

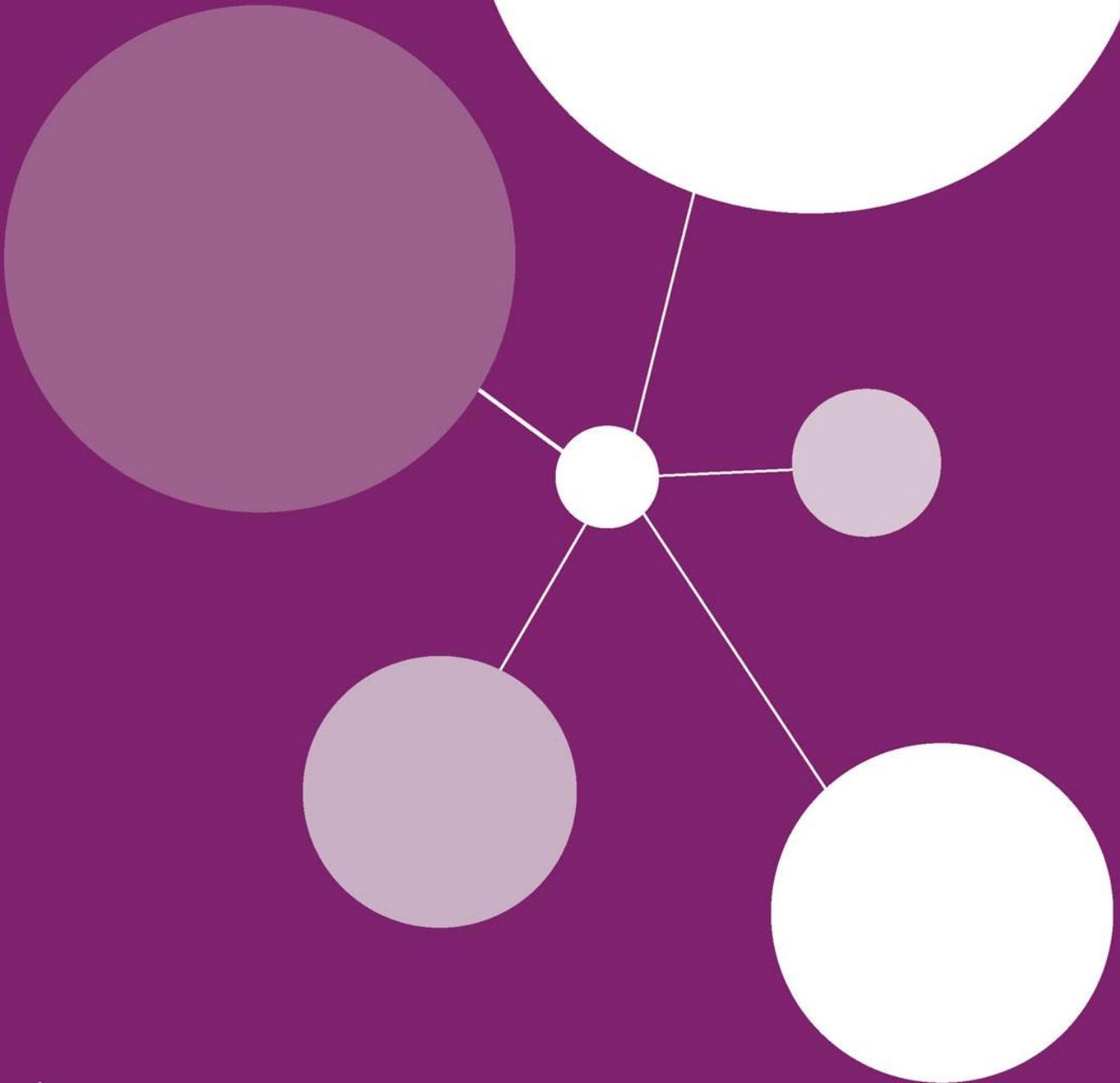


NCRI

National
Cancer
Research
Institute

NCRI Brain Group

Annual Report 2018-19



Partners in cancer research



NCRI Brain Group Annual Report 2018-19

1. Top 3 achievements in the reporting year

Achievement 1

The Brain Tumour CSG have led or been involved in the development of several new glioma studies funded by The Brain Tumour Charity (TBTC) and the National Institute for Health Research Health Technology Assessment (NIHR HTA). BRAIN MATRIX and FUTURE-GB are multi-centre glioma trials that will open across 10-15 centres which between them will recruit ~1400 patients. Two brain metastases studies, RADIANT BC and BRITEMET, have been funded by Cancer Research UK (CRUK). RADIANT BC is an interventional trial led by the Breast Cancer CSG with involvement from the Brain Tumour CSG. BRITEMET is a melanoma metastasis imaging biomarker study.

Achievement 2

The Brain Tumour CSG has appointed two medical oncologists - an academic consultant and a trainee. It is envisaged that this will lead to the development of new drug trials in brain tumours in the years to come. The CSG has also engaged with the Tessa Jowell Brain Cancer Mission with several members involved in this work with the vision to improve outcomes for patients with brain tumours.

Achievement 3

There has been a general increase in the number of brain tumour portfolio studies since the last report. The Group continue to engage with the clinical community delivering the trials in order to increase recruitment and to identify and foster new potential CIs. For example, the CSG Chair held a successful clinical research network Sub-Speciality Leads (SSLs) meeting in November 2018.

2. Structure of the Group

The structure of the CSG and Subgroups remain unchanged. Mr Michael Jenkinson continues as chair. Dr Kathreena Kurian (neuropathologist) rotated off the CSG and was replaced by Dr Juliet Brock (clinical oncologist) and Dr Juanita Lopez (medical oncologist). Ms Debbie Keatley (consumer) rotated off the CSG and the Group welcomed two new consumer members, Mr Usama Ali (joined Meningioma & Metastasis subgroup) and Ms Jessica Sass (joined Glioma subgroup). Three new trainees were appointed:

- Dr Faye Robinson – clinical oncology in Edinburgh
- Dr Cressida Lorrimer – clinical oncology in Brighton
- Dr Paul Miller – medical oncology in Oxford

3. Group & Subgroup strategies

Brain Group Strategy

Portfolio development (general)

Four new studies have been funded and will be adopted onto the NCRI CSG portfolio.

- BRAIN MATRIX (*A BRitish feasibility study of molecular stratification and targeted therapy to optimize the clinical mAnagement of parteNts with glioma by enhancing clinical ouTcomes, Reducing avoidable toXicity, improving management of post-operative residual & recurrent disease and improving survivorship*). The Brain Tumour Charity funded. CI: Colin Watts. Multi-centre study.
- FUTURE GB (*Functional and Ultrasound guided Resection of Glioblastoma*). A 2-Stage trial. Stage 1 Non-randomised learning phase evaluation of participating centres (an IDEAL study), followed by Stage 2 which is randomised, controlled Multicentre Phase III trial with 2 mechanistic substudies). NIHR Efficacy and Mechanism Evaluation (EME) funded. CI: Puneet Plaha. Multi-centre study.
- RADIANT BC (*A multi-cohort Phase 1b/expansion cohort study of the efficacy and safety of radiosurgery with durvalumab following durvalumab and standard of care systemic therapy in patients with brain metastasis secondary to breast cancer*). CRUK funded. CI: Carlo Palmieri. Cross CSG study (Brain Tumour & Breast Cancer). Multi-centre study.
- BRITEMET (*BRain dlffusion TEnsor imaging to predict immunotherapy response in METastatic melanoma*). CRUK bursary funded. CI: Rasheed Zakaria & Michael Jenkinson. Cross-CSG study (Brain Tumour & Skin Cancer). Single centre study.

Raising profile

The CSG continues to engage with aligned professional societies. Michael Jenkinson has presented at the British Neuro-Oncology Society (BNOS) (6/7/18), CNS Bootcamp (14/9/18), The Society of British Neurological Surgeons (SBNS) tumour subsection (19/3/19) and BNOS strategy day (29/3/19). This has led to increased number of researchers contacting the CSG and subgroups for input into study design and concepts. Furthermore, by raising the CSG profile, in the last recruitment round we received 8 high quality trainee applicants and 12 high calibre applicants from which we had to turn down several individuals who would have been valuable members. The CSG held a meeting with the clinical research network SSLs in November 2018 in order to increase recruitment into open trials and to identify and foster new potential trial CIs.

Strengthen UK wide & international working

ROAM continues as a UK developed trial exported internationally to European Organisation for Research and Treatment of Cancer (EORTC) and Trans Tasman Radiation Oncology Group (TROG) and will run for a further 6 years. Dr Sara Erridge is the EORTC liaison and working to ensure EORTC trials open in the UK and is involved in the upcoming i-WOT study. Michael Jenkinson is the UK lead for the International Consortium on Meningioma whose work is

focused on clinically aggressive meningiomas. Tom Santarius founded and leads AMiCo – the Anaplastic Meningioma International Consortium. These international links with meningioma researchers will be critical for developing future meningioma drug trials.

CSG structure & function

We have successfully appointed two medical oncologists to the CSG (academic consultant and trainee), which is critical to developing new drug trials. We have established a mentorship programme for the consumers – Stuart Smith and Sam Mills are working closely with the new consumer reps.

All new trainee CSG members have been assigned to work on trials in development, led by CSG or Subgroup members. Faye Robinson is working with Sara Erridge and Paul Brennan on a recurrent glioblastoma trial. Cressida Lorrimer will work with Juliet Brock on elderly glioblastoma. Paul Miller will work with the Glioma Subgroup on repurposing drugs trials. In early 2018, we held a cross CSG brain metastasis workshop in collaboration with Breast, Lung and Skin Cancer CSGs, this resulted in two CRUK funded studies which will open in 2019.

Patient & Public Involvement and Impact

Our new consumer representatives are embedding into the CSG activities. They have engaged with their mentors, attended the NIHR CRN SSLs meeting, the Supportive and Palliative Care PROMs incubator day and the annual NCRI Conference in Glasgow.

Glioma Subgroup (Chair, Dr Sara Erridge)

Develop new trials within the CSG for glioma and ensure areas of unmet need included

Two new glioma studies have been funded (see section above for details). BRAIN MATRIX will establish a rich biobank of tissue and become a platform for new drug trials. FUTURE GB will address one of the top ten research priorities within neuro-oncology, 'does extent of resection influence outcome'.

Two workshops have been held, hosted by Edinburgh members, to discuss issues related to designing trials for optimising management of recurrent glioblastoma. The first meeting was an overview of the challenges and the second on improving accuracy of diagnosis of progression. A third focussing on surgery in the recurrent setting will be held later in 2019. Studies will be developed by Drs Brennan, Erridge and Thompson around these questions. The plan is to utilise the BRAIN MATRIX trial platform which will recruit all glioma patients undergoing surgery in 10 centres and provide infrastructure for other studies that have their own funding.

The itraconazole trial was declined for funding as the reviewers required evidence that the drug would penetrate the brain. Dr Dusan Milanovic is currently accruing this evidence in a local study.

EORTC 1635 (iWOT) (Dr Erridge UK PI) a low-grade glioma trial was supported by the group but only has central funding so other sources of support are being sought.

The long-term survivor study has struggled to open due to regulatory issues related to obtaining Caldicott Guardian approval from hospitals, but Mr Brennan is developing a study as part of a neurosurgical trainee PhD.

A proton versus photon radiotherapy trial for codeleted glioma is being developed by Dr Powell (Glioma Subgroup member).

Provide feedback for non-CSG member studies

Several studies were developed by former CSG members that are recruiting or have completed recruitment:

- The PARADIGM trials (Anthony Chalmers) radiotherapy /temozolomide +/- olaparib
- Two imaging studies: DIG (Adam Waldman) and PRaM GBM (Stephen Price)
- REOgLio (Susan Short) has completed accrual

Two studies were developed by non-CSG members, but in collaboration with the Glioma subgroup and the Supportive & Palliative Care subgroup. These are open and recruiting.

- BRITER (Juliet Brock and Cressida Lorimer)
- IPIGLIO: (Dr Mulholland) Phase II of ipilimumab in glioblastoma has opened

Other studies:

- EORTC 1709 (Glioblastoma Phase III Chemo-radiation +/- marizomib has opened
- Several 'badged' commercial trials have opened Abbvie M16 (ABT ocular toxicity management) and AZ 1320 (Anthony Chalmers) Phase I re-irradiation by new agent.
- STELLAR Phase III for recurrent grade III glioma should open soon
- BRIOCHE: (Louise Murray) Randomised Phase II trial assessing role of re-irradiation or chemotherapy has been funded by Jon Moulton Charitable Foundation.

Widen the access to trials throughout the UK through a neuro-oncology network

We continue to work with CNS Bootcamp to raise the profile of the Glioma subgroup in the neuro-oncology community and our role in assisting new investigators navigate the funding and approval process to develop successful trials. Dr Sara Jeffries has stepped down as Chair in order to lead the 'New Roads in Training' aspect of the Tessa Jowell Brain Cancer Mission, through which we hope to find and develop the next generation of investigators. Michael Jenkinson is also a member of the 'New Roads in Training' group.

Meningioma, Metastases & Other Tumours Subgroup (Chair, Mr Thomas Santarius)

Support and develop new clinical trials for patients with meningioma

Tom Santarius, Michael Jenkinson and Oliver Hanemann submitted PROMISE Meningioma to the CRUK Brain Tumour Awards call. This is an international collaborative project that includes work packages for prospective recruitment of patients into imaging and tissue biomarker projects. This study was not funded and the group plans to split the programme into smaller packages and seek alternative funding streams.

Michael Jenkinson is developing STOP 'EM – a multicentre trial of prophylactic antiepileptic drugs for seizure naïve patients undergoing surgery for meningioma. This will address an important clinical problem and will be a multi-centre UK trial. A researcher-led grant was submitted to NIHR HTA on 15th May 2019.

Michael Jenkinson and Tom Santarius are developing quality of life studies for patients with meningioma. These will be part supported by funding from a grant from The Brain Tumour Charity 'Deciphering the genetic and epigenetic landscape of clinically aggressive meningioma' for which Michael Jenkinson is the UK PI. One of the workstreams is focused on quality of life. Tom Santarius submitted HuMenVac – the first-in-human autologous vaccine to treat anaplastic meningioma trial; funding was turned down by The Brain Tumour Charity and the grant will be re-worked for submission elsewhere.

Support and develop new clinical trials for patients with metastases

A cross-CSG brain metastasis workshop in February 2018 led to the development and successful funding of 2 studies:

- RADIANT BC (A multi-cohort Phase 1b/expansion cohort study of the efficacy and safety of radiosurgery with durvalumab following durvalumab and standard of care systemic therapy in patients with brain metastasis secondary to breast cancer). CRUK funded £1.3M. CI: Carlo Palmieri. Cross CSG study (brain and breast). Multi-centre study.
- BRITEMET (BRain diffusion TEnsor imaging to predict immunotherapy response in METastatic melanoma). CRUK bursary funded £24,000. CI: Rasheed Zakaria & Michael Jenkinson. Cross-CSG study (brain and skin). Single centre study.

A further study (SUPARMAN: SUPrAmarginal Resection for MetAstases of the Nervous system) is being developed with a view to NIHR HTA submission.

Support and develop new clinical trials for patients with Primary CNS Lymphoma

The IDEAL study (Improving Diagnostic EvAluation of enhancing Lesions utilising DCE-MRI in clinical practice) is in development for submission to the MRC Clinical Academic Research Partnerships (CARP) programme. CI: Sam Mills. This will be a single centre portfolio study.

Establish links with other Clinical Studies Groups for brain metastases trials

We have continued to work with the breast, lung and skin CSGs to develop new studies. The lung CSG are developing a study on MRI screening for brain metastasis in lung cancer patients, which if funded will be another example of successful cross-CSG collaboration. A follow up workshop is planned for 2020.

Define Standard Operating Procedures for meningioma studies data collection

We have published a position statement on the 'Utilisation of Volumetric Magnetic Resonance Imaging for Baseline and Surveillance Imaging in Neuro-oncology' in the British Journal of Radiology that proposes standardising imaging in meningioma and other brain tumours. We have proposed SOPs for tissue collection as part of the PROMISE Meningioma grant submitted to CRUK. Since this was not funded, it will prove challenging to implement these in neurosurgery practice across the UK.

Establish a research network with active clinicians working on meningioma

We have established a register of neurosurgeons across the UK who are interested in participating in future meningioma clinical studies. This was achieved via the Society of British Neurological Surgeons (SBSN) and the British-Irish Meningioma Society (BIMS) membership mailing lists. This list is essential to identify the PIs for any future funded studies e.g. STOP 'EM.

Supportive & Palliative Care Subgroup (Chair, Dr Robin Grant)

Encourage development of high quality clinical trials in the top 10 priority areas

Two studies have been funded and open to recruitment but do not appear on the portfolio as they do not meet the requirements. Nevertheless, this is evidence of an active research community.

- **Brainwear** – Wrist worn trackers to monitor physical activity data in patients with primary and metastatic brain tumours. Feedback given – locally funded by UCL

- **BRITER study** – Predicting who may be more likely to have side effects of treatment age >65 years (Kent Surrey & Sussex). Locally funded.

We have provided feedback for several unsuccessful trials over the last 12 months and some of these will be re-shaped based on the funding review comments:

- **BT-FIT** Brain Tumour Study: Feasibility of Exercise Intervention pre-during Treatment. (Edinburgh, Stirling, New York) (TBTC). Feedback given.
- **SmartCare UK** for neuro-oncology caregivers. Improving support for family caregivers (NIHR RfPB) (Leeds: Edinburgh; Cardiff). Not funded by TBTC or NIHR RfPB. Going to YCR – local Yorkshire funding – Feedback given
- **PREPARED** – Providing resources to Engage Patient and Relative in End of Life care Decisions (Cardiff) (MC) – Feedback given
- **Palliative Care / Supportive Care Master Protocol** – Cardiff (MC)
- **SCAN-LGG** - Symptom correlates and neuroimaging in low-grade glioma. (Edinburgh, Glasgow, Manchester (TBTC) - being re-shaped based on feedback.
- **Measuring What Matters** – measuring the impact of a brain tumour on broader aspects of life and wellbeing for patients and caregivers. (Sussex) (TBTC).

Provide early advise on study applications

Several studies are in development and planned for submission over the next 12 months:

- **Aiding Decisions About Primary Treatment in Glioma (ADAPting)**. (Edinburgh, Cardiff, Glasgow, Leeds). Being developed. Feedback given
- **SHIPPING study**. Scanning Headache to Identify Positive Predictive factors for use IN Guidelines. Being developed
- **SCARF BT**. SCARF-BT: Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour. PI S Price (Cambridge). Feedback given - Submitted RfPB

Support Research Design Service and key Clinical Trials Units involvement

We held an incubator day on 13 September 2018 on Clinical Outcome Assessments in Neuro-Oncology including: PROs, ClinROs, ObsROs and PerfROs. Following the Incubator Day that led to a position statement from the group on Clinical Outcome Assessment in BRAin Tumour Trials (COBRA NCRI Brain S&PC Position Statement 2019). Further work will be required to develop a comprehensive framework for patient centred outcomes through collaboration with CTUs in the UK and ensure the align with Brain MATRIX

Work collaboratively with relevant NCRI groups

Several subgroup members are working to increase engagement across other NCRI groups and national/international groups:

Involvement with other CSGs and Subgroups

- We have been supportive of the NCRI Supportive & Palliative Care CSG by sharing the outcomes of the PROMs Incubator Day on 13/9/18

National /International Groups

- EANO Review on Capacity to Consent. In production 2019. (RG/HB/KO/AR).
- Tessa Jowell Brain Cancer Mission (TJBCM) (HB)
- Cochrane Neuro-Oncology Group (RG / HB)

NIHR Subspecialty Leads

- Working with ABN Scientific Committee to encourage Neurology involvement (Neuroscience) ABN Scientific Chair; ABN AAG Lead; (RG / HB.) Neuroscience Involvement in Neuro-Oncology.

4. Task groups/Working parties

The Brain Group have had no task groups or working parties during the reporting year.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)					
Study	Application type	CI	Outcome	Level of CSG input	Funding amount
May 2018					
ITRARTEM: Itraconazole (ITRA) with standard radiotherapy (RT) and temozolomide (TMZ) in patients with newly diagnosed glioblastoma multiforme (GBM): a phase I/II study	Early Phase & Feasibility Study	Dr Dusan Milanovic	Not Supported	Discussed with Glioma subgroup at 2 meetings	NA
18F-DOPA PETMRI to accelerate second line treatment in patients with aggressive brain tumours	Biomarker Project Award	Dr Francesco Fraioli	Not Supported	Not discussed with CSG	NA
November 2018					
IMAGE-ID: Image-guided Multi-modal Annotation of Genetics and tumour micro-Environment In patients with Diffuse low-grade glioma	Experimental Medicine Award Outline	Dr Matthew Grech-Sollars	Invited to full	Discussed with glioma subgroup and feedback on study design provided	TBC
Other committees					
Study	Committee application type	& CI	Outcome	Level of CSG input	Funding amount
BRITEMET (BRain dlffusion TENSOR imaging to predict immunotherapy response in METastatic melanoma). CRUK bursary funded. CI: Rasheed Zakaria & Michael Jenkinson. Cross-CSG study (brain and skin). Single centre study.	CRUK Postdoctoral research bursary	Rasheed Zakaria	Funded August 2018	CSG developed	£24,000
FUTURE GB (Functional and Ultrasound guided Resection of Glioblastoma). A 2-Stage trial. Stage 1 Non-randomised	NIHR EME	Puneet Plaha	Funded March 2019	CSG supported. Michael Jenkinson is a co-applicant	£1.7M

learning phase evaluation of participating centres (an IDEAL study), followed by Stage 2 which is randomised, controlled Multicentre Phase III trial with 2 mechanistic substudies). NIHR EME funded. CI: Puneet Plaha. Multi-centre study.					
RADIANT BC (A multi-cohort Phase 1b/expansion cohort study of the efficacy and safety of radiosurgery with durvalumab following durvalumab and standard of care systemic therapy in patients with brain metastasis secondary to breast cancer). CRUK funded. CI: Carlo Palmieri. Cross CSG study (brain & breast). Multi-centre study.	CRUK	Carlo Palmieri	Funded January 2019	CSG supported. Product of the cross CSG brain metastasis workshop	£1.3M
BRAIN MATRIX (A BRITish feasibility study of molecular stratification and targeted therapy to optimize the clinical mAnagement of parleNts with glioma by enhancing clinical ouTcomes, Reducing avoidable toXicity, improving management of post-operative residual & recurrent disease and improving survivorship). The Brain Tumour Charity funded. CI: Colin Watts. Multi-centre study.	The Brain Tumour Charity	Colin Watts	Funded October 2018	CSG supported. Colin Watts is a former CSG chair.	£2.8M

6. Consumer involvement

Usama Ali

Usama is on the Meningioma & Metastasis subgroup. He has made contact with his mentor (Dr Mills) and attended a 2-day NCRI consumer training event in September 2018.

Usama also attended:

- the NIHR CRN Brain Subspecialty Meeting in November 2018.
- a PROMs incubator day in Birmingham in September 2018 where different stakeholders with an interest in implementing the use of PROMs in brain tumour studies came together to discuss ideas on how to drive this agenda forward
- the NCRI Annual Conference in November 2018.
- the NCRI Consumer Forum Meeting in March 2018 and participated in the “Dragon’s Den” workshop where he (along with other patients) provided feedback on a researcher’s proposed study which aims to investigate the issue of multi-morbidity and barriers in early diagnosis for cancer care/treatment.

Jessica Sass

Jess is on the Glioma Subgroup and has made contact with her mentor (Stuart Smith). Jess was involved as a panel member for the selection on the new NCRI Consumer Lead.

Jess also attended:

- The 2-day NCRI consumer training event in September 2018.
- The NIHR CRN Brain Subspecialty Meeting in November 2018.
- The NCRI Annual Conference in November 2018.
- The NCRI Consumer Forum Meeting in March 2018 and participated in the “Dragon’s Den” workshop to provide feedback on researchers proposed study.
- The Health Data Research UK - Frontiers Meeting for Patients, Public and Charities and participated in a discussion surrounding how patients can best be incorporated into research models and projects.

7. Priorities and challenges for the forthcoming year

Priority 1

Increase the number of interventional studies on the portfolio across all brain tumour types. We need to translate the multi-centre studies in development (e.g. STOP 'EM – prophylactic antiepileptic drugs in meningioma surgery) into successful grant applications and translate the activity in workshops (e.g. recurrent glioblastoma) into grants.

Priority 2

Provide trainee mentorship and ensure trainees are actively engaged in subgroup activity to develop clinical studies for funding. These trainees should be co-applicants on the grants. As an example two of the previous trainee members have been successful in securing study funding (Ally Rooney; BT Life, The Brain Tumour Charity) or are working up grants (Paul Brennan; Recurrent glioblastoma trials). It is vital that the current trainees are supported fully in their CSG activity.

Priority 3

Engage with professional organisations to ensure the CSG chair has representation on the British Neuro-Oncology Society committee and the SBNS tumour section committee. This will facilitate cross organisation working to develop new chief investigators and trials.

Challenge 1

Ensuring the grants submitted to NIHR have input and feedback from the Brain Tumour CSG. At the last APPG Brain Tumour meeting we understand that 20 applications have been submitted since the brain tumour highlight notice was created but only 2 have been funded and this may reflect applications of insufficient quality.

Challenge 2

Increase the number of studies on the meningioma, metastasis and other tumours portfolio. This part of the portfolio is the weakest and the tumour types are some of the more challenging to develop new studies for.

Challenge 3

Increasing the number of studies that can open in all centres across the UK since at present studies tend to open in the same higher volume sites. As an example, if funded, the STOP 'EM meningioma trial could open in all neurosurgery units in the UK.

8. Collaborative partnership studies with industry

The FUTURE GB trial involves collaboration with industry to provide intra-operative ultrasound and image-guidance systems for participating neurosurgery units to the value for approximately £1.7M. This industry support was essential to ensure the requested funds from NIHR EME represented value for money.

9. Appendices

Appendix 1 - Membership of the Brain Group and Subgroups

Appendix 2 –Brain Group and Subgroup strategies

A – Brain Group Strategy

B – Glioma Subgroup Strategy

C – Meningioma, Metastases & Other Tumours Subgroup Strategy

D – Supportive & Palliative Care Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Mr Michael Jenkinson (Brain Group Chair)

Appendix 1

Membership of the Brain Group

Name	Specialism	Location
Dr Juliet Brock	Clinical Oncologist	Brighton
Dr Sara Erridge	Clinical Oncologist	Edinburgh
Dr Juanita Lopez	Clinical Oncologist	London
Dr Paul Sanghera	Clinical Oncologist	Birmingham
Dr Cressida Lorimer*	Clinical Research Fellow	Brighton
Dr Paul Miller*	Clinical Research Fellow	Oxford
Dr Faye Robertson*	Clinical Research Fellow	Edinburgh
Dr Thomas Booth	Radiologist	London
Mr Usama Ali	Consumer	Oxford
Ms Deborah Keatley	Consumer	Belfast
Ms Jessica Sass	Consumer	London
Dr Sarah Jefferies	Clinical Oncologist	Cambridge
Dr Robin Grant	Neurologist	Edinburgh
Professor Oliver Hanemann	Neurologist	Plymouth
Professor Silvia Marino	Pathologist	London
Dr Martin McCabe	Paediatric Oncologist	Manchester
Dr Samantha Mills	Radiologist	Liverpool
Dr Igor Vivanco	Scientist	London
Dr Wendi Qian	Statistician	Cambridge
Mr Michael Jenkinson (Chair)	Surgeon	Liverpool
Mr Thomas Santarius	Surgeon	Cambridge
Mr Stuart Smith	Surgeon	Nottingham

* denotes trainee member

Membership of the Subgroups

Glioma Subgroup		
Name	Specialism	Location
Dr Paul Miller*	Clinical Research Fellow	Oxford
Dr Faye Robertson*	Clinical Research Fellow	Edinburgh
Dr Sara Erridge (Chair)	Clinical Oncologist	Edinburgh
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr Dusan Milanovic	Clinical Oncologist	London
Dr Sarah Jefferies	Clinical Oncologist	Cambridge
Dr James Powell	Clinical Oncologist	Cardiff
Ms Jessica Sass	Consumer	London
Dr Juanita Lopez	Medical Oncologist	London
Dr Igor Vivanco	Medical Oncologist	London
Dr Estelle Healey	Pathologist	Belfast
Dr Thomas Booth	Radiologist	London
Dr Darragh McArt	Senior Lecturer	Belfast
Dr Paul Brennan	Surgeon	Edinburgh
Mr Stuart Smith	Surgeon	Nottingham
Dr Gerard Thompson	Radiologist	Edinburgh

Meningioma, Metastases & Other Tumours Subgroup		
Name	Specialism	Location
Dr Joanne Lewis	Clinical Oncologist	Newcastle
Dr Paul Sanghera (Co-chair)	Clinical Oncologist	Birmingham
Dr Gillian Whitfield	Clinical Oncologist	Manchester
Mr Usama Ali	Consumer	Oxford
Professor Oliver Hanemann	Neurologist	Plymouth
Dr Samantha Mills	Neuro-radiologist	Liverpool
Dr Richard Baird	Medical Oncologist	Cambridge
Mr Michael Jenkinson	Surgeon	Liverpool
Mr Jonathan Pollock	Surgeon	Essex
Mr Thomas Santarius (Chair)	Surgeon	Cambridge
Mr Rasheed Zakaria*	Surgeon	Liverpool

Supportive & Palliative Care Subgroup		
Name	Specialism	Location
Dr Cressida Lorimer*	Clinical Research Fellow	Sussex
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr Helen Bulbeck	Consumer	Isle of Wight
Mrs Kathy Oliver	Consumer	Surrey
Dr Anthony Byrne	Director, Marie Curie Palliative Care Research Centre	Cardiff
Dr Robin Grant (Chair)	Neurologist	Edinburgh
Dr Jon Evans	Neuro-Psychologist	Glasgow
Professor Richard Neal	Professor Primary Care	Leeds
Professor Robert Hills	Professor of Statistics & Methodology	Cardiff
Dr Ann Arber	Senior Lecturer, Cancer & Palliative Care	Surrey
Dr Ally Rooney	Senior Lecturer Psychiatry	Edinburgh
Dr Florian Boele	YCR Academic Fellow	Leeds

* denotes trainee member

**denotes non-core member

Appendix 2

Group & Subgroup Strategies

A – Brain Tumour Group Strategy

Patients with brain tumours continue to suffer from poor clinical outcomes because of under-developed clinical research infrastructure, pre-clinical models that do not accurately represent clinical disease and a limited scientific base in the UK.

Aims

- To promote and support the development of clinical trials for patients with all types of brain tumours through disease-focused subgroups.
- To promote research into survivorship, quality of life and patient reported outcomes through a specific subgroup.
- To work more closely with scientists to generate added value from clinical trials and develop mechanistic and discovery science.
- To support, promote and advocate on behalf of brain tumour patients and their carers.

To achieve these aims, we have:

- Re-organised the subgroup structures to better reflect clinical research priorities.
- Appointed basic scientists to the CSG and Subgroups to encourage synergy between science and clinical trials.
- Appointed clinical trainees to the CSG to encourage the clinical investigators of tomorrow.
- Engaged with patient representative through CSG PPI members and brain tumour charities to support clinical trial development and prioritise what matters to patients.
- Worked with all our stakeholder to improve recruitment and identify barrier to recruitment into clinical trials.

The challenges of neuro-oncology research in the UK and planned strategy have been published:

Brain tumor research in the United Kingdom: current perspective and future challenges. A strategy document from the NCRI Brain Tumor CSG

Kathreena M. Kurian, Michael D. Jenkinson, Paul M. Brennan, Robin Grant, Sarah Jefferies, Alasdair G. Rooney, Helen Bulbeck, Sara C. Erridge, Samantha Mills, Catherine McBain, Martin G. McCabe, Stephen J. Price, Silvia Marino, Erica Moyes, Wendy Qian, Adam Waldman, Babar Vaqas, Debbie Keatley, Peter Burchill, and Colin Watts
Neuro-Oncology Practice. 5(1), 10–17, 2018 | doi:10.1093/nop/npx022

The timelines below outline the strategic objectives, actions, CSG leads and outcomes for each element of the strategy.

Brain Tumours CSG Strategy: April 2018 – April 2021

This strategy timeline has been produced to support the Brain Tumour CSG research strategy. It runs from April 2018 until April 2021, and will be reviewed and updated (by MDJ, SJ and RG) on a regular basis.

The document is composed of the following:

Page 2 – 4: NCRI Brain Tumour CSG Strategy: plan of implementation, containing agreed strategic objectives (1-5), specific actions, CSG leads and proposed deadlines.

Strategy document agreed by CSG on 19.4.18

Brain Tumour CSG members		Glioma subgroup		Meningioma & metastasis subgroup		Supportive & Palliative care subgroup	
MDJ	Michael Jenkinson	SJ	Sarah Jeffries (chair)	PS	Paul Sanghera (co-chair)	RG	Robin Grant (chair)
DK	Debbie Keatley	CMcB	Catherine McBain	TS	Tom Santarius (co-chair)	AA	Ann Arber
HB	Helen Bulbeck	EH	Estelle Healey	MDJ	Michael Jenkinson	AB	Anthony Byrne
IV	Igor Vivanco	GT	Gerry Thompson	DK	Debbie Keatley	CMcB	Catherine McBain
KK	Kathreena Kurian	HB	Helen Bulbeck	GW	Gillian Whitfield	DP	Diane Playford
LF	Lorna Fern	IV	Igor Vivanco	JL	Joanne Lewis	FB	Florian Boele
MM	Martin McCabe	JP	James Powell	JP	Jonathan Pollock	HB	Helen Bulbeck
OH	Oliver Hanemann	LC-H	Laura Clifton-Hadley	KK	Kathreena Kurian	KO	Kathy Oliver
PH	Phil Hexley	NC	Natalie Cook	OH	Oliver Hanemann	WH	Willie Hamilton
PH	Paul Sanghera	PB	Paul Brennan	RB	Richard Baird		
SE	Sara Erridge	SE	Sara Erridge	RZ	Rasheed Zakaria		
SJ	Sarah Jefferies	SM	Silvia Marino	SJM	Samantha Mills		
SJM	Samantha Mills	SS	Stuart Smith				
SM	Silvia Marino						
SS	Stuart Smith						
RG	Robin Grant						
WQ	Wendy Qian						
TB	Thomas Booth						

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Create a large portfolio of studies for patients with brain tumours	All	On going	Increased access to clinical studies for patients
	Review study proposal before submission to funding bodies to improve grantsmanship	All	On going	
1b. Portfolio development (glioma subgroup)	Increase trials for patients with gliomas	All subgroup members	Ongoing	Ongoing
	Studies in development: <ul style="list-style-type: none"> Repurposing Itraconazole 	SJ/SE	Nov 2017	Submitted to CRUK
	<ul style="list-style-type: none"> Adaptive glioma clinical trial 	All	August 2018	Submit to TBTC
	<ul style="list-style-type: none"> Role of revision surgery in glioblastoma 	PB/SS/SJ/SE	April 2019	Workshop planned
1c. Portfolio development (meningioma & metastases subgroup)	Increase trials for patients with meningioma, metastasis & others	All subgroup members		
	Studies in development: <ul style="list-style-type: none"> Management of incidental meningioma 	JP/MDJ/TS	Oct 2019	Submit to NIHR HTA Present at NCRI brain mets workshop 2/3/18 Present to main CSG and develop submission for NIHR RfPB
	<ul style="list-style-type: none"> Epilepsy in meningioma: NIHR HTA 	MDJ	Oct 2018	
	<ul style="list-style-type: none"> Surgical resection of brain metastases 	RZ/MDJ	Oct 2018	
<ul style="list-style-type: none"> Imaging markers of PCNSL 	SJM/MDJ	Oct 2018		

Strategic objective	Action	CSG Lead	Date	Outcomes
1d. Portfolio developments (supportive & palliative care)	<p>Increase trials for patients with brain tumours addressing symptom burden</p> <p>Cochrane Complex Reviews (interval scanning, earlier diagnosis, earlier referral to palliative care, molecular subtyping, long term effects or surgery and/or RT).</p> <p>Funded studies:</p> <ul style="list-style-type: none"> • SPRING trial (Seizure prophylaxis in glioma) • BTLife (brain tumours; lifestyle intervention and fatigue evaluation) • The KEATING Trial – a randomised study of the ketogenic diet <p>Studies in development:</p> <ul style="list-style-type: none"> • Effect of ketogenic diet on tumour growth • Palliative care supportive care master protocol • Improving support for family caregivers • Early diagnosis of primary brain tumours • Posterior Fossa 	<p>All</p> <p>RG</p> <p>RG AR/RG</p> <p>MDJ</p> <p>KO FB</p> <p>RG</p>	<p>On going</p> <p>August 2017</p> <p>April 2018 Oct 2017</p> <p>Sept 2018</p> <p>2019 2019</p> <p>2019</p>	<p>NIHR HTA funded TBTC funded</p> <p>Funded by Vitaflow</p>
2. Raising profile	<p>Routine dissemination of results from studies through speciality meetings e.g. SBNS, BNOS, CNS Bootcamp</p> <p>Presentation of NCRI CSG role and portfolio at specialty meetings:</p> <ul style="list-style-type: none"> •British Neuro-Oncology Society (BNOS) •Society of British Neurological Surgeons (SBNS) •CNS bootcamp •British Neurosurgical Research Group (BNRG) •British Neuropathology Society (BNS) •Glioma Club •Joint ABN / SBNS meeting 	<p>Study Chief Investigators</p> <ul style="list-style-type: none"> •MDJ/SS/SJ/SE/SM •MDJ/SS •SJ •MDJ •KK •SM •RG/MDJ 	<p>On going</p> <p>Annual presentations from March 2018</p> <p>Sept 2018</p>	<p>Continued engagement of investigators to recruit to studies</p> <p>Raise awareness, identify new chief investigators, encourage CSG review of proposals before submission to funders</p>

B – Glioma Subgroup Strategy

The formation of the Glioma Subgroup is to improve the access and entry of patients with a diagnosis of a glioma into clinical trials throughout the United Kingdom.

The Subgroup has been selected to have representation from centres in England, Scotland, Wales and Northern Ireland. It has neurosurgical representation to build on the successful current platform of neurosurgical trials. A medical oncologist with phase I experience has been appointed as it is recognised that this is an area that needs improvement in the current trial portfolio. A scientist with a dedicated interest in translational science has been appointed to help with this aspect within trial design. A radiologist and neuropathologist have been appointed for specialist advice in clinical trial development. It is planned to advertise for two trainees to join the Subgroup from any of the contributing disciplines to foster links with developing expertise for those working in neuro-oncology in the future.

The Subgroup will act as platform to provide support for the development of UK-led clinical trials, including commercial and academic studies. Plans are in place to provide a quick guide to apply for adoption to the portfolio for commercial studies.

We will also provide direct or targeted support for one-two grant applications per year for studies in glioma. Work is already underway for the development of a re-irradiation protocol which will be able to be utilised in multiple studies. The Subgroup also aims to develop a network for UK clinical oncologists who treat glioma.

There is a well-established group for neurosurgeons in the British Society of Neurosurgical Oncology and similarly there is a forum for basic research at the glioma club meeting. The infrastructure for an annual neuro-oncology meeting has been established at the CNS Bootcamp which aims to optimise information about current clinical trials and protocols that are in development to optimise trial entry across the UK. The ultimate aim will be to combine these three meetings to optimise clinical trial design and execution from the UK neuro-oncology community.

Strategic Aims:

1. Develop new trials within the CSG for glioma and ensure areas of unmet need included
2. Provide feedback for non-CSG member studies
3. Widen the access to trials throughout the UK through a neuro-oncology network

Strategic Components	Action	CSG Lead	Date	Outcome
1b. Portfolio Development (Glioma Subgroup)	Increase trials for patients with glioma	All	On going	On going
	Itraconazole Trial in glioblastoma	All subgroup	Submitted to CRUK Early Phase and	June 2018

			Feasibility December 2017	
	Standard ChemoRT+/- Ipilumimab in newly diagnosed GBM (Mulholland)	All subgroup	Submitted for funding 2017	Funded – aim to start recruitment in 7 UK centres Q4
	ATOMIC G	Presented CNS Bootcamp CM, NC	Submission to EME – input requested from sub-group	Resubmission later in 2018
	Role of revision surgery in recurrent glioblastoma	All subgroup	July 2018 – workshop to formalise trial design	Trial application to NIHR HTA November 2018
	Platform for radiology studies - MIMICING	GT, JP, IV	Meeting planned for 30.10.2018	Unified research platform for radiology studies
	Long-term survivor of GBM study (Brodbelt)	PB, EH, SS	All UK sites identified for data collection Pathology data set agreed April 2018	On going
2. Raising Profile	CNS Bootcamp	SJ	Meeting Planned for September 2018 2019 – joint meeting with Glioma Club at start of BNOS 2020 - EANO	Raise awareness, identify new investigators, increase clinical trial entry
3. Strengthen UK wide and international working	Engage with EORTC	SE	On going	EORTC studies on portfolio

C – Meningioma, Metastases & Other Tumours Subgroup Strategy

Vision

To create a large portfolio of clinical trials for patients with meningioma and metastases.

Mission statement

It is our goal to build on the existing portfolio and to develop new clinical trials for patients with meningioma and metastases. We will accomplish this by focusing on clinical priorities for patients, identifying research-active clinicians and providing a forum to advise on study applications. Our success will be measured by the number of successful grant applications and new studies adopted onto the portfolio.

Strengths

Two of the subgroup members (MDJ & TS) are part of the founding committee of BIMS (<https://britishirishmeningiomasociety.wordpress.com>) and have good links to the EORTC meningioma research committee (MDJ is a member) and the Society for Neuro-Oncology International Meningioma Consortium (MDJ, TS, OH & SM). These networks will be essential for developing UK trials and intergroup trials with EORTC. The group also draws on expertise in metastasis trials (GW, RB & PS).

Weaknesses

New subgroup members (JP, JL,) do not have experience of submitting grant applications. Current links with other CSGs is poor and many primary cancer trials specifically exclude patients with brain metastases.

Strategy for success

Meningioma

- Establish a network of research active clinicians (surgeons, oncologists, pathologist, radiologist) working on meningioma (via the British-Irish Meningioma Society) – in progress, expected May 2018.
- Define SOPs that will harmonise data collection for meningioma studies covering tumour tissue, blood samples and imaging (MRI) - in progress, expected May 2018.

Metastases

- Establish links with other CSGs (e.g. lung, breast, skin) to develop new trials for metastases patient groups, with reference to study design / methodology / tissue sampling for brain metastases trials.

Clinical studies under consideration/development by CSG subgroup

Strategic Components	Action	CSG Lead	Date	Outcome
1c. Portfolio Development (Meningioma & metastases)	Increase trials for patients	All	On going	On going
	Epilepsy in meningioma	MDJ	Nov 2018	NIHR HTA application planned
	Incidental meningioma management	JP/TS/MDJ/OH	2019 / 2020	
	Supramarginal resection of metastasis (SUPARMAN)	RZ/MJD/PS/TS/JL	2018 / 2019	NIHR HTA application planned
	Imaging markers and treatment pathway in PCNSL	SM/MDJ/TS	Nov 2018	RfPB application planned

D – Supportive & Palliative Care Subgroup Strategy

The NCRI Supportive & Palliative Care (S&PC) Subgroup strategy is aligned with the main NCRI brain strategy.

Key themes for the S&PC subgroup include:

Grantsmanship

- NCRI Brain S&PC subgroup will advise on applications in JLA priority areas by providing brief expert peer review via the subgroup on submissions at outline proposal stage.
- External review by the subgroup twice a year will follow the CTRad model.
- PPI on submissions review will be done through the S&PC PPI representatives.
- The breadth of experience on the S&PC Subgroup will provide feedback on JLA studies ranging from Primary care and early diagnosis to Palliative Care and End of Life studies

Research Studies & Trials

- To promote and support the development of clinical trials for patients with all types of brain tumours in JLA Priority areas
- To promote research into survivorship, quality of life and patient reported outcomes.
- To support, promote and advocate on behalf of brain tumour patients and their carers

Collaborations & Increasing reach

- Cochrane systematic review programme grant funded (Cochrane Neuro-Oncology Group & NCRI Brain CSG) (Dec 2017- Nov 2020) –to jointly evaluate evidence for future studies in 7 JLA topic areas for future possible brain trials and guidelines.
- NOCTURN (Neuro-Oncology Clinical Trials UK Research Network) website developed as an informational resource about developing trials, JLA research priorities, clinical trials units, funding deadlines relevant to Neuro-Oncology.
- Building relationships to explore ways of promoting NCRI and trials and expand the group and link with the NCRI Living With and Beyond Cancer group and other NCRI groups e.g. S&PC, Psycho-Social Oncology, Teenage & Young Adult CSGs
- NCRI Brain S&PC Newsletter (Jan 2018) distributed electronically

Clinical studies under consideration and development by the SPC Subgroup

Early diagnosis of primary brain tumours - Headache suggestive of cancer.

- A prospective multi-centre study of “headache suspicious of cancer” looking at the red flag features in the history, the value of a simple fast screening test of cognition (semantic verbal fluency test) and simple questions prior to brain imaging, (Robin Grant, Prof Richard Neal and Prof Leone Risdale)

Posterior Fossa Tumours

- Late effects of children and adults who have had Cerebellar tumour diagnosed (possible multi-centre)

Studies previously submitted– for further work and re-submission

- Improving support for family caregivers in neuro-oncology: the development of a self-monitoring and self-help mobile app and feasibility randomised controlled trial –F Boele
- PREPARED : **P**roviding **R**esources to **E**ngage **P**atients **A**nd **R**elatives in **E**nd of life care **D**ecisions – F Boele
- A Byrne - Palliative care supportive care master protocol (MC/TBTC) – not funded. Submitted as an early protocol. A Byrne
- BTFit – early neuro-rehabilitation. - A Campbell

Appendix 3 – Portfolio maps

NCRI Portfolio Maps							
Brain Tumour							
Map A – Brain metastases, meningioma, rare tumours							
↻ below to reset map							
		a) Pre-surgery	b) 1st diagnosis	c) Recurrent disease	d) Palliative care	e) Observational	
Brain meta stases	All	CamBMT1		radiation therapy in patient	CNS 2004 10	VoxTox	
						Wrist Worn Trackers for BT	
Meningio ma	All		ROAM			VoxTox	
				Genetics of End		Wrist Worn Trackers for BT	
Other studies	All			Spectral Analys		MOLGEN	
						VoxTox	
						MOT	
						Multipotent stem cell lines from	
						The PROMOTE Study	
						CRA, Liquid 13 Cis Retinoic	
						polarised 13C-Pyruvate MR	
						issue-type MRI of brain tumor	
						CIRCULATING DNA TO DE	
						ASPECT Study	
				al of ipatasertib in combinati			using plasticity to treat brain t
							Wrist Worn Trackers for BT
Rare tumours	All		SIOP Ependymoma II			BRITER study	
			CMS Study			HSI Neuro Phantom	
			PNET 5			BT-LIFE	
			Biomed			PLORAN	
					of Neratinib in Patients Wit		
					TRIDENT-1		
					VoxTox		
						ib dosing Phase I/II study C	
						Wrist Worn Trackers for BT	

Filters Used:
 Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All, LCRN: None

■ In Setup / multi res.. ■ Open / multi resea.. ■ Suspended / singl..
■ In Setup / single re.. ■ Open / single rese..



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NCRI Portfolio Maps

Brain Tumour

Map B – Gliomas, astrocytoma, glioblastoma

⌵ below to reset map

		a) Pre-surgery	b) 1st diagnosis	c) Recurrent disease	d) Palliative care	e) Observational
Anaplastic astrocytoma (grad..	All					VoxTox Imaging in Trans Glioma TSPO PET Imaging in GBM BT-LIFE
				Eforhithine with Lomustine		
Anaplastic oligodendroglioma..	All					VoxTox Imaging in Trans Glioma BT-LIFE
Glioblastoma	All					predictive molecular markers VoxTox Imaging in Trans Glioma Diffusion Imaging in Glioma Hypoxia in Cerebral Tumours PRaM-GBM TSPO PET Imaging in GBM Imaging glioblastoma pH using CE
			PARADIGM			
			ReoGlio			
			PARADIGM 2			
				radiation therapy in patient		
			IPI-GLIO			
			M16-534			
			EORTC 1709-BCG			
Low grade glioma	All					VoxTox Imaging in Trans Glioma MISSION: GliomaS Innate Dysfunction in Gliomas BT-LIFE Patients with Adv. Solid Tumour
				VINILO		

Filters Used:

Active Status: All, CSG Involvement: All, Funding Type: All, Phase: All, LCRN: None

- Open / multi resea..
- Suspended / singl..
- In Setup / single re..
- Open / single rese..



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Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
<p>KEATING trial</p> <p>1. The modified ketogenic diet in adults with glioblastoma; an evaluation of feasibility and deliverability with the National Health Service. Martin-McGill KJ, Marson AG, Tudur Smith C, <u>Jenkinson MD</u> Nutr Cancer 2018 70 (4): 643-649</p>	<p>Trial closed to recruitment and in follow-up. The study was the predecessor to KEATING.</p>	<p>Developed by CSG</p>
<p>2. Utilisation of Volumetric Magnetic Resonance Imaging for Baseline and Surveillance Imaging in Neuro-oncology Mills SJ, Santarius T, Radon M, Hanemann, O, Lewis, J, Sanghera P, Pollock J, Whitfield J, Zakaria R, Keatley D, <u>Jenkinson MD</u> British Journal of Radiology 2019 (in press)</p>	<p>Position statement about protocol for volume MRI in brain tumour management</p>	<p>Developed by CSG</p>
<p>3.</p>		
<p>4.</p>		
<p>5.</p>		

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Brain Group portfolio, 5 trials closed to recruitment and 11 opened.

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
2014/2015	716	171	716	170	15.1	3.6
2015/2016	147	112	145	106	3.05	2.23
2016/2017	189	116	188	108	3.96	2.27
2017/2018	600	259	598	245	12.58	5.15
2018/2019	305	312	295	277	2.58	2.42