replacements and a study FAIT trial looking at femoral acetabular impingement. The elective surgery study lead is Mr Vikas Khanduja. We have 2 cell therapy studies. We are the only UK centre in the ADIPOA 2 trial. (www.adipoa2.eu). This is a study using adipose/fat derived stem cells which have been cultured to treat early knee osteoarthritis. This study has now passed its ethical review and we hope will start recruitment in April. The PREOB trial is a study looking at cellular therapies for the treatment of early osteonecrosis of the femoral head.

The ARUK tissue engineering centre grant has had a successful renewal. The Arthritis Research UK tissue engineering centre is led by the University of Cambridge and has a unique collaboration of scientists and clinicians at the University of Aberdeen, Keel University, Newcastle University, the Robert Jones and Angus Hunt Orthopaedic Hospital and the University of York.

The clinical services at Addenbrooke's Hospital have also been commended during 2017. They have had significant success with the treatment and adherence to best practice for fractured neck of femur care. They have also had favourable National Joint Registry data to support elective hip and knee replacement surgery and a positive review by Professor Tim Briggs during his GIRFT (getting it right first time) visit to the Trust.

***Professor of Orthopaedic Surgery and Research Director*:** Professor Andrew McCaskie

***Senior Research Associates*:** Dr Mark Birch; Dr Roger Brooks
Senior Lecturer & Research Fellow: Dr Frances Henson
***University Lecturer & Honorary Orthopaedic Consultants*:** Mr Wasim Khan; Mr Stephen McDonnell

NIHR Academic Clinical Fellows: Dr Andrew Hotchen*;* Mr Matthew Seah
***NIHR Academic Clinical Lecturer*:** Mr Benjamin Davies
Honorary Research Consultant*:* Dr Nigel Loveridge
***Research Associates*:** Dr Virginia Piombo; Dr Karim Fekir; Dr Sarah Lindsay; Dr Helen Lydon
Research Assistants: Amal Alami; Karin Newell
PhD students: Anna Albiero; Francesca Beaton; Sophie Frankham-Wells
***MPhil student*:** Dr Jamie Roberts
***PA to Prof McCaskie*:** Mrs Chris Coulson
***Research Grant Administrator*:** Alison Sawalhi

NHS Consultants: Mr Carrothers, Mr Edwards, Mr Hopkinson-Woolley, Mr Hull, Mr Johnston, Mr Kang, Mr Keene, Mr Khanduja, Mr Krkovic, Mr Melton, Mr Norrish, Mr Owen, Mr Rehm, Mr Robinson, Miss Stohr, Mr Tytherleigh-Strong, Mr Van-Rensburg, Mr Vince

Musculoskeletal Roadshow

The 5th Roadshow took place on 28th March 2017 at the Clifford Allbutt Lecture Theatre. The feedback was good and patients enjoyed the talks. A further Roadshow will be held in 2018 at a date to be agreed.

5TH CARE WALK

The 5th CARE Walk took place on Saturday 3rd September 2016. Staff got together with a few patients and family of staff to take part in the walk this year. The longest walk was 18 miles and 6 people started at the beginning. They met with others at points throughout the walk, by the time they got back to Wandlebury it was pouring with rain but their spirits were not dampened. A welcome hot drink and cake were waiting for them in the Educational Centre along with many of their friends/family. We managed to raise £1958.15.

Collecting Boxes - 'THANK YOU' to all those who are still holding CARE collecting boxes and also to those who are new holders. The collecting boxes are emptied into a large jar when they are returned. This year we have banked **£248.00**

Rheumatology Department Staff

Chair of CARE: Professor Gaston

Consultants: Dr Clunie, Dr Hall, Dr Jadon, Dr Jordan, Dr Lillicrap, Dr Malaviya, Dr Negoescu, Dr Poole, Dr Rees, Dr Shenker.

Locum Consultants: Dr Buknall and Dr Mossawi

Rheumatology Specialist Registrars: Dr Evans and Dr Weller

Academic SpR: Dr Stober and Dr Singh-Nijjar

Rehab Trainee: Dr Mee

Senior Research Fellows: Dr Goodall

Research Fellows: Dr Htut, Dr Fifield, Dr Shaikh

Post-Doctoral Scientists: Dr Webster

Senior Research Technicians: Mrs Ellis

Research Unit Manager: Mrs Smith

Research Nurses: Ms Fan, Mrs Raut-Roy, Ms Ford, Mrs Mil and Mrs Blesic

Research Admin Assistant: Mrs Jarvis

Specialist Nurse Practitioners: Mrs Isaacson, Mrs Nash, Mrs Bloxham, Mrs Hollis, Ms Pilbrow, Ms How, Mr Cayado-Lopez.

Rheumatology Secretaries: Ms Payler, Ms Hollands, Ms Senior

Clinical 5 Staff: Ms Douglas, Ms Goodsell, Ms White

`Supporting *Care*

Care and the work of the Rheumatology Research Unit depend entirely on donated income. Much of this is in the form of grants for specific projects and comes from Foundations like the Arthritis Research Campaign. Without these big grants none of the research would be possible. But we need additional money and support which individual friends and small groups can give. Gifts come in many forms and all are very much appreciated. They can be:

- Gifts by cash, gift aid or cheque made payable to ***Care***
- By a legacy to ***Care*** in your will

Or support can be given in other ways:

- Finding locations for one or two ***Care*** collecting boxes.
- Gathering a small group of friends and arranging an event like a coffee morning, cake stall, bingo session or ..... for ***Care.***
- Putting the ***Care*** **Times** into the hands of a club Chairman, your employer, a Company Director or Trust member.
- Suggesting ***Care*** for support by the staff where you work.

To: Sheila Smith ***Care*** Rheumatology Research Unit, Box 194, Unit E6, Addenbrooke's Hospital, Cambridge CB2 OQQ
Tel: 01223 217457
Email: sheila.smith@addenbrookes.nhs.uk

From _____

Address _____

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Post Code: _____ Telephone:_____

Please send me information on:

Considering a Legacy to ***Care*** ☐ *A CARE collecting box* ☐

Care is a registered Charity, number 802862, and exists to support patient care and research in rheumatic diseases in the region around Cambridge. It shares offices with the Rheumatology Clinical Research Unit.