Glioma Clinical Trial
Call for applications

Purpose and Scope

Currently only 5.3% of brain tumour patients are enrolled onto clinical trials[1], compared with an average of 13.9% of cancer patients[2]. Research by The Brain Tumour Charity and others has shown that 81% of people believe that everyone diagnosed with a tumour should be offered a trial[3], but only 23% of those diagnosed with a brain tumour in 2016 were offered a trial[4].

The Brain Tumour Charity believe that brain tumour patients should be offered the best chance of surviving their diagnosis, and as such we are determined to see more people affected by brain tumours enter into trials. We therefore wish to fund the establishment of brain tumour trial infrastructure to facilitate increased numbers of brain tumour clinical trials, permit more newly diagnosed people to join a trial, make the UK a more attractive place to open trials, and increase the availability of banked brain tumour tissue for research.

We invite applications for funding to establish an adaptive clinical trial for glioma patients in the UK.

The planned trial must:

- Be a multicentre, interventional trial with multi-arm, multi-stage adaptive design, able to accommodate rapid inclusion of novel interventional arms as they become available.
- Be restricted to low or high grade glioma, grades 2-4.
- Have wide inclusion criteria and narrow exclusion criteria.
- Have a specified interventional research question for the "backbone" trial.
- Mandate collection of samples for molecular diagnosis and tissue banking.
- Offer optional banking of post-mortem brains to all potential participants.

See "Proposal Requirements" below for further details.

Funding

Applicants may apply for up to £500,000 per year.

The budget should cover:

- Part A costs as defined by AcoRD.
- Biobanking costs. Only directly incurred costs may be claimed, please see our ***finance guidelines*** for more information.
- Payment to collaborating centres on a per-patient basis for milestones such as recruitment and submission of biobanking samples.
- Buy-out of clinical time for a researcher to develop the additional study arms.

Clinical Research Nurse costs may **not** be included as CRN time should be available within the centre and covered by NIHR. In preparing the budget, applicants should be aware of the AcoRD guidance. As an AMRC member charity, we expect any research costs identified as 'Part B' (i.e. local study trial co-

[1] NCRI Brain Tumour Clinical Studies Group Annual Report 2015-16; http://csg.ncri.org.uk/wp-content/uploads/2014/11/NCRI-Brain-CSG-annual-report-2015-16.pdf.
[2] CSG annual reports 2015-16; http://csg.ncri.org.uk/reports-and-publications-2/annual-reports/.
[3] Charity Awareness Monitor. July 2014. nfpSynergy
[4] National Cancer Patient Experience Survey 2016; http://www.ncpes.co.uk/index.php/reports/2016-reports/national-reports-1.

ordination or data collection) that are carried out by existing staff employed by the NHS, NIHR Clinical Research Network (NIHR CRN) or other clinical organisations to be paid by the Department of Health through local networks or the NHS trust. They will not be paid by AMRC charities. Guidance can be found at: ***https://www.gov.uk/government/publications/guidance-on-attributing-the-costs-of-health-and-social-care-research***.

Application Process

The call will open for applications in late February 2018 with an application deadline in early May. Funding decisions will be communicated in October 2018.

After award of the grant to the successful CTU the expectation is that the first patient will be recruited within one year of the award date. Continued support for the second year of the grant will therefore be dependent on the first patient having been recruited.

Centres will be reviewed annually against defined performance metrics, and those recruiting poorly will be removed from the trial and alternative centres selected.

Eligibility Criteria

- The award is open to applications from UK-based universities, NHS sites or other recognised UK higher research institutions.
- The trial must be co-ordinated by a lead CTU. Experience of co-ordinating multi-centre brain tumour trials and/or opening and running an adaptive interventional study will be looked upon favourably. The CTU must be willing to facilitate arms of the trial being opened and run by Clinical Investigators from other centres.
- Clinical investigators should have a contract of employment with the host institution that exceeds the planned finish date of the research by at least 12 months.
- A CTU may lead on only one application.
- Applicants must consult The Brain Tumour Charity's Research Involvement Network (RIN) during the development of the proposal and must plan for continued RIN input as the trial is run. Details of how to access the RIN can be found at: ***https://www.thebraintumourcharity.org/our-research/for-researchers/patient-public-involvement/.***

Assessment Criteria

- The potential for the trial to facilitate increased testing of new therapeutics in the UK.
- The ability of the trial to increase the percentage of newly diagnosed patients offered a clinical trial and to increase patient access to novel therapeutics (including wide geographic spread across the UK).
- The degree to which the trial will build capacity for more trials to be designed.
- The quality and relevance of the "backbone" research question.
- The ability of the trial to improve the availability and quality of molecular diagnosis.
- The ability of the trial to improve access to high-quality well-characterised brain tumour tissue for the wider research community.

Proposal Requirements

Trial Design

The planned trial must be a multicentre, interventional trial with adaptive design and be able to accommodate rapid inclusion of novel interventional arms as they become available. Interventional arms must be capable of using multiple treatment modalities. The trial should be restricted to people with low or high grade glioma (grades 2-4), have wide inclusion criteria and narrow exclusion criteria and have a specified interventional research question for the "backbone" trial. The trial must permit the inclusion of drugs at different stages of development, and must be designed to provide data to drive decisions on compounds in a timely manner and rapid assessment of arms for removal.

While not all trial participants are expected be eligible for every arm, the criteria for participation in the "backbone" trial should facilitate the inclusion of as many patients as possible.

Tissue Banking and Molecular Diagnosis

Tumour tissue banking and molecular diagnosis

The trial protocol must mandate collection of tumour samples for future molecular diagnosis and banking of fresh frozen tissue, with a molecular testing protocol robust enough to reliably identify those eligible for other arms of the trial. Samples must be collected through shared protocols and sample storage must be managed through a centralised repository. Sample testing may be through a centralised or distributed model, and working with initiatives such as Genomics England and Generation Genome[5] should be explored to minimise duplication. The tissue banking protocols must have the potential to be rolled out as standardised best practice to laboratories outside the trial.

Brain banking

The trial must offer optional banking of post-mortem brain tissue to all potential participants. One biobank must hold all banked post-mortem tissue and samples must be available to the research community on the basis of scientific meritocracy. The biobank does not have to be physically located at the lead CTU. Plans must be set out for establishment of a tissue access committee to oversee tissue distribution, chaired by a researcher with biobanking experience but no vested interest in the stored samples, and including appropriate PPI. A charge should be made for tissue distribution in order to cover but not exceed the costs of sample storage and distribution.

Trial data

Trial data must be stored in a dedicated trial database which has the ability to facilitate straightforward data transfer to The Charity's Databank (see below).

Working with The Brain Tumour Charity

The Brain Tumour Charity will be opening a Brain Tumour Databank in mid-2018. While databank participation will not be compulsory for trial participants, participants must be informed of the option during the consent process, and trial data collection must be in a format which enables straightforward transfer of trial data to the Databank for trial participants who opt-in to data sharing. Trial participants who opt-in will have their NHS data shared with the databank straight away, and their trial data must be shared with the databank promptly after the relevant trial outcomes have been released.

The Brain Tumour Charity's Research Involvement Network (RIN) must be consulted during development of the application and must provide the PPI throughout the trial. The application must set out plans for ongoing PPI using the RIN. Details of how to access the RIN can be found at: ***https://www.thebraintumourcharity.org/our-research/for-researchers/patient-public-involvement/***.

The successful applicants must undertake to work with The Charity to provide The Charity's support information to all potential participants during the consultation for entry.

Consultation with NCRI CSG

The advice and guidance of the NCRI Brain Tumour Clinical Studies Group should be sought during the design and generation of any application. The local Clinical Research Network should be consulted during the development of the application for advice and guidance on trial set-up, design and delivery.

Performance Metrics

Applicants must suggest SMART performance metrics against which the performance of each collaborating centre could be judged, and how they expect to perform against each metric in each year of funding. Metrics should include, but not be limited to, number and quality of biobank samples and recruitment numbers.

Key Dates

The call for applications will open in late February 2018, with a submission deadline in May 2018 and funding decisions communicated in October 2018.

Further Information

If you have any queries please contact us at ***research@thebraintumourcharity.org*** or on 01252 418190.

[5] Annual report of the Chief Medical Officer 2016: Generation Genome. https://www.gov.uk/government/publications/chief-medical-officer-annual-report-2016-generation-genome.

