

## **NCRI Translational Clinical Studies Group**

### **Introduction**

The overall goal of the Translational Clinical Studies Group (TCSG) is to enhance the value of translational research conducted within the NCRI portfolio of trials. The TCSG aims to deliver this by creating an information exchange between translational research experts in each of the CSDGs and to allow an interaction with other national bodies with a strong interest/role in translational research in cancer in the UK and abroad. Over recent years the priority has markedly increased as the potential has been recognised 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.

Randomised clinical trials sometimes provide the only opportunity to ask translational questions regarding efficacy and even when the randomisation is not essential for addressing a particular question the comprehensive collection of clinical data in a consistent and high quality fashion still makes them the preferred setting for conducting translational research in most cases. It is therefore expected that nearly all trials in the NCRI portfolio will be accompanied by or have integrated into them some form of translational research.

The degree of expertise in translational research is very variable between the CSDGs and one role of the TCSG has been to support and foster the aspirations of the groups that have been less active.

There are many aspects of translational research that are common to its conduct across all tissue sites. 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. The TCSG performs a role of exchanging information on the technologies and influencing national policies and tries to ensure that the activities of one CSdG can assist and do not have to be replicated by others. Similarly, information is exchanged and activities coordinated with representatives of the Experimental Cancer Medicine Centre enterprise.

The Group had their first three year progress review in February 2009. A summary of the strengths of the Group and the issues it needs to address can be found in Appendix 1.

### **Membership and structure**

The membership is largely composed of one representative from each of the CSDGs (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, ECMC and NCRN attend the meetings. Three consumer representatives are important to the Group for their perspective and guidance on many matters.

Professor Dowsett was appointed to a second 3-year term as Chairman in July 2008.

The TCSG's activities and proposals for changes in structure were subjected to external peer review during the first part of 2009. The proposals and outcome of the review are discussed as the final part of this report. A summary of the strengths of the Group and issues the Group need to address can be found in Appendix 1.

### **Portfolio and accrual**

The TCSG is not the custodian of the translational research within the NCRl portfolio, rather, it is felt important that the individual CSDGs should take that role to ensure that the research is embedded into the trials with a clear view of the disease context. However a record of the trials from each CSDG is tabled at each meeting and highlights and difficulties identified for discussion, advice and resolution.

### **Trials in development**

Details of translational research currently held by the Secretariat and can be obtained from them.

### **Meetings**

Two meetings have been held over the last 12 months. Selected major issues are summarized below.

An important item through the year has been for members to participate in the NCRl Pathology and Research Task Force and for TCSG meetings to consider progress from that Task Force that was instigated largely as a result of the Group's expressed concerns. The Task Force identified 3 key priorities:

- the rejuvenation of histopathology research,
- a framework for sustainability and
- greater recognition of pathology research.

A series of recommendations to address this have been developed and the report will be formally launched to coincide with the NCRl conference in autumn 2009. The TCSG were pleased to note that a revised remit for OnCore UK includes the provision of the support needed to bring many of these recommendations to fruition.

In parallel with the Task Force's activities a TCSG working party under Professor Collins chairmanship is addressing the issue of costs and reimbursement of the costs of Pathology departments' supporting clinical trialists' requests for their support.

The working party worked with Cancer Research UK in the development of a Biomarkers Roadmap to guide investigators and funders in the steps needed to take a new biomarker from concept to clinical practise in each of several clinical settings. This culminated in meetings to launch the Roadmap in Leeds and then a further focused meeting with the Cancer Research UK Late Phase Forum.

Funding has been provided by NCRN for a part-time project officer to work with the TCSG and OnCore UK to create a tissue resource database that investigators can search for appropriate materials to address specific research questions. The development of this is underway in collaboration with the NCRl Informatics Initiative and launch of a usable database is targeted for end of 2009.

The Group has been kept informed of and been able to comment on developments in tissue banking and consent particularly in relation to OnCoreUK and the Confederation of Cancer Biobanks. The contributions of the consumer representatives as always have been particularly valuable in these considerations.

The Group participated in the Translational Technology in Clinical Trials meeting organised by Dr Green in November 2008 in collaboration with the ECMC and EORTC. A session has been granted to the TCSG at the NCRI meeting in 2010.

**Other activities**

The TCSG regards its interaction with the Cancer Research UK TRICC (now BIDD) as an important component of its activities. This is discharged by comment by TCSG members on outline applications to TRICC (BIDD), by the TCSG chairman's *ex officio* membership of TRICC (BIDD) and by membership of the TCSG by TRICC officials allowing a high level of information exchange. TRICC (BIDD) strategy may be influenced by TCSG and the importance of changes in that strategy may be fed through members to their respective CSGs.

An improved upwards route of communication has been achieved by the Chair becoming an *ex officio* member of the NCRI Board Clinical and Translational Subgroup.

**3-year strategy**

During the last 12 months the TCSG has reviewed its structure and made proposals for change that should best allow the discharge of its goals as summarised in the introduction. These proposals were concluded after widespread consultation including the TCSG meetings and the NCRI CSG Chair's Forum. The issues and proposals are summarised below.

A key aim of the TCSG has been to ensure strong communication between the TCSG and individual CSGs with information exchange in both directions. A TR representative was therefore appointed from each CSG and these representatives have formed the main membership of the TCSG. Other membership is largely *ex-officio* from several interested parties and consumer representatives.

The TCSG was felt to have had a number of successes including:

- creation of NCRI Task Force on Pathology and Research
- influence on the Carter report
- organisation of well attended external meetings on TR methodology and technology
- winning support from NCRN for creation of a National Clinical Trials Sample Database
- consultation and influence on TRICC strategy
- consultation on universal consent form
- networking between the TR representatives
- encouraging the set-up of TR sub-committees for the individual CSGs

There were however a number of weaknesses that needed resolution to allow the TCSG to be as effective as it would wish.

These included:

- variable expertise and involvement of CSG representatives
- vulnerability of the group's expertise from the limited appointment of members to their respective CSG

- limited expert coverage of the multiple disciplines that constitute TR
- inadequate meeting time to for the multiple issues that require a level of detailed discussion for meaningful and for authoritative recommendations to be made.

It was proposed that a structure be developed that would in part be separated from membership of CSDGs. This would allow selection of committed individuals from across the UK with expertise across TR; their membership could be assured over a given period (at least 3 years). Such membership would support the development of subgroups technologies, bioresources and imaging to be the “workhouse” of the Group.

Thus the proposed new structure was to include representatives from those CSGs with the most active TR programmes (n=6 to 8) and derive the remaining 10 to 14 by response to advertisement. Identification of the 6-8 CSGs with representatives on TCSG could be according to those with active TR Subgroups (Brain, Breast, Colorectal, Gynae, Lung, Melanoma, Radiotherapy), those with the greatest number of on going TR projects and/or the views of the respective CSDG chairmen.

It was felt that the major emphasis of the TCSG on issues relevant to TR in clinical trials should remain because of the generally greater value of TR conducted in those circumstances and the special demands that such TR has. As such communication with all CSDGs should be maintained. This might be achieved in one direction by the CSG chairman or their TR representatives requesting the TCSG to consider particular issues and in the other direction by an abridged set of TCSG minutes for the CSDGs drawing attention to issues of particular relevance.

These proposals were debated at the 2009 external review of the TCSG.

### **2009 Progress Review of TCSG**

The TCSG were congratulated on their achievements to date there having been “undoubted and invaluable progress”.

It was felt that the Groups’ proposals for change were sound and would help improve its contribution further. There should be consideration of the possibility that the group might take on a more strategic role in the conduct of translational research across the UK but subsequently it was concluded that while the strategic positioning of the various groups involved in oncological translational research in the UK should be reviewed, it was impractical for the TCSG to fulfill both its important, largely operational role as well as becoming more strategic.

On this basis the TCSG meeting of May 2009 was the last under its present structure and advertisements for interested members to form the modified structure were placed in the middle of 2009. Advertisement has been completely open with the view taken that facilitating interactions with the CSDGs be a consideration that could be included during the appointments process. Over 40 applications have been received and appointment to the revised structure is expected during Q3 2009.

Professor Mitch Dowsett, Chair

## **Appendix 1**

### **Key strengths and issues from the Progress Review, February 2009**

The key strengths of the Group identified at the February 2009 review were:

- Invaluable progress since the Group was set up.
- Leadership shown by the Chair and senior members of the team.
- Providing expertise and perspective in translational research.

The Panel identified the following issues which the Translational CSG needs to consider:

- Feeling that their expertise is under-utilised.
- Having responsibility for selecting its own membership.
- Not being well placed to assist in the determination of natural strategies or priorities.
- Expanding the Group's remit to take a more formal and influential role by setting strategies and prioritising translational research across the CSGs.
- Considering the most appropriate structure for a group with a more expanded remit.
- Considering who from its existing members and external bodies might informally strategise on a way forward.
- Identifying questions of high priority and forwarding these to CSGs for discussion and development into studies.
- Continuing the education and training work stream.
- Putting on hold the restructuring suggested in the Group's report until its new remit has been clarified and agreed.