

## **NCRI Head and Neck Clinical Studies Group**

This year has been a combination of renewal and some disappointment.

### **Portfolio and accrual**

The disappointment was centred around MARCHON, which had been funded by CTAAC in 2004. Because of the difficulties in securing a supply of the radio sensitizer Nimorizole, the funding was reviewed by CTAAC and a decision to withdraw it was made. This left the Group without a major trial in advanced head and neck cancer. This was a major disappointment and as yet a replacement has not been identified.

The other trials in our portfolio have made slow but steady progress during this year. Details are given in the table below.

The ongoing projects within the Head and Neck CSG include CHARTWEL (S Dische/M Saunders); a randomised controlled trial of CHARTWEL (a continuous hyper fractionated accelerated radiotherapy schedule) versus conventional radiotherapy in post-operative head and neck cancer patients. This study is in the follow up phase as it was closed last year.

The EaStER feasibility study (M Birchall) - this study is the prequel to a potential large phase III trial to compare the outcome of patients treated with either endoscopic excision or standard radiotherapy for early glottic cancer. Outcome measures are in terms of voice quality, quality of life, and local control.

PARSPORT (C Nutting) – This is a centred randomised trial of parotid sparing intensity-modulated radiotherapy in patients with head and neck cancer. This trial continues it's slow reccrual. However, it is an extremely important trial for the application of IMRT in head and neck cancer planning.

HOTTER (C Nutting) – a trial of hyperbaric oxygen in patients with head and neck cancer with osteoradionecrosis. An outline submission of this trial was accepted by CTAAC and a full submission is being prepared.

HiLO (J Franklyn) – a comparison of two administered doses of 131-1 (with or without rhTSH) in thyroid remnant ablation post-total thyroidectomy for thyroid cancer. The HiLo trial has been approved by CTAAC as a factorial study. There has been delay in progressing and launching the trial because of withdrawal of funding for rhTSH by Genzyme. Alternative sources of funding have been sought including the Department of Health Subvention Scheme and CRUK, without initial success. This is being pursued with individual participating Trusts R&D departments. Sufficient centres have found local sources of funding to allow finalisation of the protocol and completion of applications to COREC, MHRA and ARSAC. A launch date, planned for June incorporated feedback from centres beginning to recruit at that time. An important aspect of the HiLo trial is development of a translational component; a draft application to TRICC to support collection of patient samples is underway.

Several other proposals have been submitted to CTAAC. A proposal for a randomised trial investigating the role of radiotherapy in intermediate risk head and neck cancer post operatively, was unfortunately rejected. Two other proposal looking at a phase I/II study of Docetaxel and RAD001 (Everolimus) in advanced/recurrent or metastatic squamous cell carcinoma of the head and neck (this study incorporates important translational research) (DORA C Boshoff), and an assessment of modification of tumour invasion by 3-hydroxy-3-methylglutaryl co-enzyme A reductase inhibitors in operable head and neck cancer (MOTORCAR K

Harrington) were submitted as outlines. This proposal was accepted for full application by CTAAC and a resubmission was requested for the former. These studies have been reviewed by CTAAC. We are hopeful that we may be able to proceed with them within the next year.

The current percentage of patients with head and neck cancer recruited into NCRN trials has risen to 1.4%.

### **Progress review**

The Group had a Progress Review in June 2005. The key strengths of the Group and the issues, which the Group needs to address, identified by the Progress Review Panel are included as an appendix.

### **The Thyroid Sub-group**

The Sub-group will maintain its major commitment to successful completion of the HiLo trial, including a translational element.

The recent creation of the Thyroid Sub-group, in conjunction with the imminent publication of updated UK guidelines for thyroid cancer management, is providing impetus and a forum for development of other studies. The sub-group is keen to facilitate development of trials of new therapies in radioiodine resistant metastatic disease. They propose to consider development of on-going small scale trials of novel agents, which might include pegylated anthracycline or B raf kinase inhibitors. The sub-group aims to develop means of addressing clinical controversies e.g. the extent of surgery for small carcinomas (<2cm), role of dosimetry in comparing absorbed and administered doses of radioiodine and the role of external beam radiotherapy. The establishment of the agreed national dataset for thyroid cancer will prompt retrospective and prospective cohort studies of outcome and definition of additional markers of prognosis.

### **Membership**

As part of the renewal of the group at the end of its latest three year phase a number of changes were made in its membership, including the appointment of a new chairman, Dr Chris Nutting. We are hopeful that he will take head and neck cancer research in the UK forward in his usual highly effective fashion. We wish him well. Following the peer review, we have strived to broaden the representation on our group by the appointment of oncologists with an interest in translation research and innovatively a relevant representative from the Pharmaceutical Industry. We are hoping that this will allow us to broaden our portfolio further. 7 new members joined the Group and 9 members left the Group.

### **Three year plan**

The Group's three year plan is to -

1. To improve consumer partnership through consultation and collaboration. We are very grateful for the input from J. Sharplin, J. Bramall and E. Culling into this proposal. The consumers are very keen to provide added value to project development.

They wish to be involved from an early design stage and suggest that a designated representative be attached to each research project.

They would encourage us to provide training to improve their background knowledge and thus their confidence to provide comments regarding trials.

They regard it as a priority to agree ways to improve communication between professionals and consumer representatives so that they can make comments and receive feedback on an ongoing basis.

Once this has been developed they have produced a number of proposals, which will enable consumers to be able to exert real influence on the design of new clinical trials. We are most grateful for their efforts in this area.

2. Development of a broad portfolio of studies/trials, which incorporate important translational elements and, which look at a broad range of areas. One of the major areas we wanted to drive forward in the last three years has been the incorporation of surgical studies into our portfolio. In the next three years we would anticipate significant surgical trials to be in place.
3. New translational and basic studies will be developed as described, e.g.: MOTORCAR and DORA to improve our links with the pharmaceutical industry and new drug development.
4. We plan to encourage direct links with the pharmaceutical industry as seen by our appointment of an appropriately trained representative to the CSG. A pharmaceutically supported study in head and neck cancer is currently in the process of being submitted to CTAAC for consideration of adoption.
5. We will develop more studies, which will incorporate quality of life issues in their outcome measures. To this extent new appointments to the CSG will facilitate this process.
6. We will continue to develop studies evaluating the role of IMRT in the treatment of head and neck cancer.
7. We will plan and activate a major randomised trial in the treatment of locally advanced head and neck cancers. This remains a major challenge to the CSG.

**To summarise**

All these studies will have significant translational components. We have clearly demonstrated the ability of the group to develop a satisfactory translational component in the successful funding for the since abandoned MARCHON trial.

I am confident that we have a broad range of expertise on the new CSG and expect the new chairman to lead us into a wide ranging portfolio. It is also extremely important that these are implemented in the networks, which is a challenge for the relatively rare cancers. Regular networking meetings will be required in order to achieve this.

**Head and Neck Group Portfolio**

<b>Acronym</b>	<b>Title</b>	<b>PI(s)</b>	<b>Status</b>
MARCHON	A randomised 3 arm trial of modestly accelerated radiotherapy alone or with either synchronous nimerazole or synchronous cisplatinium chemotherapy	M Robinson	Closed
CHARTWEL	a randomised controlled trial of CHARTWEL ( a continuous hyper fractionated accelerated	S Dische M Saunders	Closed/follow up phase

	radiotherapy schedule) versus conventional radiotherapy in post-operative head and neck cancer patients		
EaStER feasibility study	this study is the prequel to a potential large phase III trial to compare the outcome of patients treated with either endoscopic excision or standard radiotherapy for early glottic cancer	M Birchall	Open
PARSPORT	This is a multi-centred randomised trial of parotid sparing intensity modulated in patients with head and neck cancer	C Nutting	Open
HOTTER	a trial of hyperbaric oxygen in patients with head and neck cancer with osteoradionecrosis	C Nutting	Proposed
HiLo	a comparison of two administered doses of 131-1 (with or without rhTSH) in thyroid remnant ablation post-total thyroidectomy for thyroid cancer.	J Franklyn	Open
DORA	a phase I/II study of Docetaxel and RAD001 (Everolimus) in advanced/recurrent or metastatic squamous cell carcinoma of the head and neck. This study incorporates important translational research.	C Boshoff	Proposed
MOTORCAR	an assessment of modification of tumour invasion by 3-hydroxy-3-methylglutaryl co-enzyme A reductase inhibitors in operable head and neck cancer. This proposal was accepted for full application by CTAAC.	K Harrington	Proposed
SEND	The role of elective neck dissection in patients with early oral squamous cell carcinoma.	I Hutchison	In Set-up

Dr Martin H Robinson, Chair

## **Appendix 1: Key strengths and issues from the Progress Review, June 2005**

### Strengths:

- The Group have developed needed, and in a number of instances, innovative studies.
- The Group are open and inclusive
- The Group have attempted to engage the wider community and are making every effort to progress with this
- The integration of translational and clinical research, as exemplified not only by MARCHON-TRANS but other examples alike is seen as strength.

### The Group needs to consider:

- Encouraging more energetic younger members of the research community to join the Group
- Extending the membership to include additional medical oncologists and health professional expertise
- How best to ensure that individuals outside the Group engage with CSG members at an early stage
- Confirming and strengthening relationships with the EORTC and USA
- Developing a joint study of palliative chemotherapy with the Palliative Care Clinical Studies Development Group
- Establishing a clear route through which new agents for Head and Neck cancer can be identified and appropriate “feeder mechanisms” put in place
- Developing a PET study and studies in other areas such as chemoprevention, secondary prevention of secondary tumours or new primaries and early diagnosis
- Developing a significant study in advanced or recurrent disease
- The relevancy of the drug proposed in the MARCHON study
- Developing studies using novel agents developed on new molecular targets or other innovative agents emerging from molecular concepts of tumour growth inhibition, anti-angiogenesis
- A detailed time frame for developing a range of studies covering important issues in the treatment of all stages of Head and Neck Cancer Research UK