Patient involvement in the design of a randomised trial of Proton Beam Radiotherapy versus standard radiotherapy for good prognosis glioma

James Powell¹, Louise Murray², Neil G Burnet³,⁴, Sharon Fernandez⁵, Zoe Lingard³, Lucy McParland⁶, Daniel J O’Hara⁷, Gillian A Whitfield³,⁴ & Susan C Short²

1. Department of Oncology, Velindre University NHS Trust, Cardiff, UK
2. St James’s Hospital and Leeds Institute of Medical Research, University of Leeds, Leeds, UK
3. Division of Cancer Sciences, Manchester Cancer Research Centre, University of Manchester, Manchester, UK
4. Department of Oncology, The Christie NHS Foundation Trust, Manchester, UK
5. Department of Oncology, Leeds Teaching Hospitals NHS Trust, Leeds, UK
6. Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, UK.

Introduction
UK neuro-oncologists and colleagues are developing one of the first randomised clinical trials of proton beam therapy (PBT) versus photon radiotherapy to compare patient reported quality of life (QOL), cognitive function and other late effects in adults with good prognosis glioma.

Methods
15 patients who had previously completed radiotherapy for oligodendroglioma and carers attended a focus group in Manchester in November 2018. We sought their views on the perceived differences between PBT and photon radiotherapy, our trial proposal including patient pathway, randomisation and outcomes, as well as their views on travel and accommodation during PBT. Group discussions centred around five questions and were facilitated by neuro-oncologists, a research radiographer, neuro-psychologist and statistician.

Results
Participants strongly endorsed the trial proposal and positively highlighted the opportunity to access PBT within a clinical trial. They supported the need for randomisation and stated this should be 1:1. Patients disliked some traditional terminology such as ‘trial’ and ‘neurocognitive tests’ and preferred ‘research study’ and ‘neurocognitive assessments’.

Patient and carers encouraged careful consideration of issues around travel costs and accommodation during PBT away from home. Some limitations of the QOL questionnaires in measuring daily wellbeing were highlighted and participants considered that standard QOL questionnaires fail to address some important areas reflecting daily wellbeing.

Conclusions
We will now incorporate these important patient and carer observations to strengthen our study and add validity to the key study endpoints.

Acknowledgements
We’d like to thank the patients and their carers who took part in the workshop and provided such valuable and insightful discussion. The development of this trial is being supported by CTRad / ART-NET group and we are grateful for the support and guidance provided by their ongoing workshops. We also acknowledge the support of our official PPI member and grant co-applicant Dr Helen Bulbeck. We are grateful to the national EPSRC Network+ on Advanced Proton Radiotherapy, run by Prof Karen Kirkby, for help to support the costs of the workshop. NGB and ZL are supported by the NIHR Manchester Biomedical Research Centre.

Randomised phase II study with internal pilot
Adult patients (age ≥25 years) diagnosed with good prognosis molecularly defined grade II and III glioma: 1p19q chromosomal deletion and IDH mutation

| 11am | Welcome and Introduction |
| 11:10 – 11:30 | Question 1: What do you think are the differences between standard radiotherapy and proton therapy? |
| 11:30 – 11:40 | Presentation: What we know about protons vs photons? |
| 11:40 – 12:00 | Introduction to Research Study: |
| 12:00 – 12:15 | Question 2: How do you feel about entering a study where there is a 50% chance of standard radiotherapy and a 50% chance of proton therapy? |
| 12:15 – 12:45 | LUNCH |
| 12:45 – 13:00 | Question 3: What are your views on the trial pathway? |
| 13:05 – 13:25 | Question 4: What are your views on the trial outcomes? |
| 13:25 – 13:50 | Question 5: What are your views on travelling and staying in Manchester/London if you are offered proton beam therapy as part of the trial? |
| 13:50 – 14:00 | Conclude |

Standard of care
54 Gy VMAT
Adjuvant PCV chemo

Investigational arm
54 Gy PBT
Adjuvant PCV chemo

Imaging follow up
QoL assessment
Neuro cognitive assessments

1st end-point: Health-related QoL @ 2y (EORTC QLQ-C30, global health and HRQoL)
Co-primary end-point: neuro cognitive decline @ 2y (standard test battery)

2nd end-points – Additional HRQoL assessment (8N20 & fatigue), PFS, OS, socio-economic status, endocrine dysfunction, health economics, imaging biomarkers of normal tissue