

MCRN/BAPN Paediatric Nephrology CSG Meeting

Friday 6th November 2009

Medical Research Council Head Office

In Attendance:

Moin Saleem - Chair	(MS)	Alan Watson	(AW)
Wendy Cook	(WC)	Kjell Tullus	(KT)
Jan Dudley	(JD)	Nick Webb	(NW)
Rodney Gilbert	(RG)	Leah Krischock	(LAK)
David Hughes	(DH)	Mark Taylor	(CMT)
Caroline Jones	(CJ)	Mine Orlu Gul	(MOG)
Larissa Kerecuk	(LK)	Amy Farmer – Minute Taker	(AF)
Manish Sinha	(MSi)		

AP = Action Point

1. Welcome, Introductions & Apologies

MS opened the meeting and welcomed new members:

- Larissa Kerecuk (North East England Representative)
- Leah Krischock (Devolved Nations Representative – Scotland)
- Mine Orlu Gul (MCRN Formulations Research Fellow)

Apologies were received from Sally Johnson, Simon Waller and Laura Pilkington.

The group then discussed the remit of the CSG, which is primarily to support the development of multi-centre clinical trials. It was noted that a number of trials have now been reviewed by the group and that there is a need to keep up this momentum. The group's activity is shaped by the changes to the research funding environment and the MCRN involvement with Industry.

AW commented that a barrier to developing research at Trust level was a shortage of research support time, e.g. Research Nursing time, although the level of portfolio related research currently undertaken within his unit perhaps doesn't warrant this time. Support of this nature should be accessed via the MCRN as and when required. It was noted that there is some variation of both coverage and processes across the MCRN network. MS has received a good level of support from the MCRN in developing the RaDaR project.

2.0 Review of Minutes and Action Points from the Previous Meeting

The following comments were made:

Page 4 – APPROVE Study (JD) - This study isn't HTA funded.

With the exception of this item, the minutes were agreed as a true and accurate record.

AP – Laura Pilkington to circulate review as per page 2 [this action point was carried in the first week of May 2009].

3.0 Updates from the MCRN Co-ordinating Centre

3.1 NIHR Paediatrics (non-medicines) Specialty Group

The inaugural meeting of the group took place on Thursday 28th May and was well attended by paediatric representatives from all of the CLRNs who indicated paediatrics (non-medicines) to be a priority area. Representatives of key stakeholder groups relevant to paediatric research and the Chairs of the MCRN CSGs were also in attendance. The meeting set the scene for how the Specialty Group will function and how it fits within NIHR structures. Discussions also focused around how CSGs could take on non-medicines related research. This was also one of the themes for discussion during the CSG Chairs' forum, which took place on the same day. William Van t'Hoff was in attendance at both meetings. Michael Beresford (Chair of the CSG Chairs Forum) has been tasked to write a document about how MCRN CSGs may potentially assist in the development of the non-medicines portfolio within the comprehensive local research network (CLRN) infrastructure – this document will be circulated to CSGs in due course.

The group discussed how non-medicines research fits with the remit of the group and also the fact that the CSG receives additional non-NIHR funding. JD briefly discussed problems encountered with the DUTY study, which is predominantly a primary care study, and was not adopted by the MCRN SW. This study was supported by the CSG and it was unclear why the study wasn't adopted. It was suggested that JD may wish to write to William, in his role as Chair of the adoptions committee, with input from MS if needed, to request feedback re adoption process.

AP – JD to write to WVT re clarification about DUTY study adoption

3.2 ERA-NET PRIOMEDCHILD

MOG has been looking into preparing a proposal looking at formulations work to target this funding in conjunction with the MCRN Respiratory CSG. Two applications are currently in the pipeline and all applications need to submit an initial four page expression of interest by the 7 January. The group discussed ideas, such as research involving high molecular weight drugs and delivery route work in relation to both ERA-NET and also the off patent FP7 call. It was felt that ERA-NET as a funding source, in terms of the area of research and also the funding criteria, was possibly not directly aligned to the research interests of the group but that possibilities could be explored.

It was also noted that the group were requested to provide feedback some time ago in relation to paediatric pharmacokinetics but no subsequent response has been received.

AP – LK and MOG to discuss cystagon/cystamine work undertaken in Newcastle (University of Durham) to explore possible collaboration.

3.3 MCRN Annual Conference

Over 300 delegates have registered for the conference. The conference will include a mixture of presentations, parallel sessions and hot topics. There will also be an opportunity to network and browse various poster/exhibition stands. Registration has now closed but there is a waiting list. A poster from the CSG will go to the event. Conference feedback will be provided at the next meeting.

AP – Conference Feedback to be added to the next agenda (LP)

4.0 Consumer Matters

MS introduced WC to the group. WC outlined that her motivation for becoming involved in nephrology research related to her own experiences as a parent. WC joined the Nephrotic Syndrome Trust (NeST), as a volunteer, in 2006. One of the reasons for setting up NeST was to provide support to families. Since 2006, NeST has joined forces with other similar organisations world-wide, including France, Holland, Italy and the USA to form Nephcure International. NeST aims to support families, who are often confused by information provided on the internet. As well as participating in the Nephcure conference in Paris, 2006, WC has presented at a number of key meetings such as the ESPN. The group commended WC for her work to date and went on to discuss their

experiences of involvement at a local level. It was suggested that a database of parents who might like to be involved might be useful and that the Paediatric Nephrology Centres could possibly promote WC's organisation.

AP – List of Paediatric Nephrology Centres with corresponding Research Leads to be provided to WC (MS)

5.0 Update on Studies in Development

5.1 APPROVE Study (JD)

The study didn't secure HTA funding. There have been two subsequent publications within the same field of research which is a possible reason for the unsuccessful bid. One such study is 'RIVER', a large study looking at the incidence of renal scarring, with good pilot data. JD requested feedback from the group about whether pursuing the APPROVE study in its current form would be productive and whether both scarring and / or prophylaxis for hydronephrosis should be considered. It was identified that across the UK, there is not a standardised operating procedure for prophylaxis in such cases and in centres such as Newcastle who actively use antibiotics, it may be difficult to randomise in view of local practice. In Birmingham there is variation between clinical teams, with neonatologists introducing prophylactic antibiotics, which may then be increased by the urologists and subsequently stopped by the nephrologists. There is also variation in incidence data, with estimates ranging from 0.2 to 5% of all pregnancies. It was also suggested that the sample size and power calculations may need to be revisited given the large numbers, and the sub-group nature of the population. A pilot study should possibly be considered, particularly as radiology costs may be high. JD will seek further input from a statistician as the numbers may turn out to be the deciding factor in terms of feasibility. Ultimately, the group felt that the question was important but that the discussed factors would need to be looked into.

AP – JD to investigate feasibility

5.2 Efficacy and Safety of Rituximab in Nephrotic Syndrome in Children and Young Adults (reviewed October 2008) (MS & RM)

Guy's CTU have reviewed the protocol and have provisionally approved it. The study is a randomised, open labelled trial. Southampton has funding for a pilot involving 5-10 children at onset of nephrotic syndrome. The ethics form for this pilot has been completed and the study is currently being reviewed by immunologist Tony Williams. The group were supportive of this project, and suggested that there is a need to keep the ball rolling. It was suggested that a timescale / deadline may be beneficial, along with improved communication to collaborators. As this is area of research is a 'hot topic', it may be necessary to keep an eye on other trials seeking to answer the same question.

AP – MS to request a protocol from Ania to share with collaborators.

5.3 ARB Study (KT)

KT received a letter on 4 Aug 2009 outlining that the funding application for this study had been unsuccessful. The reasons outlined for this are as follows:

- It was unclear why the study was so expensive
- Inadequate involvement of CTU (Statistics were calculated by the ICH Statistician, rather than CTU)
- Insufficient Patient & Public Involvement (PPI)
- Sample Size too low
- Insufficient consideration / research into other similar studies taking place

The group discussed the project in detail. The group suggested that the issues raised be addressed and re-submitted with full CSG support. It was decided that this approach would be better than targeting EU funding, given that the need to include a minimum of three countries may result in difficulty finding a sponsor organisation. The group also discussed the Co-operate RCT; which was published by the Lancet and was subsequently retracted on the 10th October 2009 following an investigation into the meta-analysis data.

AP – KT to approach HTA regarding strategy for resubmission, and to address issues raised

5.4 Does Taurolock compared with Heparin reduce the Incidence of Catheter related Infections in Paediatric haemodialysis catheters: a Double Blind Randomised Control Trial (reviewed March 2008) – AP - Item to be carried forward to next meeting in Caroline's absence

5.4 C1q Antibody Study (CMT) – See later Agenda Item

5.5 Vitamin D (ergocalciferol) Supplementation in Children with Early Chronic Kidney Disease – a Multicentre, Randomised, Double-Blinded, Placebo-Controlled Study (reviewed March 2008) (ACHIEVE Study)
Single centre research involving ~70 children with 25D levels > 40 will be taken back to the HTA. 30% of end stage children have bone pain as an adult. The study is supported by the CSG. The group discussed whether there was a need to request feedback and reassurance regarding paediatric reviewers and processes. With regard to formulations work, it was noted that the oral delivery route, although unpleasant, is the current preferred method.

AP – ACHIEVE Study Protocol to be circulated to those who haven't received it previously (MS to contact Rukshana)

6.0 Update on Funded Studies

6.1 Nephrotic Syndrome (NW) – This has now been fully funded by HTA. The group congratulated NW and team for the success with this study, and are fully supportive in participating in recruitment etc. NW is waiting for final details from HTA regarding amount and starting date. MS suggested the data collection be done via RADAR.

6.2 Rare Disease Registry RaDaR (MS & CMT) – See later Agenda Item

7.0 Rare Disease Registry and Strategy (MS & CMT)

7.1 Strategy (CMT)

In 2007/08 an EC Action for rare diseases was introduced with subsequent UK government commitment to this strategy. Rare Disease UK continue to lobby the UK government about this issue. John Feehally, Charlie Thomson, Peter Mathieson, MS and CMT developed a grant bid to develop a registry in response to an MRC Cohort call. A strategy addressing rare diseases from all angles including care pathways and patient information was developed and presented at the BAPN meetings in March and September. The registry will utilise the same technologies as the UK Renal Registry. The UK Renal Registry is funded per capitation.

7.2 Rare Disease Registry (RaDaR)

The RaDaR website is almost ready to input data. The study is MCRN adopted and Ethics approval for the study is expected shortly. Two pilot studies will access participants via the registry and will be a useful test of the functionality of the project. All RaDaR participants will give written consent for their data to be included on RaDaR and to be contacted about future research opportunities. Patients will subsequently also consent to be part of those studies. RaDaR will provide patients with information and literature and relevant information will be released back to patients. It is planned that RaDaR will be officially launched at the Renal Association conference in May. Disease Specific Research Groups (DSRGs) will be established. The process for developing the DSRGs is currently being developed and needs to be standardised, open and transparent. MS is currently awaiting ethics approval for the first pilot study, Steroid Resistance in Nephrotic Syndrome (SRNS) which will involve FSGS patients. A second study, involving MPGN patients is currently being worked on by CMT. The group asked questions in relation to the ownership of data. It was explained that information will be available at more than one level, with access controlled dependent on need and type of data. Data may be used for instance in audit and distribution analysis, or may be retained by the research team. Authorship may possibly be based on patient contributions such as with the TWIST study. The group felt that robust operating

procedures and guidelines need to be established from the outset and that the pilot studies will be a useful test of the system and were very supportive of the project.

AP – MS to resend email about SRNS Site Specific Assessment to CSG members

AP – All to register for an IRAS account as necessary so that SSI Forms can be transferred (www.myresearchproject.org.uk)

7.3 C1q Autoantibody study

The C1q study, has, to a certain extent been overtaken by the work of the MPGN group in relation to the second RaDaR pilot study. Samples have been collected by a number of sites for this study. AF will be assisting with R&D Approvals that are still pending for this study.

8.0 Industry Matters

8.1 Alexion Trial (CMT)

CMT has been in conversation with Alexion Pharmaceuticals regarding the setting up of a phase II study. Alexion have requested that this is a single centre study and further details are to be worked out in the coming year.

8.2.1 Open Studies – MCRN026

This open label study is looking at the role of Losartan in patients under seven with hypertension. The study is running in three UK centres and has proved difficult to recruit to. A total of 100 patients are needed globally.

8.2.2 Open Studies – MCRN040 & MCRN041 Alexion – Eculizumab in aHUS

These studies aren't currently open to children but it was felt that there is need for research involving children to be undertaken. The costs of this treatment are very high ~250K.

8.3.1 In the process of adoption - SD075 - Takeda – TAK-491_109 PK

This is a single dose PK, safety and tolerability study in children with hypertension. As this is a liquid formulation, it is potentially suitable for all age groups. Revisions are being undertaken and the moment and it is anticipated that the study will run in the UK and US. Manchester, Great Ormond Street, Nottingham and Bristol will potentially be involved.

8.3.2 In the process of adoption – Takeda – Candesartan

The PDP application has been refused and it is unlikely that will proceed further.

8.4 Temporarily suspended study - MCRN006 (MK0954A-327) - MSD – Hypertension

MS has circulated the feasibility documents for this study and has emailed Andrew Rose. It was discussed whether items such as this should be circulated to all, with requests for an expression of interest. It was suggested that there may be a need for commitment rather than simply an expression of interest.

9.0 Any Other Business

9.1 Kids Kidney Research Study (NW)

This is a qualitative research study adopted by the MCRN looking at styles and methods of teaching dialysis methods and techniques to parents.

AP – Circulate poster in advance of December meeting

AP – This item to be added to the next agenda (LP)

9.2 Kids Kidney Research (KKR) funding (MS)

KKR are funding £100k a year for three years through the BAPN for therapeutic clinical research. This funding is potentially being topped up by KRUK making the total available £150k. The BAPN has encountered difficulties in

identifying a suitable project for this funding. MS asked the group to consider how best the £100k funding could be used in the future, suggesting that the CSG may be used to identify suitable projects. Providing that there is a robust formal process, the £50k supplementary funding may continue. Possible avenues for the funding may include parent networks or groups, pilot work and underfunded studies.

AP – MS to discuss with Neil Turner at KRUK, BAPN President and KKR

9.3 Appointment of new CSG Members

Two applications have been received from Paediatric Urologists who are keen to be part of the group. The candidates are Mr Mark Woodward and Mr P. Godbole. Input from current members will be sought regarding appointment.

9.3 RaDaR Walk-through

AP – This item to be added to the agenda for the next meeting.

AP – MS /CMT to provide additional information / walk through of web-registry system at next meeting

9.4 Attendance Expenses

AP - Laura Pilkington to circulate forms and information about claiming meeting expenses

10.0 Date of Next Meeting

To be confirmed - suggested three meetings per year. Members of the group were reminded to add availability to the Doodle page

Agenda Item	Action	Detail
2.0	Laura	Circulate review as per page 2 of previous meeting minutes [this action point was carried out in the first week of May 2009].
3.2	LK & MOG	To discuss cystagon/cystamine work undertaken in Newcastle (University of Durham) to explore possible collaboration
3.3	Laura	Conference Feedback to be added to the next agenda
4.0	Laura / MS	List of Paediatric Nephrology Centres with corresponding Research Leads to be provided to WC
5.2	MS	To request a protocol from Ania to share with collaborators.
5.4	Laura	Item to be added to next meeting agenda
5.5		ACHIEVE Study Protocol to be circulated to those who haven't received it previously
7.2	MS	To re-send email about SRNS Site Specific Assessment to CSG members
7.2	All	To register for an IRAS account as necessary so that SSI Forms can be transferred

9.1	NW /Laura	Circulate poster in advance of December meeting [actioned]
9.1	Laura	KKR Qualitative Study – Dialysis teaching to be added to the next agenda
9.3	Laura	To add RaDaR Walk through to the next agenda
9.3	MS / CMT	to provide additional information / walk through of web-registry system at next meeting
9.4	Laura	To circulate forms and information about claiming meeting expenses [actioned]