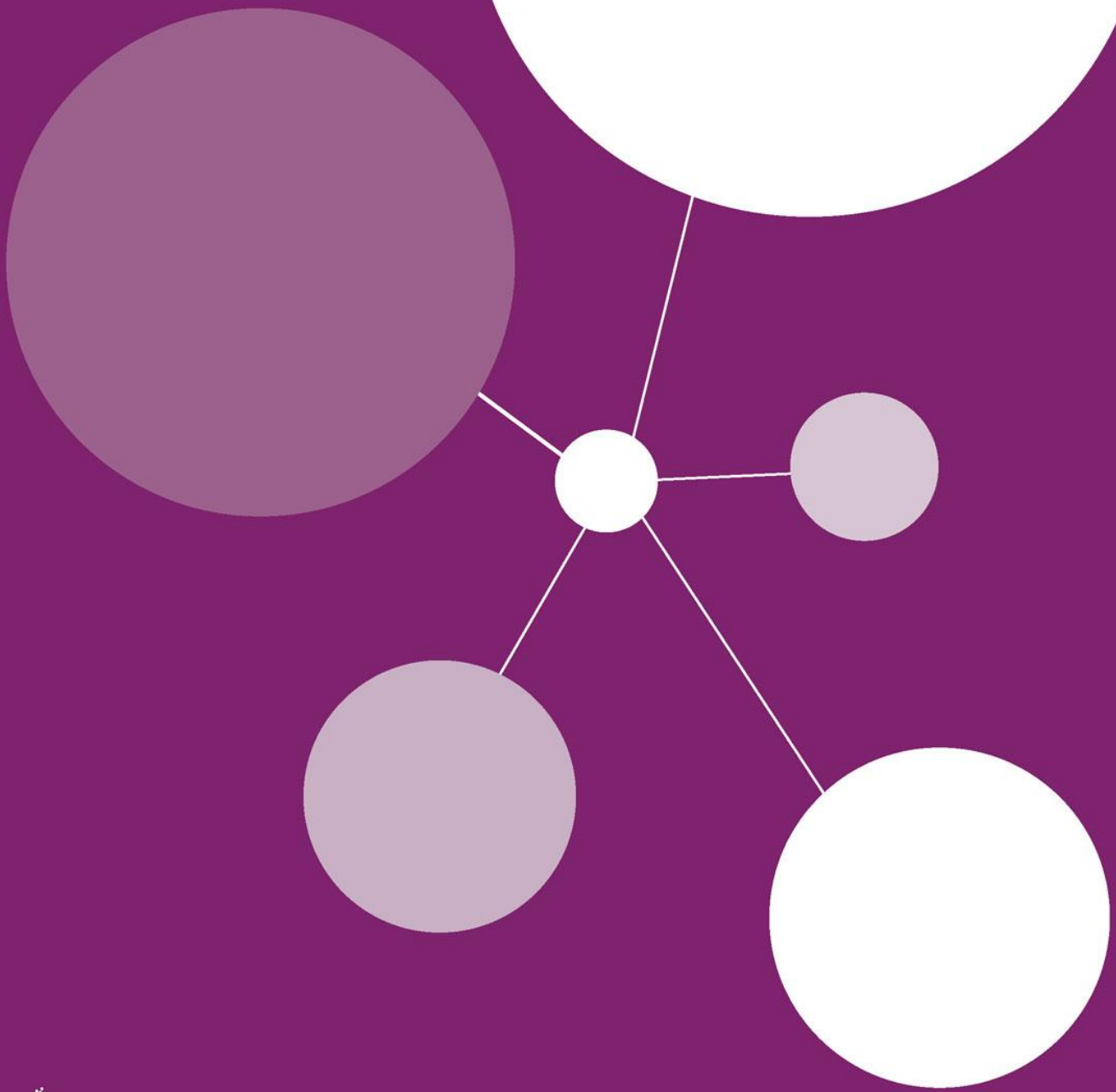
NCRI
National
Cancer
Research
Institute

NCRI Brain Tumour Clinical Studies Group

Annual Report 2014/2015



Partners in cancer research

NCRI Brain Tumour CSG Annual Report 2014/15

1. Executive Summary (including top 3 achievements in the year)

The Brain CSG continues to promote trial development and recruitment. Top achievements include:

Funding & set up of the NIHR-funded ROAM trial, which will evaluate the role of radiotherapy in the management of atypical meningioma. This study is important because it was developed through the collaboration of neurosurgeons, clinical oncologists, radiologists and neuropathologists. This was led by a CSG neurosurgeon (Mr Mike Jenkinson) and is acting as a nidus for our meningioma programme, which he leads. The trial has also resulted in significant interest within the neurosurgical community with over half of the 34 UK centres participating.

The subgroups are working well. The New Agents & Translational Subgroup has obtained funding for two early phase trials PARADIGM-2 AND ReoGlio from NAC and the Imaging & Technology Subgroup has obtained funding for an imaging biomarker study: PRaM. A medical oncologist attended the most recent New Agents & Translational Subgroup meeting and was generally recognised as having made an important and positive contribution despite not specialising in neuro-oncology. Two neuro-radiologists have been appointed to the Imaging & Technology Subgroup.

Developing trainee participation in the work of the CSG is also very important if we are to train the next generation of academic neuro-oncology specialists. Our trainee positions generated a lot of interest from oncology and neurosurgery and there was a strong field of applicants. There has also been a lot of interest among neuro-surgical trainees in the developing surgical neuro-oncology initiatives by the SBNS.

Continuing challenges revolve around the development of academic pathology and radiology and the development of medical oncology to support drug trials. Robust tissue collection remains an extremely sensitive political issue that will require further discussion if we are to establish a national resource. The infrastructure and translational expertise to support pre-clinical drug development in the UK specifically for brain cancer (including cerebral metastases) must also be addressed.

2. Structure of the Group

Professor Silvia Marino (pathology) has joined the Group and Dr Richard Shaffer and Dr Jane Fleming have both left the Group.

We have also appointed 2 senior trainee members Dr Paul Brennan (Neurosurgery) and Dr Stefan Nowicki (Clinical oncology). This is part of an initiative to encourage trainee participation in the CSG and allow greater insight into clinical trial development. These appointments are for 18 months. The Society of British Neurological Surgeons (SBNS) and The Brain Tumour Charity have agreed to fund the travel costs for attending meetings. Each trainee has been given a mentor within the group and encouraged to get involved with the subgroups(s) of their choice.

3. CSG & Subgroup strategies

Main CSG

The period 2012-14 saw the final results from several international phase III multicentre clinical trials published. Unfortunately, these trials were uniformly negative and have led to a reconsideration of trials of the format "Standard of Care + X". In the same period there have been several landmark translational studies revealing the complexity of brain cancer in terms of patterns of mutations, clonal diversity and evolutionary dynamics. In parallel, data from The Cancer Genome Atlas is paving the way for a revised classification of brain tumours (expected late 2015/16) that incorporates current validated biomarkers.

Set against this background the accelerating development of the NCRI Brain CSG is timely. Brain cancer has been prioritised by CRUK as part of its strategic planning for the next 5 years. The CSG needs to engage more actively through a closer and more confident dialogue with CRUK, CTAAC and other stakeholders including NIHR and brain tumour charities. In this way the CSG will provide clinical leadership and direction that will inform the development of translational research programmes and engagement with pharma, biotech and other potential commercial partners.

Strategic priorities for the CSG are outlined in Appendix 2A.

Imaging & Technology Subgroup (Chair, Dr Adam Waldman)

Achievements

The following imaging and radiotherapy studies have been developed within the Subgroup:

- DIG (multicentre Diffusion In Glioma platform study); opened
- PrAM study; funded by CRUK biomarker group.
- ROAM trial; funded by NIHR HTA, and opened.
- HIPPO: currently in set up
- Imaging and tissue markers of choline metabolism in glioma; opened.

There have been additional contributions by the subgroup to a substantial multicentre programme of paediatric neuroncology imaging, led by a subgroup member. Other developments include:

- UK wide survey of neurosurgery and neuroradiology units on availability and limitations to implementation of quantitative MRI in neurooncology (results presented internationally).
- Introduction of review of imaging, radiotherapy and surgical design aspects of all proposals presented to the main CSG.
- Consumer engagement in trial proposals developed by the Subgroup.

Challenges

Challenges are both technical and structural:

- Models of funding and NHS cost recovery of non standard of care imaging associated with trials
- Limited UK culture and research infrastructure in academic neuroradiology.
- Obtaining research funding to support radiotherapy trials.
- Industrial collaborations for novel technologies.
- Translation and validation of advanced imaging in multicentre platforms
- Translation of methods into clinical environment in resource-limited clinical departments
- Lack of project officer support for Subgroup activities.

New Agents & Translational Subgroup (Chair, Professor Anthony Chalmers)

Achievements

- HCQ, OPARATIC and PARADIGM trials opened and recruiting.
- ReoGlio and PARADIGM-2 trials funded by CRUK New Agents Committee.
- All the above are phase I-II studies testing novel agents in newly diagnosed GBM that have been developed within the subgroup.
- NCRI Glioma Network established with four workstreams covering trial development, molecular stratification, pre-clinical evaluation of novel combinations and building an early phase trials network.
- Increased portfolio of Industry sponsored studies.
- Worked with Brain UK to incorporate brain tumour tissue collection in this UK network of brain tissue biobanks.

Challenges

- Accessing novel agents early in the drug development process.
- Opening trials across multiple centres, each of which is likely to recruit only small numbers of patients.
- Demonstrating tumour PK and PD of novel agents in pre-clinical models and in patients.
- Obtaining programmatic research funding to support generation, validation and utilisation of clinically relevant models of primary brain tumours.
- Obtaining institutional, financial and infrastructural support for biobanking.
- Lack of project officer support for Subgroup and NCRI Glioma Network activities.

QoL/Palliative Care Subgroup (Chair, Dr Jane Fleming)

The QoL/Palliative Care Subgroup agreed at the end of the reporting year to change it's name to the Supportive & Palliative Care Subgroup to reflect more closely the relationship with the

Supportive & Palliative Care CSG. This name change was endorsed by the main Brain CSG at the April 2015 meeting.

The Subgroup was successful in bidding to host a workshop at the NCRI Conference 2014 with a focus on neuro-rehabilitation and collaboration towards future research projects. Over 60 delegates attended including two academic professors. This was sponsored by Brainstrust UK, Almac (NI) and Brain Tumour Research.

The Subgroup has the following studies in development:

- Leviteracetam at the End-of-Life : Professor Stone UCL is currently leading on this work which is being developed as two separate studies :
  - Study 1 – a pharmacokinetic study in healthy volunteers. This will be a 'proof of principle' study to demonstrate that leviteracetam is absorbed sufficiently well (and without adverse effects) to be used in patient populations.
  - Study 2 – Multi-centre, randomized pilot study in palliative care patients, comparing subcutaneous leviteracetam versus subcutaneous midazolam infusions in palliative care patients (previously on oral leviteracetam) who are unable to swallow. It is planned to study approx 30 patients in each arm.
- Supportive and palliative care for brain tumour patients' – in conjunction with the Marie Curie Trials Centre and the Wales CTU. The outcomes to be measured will be quality-of-life, functional changes and also health resources utilization. The study will be based in three possible sites – Guys/St Thomas'/Kings, Royal Marsden and Velindre Cancer centre Cardiff.

And in set-up:

- The 'Vimpat' (Lacosamide study: This study is planned to open in the UK and Ireland later in 2015. Dr Robin Grant (PI) is in contact with Mark Gilbert (USA Lead).

4. Task groups/Working parties

In October 2013 the New Agents & Translational Subgroup held a strategy day where a panel of UK brain tumour specialists discussed the landscape of current and potential novel agents for GBM and concrete methods for accomplishing the strategic aims. Several key points emerged:

- Targeting of single kinases has been repeatedly unsuccessful and vertical and horizontal combinations should be explored as in other cancers
- Large-scale molecular characterisation will be necessary going forward and importantly will identify the few tumours that harbour dominant, druggable driver mutations
- Due to heterogeneity, a renewed focus on non-specific therapies such as radiation may be sensible, and there are new opportunities in chemoradiation and possibly reirradiation
- Currently available cytotoxics and newer versions of old cytotoxics may not have been fully explored, particularly in combination

As a result of this, the following work-streams were established for development throughout 2014/15:

- Trial development
- Molecular stratification of GBM
- Establish a pre-clinical combinations network
- Develop an early phase trials network for brain tumours

This on-going work has led to several meetings to further develop strategy and funding applications as a key priority in 2015/16. This approach has already led to funding of PARADIGM 2 and ReoGlio by the Novel Agents Committee and PRaM by the Biomarker Committee.

5. Patient recruitment summary for last 5 years

Recent completion of several phase III trials means that there is limited on-going activity in this area. Currently research in the gliomas at first diagnosis is dominated by commercials studies (NCRN 396, 592, 605, 631), which are only open in a small number of centres. This is reflected in the recruitment trends seen between 2012/3 and 2013/4. Several trials have since received funding and are in set-up and is reflected in the Brain CSG portfolio to date where 4 trials closed to recruitment and 11 opened.

Table 1 Summary of patient recruitment by RCT/Non-RCT

Year	All subjects		Cancer patients only		% of cancer patients relative to incidence	
	Non-RCT	RCT	Non-RCT	RCT	Non-RCT	RCT
2010/2011	410	45	410	45	9.7	1.1
2011/2012	560	77	534	77	12.7	1.8

Table 2 Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	1594	168	927	168	19.5	3.5
2013/2014	829	136	783	136	16.5	2.9
2014/2015	716	171	716	170	15.1	3.6

6. Links to other CSGs, international groups and network subspecialty leads

The QoL/Palliative Care Subgroup has made links with other CSGs (Palliative & Supportive Care/Psychosocial Oncology & Survivorship) and with the Association of Palliative Medicine.

The Brain CSG is continuing to develop a strengthening relationship with other CSGs, in particular Breast & Lung, through engagement and support for trials in cerebral metastatic disease.

The Brain CSG is actively pursuing closer links with the EORTC, which has resulted in agreement to develop a national network of trial competent centres in the UK based on the existing EORTC centres. We are now seeking an appropriate trial to formalise this process.

We have also reached out to the US to develop collaborative adaptive trials in GBM with Harvard (Patrick Wen & Brian Alexander).

7. Funding applications in last year

The number of trial applications has fallen in 2014 for reasons that are not clear.

An NIHR study (ROAM) has been funded but does not show up on CTAAC statistics. The study is an evaluation of the role of radiotherapy on atypical meningioma. It is currently in set up.

Table 3 Funding submissions in the reporting year

Clinical Trials Advisory and Awards Committee (CTAAC)			
Study	**Application type**	**CI**	**Outcome**
July 2014			
None			
November 2014			
CORE: A randomised trial of conventional care versus radioablation (stereotactic body radiotherapy)for extracranial metastases	Full application	Dr Emma Hall	Funded
March 2015			
None			

8. Collaborative partnership studies with industry

The CSG has several industry studies on its portfolio. The CSG is usually notified about these studies when the protocol and participating centres have already been determined. The CSG usually has limited input into study design. To date no industry study has competed with other portfolio studies for patients.

Currently the Brain CSG portfolio consists of the following industry studies:

- NCRN 396: Open-label, phase II study of vemurafenib in patients with BRAF V600 mutation-positive cancers
- NCRN 592: Phase III clinical trial evaluating DCVax®-L, autologous dendritic cells (DC) pulsed with tumor lysate antigen for the treatment of glioblastoma multiforme (GBM)
- NCRN 631: ACT IV Rindopepimut/GM-CSF + Adjuvant Temozolomide in EGFRvIII-positive Glioblastoma
- NCRN 605: TAMIGA Phase IIIb:SOC +/- bevacizumab in GBM after radiotherapy + temozolomide + bevacizumab
- NCRN 2698:Pilot study to develop methodology for 2-HG MRS
- PARADIGM an AZ Alliance study on the horizon is now on the portfolio.

9. Impact of CSG activities

Clinical trials within the Brain CSG have impacted on routine UK clinical practice:

- BR12: This trial has helped rationalise the management of patients with recurrent GBM in the UK. The use of PCV versus TMZ in the context of early vs. late relapse respectively has been incorporated into clinical practice.
- EORTC 22952: randomised trial examining the role of whole brain radiotherapy after resection or radiosurgery for patients with 1-3 brain metastases. This has influenced the management of patients with cerebral metastases.
- EORTC 26052: the role of dose dense TMZ v standard protocols. The data confirms that dose dense regimens do not convey advantage.

More recently large multicentre trials have not shown impact on clinical outcome for GBM. In contrast long-term follow up of 1p19q co-deleted anaplastic oligodendrogliomas has confirmed

that radiation therapy (RT) combined with PCV chemotherapy improves survival compared to RT alone.

10. Consumer involvement

Two consumers are actively engaged with the Brain CSG. They provide the consumer voice, giving advice on PPI aspects of trial development during proposal review meetings, and contributing to the development of high quality applications.

In addition the consumers are a collective source of PPI input into the work of the Brain CSG. They flag opportunities where consumer input should be sought and seek opportunities to promote the importance of clinical trials in neuro-oncology.

The consumers also have a presence on related groups, such as the QoL/Palliative Care Subgroup, brain metastases, and New Agents & Translational Subgroup. They have contributed to the neuro-oncology symposium at NCRI 2014 and have co-developed A3 proposals.

The Chair and clinical members play a vital role in enabling consumer members to engage actively in their role. There is open communication and good facilitation. Close collaboration means that all feel supported in their role and understand what is expected of them.

Consumer engagement has been particularly involved in driving the collection of brain tumour tissue into a UK network and is widening the campaign for post surgical collection, providing insights and expertise to improve the relevance and reach of the research patients and the wider public and achieving effective consumer involvement through dissemination of information and the provision of a network and a community, led by consumers.

11. Open meetings/annual trials days/strategy days

In June 2014 the NCRI CSG held a strategy day where a panel of UK brain tumour and primary cancer specialists discussed current and potential studies for patients with brain metastases. Several key points emerged:

- There are very few trial opportunities for patients with brain metastases
- There is no clear standard for the management of brain metastases across the UK, with varying levels of access to surgery and radiosurgery
- Novel chemotherapy agents are coming on stream and may have an effect on brain metastases, potentially leading to a reduced referral rate for surgery, radiosurgery and whole brain radiotherapy
- Multi-centre trials will be required focused on specific primary cancer sites (e.g. breast only) and that genetic stratification will be required

As a result of the meeting the following work streams were established for development through 2015/16. The aim is to develop new trial opportunities for patients with brain metastases:

- Radiotherapy and surgery
- Lung cancer metastases
- Breast cancer metastases
- Patient outcomes

12. Progress towards achieving the CSG's 3 year strategy

The CSG has established closer links with the SBNS to promote surgical trials in neuro-oncology. A dedicated neuro-oncology section has been established with the approval of the SBNS council and will hold its first meeting ahead of the next SBNS. Twenty-two neurosurgical trainees attended an NCRI-sponsored workshop on surgical oncology trials. Discussions around neurosurgical trials we developed at a breakout session and are on-going. Each proposal has both a trainee and a consultant lead.

Radiotherapy trials have opened (OPARATIC, PARADIGM, HCQ) or are in development (HIPPO, ROAM). Two new trials have been funded (PARADIGM 2 & ReoGlio).

Progress on developing a meningioma programme is gaining momentum. A further study to evaluate how best to manage incidental meningiomas is now in development. A proposal to collaborate with US partners to evaluate smoothened and AKT inhibitors in meningioma are under development as part of the IRCI initiative. This has currently stalled because CTEP has yet to approve international collaborations within this initiative.

13. Priorities and challenges for the forthcoming year

Priorities for the coming year include:

- Promoting the collection of linked clinical and biological (especially genomic) data with the objective of establishing a stratified medicine programme for brain cancer within a 3-5 year time horizon.
- Developing a closer dialogue with CRUK with the following objectives:
    - establishing a translational infrastructure for adult glioma research;
    - embedding tumour banking into routine clinical practice;
    - developing better models for drug development that are relevant for brain cancer;
    - promoting surgical and radiotherapy trials

Challenges for the coming year include:

- Promoting the role of the CSG and its current agenda to the wider neuro-oncology community through out-reach at national meetings (e.g. NCRI, BNOS).
- Addressing some of the barriers to trial recruitment we have identified. Particular emphasis will be placed on strategies to mitigate geographical restriction on trial participation. PPI involvement will be of particular importance with respect to this issue.
- Promoting further recruitment to subgroups with particular emphasis on academic neuro-radiology and neuro-pathology.

14. Concluding remarks

A major challenge for the CSG is the fact that the UK has no medical oncologists subspecialising in brain cancer. It is the only major European country in this situation and within the UK brain cancer is the only cancer with negligible medical oncology input. If we are to successfully develop early-phase trials and develop better trials we need to attract academic oncologists/neurologists into neuro-oncology. This issue was raised at the strategic progress review in December 2014 however plans to address the problem remain to be developed.

15. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Imaging & Technology Subgroup Strategy
- C – New Agents & Translational Subgroup Strategy
- D – QoL/Palliative Care Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous year

Appendix 6 – Strengths & Weaknesses from the Brain CSG 2014 Progress Review

Dr Colin Watts (Brain Tumour CSG Chair)

Appendix 1

Membership of the Brain Tumour CSG

Name	Specialism	Location
Mr Neil Dickson	Chair, Brain Tumour Charity	Farnborough
Mr Paul Brennan*	Clinical Lecturer	Edinburgh
Professor Anthony Chalmers	Clinical Oncologist	Glasgow
Dr Sara Erridge	Clinical Oncologist	Edinburgh
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr Gillian Whitfield	Clinical Oncologist	Manchester
Dr Helen Bulbeck	Consumer	Isle of Wight
Ms Debbie Keatley	Consumer	Belfast
Dr Stefan Nowicki*	CRUK Clinical Research Fellow	Glasgow
Dr Kathreena Kurian	Neuropathologist	Bristol
Dr Martin McCabe	Paediatric Oncologist	Manchester
Professor Silvia Marino	Pathologist	London
Dr Samantha Mills	Radiologist	Liverpool
Dr Adam Waldman	Radiologist	London
Dr Wendi Qian	Statistician	Cambridge
Mr Michael Jenkinson	Surgeon	Liverpool
Mr Stephen Price	Surgeon	Cambridge
Dr Colin Watts (Chair)	Surgeon	Cambridge

* denotes trainee

Membership of the Subgroups

New Agents & Translational Subgroup		
Name	**Specialism**	**Location**
Professor Mike Brada	Clinical Oncologist	London
Professor Anthony Chalmers (Chair)	Clinical Oncologist	Glasgow
Catherine McBain	Clinical Oncologist	Manchester
Professor Susan Short	Clinical Oncologist	London
Dr Helen Bulbeck	Consumer	Isle of Wight
Dr Mazhar Ajaz	Medical Oncologist	Surrey
Dr Sarah Jefferies	Medical Oncologist	Cambridge
Dr Rhoda Molife**	Medical Oncologist	London
Professor Sebastian Brandner**	Neuropathologist	London
Dr Kathreena Kurian	Neuropathologist	Bristol
Dr Darren Hargrave**	Paediatric Oncologist	London
Dr Tracy Warr	Reader in Neuro-Oncology	Wolverhapton
Mr Paul Smith**	Surgeon	London
Dr Paul Roberts		Leeds

QoL/Palliative Care Subgroup		
Name	**Specialism**	**Location**
Ms Vicky Hurwitz	Clinical Nurse Specialist	London
Dr Lucy Brazil	Clinical Oncologist	Middlesex
Dr Angela Costello	Clinical Psychologist	London
Kathy Oliver	Co-Director, IBTA	Surrey
Dr Jane Neerkin	Consultant Physician in Palliative Medicine	London
Dr Helen Bulbeck	Consumer	Isle of Wight
Ms Debbie Keatley	Consumer	Belfast
Dr Lidia Yaguez	Neuropsychologist	London
Ms Vicky Hurwitz	Nurse	Middlesex
Ms Charlotte Lambourn	Nurse	London
Dr Jane Fleming (Chair)	Palliative Care Consultant	Waterford
Dr Ann Arber	Senior Lecturer, Cancer & Palliative Care	Surrey

Imaging & Technology Subgroup		
Name	**Specialism**	**Location**
Dr Jeremy Rees	Clinical Oncologist	London
Dr Paul Sanghera	Clinical Oncologist	Birmingham
Professor Susan Short	Clinical Oncologist	London
Dr Gillian Whitfield	Clinical Oncologist	Manchester
Dr Federico Roncaroli	Neuropathologist	London
Dr Alan Jackson	Radiologist	Manchester
Dr Rolf Jager	Radiologist	London
Dr Adam Waldman (Chair)	Radiologist	London
Dr Chris Clark	Reader in Imaging and Biophysics	London
Professor Franklyn Howe	Reader in MRI Physics	London
Dr Andrew Peet	Reader in Paediatric Oncology	Birmingham
Dr Andrew Brodbelt	Surgeon	Liverpool
Dr Paul Byrne	Surgeon	Nottingham
Mr Michael Jenkinson	Surgeon	Liverpool
Mr Stephen Price	Surgeon	Cambridge

*denotes trainee

** denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Specific priorities for the Brain CSG include:

- Promoting the collection of linked clinical and biological (especially genomic) data with the objective of establishing a stratified medicine programme for brain cancer within a 3-5 year time horizon.
- Developing a closer dialogue with CRUK with the following objectives:
    - establishing a translational infrastructure for adult glioma research;
    - embedding tumour banking into routine clinical practice;
    - developing better models for drug development that are relevant for brain cancer;
    - promoting surgical and radiotherapy trials
    - promote the development of academic *medical* neuro-oncology in the UK to develop early phase and multi-arm multi-stage clinical trials.

Meningiomas are the commonest primary brain tumour, but there are few study/trial opportunities. The CSG has identified this as an area for further development building on our successful development of the NIHR-funded ROAM trial, in 2015 we will explore to opportunities for further research and trials for meningiomas. The following work streams are in development:

- Development of risk stratification model for incidental meningioma (including exploration of serum biomarkers for disease monitoring)
- Development of a core outcome set for meningioma trials/studies
- Identifying actionable mutations in atypical meningioma for re-purposing of existing drugs or the development of novel agents
- Developing stratified therapeutics in rare meningiomas through the IRCI initiative

B – Imaging & Technology Strategy

The strategy of the Imaging & Technology Subgroup is to:

Improve support of clinical trials in brain tumours through:

- Development and validation of quantitative and functional imaging methods for mechanistic, PK/PD and response biomarkers in high-intensity pre-clinical and early phase clinical trials of novel therapies.
- Validation of imaging biomarkers against genetic, epigenetic and metabonomic/proteomic markers, for improved non-invasive prognostication and stratification.
- Development of imaging networks and analysis facilities across centres with expertise in quantitative imaging, for improved patient stratification and surrogate endpoints in multicentre trials.
- Establishing minimum imaging datasets for later phase, multicentre clinical trials, that can be acquired widely across UK centres.
- Provision of imaging expertise at early stages of trial development, to improve design.

Promote and facilitate development and translation of relevant technologies for brain tumour treatment by:

- In house development of trials of radiotherapy planning and delivery techniques
- Novel studies of methods to improve maximal safe surgical tumour resection, through intra-operative visualisation
- Trials of novel therapeutic modalities and delivery methods (e.g. surgically implanted delivery devices, convention enhanced delivery, high intensity focused ultrasound).

C – New Agents & Translational Subgroup Strategy

The strategy of the New Agents & Translational Subgroup is to:

Increase availability of early phase clinical trials to brain tumour patients through:

- In-house development of high quality, investigator led studies of novel agents and combinations.
- Increasing activity and quality in pre-clinical evaluation of novel agents and combinations in clinically relevant models of brain tumours, in collaboration with the UK Radiotherapy-Drug Combinations Consortium (RaDCom).
- Working towards multi-arm 'umbrella' studies that will enable large numbers of patients to participate in early and late phase trials testing a broad range of promising new agents and combinations.

Promote and facilitate translational research activity by:

- Establishing networks of laboratories, early phase clinical trial centres and brain tumour bio-repositories.
- Increasing banking of and access to high quality brain tumour tissue with associated clinical information
- Rolling out comprehensive molecular testing of all primary brain tumours to optimise diagnosis, facilitate translational research and maximise outputs from clinical trials.

D – QoL/Palliative Care Subgroup Strategy

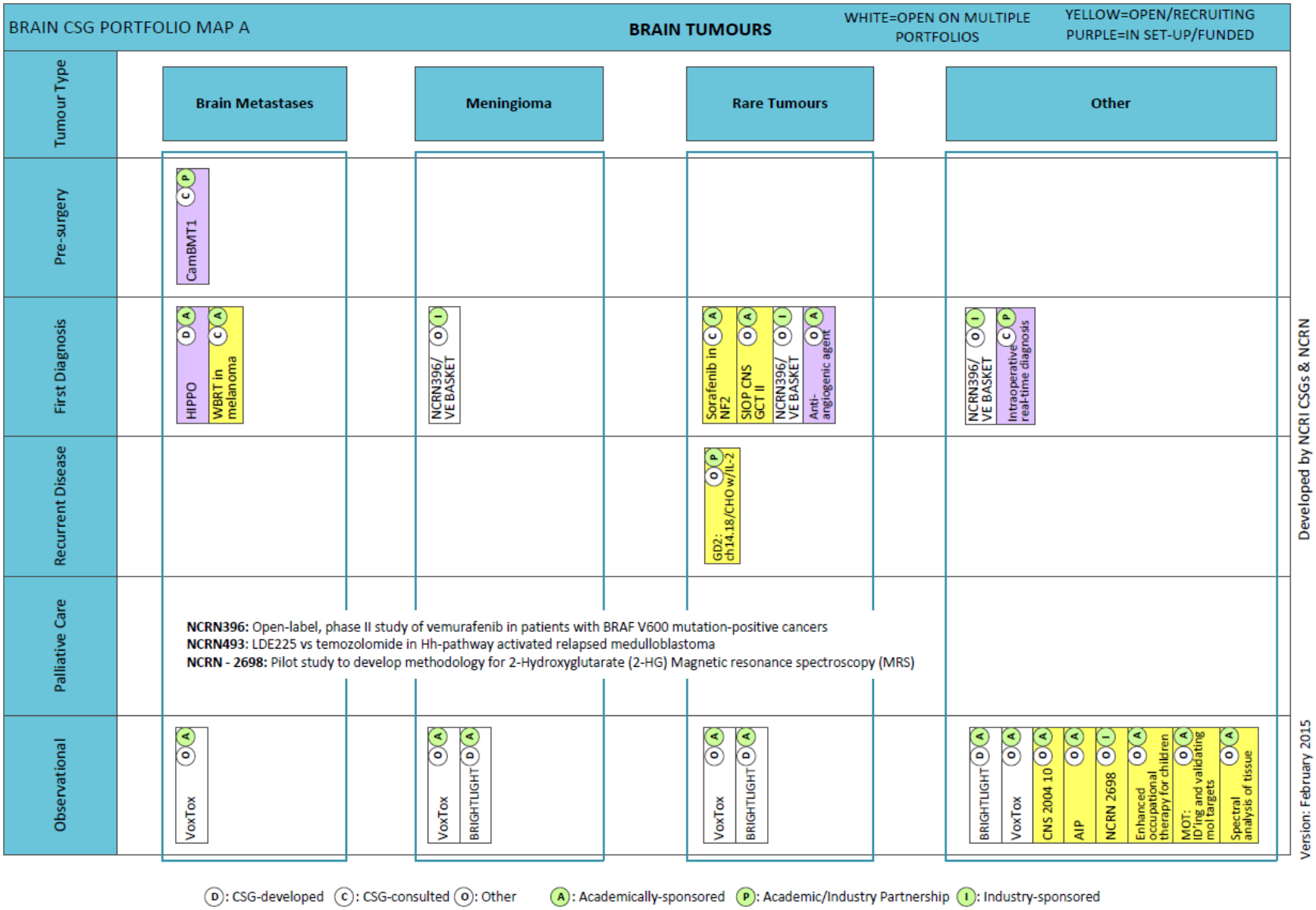
Overall objective: To improve the quality of living for those with brain tumours and their carers through evidence-based research.

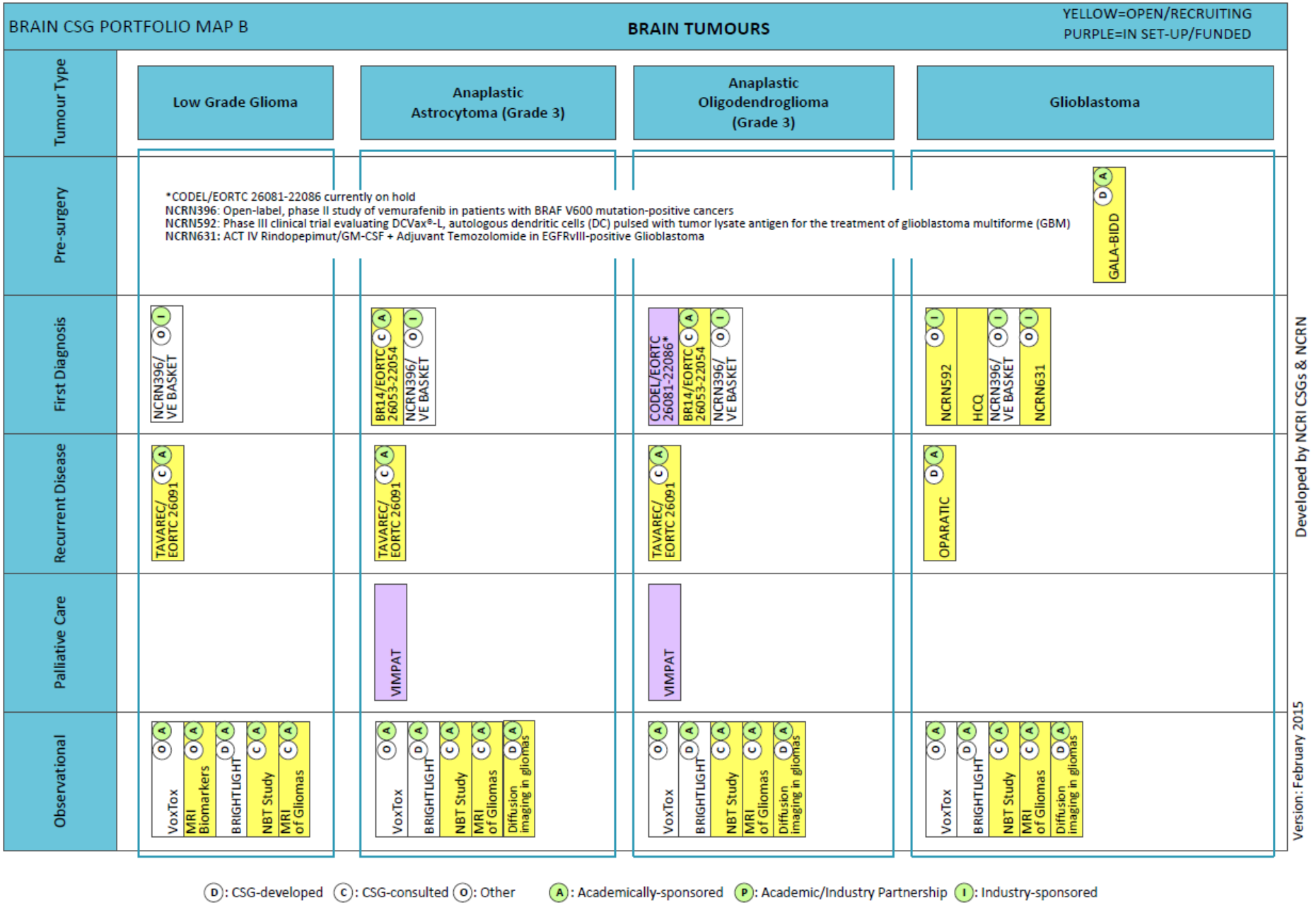
Short to medium-term objectives:

- To create a setting which is conducive to robust research by – ensuring that the composition of the sub-group covers a range of individuals from relevant areas of expertise (both formal and informal, across professions and medical specialties), ensuring that the members are actively involved in research either directly or indirectly through facilitation.
- To create an outward-looking ethos – by encouraging links with relevant individuals/bodies nationally and internationally who are involved with research in this area.
- To encourage both charitable and industry sectors to 'invest' in research projects in this area (and not to look exclusively at 'life prolonging' interventional studies)
- To promote and develop research questions for studies where the outcomes will be of direct benefit to this patient group
- To facilitate development of studies which span issues relating to the whole patient/ carer 'journey' i.e. from issues around diagnosis to disease progression and into bereavement (and also 'survivorship')
- To follow-through any recommendations raised in the most recent Progress Review Report
- To develop research projects which would address the supportive and palliative care questions developed through the James Lind Alliance process (Top 10 Uncertainties)

Appendix 3

Portfolio maps




BRAIN CSG PORTFOLIO MAP B
BRAIN TUMOURS
YELLOW=OPEN/RECRUITING
PURPLE=IN SET-UP/FUNDED
Tumour Type
Low Grade Glioma
Anaplastic Astrocytoma (Grade 3)
Anaplastic Oligodendroglioma (Grade 3)
Glioblastoma
Pre-surgery
First Diagnosis
Recurrent Disease
Palliative Care
Observational
*CODEL/EORTC 26081-22086 currently on hold
NCRN396: Open-label, phase II study of vemurafenib in patients with BRAF V600 mutation-positive cancers
NCRN592: Phase III clinical trial evaluating DCVax®-L, autologous dendritic cells (DC) pulsed with tumor lysate antigen for the treatment of glioblastoma multiforme (GBM)
NCRN631: ACT IV Rindopepimut/GM-CSF + Adjuvant Temozolomide in EGFRvIII-positive Glioblastoma
GALA-BIDD
NCRN396/ VE BASKET
BR14/EORTC 26053-22054
NCRN396/ VE BASKET
CODEL/EORTC 26081-22086*
BR14/EORTC 26053-22054
NCRN396/ VE BASKET
NCRN592
HCQ
NCRN396/ VE BASKET
NCRN631
TAVAREC/ EORTC 26091
TAVAREC/ EORTC 26091
TAVAREC/ EORTC 26091
OPARATIC
VIMPAT
VIMPAT
VoxTox
MRI Biomarkers
BRIGHTLIGHT
NBT Study
MRI of Gliomas
VoxTox
BRIGHTLIGHT
NBT Study
MRI of Gliomas
Diffusion imaging in gliomas
VoxTox
BRIGHTLIGHT
NBT Study
MRI of Gliomas
Diffusion imaging in gliomas
VoxTox
BRIGHTLIGHT
NBT Study
MRI of Gliomas
Diffusion imaging in gliomas
Developed by NCRI CSGs & NCRN
Version: February 2015
(D): CSG-developed (C): CSG-consulted (O): Other
(A): Academically-sponsored (P): Academic/Industry Partnership (I): Industry-sponsored

Appendix 4

Publications in the reporting year

ROAM

Jenkinson MD, Weber DC, Haylock BJ, Mallucci CL, Zakaria R, Javadpour M. Letter to editor: Radiotherapy versus Observation following surgical resection of Atypical Meningioma (The ROAM trial) *Neuro-Oncology* 2014 16(11): 1560-1561.

Jenkinson MD, Weber DC, Haylock BJ, Mallucci CL, Zakaria R, Javadpour M. Atypical meningioma: current clinical dilemmas and prospective clinical trials *Journal of Neurooncology* 2015 121 (1) 1-7

OPARATIC

Ajaz M, Jefferies S, Brazil L, Watts C, Chalmers A. Current and investigational drug strategies for glioblastoma. *Clin Oncol* (R Coll Radiol). 2014;26(7):419-30

CENTRIC EORTC 26071-22072 study

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Personality Changes

N. Gregg, A. Arber, K. Ashkan, L. Brazil, R. Bhangoo, R. Beaney, R. Gullan, V. Hurwitz, A. Costello, L Yágüez; Neurobehavioural changes in patients following brain tumour: patients and relatives perspective. *Supportive Care in Cancer*. Volume 22. Issue 11 (2014) Pgs 2965-2972

Appendix 5

Major international presentations in the reporting year

MR characterisation of invasive phenotypes in GBMs study

SJ Price, NR Boonzaier, V Lupson and T Larkin. "IDH-1 mutated glioblastomas have a less invasive phenotype than IDH-1 wild type glioblastomas: a diffusion tensor imaging study" oral presentation at the *Congress of Neurological Surgeons Meeting*, Boston, USA, November 2015 - This study won the AANS/CNS Section on Brain Tumors BrainLab Community Award

ROAM

Atypical meningioma: is radiotherapy necessary? Invited speaker, European Association of Neurological Surgeons, Prague, CR. 14 Oct 2014

OPARATIC

Professor Anthony Chalmers 'Drug resistance modelling: Patients, organoids and mice' session, NCRI Cancer Conference 2014.

Appendix 6

Strengths & weaknesses from the 2014 Progress Review

Strengths

- Strong leadership both at CSG and subgroup level
- A good group which has made good progress since the last review
- The Group has addressed/made progress on all the issues raised at the last review
- A well written clear report
- The merging of subgroups has been effective, synergised efforts and has helped produce better developed trials
- The development of a number of home grown trials
- The development of the QoL/Palliative Care Subgroup
- A systematic and productive approach to trials of novel agents
- The CSG are successfully reaching out to other CSGs and other collaborators
- The Group are focussing on the right strategies and developing the right sort of trials
- Plans for tissue banking are to be commended
- Good consumer involvement
- The Group is working well with the two main brain tumour charities
- Regional meetings and strategy days which have brought the right people together and have been productive

Issues for the CSG to consider

- Developing and documenting strategies for each of the subgroups
- The two other subgroups developing a more systematic approach to trial development as exemplified by the Novel Agents Subgroup
- Developing clear metrics of success for the Group
- Using the LCRNs and MDTs to identify a wider pool of potential researchers and fill gaps in the membership
- Developing a clear role/area of work for each member of the Group
- Building on the links the QoL /Palliative Care Subgroup has made with the Supportive & Palliative Care CSG
- Developing a standard QoL assessment to be included in all trials and likewise for an RT protocol
- Including supportive care in the work of the QoL/Palliative Care Subgroup and moving supportive and palliative care upstream in the disease trajectory
- Including translational work in the work of the QoL/Palliative Care Subgroup
- Developing a checklist of who should be involved at an early stage in a study's development
- Mapping and rationalising the sites involved in pilot initiatives such as the tissue banking and multi-centre diffusion platform, where practicable and possible
- Developing metrics for consumer involvement and recruiting a more 'usual' type of new consumer member
- Linking in with the LCRNs to address patchy recruitment
- Further developing international links and collaborations, particularly with the USA
- Improving the Group's international visibility and presence
- Submitting a bid for portfolio co-ordinator support to the Brain Tumour Charity