

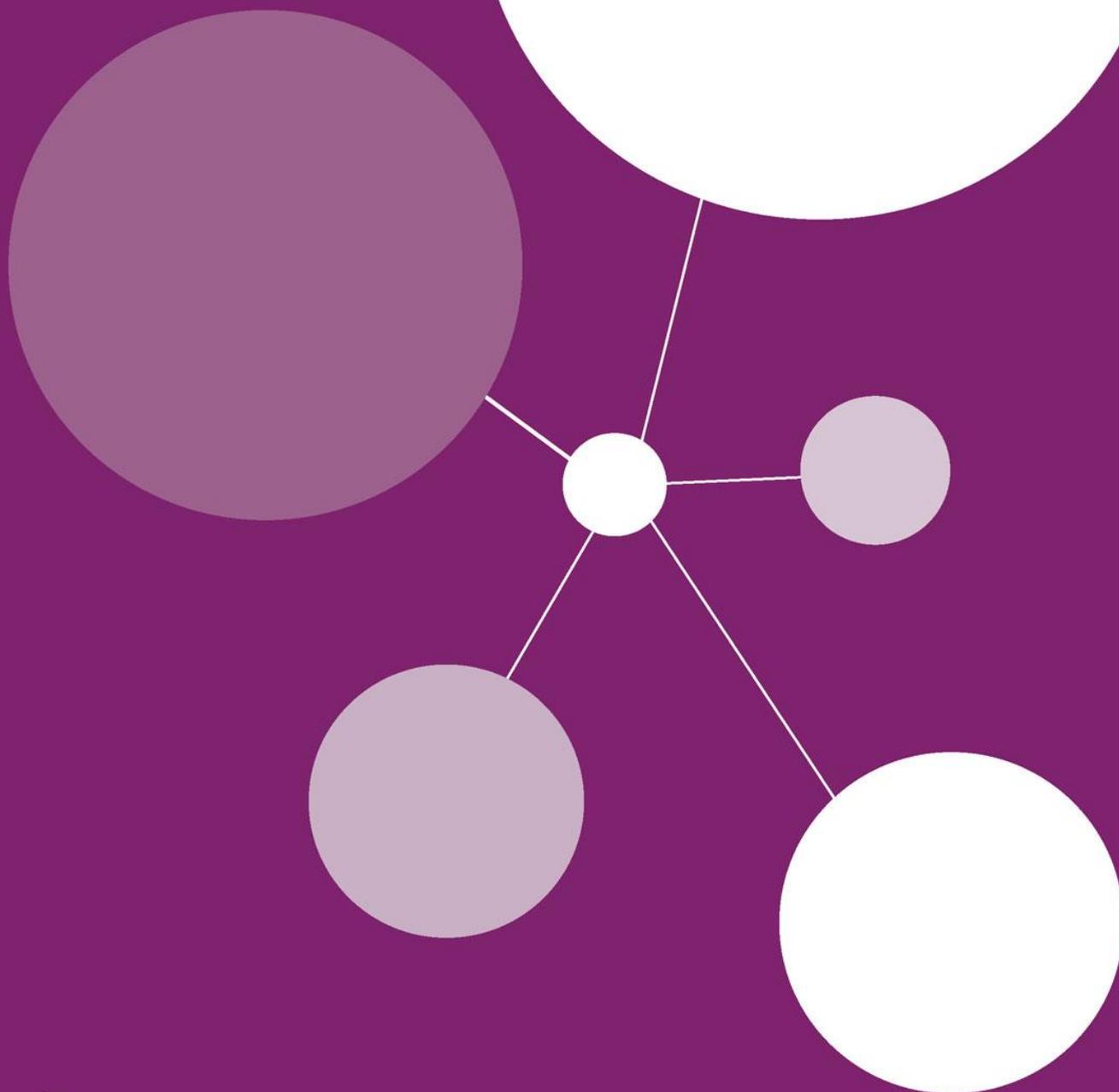


NCRI

National
Cancer
Research
Institute

NCRI Brain Tumour Clinical Studies Group

Annual Report 2017-18



Partners in cancer research



NCRI Brain Tumour CSG Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

The CSG was involved in the development of three glioma trials that secured funding from National Institute for Health Research (NIHR) Health Technology Assessment (HTA), The Brain Tumour Charity (TBTC), National Brain Appeal Charity and Bristol-Meyers Squibb.

As an exemplar the SPRING trial (Seizure PRophylaxis IN Glioma, CI: Dr Robin Grant) will open in 2019 and will be the largest glioma trial in the UK with a sample size of 804 patients. The trial will provide evidence for the role of prophylactic antiepileptic drugs in newly diagnosed glioma that will impact on future patient management.

Achievement 2

The CSG has increased engagement from the wider clinical brain tumour community in the UK. The annual CNS Bootcamp for clinical oncologists, organised by Dr Sarah Jeffries, Chair of the National Cancer Research Institute (NCRI) Glioma Subgroup, has a session dedicated to study concept development. The SBNS tumour section (led by Professor Colin Watts, former Chair of the NCRI Brain Tumour CSG) provides a similar platform and has led to an increase in studies being discussed and developed within the subgroups.

Achievement 3

The CSG worked closely with the Department of Health (DoH) Task & Finish Working Group on brain tumours which has resulted in NIHR agreeing to commit expenditure and develop specific calls for brain tumour trials. This funding is vital to develop new clinical trials for people living with brain tumours.

2. Structure of the Group

The structure of the CSG and disease specific subgroups is unchanged. Mr Michael Jenkinson was appointed as CSG chair in August 2017. Dr Catherine McBain (clinical oncologist) rotated off the CSG earlier this year and Dr Thomas Booth (neuroradiologist) joined the main CSG. Mr Peter Burchill (consumer) resigned from the CSG due to other commitments. Ms Debbie Keatley (consumer) is due to rotate off the CSG and is considering extending her term to support handover, consumer continuity and retention of institutional memory. Dr Paul Sanghera (clinical oncologist) and Mr Thomas Santarius (neurosurgeon), invited to join the CSG, became joint chairs of the Meningioma, Metastases & Other Tumours Subgroup.

3. CSG & Subgroup strategies

Main CSG

Portfolio development (general)

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

- Seizure PRophylaxis IN Glioma (SPRING), funded by the NIHR HTA. CI: Robin Grant
- BTLife (brain tumours; lifestyle intervention & fatigue evaluation) funded by TBTC. CI: Dr Ally Rooney
- Multi-centre phase II study of ipilimumab and temozolomide following surgery and chemoradiotherapy in patients with newly diagnosed glioblastoma. Jointly funded by The Brain Charity Appeal and Bristol-Meyers Squibb. CI: Dr Paul Mulholland

Raising profile

The CSG has contacted various profession societies to present annually at conferences on the role of the CSG in developing studies and supporting new researchers. Mr Jenkinson has presented at the British Neurosurgical Research Group meeting (8 March 18). Presentations at the British Neuro-Oncology Society (BNOS, 6 July 18), CNS Bootcamp (14 September 18) have been agreed. The impact will be measured on the number of researchers contacting the CSG for input into study development.

Strengthen UK wide & international working

Dr Sara Erridge has agreed to be the European Organisation for Research and Treatment of Cancer (EORTC) liaison to ensure the UK is considered for new EORTC brain tumour trials. Dr Erridge will attend the annual EORTC brain tumour group meetings and feedback to the CSG.

CSG structure & function

Dr Sanghera and Mr Santarius were appointed as joint chairs of the Meningioma, Metastases & Other Tumours Subgroup.

Patient & Public Involvement and Impact

Consumers were integral to CSG developed trials (SPRING, BTLife, MERIT) as they assisted in refining the research questions, study design and patient facing material. This contribution was reflected in 2 successful grants (SPRING, BTLife) and an invitation to re-submit (MERIT). CSG engagement with charities continues as Mr Jenkinson participated in TBTC annual away day and presented on the topic of 'Being a pioneer: a neurosurgeon's perspective'. The CSG was involved in the DoH Task and Finish group focused on lobbying Parliament for additional funding for brain tumour research. Brainstrust continues to facilitate the supportive and palliative care brain CSG and the SBNS tumour subsection. Helen Bulbeck is the PPI link with the PBT Research Strategy Group, the CTRad executive and NCRI Consumer Steering,

Activities this year include:

- Influencing strategy and service delivery/design
- Engaging with design, development and delivery in specific studies
- Raising profile with key stakeholders
- Sharing knowledge on cross-cutting themes with other NCRI consumers and beyond

Examples:

- Monitoring PPI in neuro-oncology trials to quantify impact
- Contributing to development of proactive and influential PPI practice for key stakeholders and funders such as the NIHR and CRUK
- Disseminating PPI messages to relevant CSGs (e.g Supportive & Palliative Care CSG, Clinical and Translational Radiotherapy (CTRAd) Research Working Group, Cellular Molecular Pathology Initiative (CM-Path), Lung Cancer CSG, Breast Cancer CSG and Skin Cancer CSG)
- Developing PPI think pieces on the use of brain cancer data with NCRAS/PHE
- Identifying opportunities to extend appropriate trial interventions to brain studies
- Supporting internal and external events to increase PPI awareness through the James Lind Alliance Priority Setting Partnership (JLA PSP), NIHR, Cochrane, BNOS, National Institute for Health and Care Excellence (NICE), American Association for Cancer Research (AACR) and the British Psychosocial Oncology Society (BPOS)
- Advocacy for PPI in radiotherapy research through CTRad

Glioma Subgroup (Chair, Dr Sarah Jefferies)

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

The Glioma Subgroup has developed a repurposed drug trial of Itraconazole in glioblastoma - submitted to CRUK and pending decision June 2018.

Study in development:

- Role of revision surgery in recurrent glioblastoma. A UK wide survey of clinical practice has been completed (for submission to European Association of Neuro-Oncology (EANO) meeting) and a workshop is planned for July 2018 to refine the study design.

Provide feedback for non-CSG member studies

Multi-centre phase II study of ipilimumab and temozolomide following surgery and chemoradiotherapy in patients with newly diagnosed glioblastoma (CI: Paul Mulholland) was discussed. The Glioma Subgroup advised using the Oxford Clinical Trials Unit and provided feedback to improve the study design. The study has been successfully funded (jointly between The Brain Charity Appeal and Bristol-Meyers Squibb) and will open in 7 UK centres.

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

Through the CNS Bootcamp (established by Dr Jefferies), the clinical oncology community meet annually to update knowledge and have a sandpit session to consider and develop new studies. One such study was repurposing Itraconazole in glioblastoma that was developed by the CSG and submitted to Cancer Research UK (CRUK) (pending decision June 2018). The CNS Bootcamp identified clinical oncologists interested in research and several joined the glioma subgroup to develop new trials.

Meningioma, Metastases & Other Tumours Subgroup (Chair, Mr Michael Jenkinson)

Support and develop new clinical trials for patients with meningioma

Two studies are currently in development:

- Epilepsy in meningioma: systematic review completed and published (PMID: 28625584). Clinical practice survey completed (manuscript drafted). A researcher-led expression of interest application is planned to NIHR HTA November 2018.
- Management of incidental meningioma: Clinical practice survey completed and published (PMID: 28292204). Due to the length of follow-up required (minimum 10 years) funding for this study is challenging. The study is important as it will potentially reduce the burden on health care resources – funding options are being explored.

Support and develop new clinical trials for patients with metastases

One study is in development:

- Supramarginal Resection versus Standard resection + cavity radiotherapy (SUPARMAN trial): the study was discussed at the Brain Metastasis Workshop in March and received support from CSGs and patient representatives. The technical surgical aspects of the study are being developed in consultation neurosurgeons. A researcher-led EOI application is planned for 2018/2019.

Support and develop new clinical trials for patients with PCNSL

One study is in development:

- Imaging and management pathway in PCNSL: the study has been discussed at the Lymphoma CSG and received support. An NIHR Research for Patient Benefit (RfPB) application is being developed by Dr Samantha Mills.

Establish links with other Clinical Studies Groups for brain metastases trials

The CSG hosted the Brain Metastases Workshop which took place on 2 March 18. Chairs and members from the Breast Cancer CSG, Skin Cancer CSG and Lung Cancer CSG attended. The research landscape was established and primary disease-specific breakout sessions were used to develop study ideas. A surgical study (SUPARMAN) relevant to all primary cancers was welcomed and a NIHR HTA application planned. Both the Breast and Skin Cancer CSGs developed radiosurgery + drug and immunotherapy studies. The Lung Cancer CSG considered a screening study. Following on from the success of the event a follow-up workshop is planned.

Define Standard Operating Procedures for meningioma studies data collection

Imaging and tissue sampling SOPs have been developed. A position paper is being drafted for publication that will serve as a standard for future meningioma trials.

Establish a research network with active clinicians working on meningioma

A preliminary register of neurosurgeons interested in meningioma research has been created (taken from the list of surgical PIs on the ROAM trial and attendees at the annual British and Irish Meningioma Society). Mr Jenkinson and Mr Santarius will contact the Society of British Neurological Surgeons (SBNS) to identify other individuals. The register will be used to engage sites in future meningioma studies.

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

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

We have provided support through several Incubator days on three UK-led clinical trials.

- NIHR HTA Programme: SPRING - Seizure Prophylaxis in Glioma. A Randomized Controlled Trial of Levetiracetam for Seizure Prophylaxis in patients with Suspected Glioma. April 2018-2024.
- The Brain Tumour Charity. BT Life: Brain Tumours: Lifestyle Interventions, and Fatigue Evaluation: a multi-centre, feasibility, Randomised Controlled Trial (2017-2020)
- Industry Sponsored: (Vita o International Ltd) – A Randomised Pilot Study of Ketogenic Diet (The KEATING trial). A randomised feasibility trial (NCT03075514) (Liverpool) (2017-2018)
- We have provided support to develop clinical trials and associated studies in several JLA areas through Incubator days
- NIHR Systematic Review Programme Grant: Complex Cochrane Systematic Reviews in prioritised brain tumour areas in collaboration with NCRI & NICE Oct 2017 to: Sept 2020.
- Brain Tumour Research Charity Funded - Effect of ketogenic diet on tumour growth - 2017-18 (London).
- The Brain Tumour Charity Study - Improving support for family caregivers in neuro-oncology. (awaiting decision).
- Palliative care supportive care master protocol – Cardiff Cancer Centre
- Early diagnosis of primary brain tumours - Prospective study on Headache Suspicious of brain tumour
- Early and late effects of treatment of Posterior Fossa Tumours in Children In collaboration with NCRI Teenage and Young Adults & Germ Cell Tumours CSG, and NCRI Children's Cancer & Leukaemia CSG

Provide early advise on study applications

We have advertised through the NOCTURN website, BNOS and local channels that the NCRI Brain CSG is happy to look at and advise on studies involving the JLA areas. We have provided feedback on: SPRING, BT-LIFE, KEATING Study, caregivers study and Brain Wear.

- The Brain Tumour Charity - Improving support for family caregivers in neuro-oncology (under consideration) – Dr Florian Boele (Leeds)

BRAIN WEAR feasibility phase 2 study of wrist worn trackers to monitor physical activity data in patients with brain tumours (London)

Support Research Design Service and key Clinical Trials Units involvement

- We have had the assistance of the Research Design Service (RDS) and Clinical Trials Units in our Incubator days and study submissions.
- Scottish Clinical Trials Research Unit (part of CACTUS – CAncer Clinical Trials Unit Scotland UKCRC registered) have been involved in and driving two trials – SPRING and BT Life.
- RDS provided advice for SPRING through RDS NE (Dr Luke Vale)
- There are 8 Cochrane Systematic reviews planned around JLA areas in a collaboration between NCRI and Cochrane funded by a Cochrane Systematic Review Programme Grant that will form the basis of literature search around several important areas that may be subject of future NCRI trials.

Work collaboratively with relevant NCRI groups

- Working with NCRI Teenage and Young Adults & Germ Cell Tumours CSG (Dr Angela Edgar) and NCRI Children’s Cancer & Leukaemia CSG (Dr Simon Bailey) on early and late effects of treatment of Posterior Fossa Tumours in Children
- Working with NCRI Primary Care CSG (Richard Neal) on early diagnosis of primary brain tumours
- Worked with NCRI Living with and Beyond Cancer (Dr Feng Li) on the James Lind Alliance (JLA) Priority Setting Partnership (PSP)

4. Task groups/Working parties

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

5. Funding applications in last year

The CSG had a role in developing and consulting on four studies of which three were successfully funded. The MERIT study will be resubmitted as a researcher-led application following feedback from NIHR Efficacy and Mechanism Evaluation (EME) board.

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
May 2017				
Molecular characterisation of lower-grade gliomas using advanced diffusion MRI and MR spectroscopy	Full application	Professor Mara Cercignani	Not supported	No input
November 2017				
None				
Other committees				
Study	Committee & application type	CI	Outcome	Level of CSG input
Seizure PRophylaxis IN Glioma: a randomized controlled trial (SPRING) – July 2017.	NIHR HTA research-led. EOI to full.	Dr Robin Grant	Successful	CSG developed
BTLife (brain tumours; lifestyle intervention and fatigue evaluation) – June 2017.	TBTC	Dr Ally Rooney	Successful	CSG developed
Margin Exposure for Resection of adult and paediatric brain tumours using intra-operative Imaging Technology (MERIT) - November 2017	NIHR EME commissioned call. EOI.	Mr Michael Jenkinson	Not supported. Researcher-led	CSG developed

			resubmission invited	
Multi-centre phase II study of ipilimumab and temozolomide following surgery and chemoradiotherapy in patients with newly diagnosed glioblastoma.	Joint funded by The Brain Charity Appeal and Bristol-Meyers Squibb Full application	Dr Paul Mulholland	Successful	CSG consulted

6. Consumer involvement

Debbie Keatley

Debbie Keatley is the sole consumer member of the CSG and continues to be a very active and influential presence. Activities this year include:

- ROAM study - developing patient-facing multi-media website as a central resource to support patient/carer decision making, took part in recruitment workshop December 2017
- Recruitment to CRUK Population Research Committee (September 2017) - PPI support for Catalyst Award Joint Applicant Meeting
- NCRI Supportive and Palliative Care CSG Trials Meeting September 2017
 - Subsequent collaboration on Marie Curie EoL application with Wolfson Institute (short-listed)
 - Identified potential partners for structured psychological support after diagnosis (for potential incidental meningioma study)
- Panelist at the NIHR/NHS Point of Care Trials Workshop November 2017
- Bursary award to participate in ESMO/ESO Rare Cancers Training Course December 2017
- Participant in a CMPATH led event on presumed consent (tissue/data) February 2018
- TSG Member - NI Pathways to Cancer Diagnosis (replicating Eng. Routes to Diagnosis). This work will be key to understanding barriers to earlier diagnosis and extent of emergency diagnosis of BT in NI.
- Scholarship award to participate in American Society of Clinical Oncology (ASCO) 2018
- Speaker - Complex Trials Workshop ECMC
- Speaker - BIMS 2018
- Responded to NICE draft guidelines (focusing on meningioma proposals)

Helen Bulbeck

Helen Bulbeck is a former consumer member and now a patient and charity representative for brainstrust. Helen is involved with the NCRI Consumer Steering Group that has developed core principles and a strategy to measure consumer impact across the NCRI. A range of methods will be used to develop a list that should help consumers to:

- tell their story more clearly and transparently
- focus on what is important
- enable us to do the job better
- deliver better outcomes and results for all.

7. Priorities and challenges for the forthcoming year

Priority 1

Increase the number of interventional studies on the portfolio across all brain tumour types. Only by having large-scale studies on the portfolio can we improve patient access to clinical trials across the whole of the UK. An Adaptive Glioma Trial will be submitted to TBTC (CI: Professor Watts).

Priority 2

Build on the multi-CSG Brain Metastases Workshop to develop studies for brain metastases that are both cross cutting and primary cancer specific. A follow-up workshop is planned.

Priority 3

Engage with professional organisations and groups (including SBNS, BNOS, BNRG) to promote the role and work of the Brain Tumour CSG to identify and support new clinical researchers.

Challenge 1

The Brain Tumour CSG membership (including subgroups) is composed mainly of full time NHS clinicians. Due to time constraints of members this poses a challenge for the CSG and subgroups to develop their own studies. We have addressed this by ensuring membership of each subgroup includes at least one academic clinician.

Challenge 2

Developing a mentorship programme for the next two trainee members. Each trainee will be assigned to a subgroup and participate and contribute to the development of new studies.

Challenge 3

To ensure that the NIHR commitment to fund more brain tumour studies is not missed. This will require strong leadership from the CSG to ensure that applicants consult the CSG early in the development of studies to produce competitive studies that have a high chance of being funded.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies

A – Main CSG 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 Tumour CSG Chair)

Appendix 1

Membership of the Brain Tumour CSG

Name	Specialism	Location
Dr Sara Erridge	Clinical Oncologist	Edinburgh
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr Paul Sanghera	Clinical Oncologist	Birmingham
Dr Thomas Booth	Radiologist	London
Dr Helen Bulbeck	Patient & Charity representative	Isle of Wight
Ms Deborah Keatley	Consumer	Belfast
Dr Sarah Jefferies	Medical Oncologist	Cambridge
Dr Igor Vivanco	Medical Oncologist	London
Dr Robin Grant	Neurologist	Edinburgh
Professor Oliver Hanemann	Neurologist	Plymouth
Dr Lorna Fern	Observer	London
Dr Kathreena Kurian	Pathologist	Bristol
Professor Silvia Marino	Pathologist	London
Dr Martin McCabe	Paediatric Oncologist	Manchester
Dr Phil Hexley	Project Officer	Farnborough
Dr Samantha Mills	Radiologist	Liverpool
Dr Wendi Qian	Statistician	Cambridge
Mr Michael Jenkinson (Chair)	Surgeon	Liverpool
Mr Stuart Smith	Surgeon	Nottingham

Membership of the Subgroups

Glioma Subgroup		
Name	Specialism	Location
Dr Sara Erridge	Clinical Oncologist	Edinburgh
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr James Powell	Clinical Oncologist	Cardiff
Dr Natalie Cook	Medical Oncologist	Manchester
Dr Sarah Jefferies (Chair)	Medical Oncologist	Cambridge
Dr Igor Vivanco	Medical Oncologist	London
Dr Estelle Healey	Pathologist	Belfast
Dr Paul Brennan	Surgeon	Edinburgh
Mr Stuart Smith	Surgeon	Nottingham
Dr Laura Clifton-Hadley	Trials Group Lead	London
Dr Gerard Thompson	Radiologist	Edinburgh
Dr Helen Bulbeck	Consumer	Isle of Wight

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
Ms Deborah Keatley	Consumer	Belfast
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 Tom Santarius (Co-chair)	Surgeon	Cambridge
Mr Rasheed Zakaria*	Surgeon	Liverpool

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

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG 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 NCR 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

MDJ	Michael Jenkinson
DK	Debbie Keatley
HB	Helen Bulbeck
IV	Igor Vivanco
KK	Kathreena Kurian
LF	Lorna Fern
MM	Martin McCabe
OH	Oliver Hanemann
PH	Phil Hexley
PH	Paul Sanghera
SE	Sara Erridge
SJ	Sarah Jefferies
SJM	Samantha Mills
SM	Silvia Marino
SS	Stuart Smith
RG	Robin Grant
WQ	Wendy Qian
TB	Thomas Booth

Glioma subgroup

SJ	Sarah Jeffries (chair)
CMcB	Catherine McBain
EH	Estelle Healey
GT	Gerry Thompson
HB	Helen Bulbeck
IV	Igor Vivanco
JP	James Powell
LC-H	Laura Clifton-Hadley
NC	Natalie Cook
PB	Paul Brennan
SE	Sara Erridge
SM	Silvia Marino
SS	Stuart Smith

Meningioma & metastasis subgroup

PS	Paul Sanghera (co-chair)
TS	Tom Santarius (co-chair)
MDJ	Michael Jenkinson
DK	Debbie Keatley
GW	Gillian Whitfield
JL	Joanne Lewis
JP	Jonathan Pollock
KK	Kathreena Kurian
OH	Oliver Hanemann
RB	Richard Baird
RZ	Rasheed Zakaria
SJM	Samantha Mills

Supportive & Palliative care subgroup

RG	Robin Grant (chair)
AA	Ann Arber
AB	Anthony Byrne
CMcB	Catherine McBain
DP	Diane Playford
FB	Florian Boele
HB	Helen Bulbeck
KO	Kathy Oliver
WH	Willie Hamilton

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						
Click ↓ below to reset map						
		a) Pre-surgery	b) 1st diagnosis	c) Recurrent disease	d) Palliative care	e) Observational
Brain meta stases	All				CNS 2004 10	
		CamBMT1				VoxTox
			HIPPO			SIOP Ependymoma II
Meningio ma	All		ROAM		ROAM	VoxTox
Other studies	All			Genetics of End		VoxTox
				Spectral Analys		
		PNET 5				MOT
						stem cell lines from CNS
						The PROMOTE Study
					My-CRA, Liquid 13 Cis Retinoic Acid	
						Hyperpolarised 13C-Pyruvate MRI study
						Glutamate Dysfunction in Gliomas, V1.0
						Tissue-type MRI of brain tumours
						ASPECT Study
					Brain tumour diagnostic intervals	
Rare tumours	All		SIOP CNS GCT II			VoxTox
			CMS Study			

Filters Used:

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

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



Designed and maintained by NCRI Clinical Research Groups (CRGs) & NIHR

NCRI portfolio maps

Brain Tumour

Map B – Gliomas, astrocytoma, glioblastoma

Click ↓ below to reset map

		a) Pre-surgery	b) 1st diagnosis	c) Recurrent disease	d) Palliative care	e) Observational	
Anaplastic astrocytoma (grad..)	All					MR characterisa GBM	
						VoxTox	
						Imaging in Trans Glioma	
					Diffusion imagi		
						Tissue at Operation /	
			TSPO PET Imaging in GBM	TSPO PET Imaging in GBM			
Anaplastic oligodendroglioma..	All					MR characterisa GBM	
						VoxTox	
						Imaging in Trans Glioma	
					Diffusion imagi		
Glioblastoma	All					MR characterisa GBM	
						molecular markers in	
						VoxTox	
						Imaging in Trans Glioma	
				PARADIGM			
			RTOG 3508/AbbVie M13/813				
				CANC - 4789			
		ReoGlio PRaM-GBM The KEATING trial TSPO PET Imaging in GBM PARADIGM 2	TSPO PET Imaging in GBM				
						Cerebral Tumours	
						Imaging glioblastoma pH using CEST-MRI	
Low grade glioma	All					MR characterisa GBM	
						VoxTox	
						Imaging in Trans Glioma	
					Diffusion imagi		
				VINILO			
			Biomede				
						MISSION: GliomaS	

Filters Used:

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

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



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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
1. KEATING trial: Ketogenic diets as an adjuvant therapy in glioblastoma (the KEATING trial): study protocol for a randomised pilot study. Martin-McGill KJ et al, Pilot Feasibility Stud. 2017 Nov 28;3:67	Trial closed to recruitment and in follow-up.	Developed by CSG
2. MALTING study: Subventricular Zone Involvement Characterized by Diffusion Tensor Imaging in Glioblastoma. van Dijken BRJ et al, World Neurosurg. 2017 Sep;105:697-701.	Results from MALTING have led to further study PRaM-GBM to validate findings.	Developed by CSG (former member Mr Stephen Price)
3. MALTING study: Multiparametric MR Imaging of Diffusion and Perfusion in Contrast-enhancing and Nonenhancing Components in Patients with Glioblastoma. Boonzaier NR et al, Radiology. 2017 Jul;284(1):180-190.	Results from MALTING have led to further study PRaM-GBM to validate findings.	Developed by CSG (former member Mr Stephen Price)

<p>4. Symptoms in primary care with time to diagnosis of brain tumours: Ozawa M et al Fam Pract. 2018 Feb 6. doi: 10.1093/fampra/cmz139. [Epub ahead of print]</p>	<p>Further work by S&PC Subgroup in developing studies for screening and early diagnosis.</p>	<p>Developed by CSG – SP&C Subgroup</p>
<p>5. ROAM trial:Atypical meningioma-is it time to standardize surgical sampling techniques. Jenkinson MD et al. Neuro Oncol. 2017 Mar 1;19(3):453-454.</p>	<p>Position statement about protocol for tissue sampling and reporting in meningioma surgery.</p>	<p>Developed by CSG</p>

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Brain Tumour CSG portfolio, 9 trials closed to recruitment and 13 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
2013/2014	829	136	783	136	16.5	2.9
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