

## **NCRI Brain Tumour Clinical Studies Group**

There are 3 trials currently open in the Group's portfolio and 2 are in set up. The Group is currently actively recruiting into the BR12 trial, which is comparing the efficacy of Temozolomide against PCV (Procarbazine, CCNU, Vincristine) chemotherapy in chemo-naïve patients with recurrent malignant glioma (with so far over 200 patients randomised). The trial is also examining the question of Temozolomide dosing (high dose – 100mg/m<sup>2</sup>/day for 21 days versus conventional dose 200mg/m<sup>2</sup>/day for 5 days every 28 days). A translational study linked to the BR12 trial was approved at the June 2006 TRICC meeting.

The BR11 trial run in collaboration with EORTC (EORTC 26951), which looked at the role of adjuvant PCV chemotherapy in patients with highly anaplastic oligodendroglioma, closed in 2003. The results were reported in 2005 and show no survival benefit for adjuvant chemotherapy. The Group is also collaborating with the EORTC on a randomised trial examining the role of whole brain radiotherapy after resection or radiosurgery for patients with 1-3 brain metastases although the accrual is poor.

The principal trial in development (BR14/TATA trial), approved by CTAAC, is aiming to examine the role of chemotherapy in patients with anaplastic astrocytoma (non1p,19q deleted anaplastic glioma). Following the results of EORTC trial of adjuvant and concomitant Temozolomide (with radiotherapy) in the primary treatment of glioblastoma, which show a survival benefit for chemotherapy; other tumour types need to be studied. The planned TATA trial, developed in collaboration with EORTC, RTOG and NCIC is a randomised 2x2 factorial trial design examining the separate roles of concomitant and adjuvant Temozolomide in patients with anaplastic astrocytoma. This may help in defining which of the two components of the previous empiric trial is the principal contributor to the survival benefit. The trial is also aiming to also assess the prognostic value of MGMT methylation. A phase III study comparing conventional Temozolomide with dose intensive Temozolomide in patients with newly diagnosed glioblastoma has recently been approved by CTAAC.

The Group is collaborating on the development and implementation of two brain metastases trials. The OSCAR trial developed with the Radiotherapy Group is assessing the role of radiotherapy in poor prognosis patients with multiple brain metastases from non-small cell lung cancer and will randomise patients between best supportive care and whole brain irradiation. The TACTIC trial developed in collaboration with the Lung group is assessing the value of Erlotinib (Tarceva) in addition to whole brain radiotherapy using a randomised phase II trial design in patients with inoperable brain metastases from non-small cell lung cancer. Both trials have been approved but not yet activated at the time of writing. The Group has joined the EORTC in the development and implementation of a low-grade glioma trial, which compares Temozolomide versus brain irradiation in patients with progressive grade II astrocytomas, oligodendrogliomas and mixed tumours (EORTC 22033 – 26033). The NCRI adopted multicentre trial of neoadjuvant Carboplatin was closed in 2006 due to poor accrual.

The Group was subject to an NCRI progress review in June 2005, which highlighted the problems of development and implementation of studies in less common tumours. Following the review the CSG created specific tumour and imaging subgroups to focus on the development and implementation of studies and has been successful in attracting

new group members. Susan Short, Clinical Oncologist and Scientist from University College Hospital, London has been appointed as the new chairperson of the Brain Tumour CSG from spring 2006. 3 members left the Group and 2 new members have joined the Group in early summer 2006. The accrual for 2005/06 was 3% of incidence cases.

### Brain Tumour Group Portfolio

Acronym	Title	PI(s)	Status
BR11	Adjuvant procarbazine, CCNU and vincristine chemotherapy in patients with highly anaplastic oligodendroglioma (in collaboration with the EORTC)	MJ Van Der Bent	Closed
BR12	Temozolomide vs PCV/BCNU in astrocytoma	Michael Brada, Sally Stenning Ming Lee	Open
EORTC 22952	No Radiotherapy versus Whole Brain Radiotherapy for 1 to 3 Brain Metastases from Solid Tumours after Surgical Resection or Radiosurgery. A Randomized Phase III Trial.	EORTC	Open
Neo-adjuvant Carboplatin Trial	Multicentre, Phase II Study of Carboplatin pre-irradiation in patients with primary glioblastoma multiforme following biopsy	Michael Brada	Closed
EORTC 22033 – 26033	Primary chemotherapy with Temozolomide vs radiotherapy in patients with low grade glioma	EORTC	Open
TATA/BR14	A randomised controlled trial of temozolomide as adjuvant and or concurrent treatment in anaplastic (WHO grade III glioma)	Michael Brada	In set up
	Phase III trial comparing conventional temozolomide with dose intensive temozolomide in patients with newly diagnosed glioblastoma	S. Erridge	In set up
BR12-Trans	Temozolomide vs PCV chemotherapy in the treatment of recurrent malignant glioma translational research proposal	P. Collins	In set up

Professor Michael Brada, Chair (until spring 2006)

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

### Strengths:

- 5 new trials in various stages of development.
- The hard work and effort put into the leadership of the Group was obvious

### The Group needs to consider:

- Developing a sufficient critical mass fully engaged in the work of the Group
- Appointing additional medical oncologists to exploit the use of novel agents and individuals with expertise in palliation, nursing and imaging
- Opening the Group to young energetic individuals who can champion particular trials
- How best to engage the wider research community in developing and supporting the work of the Group
- Developing a series of one day symposia on specific priorities
- Identifying 4/5 centres of excellence which may act as core support to the Group
- Widening the trials portfolio to include studies on palliative care, CNS lymphomas, CNS metastases and imaging.
- Developing a translational capability
- Contacting the Haem Onc CSG to see if the design of their study which looks a sequentially at a number of novel agents is applicable to the Brain CSG
- Establishing a dialogue with the CTAAC office in advance of submissions being made, and after funding decisions have been made
- Whether or not to resubmit their surgical trial after suitable modification
- The relevance of questions and whether or not the resources required justify a particular pathway
- Establishing an international advisory panel
- Alternative sources of funding for research nurses to support brain trials