

PEXIVAS Newsletter

Patient recruitment started

The first PEXIVAS patient was recruited in Cambridge on 8th of June 2010! So far 5 patients have been enrolled overall: 3 from Cambridge, 1 from St. George's Hospital in London and 1 from Queen Elizabeth Hospital Birmingham. Congratulations and thanks to these teams for the early successes!

Only 495 more patients needed



Thank you for your continued support!

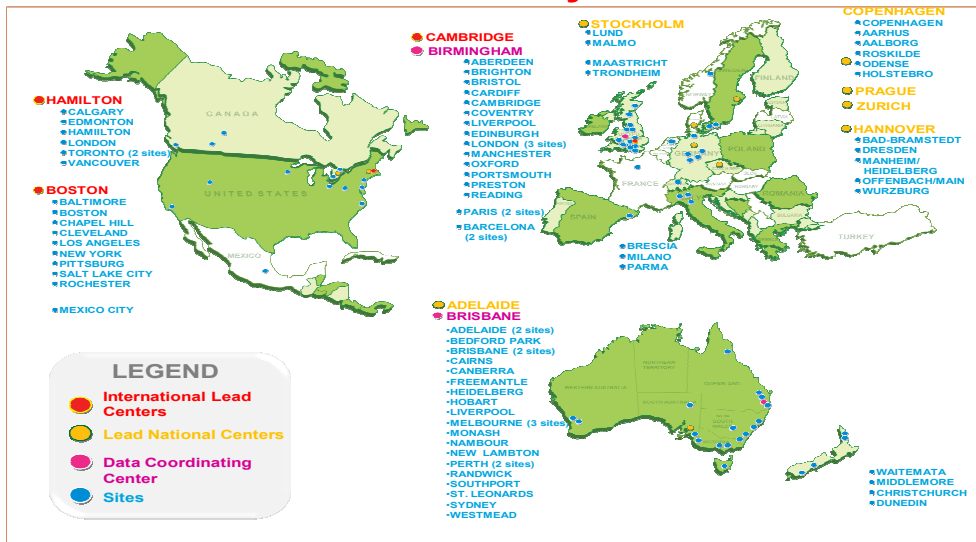
PEXIVAS will be enrolling patients from over 100 centres in the 15 countries shown below!

Electronic CRFs

The online randomization software was finalized by Birmingham Clinical Trials Unit in June 2010. The BCTU is also working on finalizing the electronic case report forms (CRFs) for recording patient's data.

www.bctu.bham.ac.uk/pexivias

PEXIVAS Study Sites



PEXIVAS will be a truly global trial: Over 100 centres from 3 continents !

Version 1.1 of the PEXIVAS protocol released
Already approved by ethics in UK and USA
(Please contact the Cambridge trial office if you have not yet received a copy of version 1.1)

New Funding Support Secured !

Congratulations to Carmel Hawley and Chen Au Peh who have negotiated with Fresenius / Gambro regarding funding support for filters in Australian centres. We are continuously seeking further funding opportunities, local trial support and for substudies. If you are planning to apply for a grant, please let the coordinating office and the PIs know—we may be able to assist you!



Special points of interest:

- First PEXIVAS patient recruited 8th of June, '10 Cambridge
- 5 PEXIVAS patients enrolled so far
- Version 1.1 of PEXIVAS protocol released and approved in UK /USA.
- Clinical trial authorization obtained by Denmark, Adelaide, New Zealand, Chapel Hill, Cleveland, Norway,
- New centres joined PEXIVAS
- Online randomization software activated on the Birmingham Clinical Trials Unit website

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Quick Reminder about the Trial Inclusion Criteria:

1. New or relapse of previous Wegener's granulomatosis or microscopic polyangiitis
2. Positive PR3-ANCA or MPO-ANCA
3. eGFR<50 mls/min (past 3 months) AND focal necrotizing GN on renal biopsy OR active urine sediment (proteinuria + haematuria/red cell casts)

OR

Pulmonary Haemorrhage (typical alveolar infiltrates on chest X-ray /CT without alternative explanation PLUS at least 1 of the following 4:

-haemoptysis, increased diffusing capacity for CO, bronchoscopic evidence, unexplained Hb<10 g/dL (Hb drop>2 g/ dL)

Trial Exclusion Criteria:

1. Vasculitis other than listed above
2. Age < 15 years
3. Anti-GBM antibody or linear glomerular IgG on renal biopsy
4. Dialysis for >21 days before randomisation or renal transplant
5. Pregnancy
6. Receipt of >1 dose iv cyclophosphamide and/or >14 days oral cyclophosphamide and/or > 14 days oral glucocorticoid and/or >1 dose rituximab during the 28 days preceding randomization
7. Any other co-morbidity that prevents enrolment into PEXIVAS in the opinion of the investigator

Medical Monitor: For non-urgent advice please E-mail PEXIVASmedicalmonitor@nhs.net. If you need to discuss urgent clinical issues please phone your regional PEXIVAS coordinator via the contact details on page 4.

Serious Adverse Event (SAE) Reporting:

An SAE is any event which is fatal, life-threatening, causes or prolongs hospitalization or results in congenital abnormality affecting the patient's baby if conceived whilst on treatment following the trial protocol. Please report all SAEs within 24 hours by E-mailing a scanned copy of the SAE case report form (download from <http://www.bctu.bham.ac.uk/pexivas/investigators/protocol.shtml>) to Biljana Jovanovska (bjovanovska@nhs.net) or fax to +441223586796 in Cambridge.

US centres: please also report SAEs to the Vasculitis Research Consortium Office in Boston: Peter Merkel (pmerkel@bu.edu) and

Carol McAlear (caking@bu.edu); Tel No: +01 617 414 2501, Fax: +01 617 414 2510

Australian / New Zealand centres: please also report SAEs to the Australasian Kidney Trials Network (Alicia Smith - a.smith18@uq.edu.au and Donna Reidlinger - d.reidlinger@uq.edu.au, Tel No: +61 732405463)

PAX Gene Tubes for Biomarker Samples:

Biomarker samples will be collected at baseline (10 mls each for RNA, DNA, serum, plasma), 2 weeks (serum, plasma), 12 weeks (RNA, serum, plasma) and 1 year (RNA, serum, plasma). Once your centre becomes ready to recruit patients the Cambridge trial office will send you instructions on how to process these samples and a supply of PAX gene tubes. Thereafter, please check the expiry date on any unused tubes and contact us in Cambridge if you need more supplies. Please inform the Cambridge trial office too if your centre does not have facilities to centrifuge or store these samples at minus 80 degrees Celsius before shipping them back to Cambridge.

Please remember to report any protocol deviations: Any protocol deviations should be recorded on the relevant case report form (CRF) and discussed via the phone with the trial management committee at the time of occurrence.

Upcoming PEXIVAS Investigators Meetings—Mark Your Calendars

Further vasculitis (VCRC/ EUVAS) investigators meetings will be:

Sunday 7 November 12-5 pm, Hilton Atlanta, Northern Court Room, 2nd floor, Room 213-214, Atlanta, USA

PEXIVAS investigators meeting from 12-1 pm, and vasculitis investigator meeting from 1-5 pm.

(A few blocks from the convention center, just before the American College of Rheumatology conference, Atlanta, USA)

Please contact Jackie Chapski (jchapski@bu.edu) if you would like to attend the Atlanta vasculitis investigators meeting

8-12th of April 2011: World Congress of Nephrology (ISN), Vancouver, Canada

Sunday 15th May 2011: ANCA Workshop, Chapel Hill, North Carolina, USA

23-26 of June 2011: European Renal Association, Prague, Czech Republic

The PEXIVAS investigators meeting held in beautiful Parma in June '10 was a professional success and an enjoyable social event. Many thanks to Augusto Vaglio and Elisa Luzi for hosting us.

Ancillary Studies

5 Sub-studies have been proposed in conjunction with PEXIVAS and now seek funding:

Dr. Wladimir Szpirt of Copenhagen (wladimir@szpirt.com) will assess the correlation between cyclophosphamide CYP2B6 / CYP2C19 genotypes and adverse events (leucopaenia and infections) with the aim to design to a better cyclophosphamide dose regimen.

If you are interested in substudy on gourmet restaurants around the world please contact Dr. Szpirt (aka foodie) as well. After visiting the top world list restaurants he is looking for matching controls.

Dr. Chen Au Peh of Adelaide (chen.peh@adelaide.edu.au) will lead a study examining the effect of Toll-like receptor stimulation with LL-37 neutrophil-derived peptide and CpG oligodeoxynucleotide on ANCA production from peripheral blood mononuclear cells. The aim is to provide further insight into the link between infection and vasculitis.

Dr. Peter Margetts of Hamilton, Canada (margetts@mcmaster.ca) will lead a study exploring the biology of circulating and renal tissue fibrocytes, currently seeking funding by the Canadian Institute of Health Research.

Dr. Janak DeZoysa (Janak.deZoysa@waitematadhb.govt.nz) and Dr. Nuala Helsby (n.helsby@auckland.ac.nz) will examine the correlation between CYP2C19 / CYP2B6 genotypes and cyclophosphamide pharmacokinetics + treatment failure.

There will be some cooperation between both studies.

Prof. Dr. Marion Haubitz of Hannover (Haubitz.Marion@mh-hannover.de) will lead a study of the elimination of pathogenic factors by plasma exchange, planning to measure osteopontin, angiotensin II, ADMA, thrombospondin, cytokines, and proteases.

All ancillary studies that utilize PEXIVAS patients and clinical data need to be formally proposed to the PEXIVAS Trial Management Committee before starting work on them, in order to help prioritize and allocate resources appropriately.

New People That Joined the Team to Help PEXIVAS Happen...

In Cambridge, Biljana Jovanovska joined David Jayne and Alina Casian at Addenbrooke's Hospital/ Biljana has started as full-time PEXIVAS trial coordinator and has a nursing background as well as a genetics BSc degree.



Lauren Scott has joined the team at the Birmingham Clinical Trials Unit as renal data manager.

Mike Walsh will soon be joined by Nicole Zytaruk in Hamilton to help coordinate the Canadian PEXIVAS centres. Nicole has valuable experience of coordinating an international study of 3600 critically ill patients for the Canadian Critical Care Clinical Trials Group

Warm welcome to colleagues who recently joined PEXIVAS !

Vancouver, Canada—Prof. Adeera Levin (ISN Secretary General)

Brighton, UK—Dr. Neil Iggo

Thessaloniki, Greece—Dr. Maria Stangou

Timisoara, Romania —Prof. Adalbert Schiller

(President of the Romanian Society of Nephrology)

— Dr. Nicu Olariu, Dr. Adelina Mihaescu

Holstebro, Denmark—Prof. Erling Pedersen

Bologna, Italy—Dr. Fausta Catapano

Madrid, Spain—Dr. Vicente Barrio

Mexico City, Mexico—Dr. Jorge Sanchez Guerrero and Andrea Hinojosa



Hamilton, Canada—Eoin Walsh (age 2) is E-mailing the trial office from his father's Blackberry and proving a dynamic, promising researcher

Key Contact Details

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Australasian Kidney Trial Network (AKTN) coordinators

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Websites Related to PEXIVAS

EUVAS: www.vasculitis.org

VCRC: rarediseasesnetwork.epi.usf.edu/vcrc/

BCTU: http://www.bctu.bham.ac.uk/pexivas

AKTN: www.uq.edu.au/aktn/

Vasculitis Foundation: www.vasculitisfoundation.org

Clinical Trials Gov: www.clinicaltrials.gov