

## **NCRI Translational Research Clinical Studies Group**

A proposal to establish a Translational Research Clinical Study Group was submitted to and accepted by the NCRI Board in February 2005. This recognised the increasing interest in the biological evaluation of patients involved in clinical trials. Until recent years this type of work has had a relatively low priority but the potential for biological analysis to allow a personalised or tailored approach to medicine and also to identify mechanisms of response and resistance to therapies and thereby identify new targets for intervention has now become widely recognised. It is therefore expected that nearly all trials in the NCRI portfolio will be accompanied by or have integrated into them some form of TR. While there was some interest and expertise in TR on most, if not all, of the CSGs this was very variable between the groups. There are many aspects of TR that are common to its conduct across all tissue sites, indeed this underpins the view of targeting therapy to molecular defects rather than organs of origin. These aspects include analytical platforms (e.g. immunohistochemistry, image analysis, expression microarrays), tissue preparation/collection, informatics, statistics, research governance, ethical frameworks, funding and national relationships with bodies such as NCRN.

### **Remit**

The overall goal of the TCSG is to enhance the value of TR conducted within the NCRI portfolio of trials. It aims to do this by creating an information exchange between the TR experts in each of the CSGs and to allow an interaction with other national bodies with a strong interest/role in TR in cancer in UK. The membership is therefore largely composed of one representative from each of the CSGs (a reserve is nominated in case of non-availability of the primary member). The Head of OnCore UK is an *ex officio* member and senior representatives from DoH, NCRI, TRICC, and NCRN attend the meetings. Two consumer representatives have a particular challenge in understanding some of the more technical language of TR but they are mentored by selected members and are important to the Group for their perspective and guidance on many matters.

The work to be undertaken by the Group is separate from early (phase I/II) drug development that is also considered as Translational Research (TR) in some quarters although cross-membership with the Cancer Research UK Phase I/II Committee allows common interests to be considered.

The Group does not, unlike the CSGs, take responsibility for the portfolio of TR in UKs clinical trials: it was felt that the integration of TR into individual trials needed a broad assessment within the CSGs that took note of the specific context and gaps and potential conflicts within the groups portfolio. An important activity of the Group is to identify issues of major importance that merit workshops and to organise such workshops to be available to the membership and, where appropriate, other interested parties.

### **Activities**

The Group has established a particularly close interaction with the Cancer Research UK Translational Research in Clinical Trials Committee (TRICC) with the Chair of the TCSG being an *ex officio* member of TRICC. Outline applications submitted to TRICC are sent to selected members of the TCSG for comment. This level of interaction allows members of TCSG to report to their parent committee on general issues related to the submission and funding process (eg common areas of strength/weakness in proposals). Joint strategic meetings to consider single matters of importance have been convened between TCSG and TRICC (see below).

The Group has met 3 times. The first was in May 2005 when there was general discussion of the Group's goals and the ways of achieving these. For the TCSG that is not responsible

for a portfolio of trials different measures of success are needed from those applying to other CSGs. Suggestions included the successful creation of a national database containing information on tissue resources linked to clinical trials: the funding of (some) TR in CSGs that were not currently active in this field; the quantity and quality of workshops organised by the Group; the development of guidance notes for various issues of importance.

A presentation was made on behalf of Dr Clark, Head of OnCore UK, who has the responsibility for creating a national cancer tissue resource that facilitates TR. This summarised Dr Clark's consultation process to date. It became clear in this first meeting that a close interaction with OnCore UK would be very helpful and would therefore be invited to be an *ex officio* member. The funding process from TRICC was summarised and clarified as supporting both the collection of tissues from CTAAC approved trials and to support research on tissues that had already been collected. The generally poor understanding of the statistical requirements for good quality TR was noted and Professor Altman was invited to present at the Group's next meeting. It was noted that a survey of tissue collections in Cancer Research UK supported centres was being undertaken by Cancer Research UK and it was felt this might underpin the goal of creating a comprehensive national database.

The second meeting was in October 2005. Major items included discussion of the development of Experimental Cancer Centres that would replace and extend the centres previously supported under NTRAC. A standing agenda item of reports from the CSG representatives was established. Professor Altman's presentation on statistics in translational research led to the agreement to develop a programme for a one-day workshop on the various issues of design needed to be considered for good quality TR. Dr Clark presented his business plan for OnCore UK which was recognised as interacting with the TR component of CSG to a greater degree than many had expected: the major basis of the collection would be from all participating patients in NCRN-supported clinical trials conducted within a selected network. This would be piloted in 4 networks with a view to comprehensive coverage of the national portfolio if the initial outcome was positive. Agreement was reached that collections which were being made for specific trials within a network would not be targeted by OnCore UK.

The third meeting was in April 2006. It was agreed that several of the action points from previous meetings had not been completed and that the committee needed to agree to focus on high priority achievable aims. The issue of generic consent across trusts was agreed to be important as a means of easing the pursuit of TR both within and outside clinical trials. Professor Collins undertook to chair a working party to provide recommendations on this issue. The industry link with NCRN was described and it was agreed that presentations from industrial colleagues would be valuable for the group and this would be organised for the second 2006 meeting. Interactions with TRICC were discussed in detail by virtue of the attendance of the meeting by the Chairman of TRICC. The goal of establishing a National Cancer Clinical Trials Tissue Resourcing Database was debated and it was agreed that this would be progressed under the auspices of Cancer Research UK and OnCore UK. It was agreed that a meeting on new technologies for TR should be organised jointly with TRICC at the NCRI national meeting. (This was subsequently found not to be feasible and instead a one-day stand alone meeting will be undertaken in December 2006).

### **Meetings/Workshops**

The first stand-alone workshop organised by the group was undertaken in Oxford in May 2006 on the subject of Design of Biomarker Studies in Clinical Trials. Presentations were made on several issues including statistical powering, reporting of studies and quality assessment. It was attended by c.80 scientists, clinicians and administrators. It was felt to be a highly successful meeting with multiple requests for slide sets from the speakers. The

success may be assessed by the acceptance by ASCO of this topic to be in their educational programme in their annual meeting in 2007.

The chairman of the TCSG attended the September 2005 meeting of the NCRI Subgroup on Clinical and Translational Research and will attend meetings annually henceforth. He also presented to the Cancer Research UK Clinical and Translational Research Committee in April 2006. This has allowed these committees to be appraised of strategic concerns and/or activities of TCSG.

### **Membership changes**

A particular challenge for the Group is the maintenance of appropriate expertise when the membership is constituted by representatives from the CSGs. As such gaps may occur and it has been recognised that this has been the case with no representative to speak to the role of PET imaging. As such we are pleased that Dr Eric Aboagye has agreed to join the group.

In summary, the Group appears to be fulfilling an important co-ordinating role in the strategic development of TR in NCRI clinical trials. Over the next year we aim to hold further workshops on matters of particular importance and to work with CRUK and OnCore UK to develop a fully functioning National Cancer Clinical Trials Tissue Resourcing Database. It will also set out to develop guidelines in key areas such as the access arrangements to tissue collection from trials.

Professor Mitch Dowsett, Chair