

## Message from the Chairs

Welcome to the eighth newsletter of the Australasian Kidney Trials Network (AKTN). The AKTN is continuing to go from strength to strength. Three AKTN-coordinated or -facilitated trials are currently recruiting, with 2 more to commence later this year, including the international collaborative trial, PEXIVAS. In addition, the ACTIVE Dialysis trial (an AKTN endorsed trial) is continuing to recruit well. Furthermore, we have seen the introduction of two new trials to the Network this year. The first of these is the ACE inhibitor trial (ACE Inhibition for the Preservation of Renal Function and Patient Survival in Kidney Transplantation) which is being led internationally by Dr Greg Knoll and the Ottawa Hospital Research Institute, and referred to locally as the AVATAR trial in Australia and New Zealand. The other is the IMPROVE trial (IMpact of Phosphate Reduction On Vascular End-points in Chronic Kidney Disease) which is a multi-centre Australian and New Zealand trial investigating phosphate reduction through Lanthanum use, and its effect on arterial compliance and vascular calcification in Chronic Kidney Disease (CKD) patients. This trial is being led by Dr. Nigel Toussaint and Dr. Eugenie Pedagogos.

As the number of trials continues to grow, so too does our staff base and we would like to welcome our new staff. Alaine Heffernan commenced with us in January as Coordinating Data Manager and is working hard on changes to the clinical trial databases and randomisation systems we are using. In addition, we would like to welcome Josie Parry. Josie commenced in April as our new Executive Support Officer and we wish her well in this position.

We thank all participating sites for your tireless efforts with patient recruitment and we encourage everyone to continue to push recruitment at their sites to ensure these Australian-led studies are a success. We look forward to meeting many of you at meetings in the coming months. The ANZSN operations staff will be well represented at the ANZSN in Perth, so please take the opportunity to visit the AKTN booth in the exhibition hall to meet the staff in person.

Best Wishes



Assoc/Prof Carmel Hawley  
Chair, Operations Secretariat



Prof Alan Cass  
Chair, Scientific Committee

# Highlights for 2010

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Donna Reidlinger, Melissa Bruce

## **AKTN Staff Graduate from further education**

We would like to congratulate our staff who have just completed further studies. Mr Charles Thompson has recently completed his Masters of Biostatistics and Ms Donna Reidlinger has completed her Masters in Public Health. In addition, Miss Alicia Smith has completed her Graduate Certificate in Clinical Trials Management and Dr Melissa Bruce has completed her Masters in Business Administration. A big congratulations to all staff for their hard work and dedication to their studies.



## **Funding secured in 2010**

This year has already proven successful with the extension of the NHMRC Enabling Grant (\$2 million over the next 5 years). In addition, the BLOCADE trial received an additional \$156,000 from Health Research Council of NZ to be used for our New Zealand sites. Despite our recent success, we are continually seeking additional funding for our current trials so if you are interested in becoming financially involved with the AKTN, please contact our Business Development Manager, Melissa Bruce for further information ([melissa.bruce@uq.edu.au](mailto:melissa.bruce@uq.edu.au)).



## **Strategic Guidance Day**

On July 15th 2010, a Strategic Guidance Day was held in Brisbane to determine the strategic direction of our Network over the next 5 years. This day enabled us to outline some goals and objectives for the Network by developing a shared understanding of the positioning of the network around patient-centred outcomes, its strategic direction and the desired outcomes for the AKTN during the period 2010 - 2015. The AKTN Business Development Manager continues to work with Strategic Planning Consultant Dr Lewie Aktinson to put the plans forged into action.



## Scholarships

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AKTN PhD scholarship applications have now opened for 2011 and will soon be released on the AKTN website. If you require information on this scholarship, please contact Melissa directly ([melissa.bruce@uq.edu.au](mailto:melissa.bruce@uq.edu.au)).



## **A randomised, controlled trial of exit site application of Medihoney™ Antibacterial Wound Gel for the prevention of catheter-associated infections in peritoneal dialysis patients**

**(ACTRN12607000537459)**

*Trial Management Committee: Prof David Johnson, Prof Alan Cass, Mr Charles Thompson, Dr Janak de Zoysa, A/Prof Carmel Hawley, Dr Steven McTaggart, Dr Geoffrey Playford, Miss Alicia Smith, Dr Liza Vergara, Dr Paul Snelling, Dr Carolyn Clark*

The HONEYPOT Trial is proceeding very well, with all 24 active sites successfully recruiting patients. A total of 278 patients have now been recruited, which represents 78% of the total recruitment target of 370 patients. The site with the most patients recruited is Princess Alexandra Hospital with 38 patients – congratulations PA! We had 2 successful Steering Committee Meetings with all site PIs and Study Coordinators in February and June this year where we discussed the barriers to recruitment and strategies to boost recruitment. 2 new sites are joining the HONEYPOT trial soon, Eastern Health (PI Prof Lawrence McMahon and Study Coordinator Annette Kent) and Western Health (PI Dr Vicki Levidiotis and Study Coordinator Donna Soraghan) who are currently completing their documentation to be able to start recruiting soon. Monitoring visits have been completed for 12 sites already this year, which has provided a great opportunity for HONEYPOT Project Officer Liza Vergara to meet the site HONEYPOT coordinators, and sort through coordination issues that commonly arise at sites. The countdown to reach recruitment of the final patient has started and we are encouraging all sites to not to let their guards down and keep on recruiting (especially incident PD patients!) to be able to reach our target of 370 patients.



## **Fish oil and Aspirin in Vascular access Outcomes in RENal Disease**

**(ACTRN12607000569404)**

*Trial Management Committee: Dr Ashley Irish, Prof Alan Cass, Dr Sharan Dogra, Mr Charles Thompson, A/Prof Carmel Hawley, Prof Peter Kerr, Dr Trevor Mori, Dr Kevan Polkinghorne, Dr Amanda Robertson, Dr David Voss, Ms Peta-Anne Paul-Brent, A/Prof Vlado Perkovic, Dr David Gracey, Dr Amanda Mather, Dr Chen Au Peh, Dr Hooi Lai Seong, Dr Chris McIntyre, Mr Colin Hutchinson*

Twenty-six Australian and New Zealand sites are actively recruiting patients with a total of 159 patients recruited and 1651 patients screened for their suitability. In addition to the Australian and New Zealand sites, significant progress has been made with the introduction of sites from Malaysia and the United Kingdom. Eight sites from Malaysia and 8 sites from the United Kingdom have been engaged to participate in the study with a target of 165 and 400 patients respectively over 3 years.

There has been an ongoing concern about the lower than expected recruitment rate with the most significant reason for screening failure is the use of aspirin (39% of excluded patients required aspirin). The FAVOURED Trial Management Committee is concerned that even with the addition of the UK and Malaysia, the recruitment rate may be affected by aspirin use and that the study target may not be met in a timely fashion. In addition, a review of the baseline characteristics of patients has shown that the current study population was both young and healthy (average age = 55 years and with only 4% ischemic heart disease). This is not representative of the average stage 4/5 Chronic Kidney Disease cohort and has the potential of reducing the failure rate of studied AVFs and generalisability of the results to the wider renal population.

With the dual aim of improving the recruitment rate and bringing the study population characteristics in line with the general renal population, the FAVOURED Trial Management Committee has decided to amend the study protocol to allow patients taking aspirin to be randomised solely to fish oil or a matched placebo. We believe this will allow us to better understand the potential added benefit of fish oil, on top of aspirin, in people at high cardiovascular risk, thus further illuminating the role of both agents in this large pool of patients.

The changes to this study will take a few months. They involve protocol changes; changes to the randomisation program; changes to the data base and detailed review of the statistical power and analysis plan. Whilst these changes are occurring we need to continue to recruit to the trial as it is currently, and keep the momentum of the study going. We are confident that with the changes to the study protocol and the engagement of our international colleagues in the UK and Malaysia we will achieve the planned recruitment targets.



## **Haemoglobin levels in patients with Erythropoietin-Resistant anaemia treated with Oxpentifylline (ACTRN12608000199314)**

*Trial Management Committee: Prof David Johnson, Mr Charles Thompson, Dr Rob Fassett, A/Prof Carmel Hawley, Prof Alan Cass, A/Prof Stephen McDonald, Miss Alicia Smith, A/Prof Rowan Walker, A/Prof Genie Pegadogos, Ms Donna Reidlinger, A/Prof Vlado Perkovic, A/Prof Carl Kirkpatrick*

Earlier this year, the HERO Trial Management Committee unanimously decided to change the primary end-point from difference in haemoglobin concentration to difference in ERI (Erythropoietin Resistance Index –  $ERI = rHuEPO \text{ dose in IU/kg body weight/week} \div Hb$ , or  $ERI = darbepoetin \text{ dose in } \mu\text{g/kg body weight/week} \div Hb$ ). This amendment was prompted by publication of the TREAT trial, which was performed in CKD patients with diabetes mellitus and anaemia. The investigators reported a significantly increased incidence of stroke and thromboembolic events in patients assigned to darbepoetin with a high haemoglobin target, vs control<sup>1</sup>. The publication is available upon request to the AKTN.

It remains unclear whether a high haemoglobin target or a high ESA dose (or both) underpin the increased incidence of these events. Nevertheless, the TREAT findings greatly strengthened the increasing evidence against the validity of haemoglobin level as a surrogate outcome measure of ESA therapy, thereby necessitating modification of the HERO trial protocol. Changes were made to the inclusion criteria, statistical calculation (recruitment target has not changed) and analysis plan.

The good news is that these amendments not only potentially increase participant safety, but also widens the patient population eligible for the trial. The next twelve months should see this trial meet its recruitment goals and provide preliminary research results for dissemination.

1. Pfeffer MA, Burdmann EA, Chen CY, et al. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. *N Engl J Med* 2009;361:2019-32.



## **Beta-blocker to Lower Cardiovascular Dialysis Events (ACTRN 12609000174280)**

*Trial Management Committee: Dr Matthew Roberts, A/Prof Frank Ierino, Prof Henry Krum, A/Prof Carmel Hawley, Mr Charles Thompson Prof Alan Cass, A/Prof Nicole Isabel, Dr Liza Vergara, A/Prof Helen Pilmore, Prof Andrew Tonkin, A/Prof Vlado Perkovic, A/Prof Amit Garg*

This trial aims to investigate whether the beta-blocker carvedilol is effective in reducing the incidence of cardiovascular morbidity and mortality in patients receiving dialysis. In the first instance the AKTN are performing a Feasibility study. The major outcomes of this Feasibility study will be to assess tolerability of carvedilol, recruitment rates, and event rates which will provide baseline data for a larger clinical endpoint study planned in the future. The trial will recruit 150 participants and will follow them for 12 months with a supervised down-titration and cessation of study drug at the end of the study. Funding for this study has been obtained from 3 grants - Jacquot grant application (\$AU700K over 3 years), Pfizer CVL (\$AU55K) and from Health Research Council of New Zealand (\$NZ156K for NZ sites only).

An NHMRC grant application was applied for this year to supplement the funding until 2013. To date, 10 sites (Australia = 7 sites, New Zealand = 3 sites) have confirmed their participation in the study. Currently, we have 6 sites (Auckland City Hospital, Austin Health, Monash Medical Centre, Royal Melbourne Hospital, Royal Prince Alfred Hospital and Westmead Hospital) with ethics approval. Procurement of study medication and manufacture of placebo are currently underway. Recruitment is expected to start by late October this year.

# Current Trials- UPDATE



## **ACTIVE Dialysis**

*Trial Management Committee: A/Prof Vlado Perkovic, Prof Alan Cass, Dr Meg Jardine, Dr Martin Gallagher, Dr Eleanora Fjälling.*

*Optional Observers (as of July 2010): Josie Raley, Sue Murray, Jason Healey, Tam Le*

ACTIVE Dialysis is a prospective, randomised trial designed to provide definitive evidence on the benefits and costs of extending weekly haemodialysis hours beyond current standards. Led by a steering committee of nephrologists and endorsed by the AKTN, the study is coordinated by the Renal Division at The George Institute for International Health. The trial is funded by a National Health and Medical Research Council (NHMRC) Project Grant with a supplementary unrestricted grant from Baxter. Participants are being enrolled from both the home haemodialysis and in-centre settings and are randomized to standard or extended weekly hours of haemodialysis for 12 months.

ACTIVE now has 40 of a planned 200 participants enrolled. 16 sites in Australia and New Zealand have joined and 11 are actively recruiting. Canada will soon join with 3 sites nearing completion of Ethics and regulatory processes. ACTIVE appears likely to provide landmark evidence on the question of the benefits and harms of extended hours dialysis. Any interested sites are still able to join the study and are invited to contact Meg Jardine ([mjardine@georgeinstitute.org.au](mailto:mjardine@georgeinstitute.org.au)) or Vlado Perkovic ([vperkovic@georgeinstitute.org.au](mailto:vperkovic@georgeinstitute.org.au)) for further information.



## **PEXIVAS TRIAL**

*Trial Management Committee: Dr Chen Au Peh, A/Prof Carmel Hawley, A/Prof Vlado Perkovic, Prof Randall Faull, Dr Janak de Zoysa, Prof Peter Kerr, Prof Robyn Langham, Dr Giles Walters, Dr Sunil Badve, Miss Alicia Smith, Ms Donna Reidlinger*

The PEXIVAS Trial is an international randomised controlled trial investigating plasma exchange and glucocorticoid dosing in the treatment of Anti-Neutrophil Cytoplasmic Autoantibody associated vasculitis. The AKTN will facilitate the Australasian arm of this multi-centre trial which is being led by Dr Chen Au Peh, an Adelaide based Nephrologist.

The first patient was randomised into PEXIVAS on the 8th June 2010 from Addenbrooke's Hospital, Cambridge, UK. Australian and New Zealand sites are currently completing regulatory and governance paperwork with most sites on track to begin recruiting to the trial in August 2010.



## **ACE inhibitor trial**

### ***ACE Inhibition for the Preservation of Renal Function and Patient Survival in Kidney Transplantation*** **(Local acronym: AVATAR - Ace inhibitors Versus p lacebo Therapy After Renal transplantation)**

Negotiations are currently underway to facilitate the Australian and New Zealand arm of an international study investigating Ace Inhibitor use in Kidney transplantation. This trial is being led internationally by Dr Greg Knoll and the Ottawa Hospital Research Institute. Dr. Helen Pilmore will chair the trial management committee for the Australian and New Zealand investigators in this trial. Funding will be provided by the Canadian Institute of Health Research. The first ANZ Trial Management Committee teleconference is to be held in August 2010, and local recruitment is expected to commence in mid 2011.



## **IMPROVE trial**

### ***IMpact of Phosphate Reduction On Vascular End-points in Chronic Kidney Disease***

Arrangements are being finalised to coordinate a multi-centre Australian and New Zealand trial investigating phosphate reduction through Lanthanum use, and its effect on arterial compliance and vascular calcification in Chronic Kidney Disease (CKD) patients. This trial is being led by Dr. Nigel Toussaint and Dr. Eugenie Pedagogos (Melbourne), and funding has been made available via an unrestricted pharmaceutical company grant. This trial will be conducted in collaboration with Dr David Wheeler in the United Kingdom, where additional sites will participate in patient recruitment. The first Trial Management Committee teleconference was conducted on the 19th of July 2010, and recruitment commencement at the Australian and New Zealand sites is likely to occur in mid 2011. This will be the first study involving a true partnership of ANZ and UK investigators. Such international collaboration is important to achieve our goal of performing studies with adequate power to address clinically relevant questions.



## **TransDiab trial**

This trial aims to investigate the potential benefits of metformin for the treatment and prevention of post-transplant diabetes mellitus. Although this treatment has been demonstrated to be effective in the general population, it has not been trialed in the transplant population. The first component of this trial will be a feasibility study to assess the tolerability and safety of metformin in this patient population. Several face-to-face meetings have been held with opinion leaders in the Transplantation community, and significant progress has been made towards finalising the protocol. The AKTN aims to initiate the TransDiab trial during 2011.

## Interested in participating in a trial?

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If you are interested in finding out more information or participating in any of the trials that you have seen advertised, please contact our Project Manager, Alicia Smith ([a.smith18@uq.edu.au](mailto:a.smith18@uq.edu.au)) for further information.

## New Staffing

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### **Mrs Josephine Parry - AKTN Executive Support Officer**

Josie joined the AKTN in April this year as Executive Support Officer. She has Diplomas in Frontline Management and Government (Investigations) from the Charles Darwin University, Northern Territory. Josie has many years experience working in key management and senior administrative roles within both the University and Public Sectors both in Queensland and the Northern Territory.



### **Ms Alaine Heffernan - AKTN Coordinating Data Manager**

Alaine joined the AKTN in February this year as Co-ordinating Data Manager. She has a Bachelor of Science (Human Nutrition and Dietetics) and has five years experience working in clinical trials as a clinical research associate and clinical data programmer. Alaine is currently working on changes to the clinical trial databases and randomisation systems to compliment protocol amendments in HERO and FAVOURED.

## Staff at the AKTN Coordinating Office

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A/Prof Carmel Hawley - AKTN Operations Secretariat, Chair  
Prof David Johnson - AKTN Operations Secretariat, Deputy Chair  
Dr Melissa Bruce - Business Development Manager  
Dr Sunil Badve - Clinical Trialist  
Mr Charles Thompson - Biostatistician  
Ms Alaine Heffernan - Coordinating Data Manager  
Mrs Josephine Parry - Executive Support Officer  
Miss Alicia Smith - Project Manager  
Ms Peta-Anne Paul-Brent- FAVOURED Project Officer  
Dr Liza Vergara - BLOCADE and HONEYPOT Project Officer  
Ms Donna Reidlinger - HERO and PEXIVAS Project Officer

## Contact us

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