



UK Medicines for Children Research Network
(MCRN)

MCRN BAPN Nephrology CSG Meeting
6 March 2008, at Institute of Child Health, London


**National Institute for
Health Research**

Minutes

Attendees: Moin Saleem (Chair) - MS
Rodney Gilbert – RG
Kjell Tullus – KT
Simon Waller – SW
Manish Sinha – MS
Caroline Jones – CJ
Nicholas Webb – NW
Mark Taylor – MT
Alan Watson – AW
William van't Hoff – WvH
Jennifer Blakeburn - JB

Apologies: Jan Dudley
Sally Johnson

Welcome Introduction & Apologies:

Moin Saleem opened the meeting welcoming all in attendance to this first meeting of the CSG. MS welcomed Jennifer Blakeburn the MCRN, CSG Administrator.

Minutes of the Last Meeting:

The minutes of the previous meeting were approved as an accurate record.

MS gave a brief introduction to the MCRN Clinical Studies Groups. It was noted that MS was appointed as Chair of the CSG through an open and competitive recruitment process and a formal application process was conducted for the appointment of scientific members of which 11 applications have been received. It was confirmed that an official letter to all successful applicants will be sent from the MCRN Coordination Centre informing them of their term of membership. Membership was further discussed in terms of non medical members. It was noted that it is important for the membership to be inclusive but not too large as to cause a problem for meetings. It was noted that there have been developments in terms of non medicines paediatrics research within the MCRN but at the current time the remit of the network still primarily focuses on medicines. It was noted that members should try to gain funding for their travel to CSG meetings from their Trust in the first instance and as such members should provide the letter of confirmation to their Trusts to add this to their job description. If unsuccessful, travel expenses can be claimed from the MCRN. JB gave a brief presentation outlining the role and remit of the MCRN Clinical Studies Groups and the Study Adoption Committee.

JB also gave a brief introduction to the ERA-NET Project which is a European funded programme to identify research priorities within medicines for children. This work is being conducted in collaboration with the MRC and aims to conduct a Delphi style consensus questionnaire to identify key research priorities within medicines for children which will go to inform a trans-national funding call. CSGs will be required to identify research priorities within their specialty area.

Action Point: All CSG members to consider key important research topics within their specialty area of Nephrology and to inform JB of any European professional societies associated to Nephrology.

Working with Industry:

The group were informed that the MCRN has currently one Industry funded study within the field of nephrology running through the network and this has been very successful. It is expected that a large number of studies will come to the network as a result of the paediatric investigation plans required as part of marketing authorisations. In these cases the CSGs need to be reactive and responsive. The response time required for liaising with Industry is very tight. It was noted that the MCRN can also adopt investigator led industry funded research. It would be beneficial for any members of the group who are approached by the pharmaceutical industry on a consultancy basis to inform them of the network and the support that it can provide and put them in contact with Dr Andrew Rose, Industry Liaison Officer, based at the Coordinating Centre.

JB informed the group of the IMI initiative which is a European wide collaboration between pharmaceutical industry and public funding bodies in the form of private money from industry and public money from FP7 being used to fund research based on the priorities identified by pharma. The first call will take place around March 2008 but at this stage it is unclear whether nephrology topics will be included in this first call. The MCRN will keep a close eye on this initiative and identify the CSG if appropriate funding calls are made for this group.

Review of Ongoing Projects:

NEPHROTIC SYNDROME – PILOT STUDY

Nick Webb updated the CSG of the progress of the Nephrotic Syndrome pilot study which has been adopted by the MCRN. NW was keen to thank the group for their efforts to recruit to this pilot study which has recruited 50 patients, 3 of whom have dropped out of the study and are currently being replaced. The team are in the process of applying to Kidney Research UK to increase recruitment to the study to a further 160 patients. They hope to be successful in this application. It was noted that the LRN teams made a huge effort to set up sites and get them up and running as promptly as possible. The research team are making an additional application to the NIHR HTA as a fall back should the application to KRUK be unsuccessful. It was noted that it would be very beneficial for CSG to officially support this application. MT raised a potential conflict of interest as he sits on the panel for Kidney

Research UK. It was noted that the CSG would need to ask if this was considered as a conflict of interest as he now sits as a CSG member.

Action Point 2: MS to write to Kidney Research UK to find their opinion on this potential conflict of interest.

Action Point 3: JB to send declaration of interest documents from the MCRN to CSG members.

Review of Proposed Projects

ARB/ACEi

Kjell Tullis presented an update on his study ARB/ACEi he plans to submit this application to the HTA in January, however there were still outstanding issues to discuss with the CSG. It was noted that most centres are happy to participate in this study once issues have been resolved.

KT raised a number of outstanding issues to discuss with the CSG members including centralisation of measurements of albuminuria and/or proteinuria, feasibility data and estimates of drop out rates, costs of the study and necessary expertise of the research team. It was recommended that a pilot study is conducted to clarify the issues in terms of current practice within the UK and its influence on recruitment. It was suggested that KT seeks advice from a Clinical Trials Unit on methodology, design etc. With acknowledged CSG support, KT will be eligible to contact Prof Paula Williamson at the MCRN CTU to request support.

Further discussion centred on the toxicology of the drug and potential drop out rates. It was felt that long term follow up could be conducted through the renal registry and this should be built into the study for data collection. The group concluded that the CSG will support the registration and will be involved in further developments.

Action Point 4: Kjell Tullis to consider conducting a pilot study of approximately 20 patients to look for side effects toxicology and drop out rates.

Action Point 5: All members to describe their current practice to Kjell to inform his study design.

TAUROLOCK STUDY

CJ informed the group that the decision has been made not to consider the inclusion of alteplase in this study. It was noted that Taurolock is not licensed for the use of children and will need to be prepared on site. 1 – 2 units have expressed that they will not participate in the study. It was agreed that the study will need interim assessment and support from a

Clinical Trials Unit for advice on costings. The statistician suggested that the study may be underpowered and interim assessment will be required. It was felt that to get 50-60 new lines, the study will need to recruit from most of the large centres in the UK and therefore to move forward the research team will need names and numbers from sites who are willing to participate to identify if enough support is available to conduct the study. If not the study design will be reconsidered, potentially to include alteplase. This study has the support of the CSG for further development.

Action Point 6: CJ to complete working up the study protocol and to cost based on the current study design. She will need to conduct a feasibility assessment to identify approximately the number of new lines which were put in, in the last year in the key sites.

THE UTI NICE TRIAL:

Following initial discussions in which it was suggested that recruitment would be difficult for this study, it has been decided to recruit through Microbiology Department, in which a letter for recruitment for the trial will be issued at the same time as a report on positive microbiology. It has taken a lot of leg work to get all key players within one area on board for this study and therefore, is likely to be unachievable in more than one centre. The plan is to take this study to the HTA for funding. The group felt that the study would benefit from a comparison of two regions and suggested that Liverpool or Glasgow may be able to develop the links to conduct this study. However, there are no trainees to do the initial work, but both of these centres have good populations and infrastructure. This study has the support of the CSG for further development.

CIQ ANTIBODIES

It was noted that this study needs local R&D approval for data collection. So far MT has not received approvals from local R & D departments. The group fed back their progress on gaining approvals in their centres and it seemed likely that at least one site would gain approval in the very near future.

William van't Hoff informed the group that for medicines studies it is the role of the MCRN Local Research Networks (LRNs) to assist research teams on achieving local approvals. The SENCE LRN in London are currently working to the target of gaining approvals within 3 days and this is monitored with a traffic light system. Although all LRNs are working in different ways it was noted that Manchester is also very good at obtaining approvals in a very short time frame. This will further be assisted with central sign off, or CPS.

USE OF TRIMETHOPRIM IN THE PROPHYLAXIS OF URINARY TRACT INFECTIONS IN BABIES BORN AFTER ANTENATAL RENAL PELVIS DILATION:

The study has been developed in partnership with Alastair Sutcliffe and has been circulated to the General Paediatric CSG for comment. The plan is to make an application to the NIHR in May and the study will be a double blind randomised controlled trial with babies

recruited on postnatal wards to be randomised to trimethoprim or placebo until further investigation of their urinary tract infection has been completed. There will be an opportunity to opt in to a DNA database. It was suggested that the study should exclude grade 1 and 2 reflux which may contaminate the data. If the researchers don't want to exclude this they will need to stratify. It was suggested that Mike Sharland, Chair of the Allergy and Infection Immunity CSG should be asked to advise on this study. Many issues relating to resistance to antibiotics were discussed. Some concern was also expressed that the proposal to identify potential recruitment through ultrasound of pregnant mothers may cause further anxiety at an ordinarily distressing time. This study has the support of the CSG for further development.

Action Point 7: It was recommended that the researchers contact Jonathan Craig to find out why the Australian study failed to complete

VITAMIN D STUDY:

It was noted that the prevalence of vitamin D insufficiency and deficiency in children with chronic kidney disease is common and that Vitamin D insufficiency and deficiency is associated with CKD-MBD. Vitamin D supplementation (ergocalciferol), as suggested in the guidelines will have a beneficial effect upon CKD-MBD (mineral and hormonal metabolism, bone health and extra-skeletal calcification). The aim of the study is to determine the prevalence of vitamin D insufficiency and deficiency in Scottish children with CKD and to investigate differences in bone mineral and hormonal metabolism, bone health, bone turnover and markers of extra-skeletal calcification between those with and without hypovitaminosis D. The CSG were very supportive of this study. Comments from the group included the following: This study would require research nurse time, approximately 3 days per week, which should be included within the grant application. There is potentially a communication issue in terms of the samples being sent from the study site to GOS for analysis and GOS being required to inform the site when the dose needs to be increased. It was suggested that the serum could be frozen and stored until all samples can be forwarded to GOS for other assays. It was suggested that the upper limit for GFRs should be 90.

Action Point 8: The research team should present the final proposal at the next CSG meeting

Funding Opportunities:

The group were informed of upcoming funding opportunities which include NIHR Invention for Innovation and NEAT which is for new and emerging technologies. The group were reminded of the academic training programmes which were available at all levels. It was suggested that the BAPN could offer registry fellowships for a Paediatric Nephrology Registry. This could be advertised on the BAPN forum and linked with a training grant. This

should be disseminated through the trainees group and if an enthusiastic individual is found the CSG will provide their support to the application.

Registries:

The group agreed that registries are difficult to run and even more difficult to gain funding and develop the infrastructure needed for a registry to be successful. There is a need for one place for all rare diseases to be registered and the best place is alongside the UKRR. This is not funded as a research outfit and would require additional funding. It was noted that the MRC Cohort Grant offers £1/2M for 3 years. Similar applications can be made to KRUK for disease registries although this funding is short-term. If the infrastructure is developed correctly, such a registry should be self propelling after 5 years, and would make the UK a good partner for EU funding. WvH informed the group that he is involved in the EU funded 'EuNephron'.

Any Other Business:

AW informed the group that he has a quality of life study in mind. QoL questionnaire are used widely and successfully in adult nephrology. A tool has been developed by a colleague of AW for service evaluation.

Action Point 9: AW to circulate QoL assessment tool to the CSG members.

It was agreed that the BAPN website should be used more. The CSG minutes and links to the MCRN website should be added to the BAPN website.

Date and location for next CSG meeting:

Thursday 16 October 2008 (venue to be confirmed)