

## **Minutes BAPN Research Meeting – Bristol 12<sup>th</sup> Oct 2007**

Present: Alan Watson, Malcolm Coulthard, Arvind Nagra, Sally Johnson, Simon Waller, Rachel Lennon, Richard Coward, Mark Taylor, Manish Sinha, Andy Lunn, Mordi Muorah, William Van't Hoff, Moin Saleem

### **Minutes of previous meeting**

- approved

### **Aims**

- restated: Structure of the group – research lead from each unit to engage with multicentre collaborative research. Propose and execute trials and registries in the new environment of research funding

### **MCRN / Renal CSG**

- WVT gave a brief presentation of the current state of clinical study groups (CSG's) within MCRN. Stated that nephrology is currently within a mixed group of CSGs, and the environment is now ripe for creating a separate nephrology CSG, which would need a small amount of funding, and structure to include a lead, working group etc.
- Agreed that it would be a positive step for the group, which would be reconfigured to fit the described structure. The research leads from each centre will be a key part of this structure, perhaps ultimately built into their job plans, with a PA .
- Discussion followed : CMT stated that this would be on the agenda for the December BAPN AGM, for ratification.
- This Research Group should be rebranded as the proposed nephrology CSG, with a name to reflect the fact it is a new entity and to have impact with e.g. funding bodies, reflecting the momentum and purpose stated above. Name not finalised - ?BAPN renal research network, or similar.
- WVT has a conflict of interest with the proposed CSG, in that he is a MCRN lead already, so will not be able to lead the CSG
- There is a potential problem in that the MCRN centres don't cover all nephrology units, though this can be worked around.
- Registries can be included in MCRN networks
- **ACTION – WVT and MAS to finalise proposal, to be presented to MCRN. CMT to put on agenda for December**

### **Funding environment**

MAS gave an update of current funding possibilities:

KKR/KRUK – the initial tranche of money from KKR (£100k) has been agreed to be administered by KRUK, with a top up from KRUK of £50k, to make a total project grant availability of £150k. This will be advertised as the KKR/KRUK paediatric renal research award – the next deadline for applications will be early March 08.

Health Technology Assessment Programme (HTA). This is a new funding stream which: “works with the research networks of the newly established [UK Clinical Research Network](#) to identify and fund clinical trials of importance to a network's topic area

Will initiate a major new programme of HTA Clinical Trials to investigate issues that are directly relevant to clinical practice in the NHS.”

[http://www.nihr.ac.uk/files/pdfs/Implementation\\_Plan\\_6.3\(a\)\\_HTA\\_programme\\_August\\_2007.pdf](http://www.nihr.ac.uk/files/pdfs/Implementation_Plan_6.3(a)_HTA_programme_August_2007.pdf)

Applications can be made any time, on a rolling basis.

NIHR research for patient benefit programme (RfPB) – max £250k. Next deadlines : intention to submit 28-4-08, outline submission 9-06-08, full submission 20-10-08.

MRC – will not support trials showing incremental benefits (?not suitable for NS trial). However, for expensive trials, this is one of the only current options. Would need to discuss each individual trial with someone at the MRC before applying.

NIHR Programme Grant – an ambitious outcome, suggested to aim for after initial success with smaller grants and the model of research planning is established.

## **Ongoing Projects**

### **NS trial**

- NW was not able to attend due to illness, therefore a full update was not available to the meeting. It was thought that about 40/50 patients have now been recruited for the pilot study. The issues to be clarified before we could consider how and where to go for funding of the full trial included:

Are there potential problems with patient recruitment – not all centres are yet participating, but perhaps this is a momentum issue, and recruitment will improve exponentially.

The flow of information to participating centres (and others) would need improving.

Detailed information about any practical issues needs to be available to discuss, before the application for full funding, in order to make it as strong as possible.

The exact costs need to be known.

**ACTION – MAS to discuss with NW regarding current status, and details as above, to clarify when funding can be applied for.**

### **ARB/ACEi study**

WVT updated on this: There are some minor revisions to the document circulated in June 07. There has been additional input from adult nephrologists in Manchester. It was pointed out that few centres had formally responded to the document from June.

Discussion points were as follows:

- Is 3 years of placebo sellable to patients. It was suggested that the trial could be done without a placebo arm (i.e. ACEi + ARB vs ACEi alone), which may

- circumvent this problem, and possibly improve compliance in the treatment group, as well as reducing cost of the study
- There is a recent study published in NDT that only patients with proteinuria benefit from the addition of ARB. This might reduce the number of recruitable patients, or confound the data, and needs to be considered
  - Some centres do not give maximum dose of ACEi before adding in an ARB, so this would vary from the protocol of the trial
  - Central collection of samples for analysis may not be necessary, and again would reduce the cost burden and improve practicalities
  - Lisinopril is available as a liquid, and all centres represented are happy to use this as their ACEi within the trial. MAS to contact the rest of the centres to check if they are prepared to participate in the same way. It was questioned whether ARBs are also available in a liquid form
  - Age – why not start at 3yrs (when GFR has matured), and finish at 17, with appropriate follow up data from adult services if transferred.
  - TIMELINE – agreed to work to a 6 month deadline to finalise protocol, ready for submission to HTA or MRC
  - ACTIONS: WVT and Kjell Tullus to consider above points and finalise protocol. Decide on best funding stream to apply to. Aim for above timeline. WVT to consider approval by MCRN, in the absence of a nephrology CSG currently active.
- MAS to contact centres not represented at meeting, to confirm willingness to participate.**

### **Taurolock study**

Document circulated from CJ discussed:

- There is anecdotal evidence from 2 centres that use of non-heparin protocols has reduced infections and clots already – Newcastle use Alteplase, and have had no clots and 1 line infection in last 3yrs. Therefore they would not participate in the trial in its current form, but willing to consider alternative protocols. Southampton are already using Taurolock, again with anecdotal evidence of low infection rate, so reluctant to participate.
- It was discussed that it is a priority for BAPN to move away from anecdotal evidence base, so need a protocol that all will sign up to. Also emphasised that this is a very important study for our clinical practice.
- Dose of heparin is a difficult issue – some units use high, some low. Risks of high dose are spillage, causing patient bleeding. Risks of low are inadequate clot prevention.
- Local antiseptic policies can be used for the trial
- Nursing input is needed regarding feasibility of e.g. double-blind usage in a busy HD unit.
- It was suggested that the practicality could be greatly improved by using Time to first Infection/clot as the primary endpoint.

- Recruitment should be of both new (after a bedding in period) and existing catheters
- Are there any safety issues with Taurolock – needs checking
- It was suggested by the group to do a 3 arm study: 1. Taurolock; 2. Alteplase. 3: Heparin – *either* Low dose or High Dose (to be decided) with appropriate warning labels about spillage. All units present agreed they would participate in this.
- FUNDING – BRS has an appropriate project grant for this – deadline ?Oct 08. Otherwise RfPB or HTA. Is there the possibility of any industry sponsorship for this – would make application much stronger.
- TIMELINE – Outline should be ready by April 08, for submission in June 08 to RfPB.
- **ACTION – Caroline Jones and Eric Finlay to work up. MAS to contact units not represented here to confirm participation**

## UTI

Andy Lunn presented a document outlining possibilities of conducting a UTI study either in primary, secondary or tertiary care, to compare outcomes of patients managed with current NICE guidelines, to those managed with 1991 guidelines. This was discussed:

- It was agreed that it is imperative for BAPN to get engaged with a UTI study in the current circumstances, though it will not be straightforward.
- All patients with UTI in the appropriate age group will be recruited, management according to current NICE guidelines logged, then investigated as per 1991 guidelines.
- Initial calculations suggest the need for 4-600 patients, based on reduction of scarring from 5% to 2.5%
- The primary care based study was thought to be the most feasible one, as GPs will not refer on cases to secondary care according to current guidelines
- It was felt that the best option would be to engage academic GP surgeries within vicinity of each BAPN centre, to recruit patients
- There may be some difficulty with ethics review regarding additional investigations planned
- The group needs parent representation, to contribute to the protocol etc.
- **ACTION – Each Unit needs to identify their local primary care academic research lead immediately, and communicate to Andy Lunn / Alan Watson AL to contact primary care lead in Trent, initially, to discuss feasibilities**
- TIMELINE – aim for document outlining protocol to be circulated by New Year (there is an urgency to do this study before the guidelines become too entrenched)

## VUR

Previous discussions about a proposed study into antibiotic prophylaxis for VUR (SF, JAD) were continued.

- It was rumoured that there are two studies about to report data, one from Sweden, one from Italy, using randomised groups. More information about these is required
- Agreed in principle that this type of study needs to be done in UK
- **ACTION – MAS to discuss current status with JAD and SF**

### **ESRD incidence study**

Document from Karl McKeever discussed. This is a proposal for BPSU to prospectively analyse incidence of ESRD in infants. This has been favourably received by the BPSU, and would benefit by ratification from the BAPN. The group supported the study, and discussed as follows:

- KM needs feedback of incidence from Centres that haven't so far replied to his survey (about 5 replies to date)
- ?ESRD is outdated terminology – should use CKD 5
- Consider using age cutoff of 3/12 rather than 4/52, to avoid patients with recovering ARF
- It was asked whether it may be possible to include surveillance of foetuses terminated for renal anomalies. Probably too difficult under BPSU methodology.
- Would the urologists (who don't get orange card?) be aware of any patients to be included, outside the radar of nephrologists
- Trainee involvement in the study should be encouraged
- **ACTION – all centres who have not responded to feedback request, please do so via your research lead**

### **C1q antibodies study**

CMT has pilot data suggesting high incidence of anti-C1q Abs in MCGN. Not clear if this is pathogenic, prognostic or diagnostic. Therefore it needs a national study to recruit all patients. Leads will be CMT, Steve Marks, Sally Johnson.

Needs 1 extra blood sample, access to pathology and 6 monthly data collection. Ethical approval is in progress. It is envisaged to be a 2 year study.

Discussion:

- It was felt this needs to be done via a MCGN registry (see below)
- Could be done as a proposal to set up a registry, with a significant research component added on as outlined above (*post hoc thought from me – what about being more ambitious, and randomising all new pts to a treatment arm? Would show proof of principle that we can do such a study*)
- **TIMELINE** – need estimate of numbers from each Centre. Aim for draft proposal by end of the year to be circulated.
- **ACTION – ALL Centres (research leads) to give estimate of incidence/prevalence of MCGN I + II + III from last 3 years to CMT**

### **Renal Association / Renal Clinical Trials Network**

MAS informed group that the Renal Association is proposing a UK renal research consortium, as an entity within the NIHR framework. BAPN is a partner in this, and it may be an important link in the future for studies planning follow-on into adulthood.

### **Disease registries**

There are several small ad hoc registries at present, and it was discussed whether this could be formalised into a more concrete format, with funding, and an office (or virtual office) for co-ordination. This could be part of a UK rare disease registry, with inclusion of follow-through to adult care. Will need funding.

- this could be extended to include interventional studies on rare diseases, by recruiting all patients into randomised studies.

Cystinosis is part of a European grant recently awarded – registry for rare nephropathies

**ACTION – CMT to talk to Caroline Savage about getting Renal Association support, and possibly do this as a joint approach. MAS to talk to Charlie Tomson at the Renal Registry.**

### **Future plans**

- Transplantation studies – discussed that TWIST study has come to an end, and discussions are ongoing about further trials, though no details were available to this group.

### **AOB**

VUR genetics project discussed. ASW has communicated that the analyses are all moving ahead - being led by Newcastle – with the hope of a clinical and a genetics abstract to present at a major renal meeting in 2008

### **Date of next meeting**

6 months – to be finalised