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COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

The achievement of better health outcomes for patients and those affected by brain tumours through clinical trials research

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15th COGNO ANNUAL SCIENTIFIC MEETING

Bridge to the Future: Biomarkers in Brain Tumour Care

Sunday 8th October – Tuesday 10th October 2023

Hilton Sydney, NSW, Australia

CONFERENCE BOOKLET

COGNO

COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

CONTENTS

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- Dr Keryn Davidson, Co-convenor (Neurosurgeon)
- Dr Kimberley Alexander (Biomedical Scientist / Cancer Researcher)
- Mrs Diana Andrew (COGNO Consumer Advisory Panel Member)
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Co-Convenors' Welcome

Dear Colleagues

We are honoured to extend our warmest welcome to you for the 15th COGNO Annual Scientific Meeting for 2023, "*Bridge to the Future: Biomarkers in Brain Tumour Care*," held at the Hilton Sydney, NSW, Australia, from Sunday 8th October - Tuesday 10th October 2023. We are thrilled to be able to meet in person once again and to have the opportunity to network with likeminded individuals working in the brain tumour research and supportive care space.

Our program this year will be informative, featuring renowned international and local speakers running over two days with pre-ASM satellite meetings on Sunday 8th October 2023. We look forward to meeting you all!

Dr Adrian Lee
Co-convenor
COGNO ASM 2023

Dr Keryn Davidson
Co-convenor
COGNO ASM 2023

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ORAL ABSTRACT LISTING

Session 2 – Oral Abstracts

1 Harmonised database infrastructure to support local brain cancer biobanking and data registries for national linkage

Jackie Yim, Cassandra Griffin, Laveniya Satgunaseelan, Marina Kastelan, Helen Wheeler, Michael Back, James Lynam, Mike Fay, Hao-Wen Sim, Brindha Shivalingam, Kimberley L. Alexander

2 Glioblastoma biomarkers in urinary extracellular vesicles reveal the potential for a 'liquid gold' biopsy

Susannah M. Hallal, Agota Tűzesi, Liam A. Sida, Elissa Xian, Daniel Madani, Krishna Muralidharan, Brindha Shivalingam, Michael E. Buckland, Laveniya Satgunaseelan, and Kimberley L. Alexander

3 Machine learning models detect blood 'fingerprints' for accurate glioblastoma tumour surveillance

Susannah M. Hallal, Agota Tűzesi, Brindha Shivalingam, Michael E. Buckland, Laveniya Satgunaseelan, Hao-Wen Sim, Abhishek Vijayan, Fatemeh Vafaee, and Kimberley L. Alexander

4 Targeting GBM Heterogeneity using a Novel ephrin A5 Antibody Therapy

Rochelle CJ Dsouza, Niclas Skarne, Lachlan Harris, Seckin Akgul, Carolin Offenhauser, Quan Ngyuen, Craig Bell, Kris Thurecht, Ulrich Baumgartner, Fiona Smith, Rosalind Jeffree, Po-ling Inglis, Zarnie Lwin, Hamish Alexander, Andrew W Boyd and Bryan W Day

5 "Just being alive was exhausting": A qualitative exploration of patient, caregiver, and healthcare professional experiences of cancer-related fatigue in people with brain tumour

Rachel Campbell, Hannah Banks, Thomas Carlick, Mona Faris, Megan Jeon, Joanne Shaw, Haryana Dhillon

6 An Evaluation of Brain Tumour Information Resources: Current State and Next Steps

Thomas Carlick, Hannah Banks, Jill Chen, Joanne Shaw, Haryana Dhillon

7 Determining items for a brief screening tool for brain tumour caregivers' unmet needs

Jill Chen, Haryana Dhillon, Joanne Shaw, Georgia Halkett, Rachel Campbell for the BRAINS Authorship Group

8 Design of Patient-Centered Digital Health Interventions: Leveraging Input from Patients with Brain Tumours for Unmet Supportive Care Needs

Mahima Kalla, Ashleigh Bradford, Verena Schadewaldt, Kara Burns, Sarah Bray, Sarah Cain, Heidi McAlpine, Rana Dhillon, Wendy Chapman, James R Whittle, Katharine J Drummond, and Mei Krishnasamy

9 Participant Experiences of the LaTCH Program for Brain Tumour Survivors: A Preliminary Qualitative Analysis

Ellie Piggott, Sian Virtue-Griffiths, Haryana Dhillon, Joanne Shaw, Dianne Legge, and Kerryn Pike

10 IPAX-2: Phase 1 Safety and Dose Finding Study of [131I]IPA Plus Standard of Care in Patients With Newly Diagnosed Glioblastoma

Tracey Brown, Brenda Cerqueira, Stefanie Martina, Colin Hayward, and Hui K. Gan

POSTER ABSTRACT LISTING

11 When IDH1wt is not enough.... Clinical algorithm to enrich for novel mutations

Dr Lawrence Cher, Professor Hui Gan, Dr Anthony Uccellini, Dr Jonathan Clark

12 The EphA3 receptor is a tumour-specific therapeutic target and promotes tumourigenicity in medulloblastoma

Carolin Offenhauser, Fiona Smith, Kathleen Ensbey, Michelle Li, Rochelle D'Souza, Zara Bruce, Craig Bell, Kristofer Thurecht, Andrew Boyd, Bryan Day

14 Dendritic Cell Defects in Patients and Mice with Brain Tumours

Bryan Gardam, Tessa Gargett, Michael P Brown, Lisa M Ebert

15 ROR1 Expression in Glioma – A Novel Prognostic Biomarker

Daniel Madani, Miya John, Laveniya Satgunaseelan, Brindha Shivalingam, Caroline Ford

16 Targeting androgen signaling in glioblastoma

Sofia Mason, Sylvia A Chung, Hao-wen Sim, Beatriz P San Juan, Rachel F Dear, Bryan Day, Jeff Holst, Christine L Chaffer

17 High throughput strategies for brain cancer drug discovery

Ganes Pranavan, Peter Mews, Mitali Fadia, Naomi Mitchell, Olga Zaytseva, Brooke Kinsela, Tanya Jaivad, Tom Gibbs, Ross Hannan, Amee George, Lee Wong, Nadine Hein and Leonie Quinn

18 Developing a Preclinical Pipeline for Advancing Cancer Therapeutics (PACT) and its deployment as a pilot business model

Aude EM Touffu, Amanda L Hudson, Kelly J McKelvey, Alexander Yuile, Helen R Wheeler, Shihani P Stoner

20 Targeting RNA Polymerase I as a therapeutic strategy to treat paediatric gliomas

Andrew Garvie, Maheshi Udugama, Linda Hii, Hsiao PJ Voon, L Quinn, R Hannan, Lee H Wong

23 Clinical quality indicators in high-grade glioma cohort from South Western Sydney: feasibility of data extraction and reporting towards building an Australian Brain Cancer Registry

Mirette Abraham, Joe Chang, Vanessa Estall, Adam Cooper, Annette Tognela, Kate Wilkinson, Wafa Trad, Teresa Simpson, Ganesh Shivapathasundram, Sugendran Pillay, Ramesh Cuganesan, Ruwanthie Fernando, Rosalind L. Jeffree, Eng-Siew Koh

24 Exploring the Role of Germline DNA in the Brain Location of Adult Glioma Tumours

Karen Alpen, Miroslaw Kapuscinski, Robert MacInnis, Claire Vajdic and Enes Makalic

25 Descriptive epidemiology of glioma patients in Australia's multi-site BRAIN registry from 2016-2023

Rose Clarke, Anthony Dowling, Katharine Drummond, Iwan Bennett, Claire Philips, Elizabeth Ahern, David Campbell, Rosemary Harrup, Ross Jennens, Robert Campbell, Ronnie Freilich, Simone Reeves, Mark Rosenthal, Ian M Collins, Julie Johns, Peter Gibbs, Lucy Gately

26 Exploring barriers to EX-TEM recruitment using the BRAIN registry

Lucy Gately, Katharine Drummond, Anthony Dowling, Iwan Bennett, David Campbell, Claire Philips, Simone Reeves, Ronnie Freilich, Sanjeev Gill, Zarnie Lwin, Rosemary Harrup, Anne Long, Elizabeth Ahern, Mark Wong,

Robert Campbell, Katharine Cuff, Ross Jennens, Craig Underhill, Adam Cooper, Stephen Brown, Mark Rosenthal, Javier Torres, Ian M Collins, Megan Dumas, Peter Gibbs

27 Exploring current practice patterns in grade 2 glioma using the BRAIN registry

Lucy Gately, Katharine Drummond, Anthony Dowling, Iwan Bennett, Ronnie Freilich, Claire Philips, Elizabeth Ahern, David Campbell, Robert Campbell, Rosemary Harrup, Simone Reeves, Ian M Collins, Peter Gibbs

28 The [18F]-fluoroethyl-L-tyrosine (FET) in glioblastoma (FIG) TROG 18.06 study: prospective, multicentre Australian-led collaboration: trial in progress

Eng-Siew Koh, Roslyn J.Francis, Martin A.Ebert, Hui K.Gan, Sze T.Lee, Eddie Lau, Alisha Moore, Hamish Evans, Bradford A. Moffat, Dale L. Bailey, Sweet P. Ng, Mori Wada, Claire Phillips, Joseph Sia, Tim Akhurst, Ramin Alipour, Suki Gill, Jeremy Croker, Nicholas Bucknell, Elizabeth L.Thomas, Michael Back, Geoffrey P.Schembri, Edward Hsiao, Benjamin Chua, Catherine Bettington, David A. Pattison, Paul Thomas, Joe Chang, Peter Lin, Tam Ly, June Yap, Peter Gorayski, Hien Le, Ian Kirkwood, Wilson Vallat, Farhan Syed, Kylie Jung, Shahroz Khan, Dayanethee Krishna, Mark B. Pinkham, Andrew P. Pullar, Stanley Ngai, Chris Yu, Andrej Bece, Catherine Clark, Scott Beuzeville, Tow C. Yeow,Alana Rossi, Rachael Dykyj, Olivia Cook, Angela Whitehead, Caterina Brighi, Greg Fitt, Ramesh Cuganesan, Sugendran Pillay, Nathaniel Barry, Arian Lasocki, Fiona E.Scott, Elizabeth H Barnes, Lucas Adda, Richard De Abreu Lourenco, Anna K.Nowak, Mark Rosenthal, Mustafa Khasraw, Jodie Palmer, Andrew M.Scott

29 Exploring molecular biomarkers in astrocytomas using comprehensive genomic profiling (CGP)

Nicholas McNamee, Frank Lin, Hao-Wen Sim, Christine Napier, David Thomas, John Simes, Subotheni Thavaneswaran

30 Using neuroanatomical subsite to predict patterns of Glioblastoma infiltration: potential for individualising radiation therapy target volume delineation of the parietal and posterior frontal regions.

Michael Back, Jackie Yim, Patrick Horsley and Jamie Drummond

31 Combining Open and Endovascular Techniques in "Hybrid" Theatre for Complex Cerebrovascular Cases: A 10-Year Retrospective Review at a Single Australian Institution

Daniel Madani, Elissa Xian, Thomas Morrison, Patrick Tang, Rodney Allan, Johnny Wong

32 Intraoperative MRI for Brain Tumours: A 15-Year Retrospective Review at a Single Australian Institution

Daniel Madani, Krishna Muralidharan, Nicholas Andrew Chang, Patrick Tang, Johnny Wong

33 Queensland Brain Cancer Index demonstrates feasibility and challenges in automated electronic data collection for an Australian Brain Cancer Registry

Rosalind L. Jeffree, Mark B. Pinkham, Catherine Bettington, Nicole Buddle, Kimberley Budgen, Robert A. Campbell, Alessaandra Francesco

34 Application of radiomics to pre-operative imaging to predict survival in people with glioma

Aleksandra Kazi, Daniel Arrington, Prabhakar Ramachandran, Mark Pinkham and David Reutens

35 Creating a visually accessible online portal for people with brain tumour: preliminary findings

Mona Faris, Haryana Dhillon, Sharon He, Thomas Carlick, Jill Chen, Hannah Banks, Megan Jeon, Rachel Campbell, Raymond Chan, Georgia Halkett, Dianne Legge, Robyn Leonard, Annie Miller, Tamara Ownsworth, Kerryn Pike, and Joanne Shaw

36 Online resources from the Cancer Australia Quality of Life Technical Service (CQUEST)

Carrie-Anne Ng, Tim Luckett, Brendan Mulhern

37 **Recruitment and Baseline Characteristics of Participants Enrolled in the RCT of the Cognitive Rehabilitation Program, LaTCH; for Brain Cancer**

Sian Virtue-Griffiths, Dianne Legge, Ellie Piggott, Joanne Shaw, Haryana Dhillon, & Kerryn Pike

38 **Exploring approaches to neuro-oncology care coordination in Australia: A scoping review**

Megan Jeon, Joanne Shaw, Sharon He, Hannah Banks, Thomas Carlick, Mona Faris, Rachel Campbell, Brian Kelly, Eng-Siew Koh, Georgia BK Halkett, Dianne Legge, Tamara Ownsworth, Raymond J. Chan, Mark Pinkham, Ursula M. Sansom-Daly, Haryana M Dhillon

39 **Using computer adaptive testing to assess Quality of Life in Cancer clinical trials**

Brendan Mulhern, Tim Luckett and Carrie-Anne Ng

40 **Challenges In NF2-related Schwannomatosis Treated With Stereotactic Radiosurgery**

Molly Reynolds, Katrina Morris

42 **A retrospective state-wide audit of elderly glioblastoma patient outcomes following long course chemoradiotherapy after neurosurgical intervention in Tasmania**

Jim Weston, Nova Thani, Richard Foster, Patrick Dyer, and Rosemary Harrup

43 **Use and impact of single agent bevacizumab for recurrent glioblastoma: a real-world study**

Matthew Loft, Sam Smith, Katharine Drummond, Mark Rosenthal, Anthony Dowling, Claire Phillips, Simone Reeves, Iwan Bennett, David Campbell, Robert Campbell, Peter Gibbs, Lucy Gately

ORAL ABSTRACTS

1

Harmonised database infrastructure to support local brain cancer biobanking and data registries for national linkage

Jackie Yim[1,2,3], Cassandra Griffin[4,5,6], Laveniya Satgunaseelan[7,8,9,10], Marina Kastelan[1], Helen Wheeler[1,11], Michael Back[1,2], James Lynam[5,6,12], Mike Fay[5,13], Hao-Wen Sim[7,14,15], Brindha Shivalingam[7,10,15,16], Kimberley L. Alexander[7,8,10,17]

[1] The Brain Cancer Group, Royal North Shore Hospital, St Leonards, NSW, Australia
[2] Department of Radiation Oncology, Northern Sydney Cancer Centre, Royal North Shore Hospital, St Leonards, NSW, Australia
[3] Centre for Health Economics Research and Evaluation, Faculty of Health, University of Technology Sydney, NSW, Australia
[4] Mark Hughes Foundation Biobank, Hunter Medical Research Institute, The University of Newcastle, NSW, Australia
[5] Mark Hughes Foundation Centre for Brain Cancer Research, The University of Newcastle, NSW, Australia
[6] College of Health, Medicine and Wellbeing, The University of Newcastle, NSW, Australia
[7] The Sydney Brain Tumour Bank, Sydney Local Health District, NSW, Australia
[8] Department of Neuropathology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
[9] Sydney Medical School, Faculty of Medicine and Health, University of Sydney, NSW, Australia
[10] Department of Neurosurgery, Chris O'Brien Lifehouse, Camperdown, NSW, Australia
[11] Department of Medical Oncology, Northern Sydney Cancer Centre, Royal North Shore Hospital, St Leonards, NSW, Australia
[12] Department of Medical Oncology, Calvary Mater Hospital, Newcastle, NSW, Australia
[13] GenesisCare, Newcastle, NSW, Australia
[14] Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, NSW, Australia
[15] Central Clinical School, The University of Sydney, Camperdown, NSW, Australia
[16] Neurosurgical Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
[17] School of Medical Sciences, Faculty of Medicine and Health, University of Sydney, NSW, Australia

Abstract

Capturing clinical information and annotating biospecimens is crucial for high-impact translational brain cancer research. Historically, individual sites have devised their own data language and infrastructure to capture, record and interrogate clinicopathologic data. This entire process is notoriously time-consuming and an insuperable task for many sites. Important clinical parameters are often not recorded in a readily extractable form and require interpretation, relying on the cooperation of multiple sub-specialties. Duplicated efforts at individual sites drain limited resources and have led to fundamental differences in what clinicopathological data is captured and how parameters are defined and stored. A critical prerequisite step towards linking sites to a national brain cancer registry is to unify local database infrastructure. Drawing on expertise in glioma surgery, neuropathology, and medical and radiation oncology across three NSW Health districts, each with established brain tumour biobanks and translational research programs, we harmonised the data dictionaries of our existing and prospective bio-specimen and data collections. We co-designed modern, secure, web-based REDCap database infrastructure for capturing participant identifiers, consents, demographics, lifestyle factors and medical histories. Database pages for radiation and systemic therapy, radiographic assessments and clinic encounters are repeatable allowing longitudinal data capture, and neurosurgery and integrated diagnostics pages are synchronised so that pathology and molecular findings are matched to each surgical intervention. Our design incorporates branching logic to enhance usability and data piping to automatically generate treatment summaries and compute key parameters, including time-totreatment change, progression-free and overall survival. Our consolidated data dictionary has enabled future data capture and reporting strategies to be aligned across multiple biobanking and registry sites. A harmonised data dictionary fosters research collaboration and the pooling of better-defined cohorts for the rapid translation of research results into clinical care. We invite any interested groups to contact us to implement a version of this resource at their site.

Theme
Basic / Translational Science

2

Glioblastoma biomarkers in urinary extracellular vesicles reveal the potential for a 'liquid gold' biopsy

Susannah M. Hallal[1,2,3], Agota Tűzesi[2,3], Liam A. Sida[3], Elissa Xian[1,4], Daniel Madani[1,4], Krishna Muralidharan[1,4], Brindha Shivalingam[1,4,5], Michael E. Buckland[2,3], Laveniya Satgunaseelan[1,2,5], and Kimberley L. Alexander[1,2,3]

[1] Neurosurgery Department, Chris O'Brien Lifehouse, Camperdown, NSW, Australia
[2] Department of Neuropathology, Royal Prince Alfred

Hospital, Camperdown, NSW, Australia
[3] School of Medical Sciences, Faculty of Medicine and Health Sciences, The University of Sydney, Camperdown, NSW, Australia
[4] Neurosurgery Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
[5] Sydney Medical School, Faculty of Medicine and Health Sciences, The University of Sydney, Sydney, NSW, Australia.

Background: Biomarkers that reflect glioblastoma tumour activity and treatment response are urgently needed to help guide clinical management, particularly for recurrent disease. As the urinary system is a major clearance route of circulating extracellular vesicles (EVs; 30-1000 nm nanoparticles) we explored whether sampling urinary-EVs could serve as a simple and non-invasive liquid biopsy approach for diagnosing and monitoring glioblastoma.

Methods: Fifty urine specimens (15-60 ml) were collected from 24 catheterised glioblastoma IDH-wildtype patients at three clinical time points, immediately before (Pre-OP, n=17) and after (Post-OP, n=9) gross total resection of a *de novo* tumour, prior to recurrence surgery (REC, n=7), and from age/gender-matched healthy participants (n=14; accessed from the Sydney Brain Tumour Bank). EVs isolated by differential ultracentrifugation were characterised and extracted proteomes were analysed by high resolution data-independent acquisition liquid chromatography tandem mass spectrometry (DIA-LC-MS/MS).

Results: Overall, 6857 proteins were confidently identified in urinary-EVs (q-value≤0.01), including 94 EV-marker proteins. A stepwise logistic regression identified uEV biomarker proteins (*KRT19, RPS2, RPL18, RPL28, RPL7A*) with significantly higher levels in Pre-OP glioblastoma relative to controls, and an excellent accumulative diagnostic performance of 95.8% (AUC=0.958). Strikingly, uEV protein levels were able to differentiate glioblastoma patients at the three clinical timepoints (FC≥|2|, adj.p-val≤0.05, AUC>0.9) and many of the significant differentially abundant proteins included previously defined EV-biomarkers from glioblastoma cell culture, neurosurgical fluids, and plasma [1-3]. Of note, we identified three uEV proteins, GGH, GRN and ITM2B, with excellent sensitivity and specificity for glioblastoma recurrence (AUC>0.92), with known links to glioblastoma progression and/or temozolomide resistance [4-8].

Conclusion: In-depth DIA-LC-MS/MS characterisation of urinary-EVs substantiates urine as a viable source of glioblastoma biomarkers. The promising 'liquid gold' biomarker panels identified here warrant further investigation.

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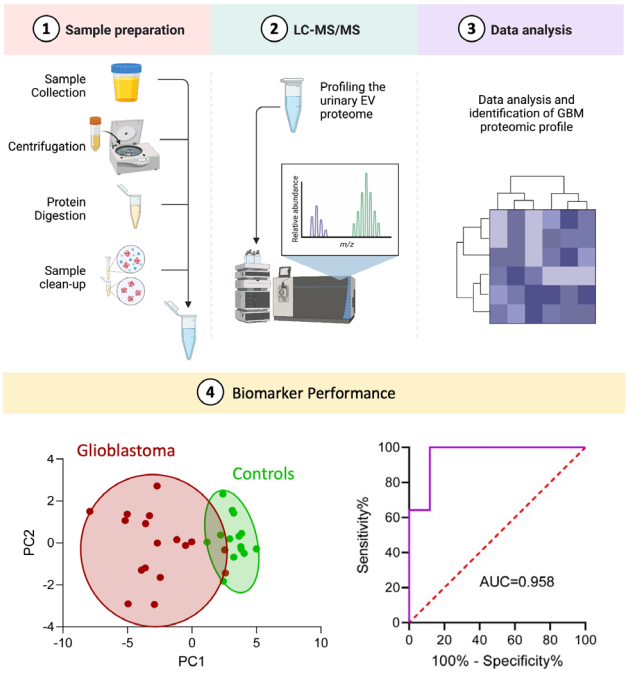
Theme
Basic / Translational Science



3

Machine learning models detect blood 'fingerprints' for accurate glioblastoma tumour surveillance

Susannah M. Hallal[1,2,3], Agota Tűzesi[2,3], Brindha Shivalingam[1,4,5], Michael E. Buckland[2,3], Laveniya Satgunaseelan[1,2,5], Hao-Wen Sim[6, 7, 8], Abhishek Vijayan[9], Fatemeh Vafaee[9], and Kimberley L. Alexander[1,2,3]

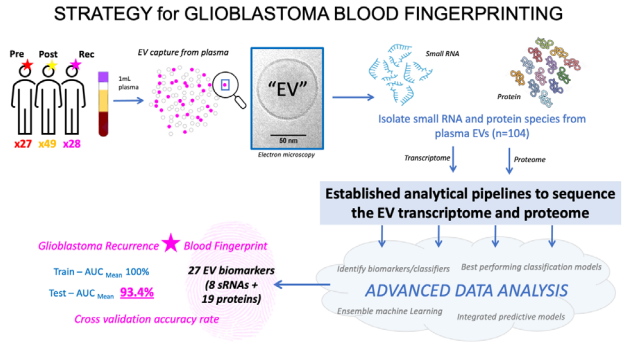
[1] Neurosurgery Department, Chris O'Brien Lifehouse, Camperdown, NSW, Australia
[2] Department of Neuropathology, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
[3] School of Medical Sciences, Faculty of Medicine and Health Sciences, The University of Sydney, Camperdown, NSW, Australia
[4] Neurosurgery Department, Royal Prince Alfred Hospital, Camperdown, NSW, Australia
[5] Sydney Medical School, Faculty of Medicine and Health Sciences, The University of Sydney, Sydney, NSW, Australia.
[6] The Sydney Brain Tumour Bank, Sydney Local Health District, NSW, Australia
[7] Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, NSW, Australia
[8] Central Clinical School, The University of Sydney, Camperdown, NSW, Australia
[9] School of Biotechnology and Biomolecular Sciences, University of New South Wales

Introduction: Circulating biomarkers that offer early and accurate indications of glioblastoma recurrence will likely have significant clinical utility. We have developed a novel, extracellular vesicle (EV)-based multianalyte liquid biopsy strategy (see Figure) to detect sensitive biomarker signatures or 'blood fingerprints' for routine assessment of glioblastoma tumour activity and treatment response.

Methods: We isolated extracellular vesicles (EVs) from 104 serial plasma specimens from 50 patients diagnosed with glioblastoma, IDH-wildtype, CNS WHO grade 4 (2021). Plasma samples were collected at three clinical time points, before (Pre-OP, n=27) and after (Post-OP, n=49) first tumour resection surgery and at path-proven recurrence (REC, n=28; accessed from the Sydney Brain Tumour Bank and Mark Hughes Foundation Biobank). Captured plasma-EV populations were analysed using our established, complementary EV proteomics and small-RNA sequencing platforms. Filtered and normalised proteomics and sRNA datasets were passed through a cross-validation pipeline (repeated 30x; 80%-train:20%-test) using multiple feature selection methods and classification models. The best performing protein and sRNA candidate biomarkers, identified separately, were those most frequently selected by the highest-performing classification models. Finally, we used ensemble stacking machine learning to build multianalyte models comprising candidate sRNA and protein biomarkers.

Results: Our pipeline generated 272 sRNA transcripts and 4117 protein species common to all plasma specimens. We described three blood fingerprints, comprising the best-performing sRNA and protein biomarkers, for classifying patients according to glioblastoma tumour burden (Pre-OP vs. Post-OP), recurrence (Post-OP vs. REC) and treatment resistance (Pre-OP vs. REC). All models had a training performance of 100%, and cross-validation test accuracy rates ranged from 89.9% - 93.4%.

Conclusions: Our EV-based liquid biopsy strategy shows exciting promise for monitoring glioblastoma patients and distinguishing recurrence from treatment effects. Independent validation of our blood fingerprints is underway utilising plasma specimens and clinicopathologic data captured during the VERTU study (trial ACTRN12615000407594) and GlioNET Observational study.



Theme
Basic / Translational Science

4

Targeting GBM Heterogeneity using a Novel ephrin A5 Antibody Therapy

Rochelle CJ Dsouza[1], Niclas Skarne[1], Lachlan Harris[1], Seckin Akgul[1, 3], Carolin Offenhauser[1], Quan Ngyuen[2], Craig Bell[2], Kris Thurecht[2], Ulrich Baumgartner[1], Fiona Smith[1], Rosalind Jeffree[4], Po-ling Inglis[4], Zarnie Lwin[4], Hamish Alexander[4], Andrew W Boyd[1] and Bryan W Day[1]

[1] QIMR Berghofer Medical Research Institute
[2] University of Queensland
[3] Griffith University
[4] Neurosurgery Department, Royal Brisbane and Women's Hospital

Introduction: Glioblastoma (GBM) is an aggressive brain cancer and is associated with very poor prognosis in large part due to tumour heterogeneity. This study examines the role of ephrin A5, a tumour specific cell surface antigen with known oncogenic roles. The study also demonstrates that an ephrin A5 antibody drug conjugate (ADC) when used in combination with EphA3 ADC can be used to more effectively target GBM.

Results: Previous findings have shown that the EphA3 receptor is frequently elevated in GBM, particularly in the mesenchymal subtype and is expressed on tumour-initiating cells (Day *et al*. Cancer Cell 2013). Our data in GBM tissue shows that tumour cells expressing the high-affinity EphA3 ligand, ephrin A5; are distinct from EphA3 expressing cells. IHC staining quantification, revealed a combined receptor/ligand coverage >75%. *In-vivo* ephrin-A5 over-expression studies showed a moderate reduction of GBM aggressiveness and downregulation of known GBM stem cell markers. Spatial transcriptomics of ephrin-A5 over-expressing xenograft tumours revealed a reduction in proliferation markers including Ki67, MCM7 and PCNA. We detected an increase in expression of AC-like cell-state markers with a concomitant reduction of the MES-like and NPC-like GBM cell-states. Consistently, over-expression of ephrin-A5 in primary GBM lines led to a reduction in neurosphere formation, Ki67 staining and overall growth rate. Dual targeting in explant GBM organoid models demonstrated potent but heterogeneous killing responses, demonstrating the ability of EphA3 and ephrin A5-ADCs to target GBM heterogeneity.

Conclusion: This project has increased our understanding of ephrin A5 tumour biology in GBM and importantly has shown enriched expression on the AC-like tumour compartment. Future studies will expand upon these initial promising findings to validate dual EphA3 and ephrin A5 antibody drug conjugate targeting. Ultimately, these therapies may greatly reduce off target toxicities and extend GBM patient survival.

Theme
Basic / Translational Science

5

“Just being alive was exhausting”: A qualitative exploration of patient, caregiver, and healthcare professional experiences of cancer-related fatigue in people with brain tumour.

Rachel Campbell[1], Hannah Banks[1], Thomas Carlick[1], Mona Faris[1], Megan Jeon[1], Joanne Shaw[1], Haryana Dhillon[1,2]

[1] The Psycho-oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, Australia
[2] Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), The University of Sydney, Sydney, Australia

Aim: Cancer-related fatigue (CRF) is one of the most common symptoms reported by people with brain tumour (PwBT). Previous research has predominantly focused on examining CRF using quantitative assessments, thus failing to capture the rich, nuanced insight that can be garnered through exploring individuals’ lived experiences. We aimed to address this gap by qualitatively exploring PwBTs’ experiences of the nature and impact of CRF.

Methods: Semi-structured teleconference interviews were conducted with 24 PwBT, 5 caregivers of PwBT, and 11 healthcare professionals (HCPs) who treat PwBT. Interviews explored the experience, impact, and management of CRF, including the type of support provided by HCPs. Data was analysed using a Framework Approach.

Results: Qualitative analysis identified four themes: (1) pervasiveness of CRF; (2) impacts of CRF; (3) advice and support provided by HCPs; and (4) CRF self-management strategies. All participants identified CRF as an important issue for PwBT. Aligning with conceptual definitions, CRF was experienced as physical, emotional, and cognitive in nature, and had profound psychosocial and functional impacts on everyday life. Almost all HCPs reported routinely assessing patients’ fatigue through informal enquiry and typically recommended pharmacological (e.g., adjusting medications) and/or non-pharmacological management (e.g., increasing physical activity). In contrast, PwBT and caregivers reported that CRF assessment, advice and support was rarely provided by their HCPs. As a result, PwBT and caregivers felt the need to develop their own management strategies using trial and error. All participants identified a lack of CRF information resources specific to PwBT and their caregivers.

Conclusion: Our findings provide rich insight into the impact of CRF on PwBT and their caregivers. Our findings also highlight a lack of support and information available for those experiencing CRF in Australia. These results highlight a critical need for efficacious and empirically derived fatigue interventions and information resources to improve support of PwBT.

Theme
Survivorship, Psychology, and Supportive Care

6

An Evaluation of Brain Tumour Information Resources: Current State and Next Steps

Thomas Carlick[1], Hannah Banks[1], Jill Chen[1], Joanne Shaw[1], Haryana Dhillon[1,2,]

[1] The Psycho-oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, Australia
[2] Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), The University of Sydney, Sydney, Australia

Aim: Brain tumours and treatments often lead to cognitive decline, visual changes, and fatigue. Information for this population must be understandable and useful for diverse backgrounds, cognitive abilities, and health literacy levels. We aimed to critically evaluate the information resources currently available for people with brain tumour (PwBT).

Methods: Information resources were selected from the first results page from a Google search using terms related to brain tumours. Three raters used the Patient Education Materials Assessment Tool (PEMAT) to evaluate understandability and actionability. Understandability refers to whether a resource can be processed by consumers of diverse backgrounds. Actionability refers to whether a resource guides consumers about what to do with the information presented. Readability of written materials was assessed using the Sydney Health Literacy Lab editor, Gunning Fog Index, Coleman Liau Index, Flesch Grade Level, Automated Readability Index, and the Simple Measure of Gobbledygook. These indexes indicate the minimum education years required to comprehend the material. We also assessed resources' accessibility options (e.g., text-to-speech), representation of diverse populations, and information transparency (e.g., providing references).

Results: We identified 27 organisations from four countries (Australia, New Zealand, United Kingdom, and Canada) and assessed 376 resources (351 written materials and 25 videos). The mean understandability and actionability of all resources were 52% and 21% respectively. The mean readability score of written materials was 10.6 years. Most resources lacked accessibility options and had limited representation of underserved populations. The transparency of information was mixed.

Conclusion: The available resources online for PwBT require improvement. Resources are not easily understandable to the public and poorly communicate how the information can be used. These issues are likely to be compounded by the cognitive challenges associated with brain tumours. Information resource developers must consider their target population and critically evaluate the readability, understandability, and actionability of the information.

Theme
Survivorship, Psychology, and Supportive Care

7

Determining items for a brief screening tool for brain tumour caregivers' unmet needs

Jill Chen[1], Haryana Dhillon[1,2], Joanne Shaw[1], Georgia Halkett[3], Rachel Campbell[1,2] for the BRAINS Authorship Group

[1] The Psycho-oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, NSW, Australia
[2] Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), The University of Sydney, Sydney, NSW, Australia
[3] Curtin School of Nursing/Curtin Health Innovation Research institute (CHIRI), Curtin University, Perth, WA, Australia

Aims: Caregivers of people with primary brain tumour (PwBT) experience high unmet needs. Within the **B**rain cancer **R**ehabilitation, **A**ssessment, **I**nterventions for survivorship **N**eed**S** (BRAINS) program, we aimed to develop a brief version of the 44-item Supportive Care Needs – Partners & Caregivers (SCNS-P&C) survey to identify the unmet needs of PwBT caregivers.

Methods: Secondary analysis was performed on baseline data by 188 caregivers of people with high grade glioma who completed the SCNS-P&C in the CARE-IS study. Items were assessed against four criteria: factor loadings; prevalence; variation in domain score; diagnostic accuracy. Feedback from BRAINS stakeholders and investigators was sought to explore suitability of items for PwBT caregivers.

Results: Six items capturing two caregiving domains were selected. Three items were in the *Cancer Impact* domain: "The impact of caring for the person with cancer has had on your working life, or usual activities"; "Understanding the experience of the person with cancer"; and "Getting emotional support for yourself". Three items were in the *Information and Communication* domain: "Accessing information relevant to your needs as a carer/partner"; "Accessing information on what the person with cancer's physical needs are likely to be"; and "Having opportunities to discuss your concerns with the doctors". The six items failed to identify only 7.4% of caregivers with other unmet needs. Feedback from BRAINS stakeholders and investigators included: changes to wording (e.g., changing 'cancer' to 'brain tumour'); and, suggestions

to improve understandability.

Conclusion: The low proportion of individuals missed by the proposed six-item scale demonstrates strong clinical potential for this screening tool. To address issues raised by stakeholders and investigators, we will invite PwBT caregivers to review the items to explore necessary changes. Routine use of this tool in clinical practice will enable PwBT caregivers to be triaged for suitable and timely support.

Theme
Survivorship, Psychology, and Supportive Care.

8

Design of Patient-Centered Digital Health Interventions: Leveraging Input from Patients with Brain Tumours for Unmet Supportive Care Needs

Mahima Kalla[1, 2], Ashleigh Bradford[3], Verena Schadewaldt[4], Kara Burns[1, 2], Sarah Bray[4], Sarah Cain[4], Heidi McAlpine[4], Rana Dhillon[5, 6], Wendy Chapman[2] , James R Whittle[7, 8, 9], Katharine J Drummond[10], and Mei Krishnasamy[3, 11, 12]

[1] Uni of Melbourne, Carlton, VIC, Australia
[2] Centre for Digital Transformation of Health, University of Melbourne, Melbourne
[3] Peter MacCallum Cancer Centre, Melbourne
[4] Royal Melbourne Hospital, Melbourne
[5] Barwon Health, Geelong
[6] St Vincent's Hospital , Melbourne
[7] Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne
[8] Personalised Oncology Division, WEHI, Melbourne
[9] Department of Medical Biology, University of Melbourne, Melbourne
[10] Department of Neurosurgery, University of Melbourne, Melbourne
[11] Department of Nursing, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne , Melbourne
[12] VCCC Alliance, Melbourne

Background and Aim: Typically, people who have brain tumours will experience persistent, distressing and disabling physical, psychosocial, cognitive, and financial challenges. These challenges are compounded by the difficulties in connecting and communicating with their treating team, establishing peer support networks, managing their symptoms, and accessing personalised supportive care, especially for rural patients. Digital health interventions can address access and equity barriers to cancer services by overcoming geographic, physical, and psychological barriers, facilitating access to treatment, support, and education for patients within convenient timeframes and their own environments. Our team set out to co-design a supportive care digital resource to mitigate the unmet needs of Australians affected by brain tumours, no matter where they live. Using an evidence informed framework and data from studies previously undertaken by members of our team, we developed *Brain Tumours Online,* a novel Australian digital health solution.

Methods: This paper focuses specifically on one step in the co-design process - a qualitative interview study with consumers and multidisciplinary health care professionals to generate an in-depth understanding of needs and preferences for a digital health solution, to address needs currently unmet by face-to-face care delivery approaches.

Results and Conclusion: True to consumers' preferences expressed in our co-design activities, our platform provides supportive psychosocial care for patients and their carers, via three key pillars: a) Learn: a curated repository of vetted evidence-based information about symptoms, treatment options, available psychosocial / allied health supports, and other practical information (e.g. preparing for return to work/study, navigating welfare support etc.); b) Connect: an online peer support community that allows patients and their informal caregivers to connect with each other and healthcare professionals in a variety of formats; and c) Toolbox: a selection of validated self-management digital health tools to support symptom management and self-care for other psychosocial needs.

Theme
Survivorship, Psychology, and Supportive Care.

9

Participant Experiences of the LaTCH Program for Brain Tumour Survivors: A Preliminary Qualitative Analysis

Ellie Piggott[1], Sian Virtue-Griffiths[2], Haryana Dhillon[3,4], Joanne Shaw[3,4], Dianne Legge[5], and Kerryn Pike[1,2]

[1] School of Applied Psychology, Griffith Centre for Mental Health and Menzies Health Institute Queensland, Griffith University, Gold Coast and Brisbane, Australia.
[2] Department of Psychology and Counselling, School of Psychology and Public Health, La Trobe University, Melbourne, Australia.
[3] Centre for Medical Psychology and Evidence-Based Decision-Making (CeMPED), University of Sydney, Sydney, Australia.
[4] Psycho-Oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, University of Sydney, Sydney, Australia.

[5] *Olivia Newton-John Cancer Wellness and Research Centre, Austin Health, Melbourne, Australia.*

Introduction: Cognitive impairment can reduce the quality of life and everyday functioning of brain tumour survivors. Despite this, few interventions are available to support those requiring cognitive rehabilitation following brain tumour diagnosis and treatment. LaTCH, a cognitive rehabilitation program, has the potential to address cognitive impairment in this population. Originally developed for older adults experiencing age-related cognitive decline, the LaTCH program is a telehealth-delivered intervention adapted to improve the everyday memory performance of brain tumour patients in Australia.

Aim: The current study aimed to explore participants' perceptions of the value, applicability, and feasibility of the LaTCH program for brain tumour survivors.

Method: The LaTCH program is a group-based intervention comprising six two-hour interactive sessions delivered online by two neuropsychologists. We are currently conducting a randomised phase II study evaluating the efficacy of LaTCH against a wait-list control condition, with 56 (of 100) participants now recruited. We conducted semi-structured interviews with participants following completion of the program (up to 11 weeks post-intervention). Qualitative accounts were audio-recorded, transcribed, and analysed for preliminary themes.

Results: We interviewed 10 participants, eight women and two men with a median age of 51 years. Overall, participants reported that the LaTCH program helped them implement new strategies to improve their memory in everyday life. They further reported that LaTCH increased feelings of acceptance, self-efficacy, and hope for the future. Few improvements, other than shorter sessions, were proposed. All agreed that LaTCH should be available to the wider population of brain tumour survivors. Participants suggested possible locations, facilitators, and referral pathways for potential future implementation, and identified financial costs and travel requirements as likely barriers to participation.

Conclusion: Participants perceive the LaTCH program to be a valuable, applicable, and feasible cognitive rehabilitation intervention for brain tumour survivors in Australia.

Theme
Survivorship, Psychology, and Supportive Care.

10

IPAX-2: Phase 1 Safety and Dose Finding Study of [^{131}I]IPA Plus Standard of Care in Patients With Newly Diagnosed Glioblastoma

Tracey Brown[1], Brenda Cerqueira[1], Stefanie Martina[1], Colin Hayward[1], and Hui K. Gan[2]

[1] *Telix Pharmaceuticals, Melbourne, Australia*
[2] *Austin Hospital, Melbourne, Australia*

Introduction: Glioblastoma (GBM) accounts for nearly 60% of all central nervous system tumors, with poor prognosis and high recurrence rate. Many tumor types, including GBM, overexpress the L-type amino transporter 1 (LAT-1), which is the target for the small-molecule amino acid derivative, 4-L-[^{131}I] iodo-phenylalanine ([^{131}I]IPA). LAT-1 also mediates ^{18}F-FET uptake; thus, ^{18}F-FET PET may help select patients with overexpressed LAT-1 for (^{131}I]IPA treatment and provide follow-up informarmation on tumor status. Preliminary effiacy and safety results from a phase 1 study of [^{131}I]IPA + XRT in patients with recurrent GBM are promising.

Aim: The objective of IPAX-2 is to evaluate the safety and tolerability of [^{131}I]IPA in patients newly diagnosed with GBM.^{18}F-FET PET will be used for pre- and post-treatment evaluations.

Methods: IPAX-2 is a phase 1, multicentre, open label, single arm, parallel group, dose finding study to evaluate the safety of ascending radioactive dose levels of [^{131}I]IPA + best standard of care in newly diagnosed patients with GBM. Eligible participants (n=12) will inlude patients aged 18-65 years of age (inclusive) with 1) histologically confirmed intracranial GBM following surgial resection, 2) no prior systemic therapy or radiation for GBM; 3) a Karnofsky Performance Status ≥70; 4) a plan to begin chemoradiation 3-6 weeks after surgical resection with Stupp regimen; 5) have adequate organ function; and 6) have adequate tissue samples previously archived. Primary outcome measures are 1) the incidene rate and severity of dose-limiting toxicities, and 2) the safety, tolerability, and recommended phase 2 dose.

Results: This study is currently enrolling patients, and no results are available at the time of this abstract.

Conclusion: [^{131}I]IPA unique characteristic including its specific and sustained tumor accumulation, and intrinsic cytostatic and radiosensitizing effect, make it an extremely attractive therapeutic probe against GBM.

Disclosures: Telix Pharmaceuticals is the sponsor of this study.

Theme
Therapeutics in Clinical Care.

11

When IDH1wt is not enough.... A clinical algorithm to enrich for novel mutations

Dr Lawrence Cher[1], Professor Hui Gan[1], Dr Anthony Uccellini[1], Dr Jonathan Clark[1]

[1] Austin Health, Heidelberg VIC, Australia

Introduction: The division of gliomas into two broad groups characterised by the presence or absence of an IDH mutation was a crucial juncture in understanding glioma biology. While most IDH wild type tumours in adults are essentially grade IV astrocytomas with relatively poor prognosis we now appreciate that there are a range of other mutations that are of major importance in prognosis that have been identified and can potentially have therapeutic implications. We present a clinically based approach to enriching for a population of patients in which more detailed molecular profiling is important for treatment or prognosis.

Methods: In clinical practice we identified several clues that can identify patients with unusual molecular profiles that improve our understanding of the patient's prognosis or treatment.

Results: A history of symptoms extending longer than normally expected for a typical IDHwt tumour is an important clue in identifying rarer tumour subtypes. In addition, imaging can be important. Looking at prior imaging that shows a precursor lesion which may have been missed is important to suggest a different molecular profile. As well, imaging characteristics such as a midline tumour should prompt for assessment of H3K27M mutations. IDHwt non-enhancing tumour followed for a period of time should also be assessed particularly in older patients who may have a FGFR3-TACC3 mutation for example. FGFR directed therapy may also be considered although there is little data at present in this subgroup.
In addition, patients who live longer than expected should also be evaluated retrospectively. In young adults it is important to consider the range of paediatric brain tumour types should also be considered. BRAF V600E mutations can affect a range of tumours such as pilocytic tumours and PXAs and combined MEK inhibition is a treatment option.

Conclusion: We will provide clinical examples of all these as part of our presentation to illustrate our approach, to a clinically based method of enriching for molecular characterisation of glioneuronal tumours.

Theme
Adolescent and Young Adult, Paediatric and Rare CNS Tumours

12

The EphA3 receptor is a tumour-specific therapeutic target and promotes tumourigenicity in medulloblastoma

Carolin Offenhauser[1], Fiona Smith[1], Kathleen Ensbey[1], Michelle Li[1,2], Rochelle D'Souza[1,2], Zara Bruce[1], Craig Bell[4,5], Kristofer Thurecht[4,5], Andrew Boyd[1,3], Bryan Day[1,2,6].

[1] QIMR Berghofer Medical Research Institute, Brisbane, Australia
[2] School of Biomedical Sciences, The University of Queensland, Brisbane, Australia
[3] School of Medicine, The University of Queensland, Brisbane, Australia.
[4] Australian Institute for Bioengineering and Nanotechnology, The University of Queensland, Brisbane, Australia
[5] Centre for Advanced Imaging, The University of Queensland, Brisbane, Australia
[6] School of Biomedical Sciences, Faculty of Health, Queensland University of Technology, Brisbane, Australia.

Introduction/Aims: Medulloblastoma is the most common central nervous system malignancy in children. With aggressive therapy, 5-year survival rates range from <50 to >90%, depending on subtype and risk stratification. Novel therapeutic approaches are needed to improve survival and reduce the significant long-term side effects associated with current therapies. In this context, we investigated the receptor tyrosine kinase EphA3 as a potential tumour-specific therapeutic target in medulloblastoma and examined its oncogenic functions.

Methods: EphA3 expression was analysed in cell lines, patient-derived xenograft tissues and public gene expression datasets. Oncogenic functions of EphA3 were investigated using shRNA-mediated EphA3 knockdown to assess its effects on drug sensitivity, invasiveness and tumour formation using *in vitro* cell-based assays and *in vivo* animal studies. EphA3-targeting ADCs were generated and anti-tumour efficacy was assessed *in vitro* and *in vivo* using preclinical animal models.

Results: EphA3 is elevated in a significant proportion of medulloblastoma tumours; this is particularly the case for the WNT and Group 4-alpha subtypes. Our EphA3 knockdown studies suggest that EphA3 expression promotes 3D tumour cell invasion, chemotherapy resistance and tumour initiation and/or progression. Our EphA3-targeting ADCs effectively induced caspase-mediated cell death *in vitro* and were found to be relatively tumour-specific and well-tolerated in preclinical animal studies. The ADC alone showed minimal efficacy; however, in combination with de-

escalated radiation we observed a synergistic anti-tumour response.

Conclusions: Our study identifies the EphA3 receptor as a promising novel therapeutic target for medulloblastoma and suggests that EphA3 has a functional, pro-tumorigenic role. Our study further demonstrates safety and efficacy of anti-EphA3 ADCs in combination with de-escalated radiotherapy in preclinical models of medulloblastoma.

Themes
Basic/ Translational Science, Adolescent and Young Adult, Paediatric and Rare CNS Tumours

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14

Dendritic Cell Defects in Patients and Mice with Brain Tumours

Bryan Gardam[1,2], Tessa Gargett[1,2,3], Michael P Brown[1,2,3], Lisa M Ebert[1,2,3]

[1] Adelaide Medical School The University of Adelaide, Adelaide, South Australia, Australia
[2] Translational Oncology Laboratory, Centre for Cancer Biology, University of South Australia and SA Pathology, Adelaide, South Australia, Australia.
[3] Cancer Clinical Trials Unit, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Glioblastoma is an aggressive form of brain tumour that is the leading cause of death from cancer in people under 40 in Australia. Glioblastoma has seen few advances in treatment for over 20 years, highlighting the urgent need for new and innovative treatments. Dendritic cells are professional antigen-presenting cells required for priming and activating T cells and for initiating effective immune-mediated tumour control. Several studies have reported reduced dendritic cells in glioblastoma patients' peripheral blood compared to healthy controls, and a paucity of these cells within glioblastoma tumours. However, it is currently unclear which dendritic cell subsets are most affected. Here we aim to determine the affected dendritic cell subsets and an appropriate murine model to replicate these results to allow us to investigate potential methods to restore dendritic cells in glioblastoma patients.
In this study, we show a systemic reduction in dendritic cells in glioblastoma patients' peripheral blood compared to healthy donors by high-parameter flow cytometry. The most significant reduction was seen in $CD5^{+}$cDC2s, $CD14^{-}$DC3s, and pDCs. At the same time, all other subsets were also reduced. Our investigation also identified changes in dendritic cell functional markers in both tumour and blood, including markers indicating reduced antigen presentation and lymph node homing, while PD-L1 was increased.
Next, we explored the dendritic cells in four murine models of glioblastoma to evaluate their suitability as a model system.
In our evaluation of two syngeneic and two patient xenograft murine models, we found no significant difference in dendritic cell number in tumour and other tissues across the models. However, the change in functional markers was best reflected in the syngeneic model, indicating a potentially suitable model to explore growth factor treatments to expand and restore the dendritic cell populations.

Theme
Basic / Translational Science

15

ROR1 Expression in Glioma – A Novel Prognostic Biomarker

Daniel Madani[1], Miya John[2], Laveniya Satgunaseelan[3], Brindha Shivalingam[1], Caroline Ford[2]

[1] Department of Neurosurgery, Chris O'Brien Lifehouse Hospital, Royal Prince Alfred Hospital, Sydney, Australia
[2] Gynaecological Cancer Research Group, Lowy Cancer Research Centre, School of Women's and Children's Health, Faculty of Medicine and Health, University of New South Wales, Sydney, Australia
[3] Department of Neuropathology, Royal Prince Alfred Hospital, Australia Sydney medical School, Faculty of Medicine and Health Sciences, The University of Sydney, Sydney, Australia

Background: Glioblastoma is the most common and aggressive primary brain tumour in adults. Despite maximal surgical resection followed by concomitant chemo-/radiotherapy, the three-year survival remains less than 5%. Receptor tyrosine kinase-like orphan receptor 1 (ROR1) overexpression is associated with poor prognosis in several cancers. ROR1 therapeutics are in Phase I/II trials making it an exciting novel target with translational potential to explore for glioblastoma treatment. The aim of this study was to examine the association between ROR1 mRNA expression and overall survival, by applying the WHO 2021 classification to transcriptomic glioma datasets.

Methods: Clinical, histological, and molecular data was extracted from The Cancer Genome Atlas (TCGA), Chinese Glioma Genome Atlas (CGGA), Repository for Molecular Brain Neoplasia (REMBRANDT), and GSE16011 (GRAVENDEEL) projects via the GlioVis portal. Using the WHO 2021 classification, the dataset was appropriately re-classified. Only confirmed cases of astrocytoma, oligodendroglioma, or glioblastoma, and ROR1 mRNA expression data were included in the

analysis, which included a total of 2,303 cases. 981 cases comprised the low-grade glioma cohort and 1322 cases were included in the high-grade glioma cohort. ROR1 mRNA expression from the four datasets was normalised within each dataset, combined, and divided into high and low expression groups. ROR1 expression and survival correlations were estimated with Kaplan-Meier survival analysis and Mantel-Cox test using GraphPad Prism v9.

Results: Those with high ROR1 expression had an overall median survival of 4.5 months, as compared to 21.4 months in the low ROR1 expression cohort (p< 0.0001). High-grade gliomas had the highest ROR1 mRNA expression across the consortium when compared to the low-grade glioma cohort (p< 0.0001).

Conclusion: The results of this study indicate an association between overall survival in glioma and ROR1 expression. In addition, targeting ROR1 could hold translational importance for novel putative treatment in glioblastoma patients.

Clinical Characteristics of Glioma Datasets				
Dataset	**TCGA**	**CGGA**	**REMBRANDT**	**GRAVENDEEL**
SUB HEADING: 2021 WHO Classification of Tumours of the Central Nervous System and grade *n* (%)				
Astrocytoma	258	247	147	53
Grade 2	113	116	64	6
Grade 3	96	131	58	15
Grade 4	30	-	-	32
Unreported grade	19	-	25	-
Oligodendro-glioma	169	167	67	23
Grade 2	85	95	30	4
Grade 3	72	71	23	18
Unreported grade	12	1	14	1
Glioblastoma	408	388	219	128
Primary Grade 4	408	388	132	126
SUB HEADING:Demographics				
Median age in years (range)	47 (14 – 89)	43 (8 – 79)	50 (15 – 89)	52 (14 – 81)
Male	355	595	214	180
Female	254	414	126	88
Unreported	58	1	46	0
SUB HEADING: Total	631	802	433	211

*Not otherwise specified (NOS) - unreported grade
TCGA total 631
CGGA 802
REMBRANDT 433
GRAVENDEEL 211

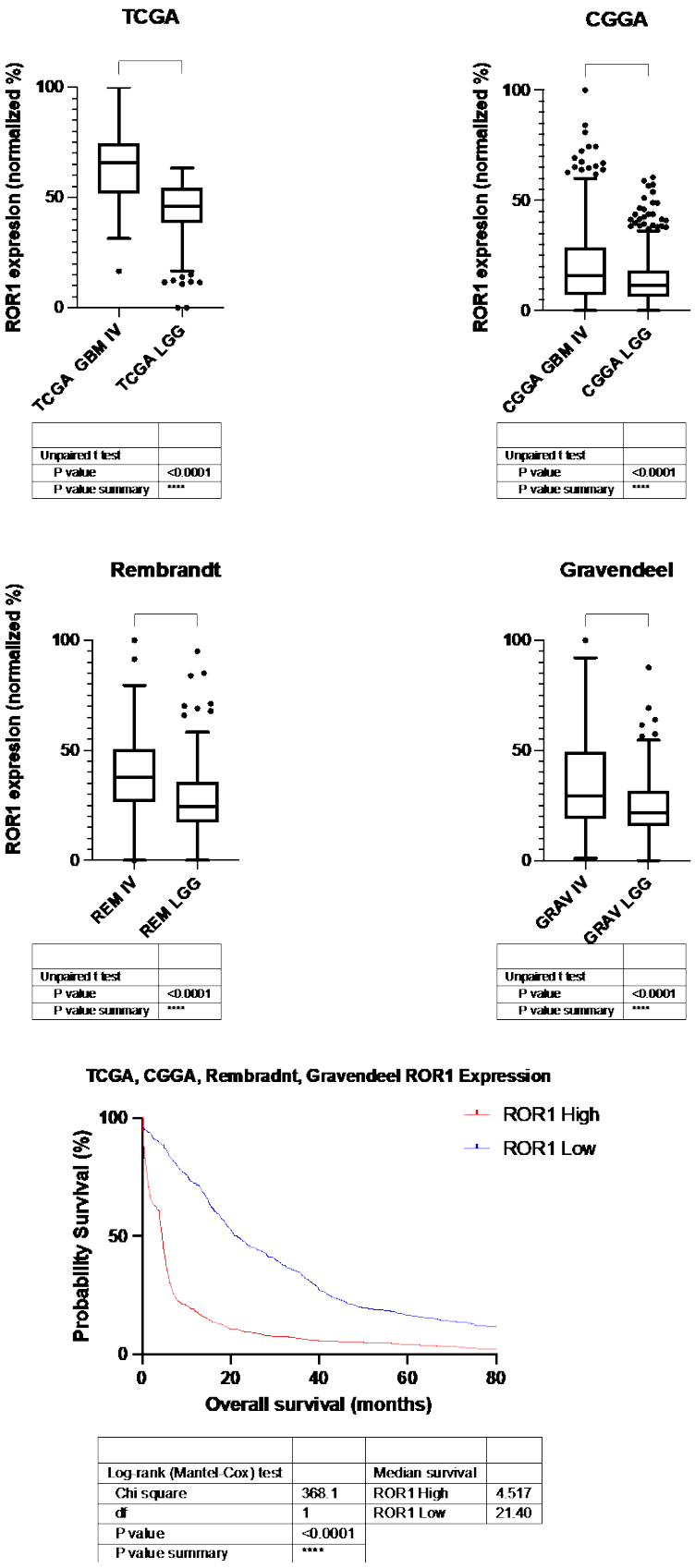


Figure #. Kaplan-Meier survival curves of four independent datasets in glioma patients. Survival benefit was observed in the ROR1 low expression glioma cohort (p <0.0001)

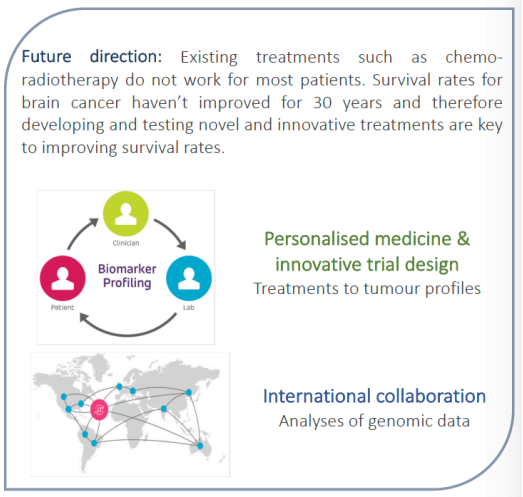
Future direction: Existing treatments such as chemo-radiotherapy do not work for the vast majority of glioma

of patients. Survival rates for brain cancer haven't improved for 30 years and therefore developing novel and innovate treatments are key to improving survival rates

Advances in next generation sequencing
- Identification of cancer stem cell

Analysis of genomic data
- ROR1 as a therapeutic target for glioma

Personalised medicine
- Innovative glioma trial design



Theme
Basic / Translational Science

16

Targeting androgen signaling in glioblastoma

Sofia Mason[1,2,3], Sylvia A Chung[4,5], Hao-wen Sim[1,2,3], Beatriz P San Juan[1,2,3], Rachel F Dear[1,2,3], Bryan Day[6,7], Jeff Holst[4,5], Christine L Chaffer[1,2,3]

[1] The Garvan Institute of Medical Research, Darlinghurst, NSW, Australia
[2] St. Vincent's Clinical School, UNSW Medicine, UNSW Sydney, NSW, Australia
[3] The Kinghorn Cancer Centre, Darlinghurst, NSW, Australia
[4] School of Biomedical Sciences, UNSW Sydney, NSW, Australia
[5] Adult Cancer Program, Lowy Cancer Research Centre, UNSW Sydney, NSW, Australia
[6] QIMR Bergdorfer Medical Research Institute, Herston, Queensland, Australia
[7] University of Queensland, Brisbane, Queensland, Australia

Aims: Glioblastoma is a lethal brain cancer. Androgen receptor (AR) transcript levels and protein expression are upregulated in glioblastoma compared to normal brain. AR signalling has a role in cancer stem cell function in various cancers. Stem cell activity and cancer cell plasticity represent key resistance mechanisms in glioblastoma. We hypothesise that potent brain-penetrant anti-androgen therapies have the potential to improve response to treatment in glioblastoma.

Methods: Clinical samples and patient derived xenografts were assessed for AR expression by immunohistochemistry. Cytoplasmic AR+ and AR- glioblastoma patient-derived xenografts maintained under stem cell conditions were tested *in vitro* for their response to anti-androgen therapies (abiraterone, enzalutamide and seviteronel). Stem cell function was assessed using a tumoursphere assay. Changes in plasticity markers, including ZEB1, were measured with immunofluorescence.

Results: ~55% of people with glioblastoma have detectable cytoplasmic AR based on immunohistochemistry. AR-positive patient derived glioma stem cell line RN1 was inhibited by low concentrations of anti-androgen agents, with seviteronel having the lowest half maximal inhibitory concentration (IC50) (at 96 hours: enzalutamide 52μM, abiraterone 12μM, seviteronel 7μM). AR negative line WK1 was also inhibited though with higher IC50s (at 96h: enzalutamide 63μM, seviteronel 21μM). Conventional cell lines U87 and U251 were also inhibited by anti-androgen monotherapy. Tumoursphere assays demonstrated that anti-androgen agents inhibit the tumour-forming ability of cells, with seviteronel and abiraterone showing more inhibition than enzalutamide. Immunofluorescence analysis showed downregulation of plasticity marker ZEB1 with anti-androgen treatment (normalised mean fluorescent intensity: abiraterone 0.84, enzalutamide 0.91, seviteronel 0.74).

Conclusions: Glioblastoma is a devastating disease, lacking effective or targeted treatments. Targeting AR with repurposed anti-androgen drugs may be a promising therapeutic strategy, with the potential to abrogate treatment resistance. We are now evaluating these anti-androgen regimens in animal experiments, which will provide a more replicative microenvironment and confirm blood-brain barrier penetrance.

Theme
Basic / Translational Science

17

High throughput strategies for brain cancer drug discovery

Ganes Pranavan[1], Peter Mews[1], Mitali Fadia[1], Naomi Mitchell[2], Olga Zaytseva[2], Brooke Kinsela[2], Tanya

Jaivad[2], Tom Gibbs[2], Ross Hannan[2], Amee George[2], Lee Wong[3], Nadine Hein[2] and Leonie Quinn[2]

[1] The Canberra Hospital, ACT Health, Canberra, ACT
[2] John Curtin School of Medical Research, Australian National University, Canberra, ACT
[3] Monash Biodiscovery Research Institute, Monash University, Clayton, VIC.

A major challenge in the brain cancer field is development of efficacious therapies. This has been hampered by the inherent disconnect between fundamental research and the clinic, together with the lack of effective pre-clinical models for drug screening studies. The Canberra Brain Cancer Collaborative (CBCC) comprises an interdisciplinary research team that connects our drug discovery research at Australian National University (ANU) with The Canberra Hospital (TCH) oncology, neurosurgery, and neuro-pathology units. Thus, we have also established the ACT node of Brain Cancer Biobanking Australia (BCBA), which will provide the diversity of glioma genotypes necessary for robust drug discovery. Moreover, through whole genome and transcriptome sequencing, we are developing the deep molecular classification of glioma samples, with integrated patient and histopathological data, essential for robust genomics-based drug discovery.
Our exciting preliminary data demonstrate *ATRX* and *IDH1* mutant glioma are hypersensitive to the first in class RNA Polymerase I (Pol I) inhibitor CX-5461. Importantly, we have developed a second-generation Pol I inhibitor PMR-116 (with Pimera Australia) which can cross the blood brain barrier. We are building on our observation that these glioma subtypes are sensitive to Pol I inhibitors by testing for efficacy of PMR-116 in combination with Temozolmide. To extend the longevity of PMR-116 in clinic, we are using 3D glioma models, together with High Throughput Screening, to identify drugs with efficacy in combination with the Pol I inhibitor. For rapid translation to clinic, we will first test FDA approved agents for efficacy in combination with PMR-116. In addition to screening *IDH1* and *ATRX* mutant tumours, in future, we aim to identify agents with efficacy for a broader range of gliomas.

Theme
Basic / Translational Science

18

Developing a Preclinical Pipeline for Advancing Cancer Therapeutics (PACT) and its deployment as a pilot business model

Aude EM Touffu[1,2,3], Amanda L Hudson[2,3], Kelly J McKelvey[3], Alexander Yuile[2,3,4,5], Helen R Wheeler[2,3,4,5], Shihani P Stoner[1,2,3]

[1] Mark Hughes Foundation, University of Newcastle, Callaghan, 2308 NSW, Australia.
[2] Bill Walsh group, The University of Sydney, Kolling Institute, St Leonards, 2065 NSW, Australia.
[3] Faculty of Medicine and Health, The University of Sydney, Camperdown, 2006 NSW, Australia.
[4] Royal North Shore Hospital, Reserve Road, St Leonards, 2065 NSW, Australia.
[5] The Brain Cancer Group, Westbourne St, St Leonards, 2065 NSW, Australia.

Background: Glioblastoma is the most common primary brain malignancy in adults and has a poor prognosis with a median survival of 14 months. While there have been major breakthroughs in understanding glioblastoma pathophysiology, this growing body of evidence has been slow to translate to clinical trials and is yet to change the standard of care. This is partly due to unique challenges in developing glioblastoma animal models. Barriers specific to neuro-oncology models include simulating major physiologic processes such as the blood-brain barrier, recreating standard of care treatments of localised radiotherapy and systemic temozolomide, and difficulties with orthotopic intra-cranial inoculation of glioblastoma cells. All of the above require specific skill sets and can be cost prohibitive in many situations. To improve access to animal models for Australian researchers, we developed a preclinical pipeline that maximizes cost-efficiency and scalability, which can serve as a sustainable business model.
Methods: Following institutional approvals, protocols for pragmatic and scalable animal models were optimised to simulate clinical care. Through funding from the Mark Hughes Foundation, these protocols were launched as a pilot business model with the aim of improving access to pre-clinical models in Australia.

Results: Our pipeline utilizes our Small Animal Radiation Research Platform (SARRP) to simulate brain cancer models. It delivers targeted radiation therapy that is CT image-guided to optimise radiation localisation. Figure 1 demonstrates use of this pipeline to investigate differential effects of radiation fractionation on glioblastoma. Since establishing PACT as a business in 2019, eight brain cancer projects have been completed for five different collaborators. These projects have investigated both therapeutics and diagnostic techniques.

Conclusion: We have demonstrated how a streamlined protocol can be deployed to provide rapid development of animal models for glioblastoma and how access to this pipeline can be increased through use of a sustainable business model.

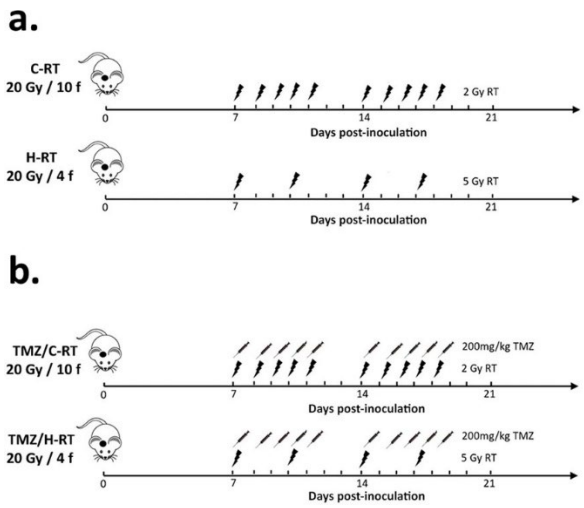


Figure 1. Schematic representation of the in vivo conventional radiotherapy (C-RT) or hypofractionated radiotherapy (H-RT) regimens alone (**a**) or with temozolomide (TMZ) (**b**).

Theme
Basic / Translational Science

20

Targeting RNA Polymerase I as a therapeutic strategy to treat paediatric gliomas

Andrew Garvie[1], Maheshi Udugama[1], Linda Hii[1], Hsiao PJ Voon[1], L Quinn[1], R Hannan[2], Lee H Wong[1]

[1] Biomedicine Discovery Institute, Monash University; [2] John Curtin School of Medical Research, Australian National University.

Background and Aim: The incorporation of the histone variant H3.3 into DNA is orchestrated by ATRX (alpha thalassemia/mental retardation X-linked), facilitating the assembly of DNA repeats like telomeres and ribosomal DNA repeats (rDNA) into regions of silenced chromatin. Notably, a remarkable discovery in the realm of cancer epigenetics is the identification of H3.3 mutations, particularly H3.3K27M and H3.3G34R, which are frequently found in paediatric gliomas.

Of significance, the H3.3G34R mutation often co-occurs with ATRX mutations. Loss of ATRX is strongly linked to the activation of the ALT telomere maintenance pathway, which confers cellular immortality in 15% of human cancers. Mutations in the Krebs cycle gene IDH1 (IDH1R132H) also frequently coincide with ATRX mutations, though they are more prevalent in adult gliomas.

We have previously reported that ATRX-depleted cells experience substantial loss of rDNA copies, resulting in reduced production of ribosomal RNA (rRNA) transcripts and increased sensitivity to inhibition of RNA polymerase I (1,2). Consistently, human cancers with ATRX mutations exhibit extensive reductions in rDNA copy numbers and manifest sensitivity to RNA Polymerase I inhibition.

Results and Conclusion: Our findings indicate that H3.3 and IDH1 mutations in gliomas introduce notable stressors to the rRNA transcription pathway. This stress arises due to severe disruption of chromatin organization at rDNA repeats caused by H3.3, IDH1, and ATRX mutations. Correspondingly, our investigations reveal that gliomas with H3.3/IDH1/ATRX mutations display heightened sensitivity to treatment with RNA Polymerase I inhibitors, such as CX5461 (3, 4) and PMR116 (which are capable of crossing the blood-brain barrier). In light of these findings, we propose the therapeutic potential of RNA polymerase I transcription inhibitors as a viable treatment approach for H3.3/IDH1/ATRX-mutated gliomas.

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Theme
Basic / Translational Science

23

Clinical quality indicators in high-grade glioma cohort from South Western Sydney: feasibility of data extraction and reporting towards building an Australian Brain Cancer Registry

Mirette Abraham[1], Joe Chang[1], Vanessa Estall[1], Adam Cooper[2], Annette Tognela[3], Kate Wilkinson[2], Wafa Trad[4], Teresa Simpson[4], Ganesh Shivapathasundram[5], Sugendran Pillay[6], Ramesh Cuganesan[6], Ruwanthie Fernando[7], Rosalind L. Jeffree[8], Eng-Siew Koh[1,9]

[1] Department of Radiation Oncology, Liverpool Cancer Therapy Centre, Liverpool, NSW, Australia
[2] Department of Medical Oncology, Liverpool Cancer Therapy Centre, Liverpool, NSW, Australia
[3] Department of Medical Oncology, Macarthur Cancer Therapy Centre, Macarthur, NSW, Australia
[4] Liverpool Cancer Therapy Centre, Liverpool, NSW, Australia
[5] Department of Neurosurgery, Liverpool Hospital, Liverpool, NSW, Australia
[6] Department of Radiology, Liverpool Hospital, Liverpool, NSW, Australia
[7] Department of Palliative Care, Liverpool Hospital,

Liverpool, NSW, Australia
[8] Department of Neurosurgery, Hospital, Royal Brisbane Women's Hospital, Herston, QLD, Australia
[9] South Western Sydney Clinical School, University of New South Wales, Australia

Purpose: In 2022, 58 Clinical Quality Indicators (CQI) embedded within an Australian brain cancer registry spanning key aspects of high-grade glioma (HGG) and low-grade glioma were developed via Delphi process [1]. This study focuses on 1) describing CQI within a HGG subgroup and 2) ascertaining feasibility of CQI data extraction.

Methods and Materials: A retrospective audit of HGG patients diagnosed in South Western Sydney between 1/1/2019 and 31/12/2020 was undertaken. Data sources included hospital/oncology EMR, MDT minutes and correspondence letters. Of the 58 CQI, 19 were excluded (LGG/paediatrics/salvage therapy). Thirty-nine CQI covering HGG including ECOG, histological/ molecular diagnostics, extent of resection (EOR), post-operative MRI, guideline-concordant radiotherapy (RT) (standard/ hypofractionated), concurrent and/or adjuvant chemotherapy (CT). MDT discussions, clinical trial screening and key referrals (allied health, palliative care) were analyzed.

Results: To date, the 61 patients analyzed are Grade IV glioma (n=54), Grade III (n=7) with anaplastic astrocytoma (n=4) and oligodrendroglioma (n=3). Of these, 55/61 (90%) were discussed at initial diagnosis in an MDT. Adjuvant RT (40.05-60Gy) was recommended in n=54, concurrent CT in n=53, adjuvant CT in n=47. Ten patients were deemed suitable for at least one clinical trial.
Despite guideline-concordant recommendations, n=16/55 (29%) were subsequently unable to complete full adjuvant therapy due to: disease progression n=9/55 (16%), patient decision n=3/55 (5.5%), change in performance status/ terminal care n=3/55 (5.5%) or move to another treatment centre n=1/55 (2%).
Although referrals and indications for MDT discussion were automated, actual MDT recommendations and eventual outcomes data required manual extraction.

Conclusion: Given that CQI and MDT recommendations facilitate optimal care for HGG patients, tailored documentation and data systems which facilitate efficient capture and extraction of CQI are needed. Future initiatives aim to enable CQI and clinical outcomes to be compared longitudinally and benchmarked against other patient cohorts.

References
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Theme
Other

24

Exploring the Role of Germline DND in the Brain Location of Adult Glioma Tumours

Karen Alpen[1], Miroslaw Kapuscinski[1], Robert MacInnis[1,2], Claire Vajdic[3] and Enes Makalic[1]

Affiliations:
[1] Centre of Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Parkville, Victoria, Australia
[2] Cancer Epidemiology Division, Cancer Council Victoria, East Melbourne, Victoria, 3002, Australia
[3] The Kirby Institute, UNSW Sydney, Sydney NSW 2052, Australia

Background/Aim: Adult glioma tumours are non-uniformly distributed throughout the brain with oligodendroglioma having a higher proportion of frontal lobe tumours than astrocytoma or GBM[1]. With few known environmental risk factors for glioma, what is driving this non-uniform distribution? Are individuals born with variation in their DNA that makes them susceptible to tumours in a particular brain location?

Methods: Using tumour location data of two independent studies, the Australian AGOG study and European GliomaScan study, we conducted a genome-wide association study stratified by sex and tumour location (frontal, parietal and temporal lobes) to investigate whether the known germline risk variants (e.g., variants in *TERT, TP53, EGFR, CCDC26, RTEL1, CDKN2BAS*) are associated with tumour location and to identify novel risk variants or genomic regions that may be associated with the location of glioma tumours.

Results: The established germline glioma risk variants do not appear to be drivers of the location of glioma tumours. We identified ten novel genomic regions associated with risk of glioma in either the frontal, temporal or parietal lobe which replicated across both studies. Most of these location-specific risk regions were discovered in sex-specific data.

Conclusion: Our findings suggest that risk factors other than the known genetic risk variants are driving glioma tumour location. These unknown risk factors may be novel genetic risk regions such as those identified in this analysis and/or unidentified environmental risk factors. Our analysis was limited by small sample sizes and additional datasets are required to provide further evidence to support our findings.

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Theme
Other

25

Descriptive epidemiology of glioma patients in Australia's multi-site BRAIN registry from 2016-2023

Rose Clarke[1,2], Anthony Dowling[2], Katharine Drummond[3,4], Iwan Bennett[5,6], Claire Philips[7], Elizabeth Ahern[8,9], David Campbell[10], Rosemary Harrup [11,12], Ross Jennens[13], Robert Campbell[14], Ronnie Freilich[15], Simone Reeves[16], Mark Rosenthal[17], Ian M Collins[18], Julie Johns[1], Peter Gibbs[1,19], Lucy Gately[1,20]

[1] The Walter and Eliza Hall Institute of Medical Research, 1G Royal Parade, Parkville, Melbourne, VIC, 3052, Australia.
[2] Department of Medical Oncology, St Vincent's Hospital Melbourne, Melbourne, VIC, Australia.
[3] Department of Neurosurgery, Royal Melbourne Hospital, Parkville, VIC, Australia.
[4] Department of Surgery, University of Melbourne, Parkville, VIC, Australia.
[5] Department of Neurosurgery, Alfred Health, Melbourne, VIC, Australia.
[6] Department of Neurosciences, Monash University, Clayton, VIC, Australia.
[7] Department of Radiation Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia
[8] Department of Oncology, Monash Health, Melbourne, VIC, Australia.
[9] School of Clinical Sciences, Monash University, Melbourne, VIC, Australia
[10] Department of Medical Oncology, University Hospital Geelong, Barwon Health, Geelong, VIC, Australia.
[11] Cancer & Blood Services, Royal Hobart Hospital, Hobart, TAS, Australia.
[12] Menzies Research Institute, University of Tasmania, Hobart, TAS, Australia.
[13] Department of Medical Oncology, Epworth Healthcare, Richmond, VIC, Australia.
[14] Department of Medical Oncology, Bendigo Health, Bendigo, VIC, Australia.
[15] Department of Neurology, Cabrini Hospital, Malvern, VIC, Australia.
[16] Department of Radiation Oncology, Ballarat Austin Radiation Oncology Centre, Ballarat, VIC, Australia.
[17] Department of Medical Oncology, Royal Melbourne Hospital, Parkville, VIC, Australia.
[18] Department of Medical Oncology, Southwest Healthcare, Warrnambool, VIC, Australia.
[19] Department of Medicine, University of Melbourne, Melbourne, VIC, Australia.

Table 1: Demographics of glioma patients in the BRAIN registry.

Patient Demographics		**Total N (%)**	**WHO Grade 1 N (%)**	**WHO Grade 2 N (%)**	**WHO Grade 3 N (%)**	**WHO Grade 4 N (%)**	**Unknown/ Missing N (%)**
New Diagnosis		1313	31 (2)	208 (16)	112 (9)	859 (65)	103 (8)
Median Age (Range)		60 (18-93)	31 (18-62)	38 (19-85)	45 (22-86)	64 (18-93)	62 (18-86)
Gender	Female	519 (40)	15 (3)	83 (16)	46 (9)	331 (64)	44 (8)
	Male	794 (60)	16 (2)	125 (16)	66 (8)	528 (67)	59 (7)
ECOG at Diagnosis	ECOG 0	652 (50)	22 (3)	140 (22)	70 (11)	392 (60)	28 (4)
	ECOG 1	228 (17)	6 (3)	23 (10)	12 (5)	177 (78)	10 (4)
	ECOG 2	107 (8)	1 (1)	8 (7)	3 (3)	90 (84)	5 (5)
	ECOG 3	41 (3)	0 (0)	4 (10)	2 (5)	31 (75)	4 (10)
	ECOG 4	8 (1)	0 (0)	1 (12.5)	0 (0)	7 (87.5)	0
	Unknown	277 (21)	2 (1)	32 (12)	25 (9)	162 (58)	56 (20)
Indigenous Status	Indigenous	16 (1)	1 (6)	6 (38)	1 (6)	8 (50)	0 (0)
	Non-Indigenous	1024 (78)	20 (2)	171 (16)	88 (9)	665 (65)	80 (8)
	Not stated	273 (21)	10 (4)	31 (12)	23 (8)	186 (68)	23 (8)
Median Socio economic Status (IRSAD Decile)		6	6	7	6	6	6.5

[20] *Department of Medical Oncology, Alfred Health, Melbourne VIC, Australia.*

Background: The BRAIN (Brain tumour Registry: Innovation And translatioN) Registry is a large collaborative multi-site real-world data collection effort in brain cancer in Australia. Institutional recruitment is steadily growing across public, private and regional sites. Here we examine the demographics and treatment location for patients with glioma.

Methods: Adult patients diagnosed with a glioma between 1/1/2016 and 31/6/2023 were identified in the BRAIN registry. Descriptive statistics were used to describe patient demographics.

Results: 1313 patients were identified from 12 centres (6 metropolitan, 4 regional, 2 private). Majority of patients were male and non-Indigenous with ECOG 0-2 (see Table 1). Median socioeconomic status was 6 (ISRAD Decile). Median age was 60 years. 90% of patients underwent surgery at public institutions, with 10% in private hospitals. Following surgery, 76% were flagged for further treatment. Management following surgery commonly occurred at the same location as surgery (69%) with one-third referred to another centre. Of these, 68% were referred to a regional centre, 29% to another metropolitan centre and 3% to a private institution. Median age increased with tumour grade (grade 1-4: 31yrs vs 38yrs vs 45yrs vs 64yrs, $p<0.0001$), as did receipt of post-operative radiotherapy (grade 1-4: 19% vs 34% vs 77% vs 67%, $p<0.0001$) and/or chemotherapy (grade 1-4: chemotherapy 19% vs 29% vs 71% vs 60%, $p<0.0001$). Proportion of patients referred to a regional centre also increased with tumour grade (grade 1-4: 7% vs 13% vs 22% vs 32%, $p<0.0001$), however, referrals to private did not ($p=0.17$).

Conclusions: The BRAIN registry provides real-world data about patients diagnosed with glioma. Approximately one-third of patients are referred to another centre for ongoing management following surgery, highlighting the importance of engaging a broad range of sites to improve data capture along the treatment continuum. Further work into decision making and patterns of care is underway.

Theme
Other

26

Exploring barriers to EX-TEM recruitment using the BRAIN registry

Lucy Gately[1,2], Katharine Drummond[3,4], Anthony Dowling[5,6], Iwan Bennett[7], David Campbell[8], Claire Philips[9], Simone Reeves[10], Ronnie Freilich[11], Sanjeev Gill[2], Zarnie Lwin[12], Rosemary Harrup[13,14], Anne Long[15], Elizabeth Ahern[16,17], Mark Wong[18], Robert Campbell[19], Katharine Cuff[20], Ross Jennens[21], Craig Underhill[22], Adam Cooper[23], Stephen Brown[24], Mark Rosenthal[25], Javier Torres[6,26], Ian M Collins[27], Megan Dumas[1], Peter Gibbs[1,6]

[1] *Personalised Oncology Division, The Walter and Eliza Hall Institute of Medial Research, Parkville, VIC, Australia*
[2] *Department of Medical Oncology, Alfred Hospital, Prahran, VIC, Australia*
[3] *Department of Neurosurgery, Royal Melbourne Hospital, Parkville, VIC, Australia*
[4] *Department of Surgery, University of Melbourne, Parkville, VIC, Australia*
[5] *Department of Medical Oncology, St Vincent's Hospital Melbourne, VIC, Australia*
[6] *Department of Medicine, University of Melbourne, Melbourne, VIC, Australia*
[7] *Department of Neurosurgery, The Alfred, Melbourne, VIC, Australia*
[8] *Department of Medical Oncology, University Hospital Geelong, Barwon Health, Geelong, VIC, Australia*
[9] *Department of Radiation Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia*
[10] *Ballarat Austin Radiation Oncology Centre, Ballarat, VIC, Australia*
[11] *Cabrini Hospital, Malvern, VIC, Australia*
[12] *Department of Medical Oncology, Cancer Care Services, Royal Brisbane and Women's Hospital, and The University of Queensland, Brisbane, QLD , Australia*
[13] *Cancer & Blood Services, Royal Hobart Hospital, Hobart, TAS, Australia*
[14] *Menzies Research Institute, University of Tasmania, Hobart, TAS, Australia*
[15] *Department of Medical Oncology, Sir Charles Gairdner Hospital, Perth, WA, Australia*
[16] *Department of Oncology, Monash Health, Melbourne, VIC, Australia*
[17] *School of Clinical Sciences, Monash University, Melbourne, VIC, Australia*
[18] *Department of Medical Oncology, Westmead Hospital, New South Wales, Australia*
[19] *Bendigo Health, Bendigo, VIC, Australia*
[20] *Department of Medical Oncology, Princess Alexandra Hospital, Brisbane, QLD, Australia*
[21] *Epworth HealthCare, Melbourne, VIC, Australia*
[22] *Border Medical Oncology Research Unit, Albury, VIC, Australia*
[23] *Department of Medical Oncology, Liverpool Cancer Therapy Centre, Sydney, NSW, Australia*
[24] *Department of Medical Oncology, Grampians Health, Ballarat, VIC, Australia*
[25] *Medical Oncology, Royal Melbourne Hospital, Melbourne, VIC, Australia*

[26] *Department of Medical Oncology, Goulburn Valley, VIC, Australia*
[27] *Department of Medical Oncology, South West Regional Cancer Centre, Victoria, Australia*

Background: Registry trials, with less stringent entry criteria, are anticipated to recruit a more real-world patient population. Recruitment to EX-TEM, a phase III registry trial assessing utility of extended temozolomide in glioblastoma, was slower than anticipated. Only 46 patients who had completed standard STUPP protocol without disease progression were recruited from 16 sites over a 33-month period. A combined analysis of EX-TEM with a Spanish study with similar recruitment parameters demonstrated no benefit from extended temozolomide. Here we explore recruitment challenges.

Methods: Data on study eligible patients during the trial recruitment period (1/1/2019-16/09/2022) was extracted from the multi-site BRAIN registry[1], which collects data on consecutive patients diagnosed with glioblastoma. "EX-TEM candidates (EC)" were defined as patients who met the inclusion criteria but were not enrolled in EX-TEM. "EX-TEM participants (EP)" were defined as enrolled EX-TEM participants. Relevant intergroup statistics were used to identify differences in tumour, treatment, and outcome characteristics. Survival was estimated using Kaplan-Meier method.

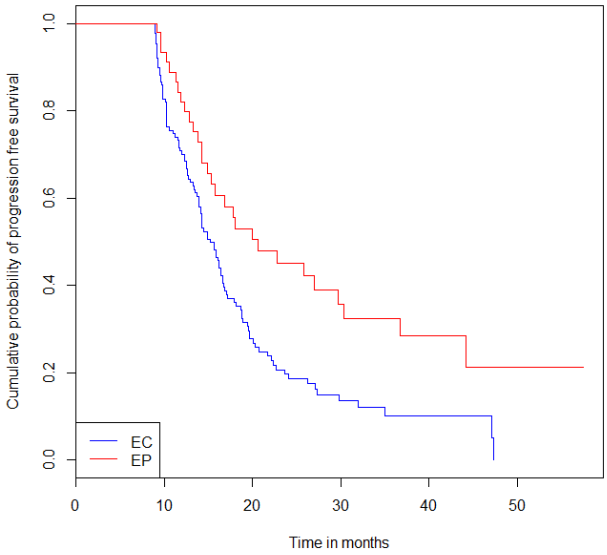
Results: 550 patients diagnosed with glioblastoma were identified between 1/4/2018-31/12/2021 (coinciding with completion of Stupp protocol during the EX-TEM recruitment period). Of these, 347 (63%) commenced treatment with Stupp protocol, but only 173 (50%) completed treatment with an ECOG 0-2, of which 46 (27%) EP and 127 (73%) EC. Compared with EC, EP were younger and more likely to be ECOG 0-1, and undergone initial macroscopic resection (see Table 1). Progression-free (PFS) and overall survival (OS) were significantly longer in EP compared to EC (see Fig 1). On multivariate analysis, EP was an independent marker for improved PFS (HR 0.6 [(0.37-0.99)], p=0.04) and both age<65years and EP were independent markers for improved OS (age: HR 0.57 [(0.38-0.87)], p=0.008; EX-TEM: HR 0.5 [(0.28-0.88)], p=0.02).

Conclusion: In the real-world setting, glioblastoma patients commencing Stupp protocol is lower than expected at 63%, but the proportion completing treatment is similar to previous trials. Additionally, less than 30% of eligible patients were enrolled in EX-TEM, mostly a younger fitter population, with improved survival outcomes. Recruitment to registry trials is impacted similar to standard trials.

Theme
Other

Figure 1: Survival curves for EC vs EP: **(A)** PFS (EC vs EP: 15.2months vs 20.6 months, p=0.003); and **(B)** OS curves (EC vs EP: OS 20.3 months vs 32.9 months, p<0.001)

A



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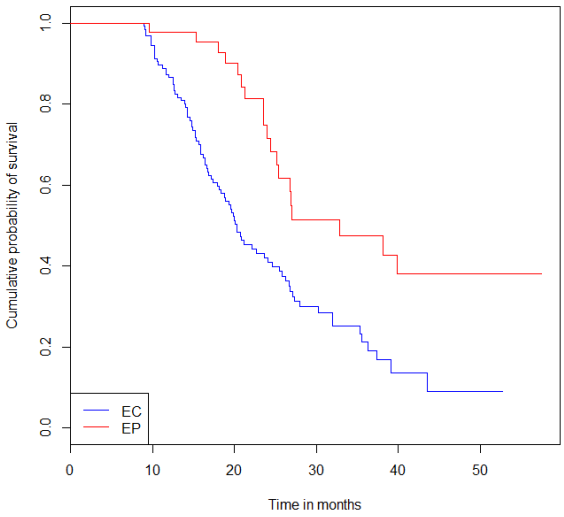


Table 1: Baseline characteristics for EP vs EC

Characteristic	EX-TEM participant (EP) n=46	EX-TEM candidate (EC) n=127	p value
Age			
Median age	57 years	60 years	**<0.001**
(range)	(27-86)	(22-86)	
Age > 65	8 (17%)	54 (43%)	
Gender			
Male	28 (60%)	73 (57%)	**0.07**
Female	16 (40%)	54 (43%)	
ECOG			
0-1	46 (98%)	119 (94%)	**0.002**
2	1 (2%)	8 (6%)	
Extent of resection			
Biopsy	3 (6%)	25 (20%)	**0.0004**
Partial resection	0 (0%)	3 (2%)	
Subtotal resection	12 (26%)	50 (40%)	
Macroscopic resection	30 (64%)	40 (31%)	
Molecular			
IDH widltype	32/42 (76%)	115/122 (94%)	**0.001**
MGMT methylated	11/16 (69%)	26/43 (60%)	**0.9**
Survival			
PFS	20.6 [15.8-36.7]	15.2 [13.9-16.7]	**0.003**
OS	32.9 [25.4-na]	20.3 [18.4-25.5]	**<0.001**

27

Exploring current practice patterns in grade 2 glioma using the BRAIN registry

Lucy Gately[1,2], Katharine Drummond[3,4], Anthony Dowling[5,6], Iwan Bennett[7], Ronnie Freilich[8], Claire Philips[9], Elizabeth Ahern[10], David Campbell[11], Robert Campbell[12], Rosemary Harrup[13,14], Simone Reeves[15], Ian M Collins[16], Peter Gibbs[1]

[1] Personalised Oncology Division, The Walter and Eliza Hall Institute of Medial Research, Parkville, VIC, Australia
[2] Department of Medical Oncology, Alfred Health, Melbourne VIC
[3] Department of Neurosurgery, Royal Melbourne Hospital, Parkville, VIC, Australia
[4] Department of Surgery, University of Melbourne, Parkville, VIC, Australia
[5] Department of Medical Oncology, St Vincent's Hospital Melbourne, VIC, Australia
[6] Department of Medicine, University of Melbourne, Melbourne, VIC, Australia
[7] Department of Neurosurgery, The Alfred, Melbourne, VIC, Australia
[8] Cabrini Hospital, Malvern, VIC, Australia
[9] Department of Radiation Oncology, Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia
[10] Department of Medical Oncology, Monash Health
[11] Department of Medical Oncology, University Hospital Geelong, Barwon Health, Geelong, VIC, Australia
[12] Bendigo Health, Bendigo, VIC, Australia
[13] Cancer & Blood Services, Royal Hobart Hospital, Hobart, TAS, Australia
[14] Menzies Research Institute, University of Tasmania, Hobart, TAS, Australia
[15] Ballarat Austin Radiation Oncology Centre, Ballarat, VIC, Australia
[16] Department of Medical Oncology, South West Regional Cancer Centre, Victoria, Australia

Background: Grade 2 gliomas (G2-glioma) are uncommon, accounting for 10% of all primary brain

tumours[1]. In 2016, a new standard-of-care was established in high-risk patients[2]. Here we explore the impact of these guidelines on practice patterns in G2-glioma within a Victorian context.

Methods: Data was extracted from the BRAIN registry[3] for histologically diagnosed patients from 1/1/2016-30/9/2022. Descriptive statistics were used to describe the population. Survival was estimated using Kaplan-Meier method. Multivariate analyses were conducted using known prognostic factors including age, ECOG status, extent of resection, and risk category.

Results: Of the 1129 patients with glioma registered in BRAIN, 233 (21%) were deemed G2-glioma with 75% IDH-mutant on immunohistochemistry. Median follow-up was 2.5 years. Baseline characteristics are shown in table 1. Overall, 16% were deemed low-risk, with 92% undergoing observation (Fig 1A). 83% were deemed high-risk. Of these, 60% underwent observation and 25% received combination chemotherapy and radiotherapy (CRT) with majority receiving temozolomide (Fig 1B). Patients aged<40 years at diagnosis or who underwent resection beyond biopsy were more likely to undergo observation rather than CRT (aged<40 years: 50% vs 25%, p=0.005; resection: 73% vs 55%, p=0.01). Median PFS was improved in high-risk patients with receipt of therapy (observation vs radiotherapy alone vs CRT: 33.8 months vs 45.8 months vs NR, HR 0.69, p=0.01). On multivariate analysis, younger age, ECOG0-1 and CRT were independent markers for improved PFS (aged<40: HR 0.57 [(0.35-0.93)], p=0.02; ECOG0-1: HR 0.15 [(0.07-0.32)], p<0.0001; CRT: HR 0.26 [(0.13-0.53)], p=0.0002). OS data remains immature.

Conclusion: Selection and timing of treatment following surgery in G2-glioma is complex and multi-factorial. Whilst CRT is associated with an improved PFS in high-risk G2-glioma, there is limited uptake of this approach. Most undergo observation following initial surgery, especially those that are young and undergo resection. Further analysis of practice patterns over time are underway.

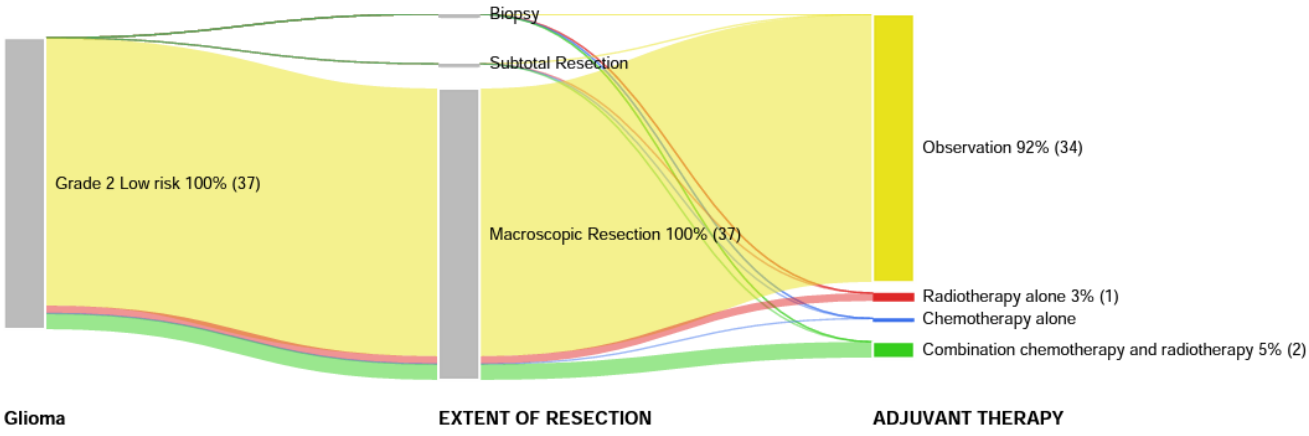
Acknowledgement: This analysis was supported by funding from Servier.

Theme

Other

Figure 1: Patient treatment flows in first line setting for all patients with low-risk grade 2 glioma (A) and high-risk grade 2 glioma (B)

A



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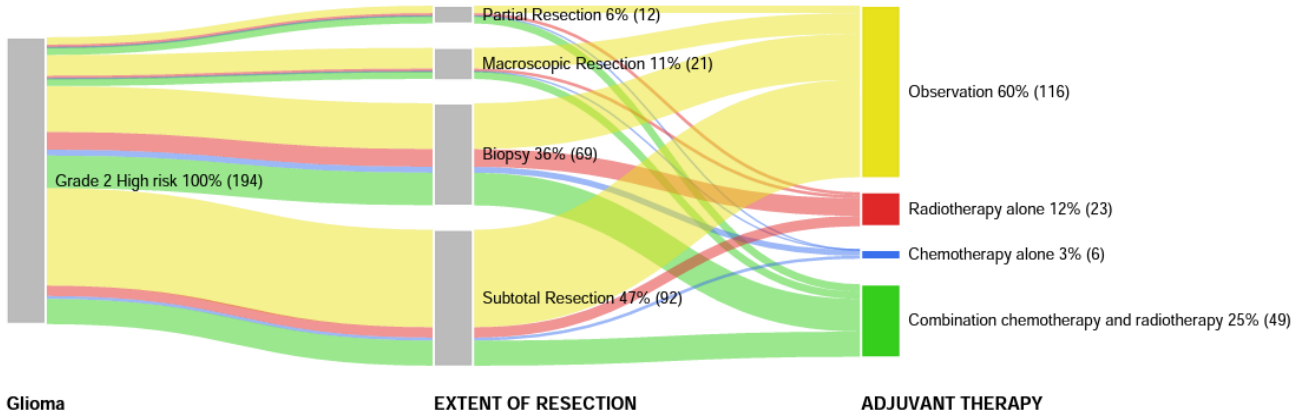

Table 1: Baseline characteristics

Characteristic	Grade 2 glioma		
	All n=233	High risk* n=194	Low risk n=37
Gender			
Male	140 (60%)	116 (60%)	24 (65%)
Female	93 (40%)	78 (40%)	13 (35%)
Age			
Median age (range)	40 years	44 years	31 years
	(20-85)	(20-85)	(20-39)
18-29 years	46 (20%)	30 (15%)	16 (43%)
30-39 years	69 (30%)	48 (25%)	21 (57%)
40-64 years	87 (37%)	85 (44%)	0 (0%)
Over 65 years	31 (13%)	31 (16%)	0 (0%)
ECOG			
0	162 (70%)	133 (69%)	27 (73%)
1	28 (12%)	22 (11%)	6 (15%)
2	12 (5%)	12 (6%)	0 (0%)
3+	7 (3%)	7 (4%)	0 (0%)
Missing	24 (10%)	20 (10%)	4 (10%)
Tumour location			
Frontal	158 (68%)	129 (66%)	28 (76%)
Parietal	45 (19%)	39 (20%)	5 (14%)
Occipital	7 (3%)	7 (4%)	0 (0%)
Temporal	66 (28%)	59 (30%)	7 (19%)
Deep structures	19 (8%)	19 (10%)	0 (0%)
Multifocal	12 (5%)	12 (6%)	0 (0%)
Extent of resection			
Biopsy	69 (30%)	69 (36%)	0 (0%)
Partial resection (<50%)	12 (5%)	12 (6%)	0 (0%)
Subtotal resection (50-95%)	92 (40%)	92 (47%)	0 (0%)
Macroscopic resection	58 (25%)	21 (11%)	37 (100%)
Missing	2 (<1%)	0 (0%)	0 (0%)
Molecular markers			
IDH-wildtype**	46 (20%)	44 (27%)	2 (6%)
IDH-mutant + 1p19q non-codeleted	96 (41%)	74 (38%)	20 (54%)
IDH-mutant + 1p19q co-deletion	90 (39%)	75 (39%)	15 (40%)
IDH status unknown	1 (<1%)	1 (<1%)	0 (0%)
Adjuvant treatment			
Observation	150 (65%)	116 (60%)	34 (92%)
Radiotherapy alone	25 (10%)	23 (12%)	1 (3%)
Chemotherapy alone	6 (3%)	6 (3%)	0 (0%)
Combination chemotherapy and radiotherapy	51 (22%)	49 (25%)	2 (5%)

*defined as aged≥40 years or subtotal resection

**on immunohistochemistry

28

The [18F]-fluoroethyl-L-tyrosine (FET) in glioblastoma (FIG) TROG 18.06 study: a prospective, multi-centre Australian-led collaboration: trial in progress

Eng-Siew Koh[1,2], Roslyn J.Francis[3,4], Martin A.Ebert[5,6], Hui K.Gan[7,8], Sze T.Lee[7,8,9], Eddie Lau[9,10], Alisha Moore[11], Hamish Evans[11], Bradford A. Moffat[12,] Dale L. Bailey[13,14], Sweet P. Ng[15], Mori Wada[15], Claire Phillips[16], Joseph Sia[10,16], Tim Akhurst[10,17], Ramin Alipour[17],Suki Gill[6], Jeremy Croker[6], Nicholas Bucknell[6], Elizabeth L.Thomas[4], Michael Back[18],Geoffrey P.Schembri[14], Edward Hsiao[14], Benjamin Chua[19], Catherine Bettington[19], David A. Pattison[20], Paul Thomas[20], Joe Chang[1], Peter Lin[2,21], Tam Ly[21], June Yap[21],Peter Gorayski[22], Hien Le[22], Ian Kirkwood[23], Wilson Vallat[23], Farhan Syed[24], Kylie Jung[24], Shahroz Khan[25], Dayanethee Krishna[25],Mark B. Pinkham[26], Andrew P.Pullar[26], Stanley Ngai[27], Chris Yu[27], Andrej Bece[28], Catherine Clark[28], Scott Beuzeville[29], Tow C. Yeow[29],Alana Rossi[11], Rachael Dykyj[11], Olivia Cook[11], Angela Whitehead[11], Caterina Brighi[13], Greg Fitt[10,30], Ramesh Cuganesan[31], Sugendran Pillay[31], Nathaniel Barry[5], Arian Lasocki[17,32], Fiona E.Scott[7], Elizabeth H Barnes[33], Lucas Adda[34], Richard De Abreu Lourenco[35,] Anna K.Nowak[3,36], Mark Rosenthal[10,37], Mustafa Khasraw[38], Jodie Palmer[7], Andrew M.Scott[7,8,9].

[1] Department of Radiation Oncology, Liverpool Cancer Therapy Centre, Liverpool, NSW, Australia
[2] South Western Sydney Clinical School, University of New South Wales, Australia
[3] Medical School, University of Western Australia, Perth, WA, Australia
[4] Department of Nuclear Medicine, Sir Charles Gairdner Hospital, Nedlands, WA, Australia
[5] School of Physics, Mathematics and Computing, University of Western Australia, Crawley, WA, Australia
[6] Department of Radiation Oncology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia
[7] Tumour Targeting Program, Olivia Newton-John Cancer Research Institute, Heidelberg, VIC, Australia
[8] School of Cancer Medicine, La Trobe University, Heidelberg, VIC, Australia
[9] Department of Molecular Imaging and Therapy, Austin Health, VIC, Australia
[10] Department of Medicine, University of Melbourne, VIC, Australia
[11]Trans Tasman Radiation Oncology Group (TROG) Cancer Research, Newcastle, NSW, Australia
[12] Melbourne Brain Centre Imaging Unit, Department of Radiology, University of Melbourne, VIC, Australia
[13] Faculty of Medicine & Health, University of Sydney, Camperdown, NSW, Australia
[14] Department of Nuclear Medicine, Royal North Shore Hospital, St Leonards, NSW, Australia
[15] Department of Radiation Oncology, Austin Health, Heidelberg, VIC, Australia
[16] Department of Radiation Oncology, Peter MacCallum Cancer Centre, VIC, Australia
[17] The Sir Peter MacCallum Department of Oncology, Melbourne, VIC, Australia
[18] Department of Radiation Oncology, Royal North Shore Hospital, St Leonards, NSW, Australia
[19] Department of Radiation Oncology, Royal Brisbane Women's Hospital, Herston, QLD, Australia
[20] Department of Nuclear Medicine, Royal Brisbane and Women's Hospital, Herston, QLD, Australia
[21]Department of Nuclear Medicine, Liverpool Hospital, Liverpool, NSW, Australia
[22]Department of Radiation Oncology, Royal Adelaide Hospital, Adelaide, SA, Australia
[23]Department of Nuclear Medicine, Royal Adelaide Hospital, Adelaide, SA, Australia
[24]Department of Radiation Oncology, The Canberra Hospital, Woden, ACT, Australia
[25]Department of Nuclear Medicine, Canberra Hospital, Woden, ACT, Australia
[26]Department of Radiation Oncology, Princess Alexandra Hospital, Woolloongabba, QLD, Australia
[27]Department of Nuclear Medicine, Princess Alexandra Hospital, Woolloongabba, QLD, Australia
[28]Department of Radiation Oncology, St George Hospital, Kogarah, NSW, Australia
[29]Department of Nuclear Medicine, St George Hospital, Kogarah, NSW, Australia
[30]Department of Radiology, Austin Health, Heidelberg, VIC, Australia
[31]Department of Radiology, Liverpool Hospital, Liverpool, NSW, Australia
[32] Centre for Cancer Imaging, Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia
[33]Faculty of Medicine and Health, NHMRC Clinical Trials Centre, University of Sydney, NSW Australia
[34]Consumer Advisory Panel, Cooperative Trials Group for Neuro-Oncology (COGNO), Sydney, NSW, Australia
[35]Centre for Health Economics Research and Evaluation, University of Technology Sydney, Sydney, NSW, Australia
[36] Department of Medical Oncology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia
[37] Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia
[38] Department of Neurosurgery and Preston Robert Tisch Brain Tumor Center, Duke University School of Medicine, Durham, North Carolina, USA

Aim: The FET-PET In Glioblastoma (FIG) study is an active prospective multi-centre study open across 10 Australian sites evaluating the impact of serial [18F] fluoroethyl-L-tyrosine positron emission tomography (FET-PET) imaging on the management of up to 210 adult Glioblastoma participants. We provide here a 'trial in progress' update.

Methods: Participants undergo FET-PET imaging at three time-points: pre-chemo-RT [CRT] (FET-PET1),

one month post CRT (FET-PET2) with FET-PET3 triggered at suspected progression. FET-PET analysis is both qualitative and quantitative including biologic target volume (BTV) delineation by site Nuclear Medicine (NM) physicians. Radiotherapy (RT) is per standard of care (60Gy/30 or 40.05Gy/15 daily fractions) with the site Radiation Oncologist (RO) deriving post-hoc hybrid RT volumes incorporating the BTV. A comprehensive NM and RO credentialing program before site activation has been undertaken (1,2). The study's co-primary outcomes are 1) to investigate how the addition of FET-PET versus standard MRI impacts radiation volume delineation and 2) to determine the accuracy and management impact of FET-PET in distinguishing pseudoprogression versus true tumour progression and/or recurrence. Secondary outcomes include investigating relationships between FET-PET parameters (including dynamic uptake, tumour to background ratio, metabolic tumour volume) with progression-free and overall survival, FET-PET versus MRI-determined sites of progression and a health-economic analysis. Exploratory outcomes include correlation of multimodal imaging, blood and tumour biomarkers with patterns of failure and survival.

Results: Recruitment commenced in January 2021. To date, 142 (n=86 Group 1 and n=56 Group 2) participants have been recruited, aiming for a target 140 Group 1 participants nationally. Important measures including site MRI quality assurance and a checklist ensuring accurate modified RANO assessment and triggering of timepoint 3 have been implemented.

Conclusions: The FIG study is the largest prospective multi-site study of its kind addressing FET-PET's role in management of pseudoprogression, prognostication and impact on adjuvant radiation planning.

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2. Barry N, Francis RJ, Ebert MA, Koh E-S, Rowshanfarzad P, Hassan GM, et al. Delineation and agreement of FET PET biological volumes in glioblastoma: results of the nuclear medicine credentialing program from the prospective, multi-centre trial evaluating FET PET In Glioblastoma (FIG) study—TROG 18.06. *European Journal of Nuclear Medicine and Molecular Imaging.* 2023. doi:10.1007/s00259-023-06371-5.

Theme
Other

29

Exploring molecular biomarkers in astrocytomas using comprehensive genomic profiling (CGP)

Nicholas McNamee[1,2], Frank Lin[2], Hao-Wen Sim[1,2,3,4], Christine Napier[2], David Thomas[2], John Simes[3,4], Subotheni Thavaneswaran[1,2,3]

[1] The Kinghorn Cancer Centre, St Vincent's Hospital, Darlinghurst, Sydney NSW
[2] Garvan Institute of Medical Research, School of Clinical Medicine, Faculty of Medicine and Health, UNSW, Darlinghurst, Sydney NSW
[3] The NHMRC Clinical Trials Centre, University of Sydney, Camperdown, Sydney NSW
[4] Chris O'Brien Lifehouse, Camperdown, Sydney NSW

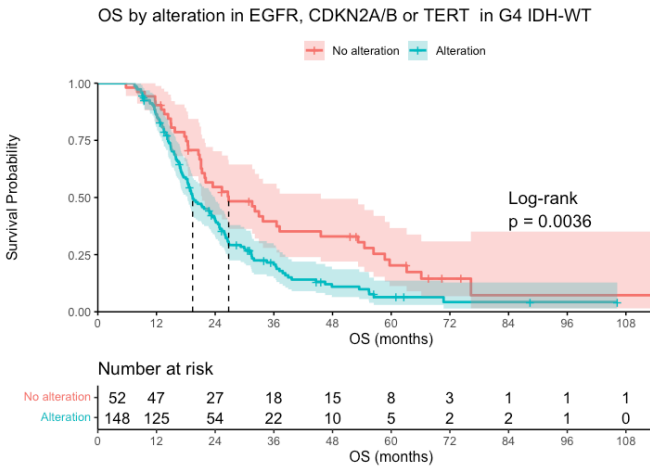
Aims: Astrocytomas exhibit molecular heterogeneity with prognostic implications for genomic alterations, including *IDH*, *EGFR*, *TERT* promoter and *CDKN2A/B*. Greater access to comprehensive genomic profiling (CGP) provides an opportunity to characterise the genomic landscape of these tumours and their clinical implications.

Methods: Patients with astrocytomas undergoing CGP through the Australian Molecular Screening and Therapeutics (MoST) precision oncology program between March 2017 and January 2022 were identified and the frequencies of genomic alterations assessed. Associations between overall survival (OS) and alterations in *EGFR*, *TERT* promoter and/or *CDKN2A/B* were estimated using Kaplan-Meier methods. The correlation between temozolomide (TMZ) exposure and tumour mutational burden (TMB) was also assessed.

Results: Our cohort encompassed 278 patients with astrocytomas, with median age of 48 years, 93% ECOG performance status 0-1 (N=259/278) and 84% histological grade 4 (N=234/278). The median OS (mOS) for the cohort was 26.6mo (95%CI 24.0-31.4). For histological grade 2/3 *IDH*-mutant tumours, mOS was 31.3mo (N=3) and 118.6mo (N=20, 95%CI 96.5-NA) for those with or without alterations in *EGFR*, *TERT* promoter and/or *CDKN2A/B*, respectively. For histological grade 2/3 *IDH*-wildtype tumours, mOS was 20.7mo (N=8, 95%CI 16.2-NA) and 45.2mo (N=11, 95%CI 19.2-NA), respectively. For histological grade 4 *IDH*-mutant tumours, mOS was 81.4mo (N=4, 95%CI 32.7-NA) and 71.1mo (N=21, 95%CI 43.8-NA), respectively. For histological grade 4 *IDH*-wildtype tumours, mOS was 19.4mo (N=148 [55% *TERT* promoter, 42% *EGFR*, 17% *CDKN2A/B*], 95%CI 18.3-23.9) compared with 26.8mo (N=52, 95%CI 21.3-45.6; logrank P=0.0036), as shown in figure 1. Co-occurring molecular alterations in grade 4 *IDH*-wildtype tumours included *PTEN* (37%), *TP53* (32%), *NF1* (22%), *CDK4* (14%), *RB1* (12%), and *PIK3CA* (7%). Exposure to TMZ prior to sequencing was associated with increased

TMB (mean 3.5mut/Mb TMZ-naïve vs 16.8mut/Mb TMZ-exposed; two-sample t-test P=0.026).

Conclusion: CGP provides prognostic information that complements histological grading and demonstrates incremental value in understanding the molecular heterogeneity of astrocytomas.



Theme
Pathology; Therapeutics in Clinical Care

30

Using neuroanatomical Subsite to predict patterns of Glioblastoma infiltration: potential for individualising radiation therapy target volume delineation of the parietal and posterior frontal regions

Michael Back[1], Jackie Yim[2], Patrick Horsley[1] and Jamie Drummond[1]

[1] Royal North Shore Hospital
[2] The Brain Cancer Group

Background: Radiation therapy(IMRT) protocols for glioblastoma utilize isotropic margin expansion around neurosurgical cavities/residual contrast enhancing(T1gd) disease. However pathways of infiltration may be associated with white matter tract(WMT) involvement varying between neuroanatomical subsites. Posterior frontoparietal tumours involving posterior cingulate region (PostCing) may have extensive infiltration centrally. This study aims to quantify the PostCing infiltration pathway/relapse sites.

Methods: Consecutive patients managed for GBMwt with IMRT between 1/2016-6/2022 were classified into 15 neuroanatomical subsites. Tumour segmentation on T1-gadolinium-enhanced(T1gd) and T2-weighted(T2) sequences was performed at diagnosis/relapse. Subsites of Frontal Lobe (Posterior) and Parietal Lobe (Superior/Posterior/Lateral) were identified. On both sequences involvement of adjacent/distant regions (cingulate gyrus, cingulum, splenium, ventricular trigone, parahippocampal-hippocampal gyrus) were identified; as were major WMT: cingulum-parahippocampal formation(CING-PHG), and arcuate fasciculus–inferior longitudinal fasciculus(AF-ILF). Survival was analysed in relation to pattern of infiltration and site of relapse.

Results: Of 348 patients with glioblastoma, fifty-five(16%) involved PostCing region. Pre-IMRT features included near-total resection in 25%; impaired ECOG 2-3 in 47%; and 58% MGMT-methylated. Parietal lobe tumours(67%) were predominantly posterior(42%) with only 7% lateral parietal. WMT involvement was evident in 94% with T1gd(62%), and T2 alone(33%) abnormality. Infiltration to distal sites of cingulum/splenium/PHG was frequent and predictable; correlating to cingulum pathway involvement in 70% of patients. Median RFS and OS was 13.2 months (95%CI: 11.8-14.8) and 16.6 months (95%CI:14.8-18.5) respectively. Distant relapse was evident in 53% of relapses. In the forty-four Stupp60Gy patients, distant relapse occurred later and was associated with improved overall survival(p=0.02). No difference in RFS(p=0.82) or OS(p=0.31) was noted if tract involvement was either T1gd or T2 alone abnormality.

Conclusion: For glioblastoma in posterior cingulate region, the infiltration and relapse pathways followed white matter tracts in a predictable distribution with high rate of distant disease at diagnosis and relapse. IMRT potentially may be individualised for neuroanatomical subsite and non-isotropic target volume expansion

Theme
Radiology; Other

31

Combining Open and Endovascular Techniques in "Hybrid" Theatre for Complex Cerebrovascular Cases: A 10-Year Retrospective Review at a Single Australian Institution

Daniel Madani[1], Elissa Xian[1], Thomas Morrison[1], Patrick Tang[1], Rodney Allan[1], Johnny Wong[1]

[1]Department of Neurosurgery, Royal Prince Alfred Hospital, Sydney

Purpose: Complex cerebrovascular conditions may require open microsurgical and endovascular strategies. The "hybrid" theatre is a multimodal suite

designed to accommodate both techniques. The aim of this study was to evaluate the impact on treatment of combined cerebrovascular cases and present our 10-year hybrid theatre experience, with illustrative cases demonstrating its utility.

Methodology: A retrospective cohort analysis was conducted to include all cerebrovascular cases in the hybrid theatre (2013–2023). Clinical and intraoperative data was extracted on aneurysms, arteriovenous malformations, dural arteriovenous fistulas, and bypass procedure cases only. The cases were categorised into: (1) intraoperative angiogram only; (2) endovascular surgery with open access (ESOA); and (3) open surgery with endovascular adjunct (OSEA). The impact of intraoperative angiogram on operative outcome and workflow was reviewed. Anaesthetic and operative times were compared with matched cohorts in a standard neurosurgical theatre.

Results: Fifty-seven combined cases were identified, consisting of 30 (52%) aneurysms, 11 (19%) AVMs, 6 (11%) dAVFs and 10 (18%) bypass procedures. Hybrid theatre utilization increased from 26 to 31 cases between the first and second 5-year intervals. Intraoperative angiogram only was performed in 33% of cases (*n*= 19), while ESOA and OSEA represented 18% (*n*= *10*) and 49% (*n*= *28*), respectively. Intraoperative angiogram resulted in clip adjustment in 36% of aneurysm cases and revealed 1 incomplete AVM resection. Average anaesthetic set-up and procedural time were 5.6h and 4.3h respectively, which compared favourably with matched cohort (*n*= 243) of 6.4h and 4.8h, respectively (*p< 0.0001*, one sample *t-test* analysis). No significant difference in complication rates were detected.

Conclusion: The hybrid theatre provides opportunities to improve operative workflow by reducing subsequent angiographic procedures and improving patient outcome in complex cerebrovascular cases.

Theme
Radiology; Surgery

32

Intraoperative MRI for Brain Tumours: A 15 Year Retrospective Review at a Single Australian Institution

Daniel Madani[1], Krishna Muralidharan[1], Nicholas Andrew Chang[1], Patrick Tang[1], Johnny Wong[1]

[1] Department of Neurosurgery, Royal Prince Alfred Hospital, Sydney

Purpose: Maximal safe resection is the objective of most neuro-oncological operations. Extent of resection can be maximized using imaging updated intra-operatively, including intraoperative MRI (iMRI) theatre, which may translate to improved overall survival. The aim of this study was to present our 15-year iMRI theatre experience and review its utility.

Methodology: A retrospective cohort analysis was conducted to include all intracranial tumour operations performed in the iMRI theatre (2007–2022). Casfes were classified according to their histopathology: low- and high-grade gliomas (LGG and HGG respectively), meningiomas, pituitary adenomas, and metastases. Demographic, clinical and histological data was extracted from SurgiNet and analyzed by using the WHO 2021 classification. The impact of intraoperative MRI on operative outcome was reviewed.

Results: A total of 478 neuro-oncology cases were identified, consisting of 194 pituitary adenomas (*n*= 69 cases via microscope), 162 HGG, 108 LGG (*n*= 7 cases for biopsy), 10 cerebral metastases, and 4 meningiomas. Intraoperative MRI theatre utilization averaged 41 cases per year throughout our 15-year experience. The median age was 47 years old (range 35-59 yo.) with a slight predominance in the female population (*n*= 298, 52%). We identified 85 (17.8%) re-do cases, which include: pituitary adenoma (*n*= 15, 17.6%), glioma (*n*= 68, 80%), and intracranial metastasis (*n*= 2, 2.4%). Of the 10 intracranial metastases, melanoma consisted of 5, lung carcinoma of 3, and renal cell- and colorectal-carcinoma represented 1 case, respectively. Intraoperative MRI confirmed complete resection in all meningioma cases.

Conclusion: In this series, iMRI has been utilised mostly for pituitary adenoma resection and gliomas. It provides near real-time intraoperative navigation and imaging to maximise extent of resection, prevent injury to important structures and improve patient outcome in tumour resections.

Theme
Radiology; Surgery

33

Queensland Brain Cancer Index demonstrates feasibility and challenges in automated electronic data collection for an Australian Brain Cancer Registry

Rosalind L. Jeffree[1], Mark B. Pinkham[2], Catherine Bettington[1], Nicole Buddle[3], Kimberley Budgen[1], Robert A. Campbell[4], Alessaandra Francesconi[5], Zarni Lwin[1,6], Suzanne Poulgrain[7], Cassie Turner[1], & Danica Cossio[8]

[1] Department of Neurosurgery, Hospital, Royal Brisbane Women's Hospital, Herston, QLD, Australia

[2] *Department of Radiation Oncology, PrincessAlexandra Hospital, Woolloongabba, QLD, Australia*
[3] *Radiation Oncology, Sunshine Coast University Hospital*
[4] *Mater Centre for Neuroscience & Brisbane Clinical Neuroscience Centre & UQ*
[5] *Medical Oncology Sunshine Coast Hospital and Health Services & Griffith University*
[6] *Cancer Care Services*
[7] *Medical Oncology, Queensland Health*
[8] *Cancer Alliance Queensland*

Aims: This project aimed to assess patterns of care and outcomes for brain cancer patients in Queensland diagnosed from 2011-2020. Data were used to test which Clinical Quality Indicators (CQIs), as published by Brain Cancer Biobanking Australia (BCBA) (Matsuyama 2022), could be reported using existing, automated data collection infrastructure.

Methods: We mined data from the Queensland Oncology Repository, a comprehensive clinical cancer database that routinely links diagnostic information from the Queensland Cancer Register with treatment, admissions (for both public and private hospitals), and outcome data. A Queensland Brain Cancer Committee was formed to review and report on this data.

Results: During the study period, 3,228 people with primary brain cancer were identified. Fifteen of 58 CQIs could be reported, covering 4 of 6 treatment domains: Diagnosis, Imaging, Surgery and Radiotherapy. Challenges included determining extent of resection from admissions data and segregation of radiotherapy dose into appropriate groups. Meaningful data were not available for optimal molecular testing (eg IDH mutation), oral Chemotherapy, or Other Care. Overall, the quality of care was very good. Most people had a histological diagnosis (86%), underwent surgery in a tertiary hospital (95%) and received radiotherapy within an appropriate timeframe (93%).
Variation in care between hospitals was noted, eg craniotomy rate (versus biopsy alone) ranged 40-80% and rate of MRI within 72 hours after resection of high-grade glioma ranged 60-80%. For people with low-grade glioma receiving radiotherapy, only 50% received the standard dose of 45-54Gy.
The Queensland Brain Cancer Index is available here: https://cancerallianceqld.health.qld.gov.au/publications/

Conclusions: Automated data collection of a limited number of CQIs is feasible. In Queensland, next steps are to examine variations in practice, consider whether improvements are possible, and iterate reporting to evaluate changes over time. BCBA has funding to start an Australian Brain Cancer Registry, reporting in other states and collecting additional CQIs.

Reference: Matsuyama M, et al Neurooncol Pract. 2022;9(1):68-78. doi: 10.1093/nop/npab055.

Theme
Radiology; Surgery, Therapeutics in Clinical Care; Other

34

Application of radiomics to pre-operative imaging to predict survival in people with glioma

Aleksandra Kazi[1,2], Daniel Arrington[1], Prabhakar Ramachandran[1], Mark Pinkham[1] and David Reutens[2]

[1] *Department Radiation Oncology, Princess Alexandra Hospital, Brisbane, Australia*
[2] *University of Queensland, Brisbane, Australia*

Introduction: In recent times, a range of machine learning-based methods have been employed to model outcomes by considering image factors such as shape, intensity, and texture. The objective of this research was to predict the overall survival (OS) of individuals with glioma, leveraging preoperative MRI scans.

Methods: Preoperative MRI scans of 115 consecutive glioma patients were identified from our institution database. Each patient's multimodal scans include T1, postcontrast T1-weighted (T1c), T2-weighted, and T2 Fluid Attenuated Inversion Recovery (FLAIR) as a minimum. Tumour segmentation was performed according to the FLAIR images and, when appropriate, the T1c. The process involved image resampling, intensity normalization (z-score), and wavelet transformation. Radiomics feature extraction was computed with in-house developed MATLAB software. For predicting 6- and 12-month survival, two classifiers were trained and validated, using features determined as statistically different using ANOVA and Chi2, followed by recursive elimination.

Results: The cohort consisted of 5, 11 and 98 patients with WHO grade 2, 3 and 4 gliomas, respectively. All of them were IDH wild-type, median age at diagnosis was 58 years (range: 17-83) and the median survival (excluding 26 patients alive at the time of study) was 1.1 years (range: 0.2 to 7.5years). At 6- and 12-months, the Area Under the Receiver Operator Characteristic Curves following leave-one-out validation were 0.906 and 0.824, respectively. The optimal True Positive rates were 0.871 and 0.764, while False Positive rates were 0.143 and 0.209. Feature analysis with ANOVA and Chi2 heavily favoured radiomics from wavelet-filtered volumes, with First Order features the dominant category.

Conclusions: Radiomics-driven classification models capable of forecasting 6- and 12-month overall survival (OS) based on preoperative MRI scans demonstrate promising sensitivity and specificity. Incorporation of

wavelet transformation played a crucial role in achieving this outcome, thus future work will include further exploration of the MRI pre-processing options.

Theme
Radiology; Survivorship, Psychology and Supportive Care

35

Creating a visually accessible online portal for people with brain tumour: preliminary findings

Mona Faris[1], Haryana Dhillon[1,2], Sharon He[1], Thomas Carlick[1], Jill Chen[1], Hannah Banks[1], Megan Jeon[1], Rachel Campbell[1], Raymond Chan[3], Georgia Halkett[4], Dianne Legge[5,6], Robyn Leonard[7], Annie Miller[8], Tamara Ownsworth[9], Kerryn Pike[10,11], and Joanne Shaw[1]

[1] The Psycho-oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, Australia
[2] Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), The University of Sydney, Sydney, Australia
[3] Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Bedford, Australia
[4] Curtin School of Nursing/Curtin Health Innovation Research institute (CHIRI), Curtin University, Perth, Australia
[5] Oliva Newton-John Cancer and Wellness Centre, Austin Hospital, Heidelberg, Australia
[6] Curtin School of Nursing/ Curtin Health Innovation Research Institute, Faculty of Health Sciences, Curtin University, Bentley, Australia
[7] Brain Cancer Biobanking Australia, NHMRC Clinical Trials Centre, University of Sydney
[8] Cancer Council NSW, Woolloomooloo, Australia
[9] School of Applied Psychology & Menzies Health Institute of Queensland, Brisbane, Australia
[10] School of Applied Psychology, Griffith Centre for Mental Health, & Menzies Health Institute Queensland, Griffith University, Australia
[11] School of Psychology & Public Health & John Richards Centre for Rural Ageing Research La Trobe University, Australia

Introduction: People with brain tumour (PwBT) experience a range of symptoms and needs. Within the **B**rain cancer **R**ehabilitation, **A**ssessment, **I**nterventions for survivorship **N**eeds (BRAINS) program, we are implementing screening to identify distress and unmet needs in PwBT and caregivers using an online portal called ADAPT BRAINS. With one in three PwBT reporting visual difficulties such as reading or visual processing issues, we modified the portal to improve visual accessibility.

Aim: To obtain feedback from end-users on the visual accessibility and useability of the ADAPT BRAINS portal.

Methods: Modifications were made to an existing online portal (e.g., design and layout, incorporating a visual accessibility tool). Semi-structured cognitive walkthrough interviews were conducted with PwBT, caregivers of PwBT, and health care professionals (HCP) who provide care to PwBT, as they navigated the portal. Perceptions around the portal's useability and user interface were discussed. Recruitment and data collection are ongoing, with analysis of interviews conducted using a Framework Approach.

Results: To date, interviews with five PwBT, three caregivers, and four HCP have been conducted. Overall, the portal was viewed positively. Some acknowledged the usefulness of having a caregiver to assist with navigating the portal. Incorporating images, icons, or colours was recommended to further clarify or emphasise text. Suggestions for Improvements included: reducing text-heavy sections by minimising text or chunking. All participants considered the accessibility tool to be useful but indicated it should be made more obvious for users. Participants expressed the importance of portal content being adaptable across devices and platforms.

Conclusions: Recommendations for improving visual accessibility include the use of visuals (e.g., images, icons), limiting text on the screen, allow users to alter the screen presentation to suit their needs, and ensuring content and design is compatible with different devices. These changes will be incorporated into the portal prior to implementation.

Theme
Survivorship, Psychology and Supportive Care

36

Online resources from the Cancer Australia Quality of Life Technical Service (CQUEST)
Carrie-Anne Ng[1], Tim Luckett[1], Brendan Mulhern[1]

[1] Cancer Australia Quality of Life Technical Service (CQUEST)

Background and aims: The Cancer Quality of Life Expert Service Team (CQUEST) is the Cancer Australia funded Quality of Life Technical Service, hosted by UTS (University of Technology Sydney).
One of CQUEST's aims is to support the use of patient-reported outcome measures (PROMs) in cancer clinical trials by developing up-to-date, practical, and accessible resources. This poster will introduce three

online resources for COGNO members, and provide an opportunity for members to request further resources.

Methods: The CQUEST website (www.uts.edu.au/cquest) includes a repository with the following resources:
1. A list of translated and culturally validated PROMs that will improve access to cancer trials for patients from culturally and linguistically diverse and Indigenous backgrounds. The list currently includes 76 PROMs commonly used in cancer clinical research and will be updated periodically over time.
2. Informative graphics and videos that will help improve PROM data quality and minimise missing data by educating patients and clinical trial staff on rationales and processes for PROM data collection.
3. Updated resources for the two most utilised PROM suites in cancer clinical trials (EORTC and FACIT). This includes a calculator which converts raw mean scores from the EORTC QLQ-C30 and FACT-G into norm-based T-scores which allow for comparison with the general Australian cancer population.

Results: CQUEST's online resources will help COGNO members increase access to trials, improve PROM data quality, and enrich data interpretation for the EORTC QLQ-C30 and FACT-G.
COGNO members are invited to request further online resources that will improve use of PROMs in their research. These can be suggested to the CQUEST team during discussion of the poster.

Conclusion: CQUEST invites COGNO members to engage with our online resources to improve the use of PROMs in cancer clinical trials.

Theme
Survivorship, Psychology and Supportive Care

37

Recruitment and Baseline Characteristics of Participants Enrolled in the RCT of the Cognitive Rehabilitation Program, LaTCH; for Brain Cancer

Sian Virtue-Griffiths[1], Dianne Legge[2], Ellie Piggott[3], Joanne Shaw[4,5], Haryana Dhillon[4,5], & Kerryn Pike[1,3]

[1] Department of Psychology and Counselling, School of Psychology and Public Health, La Trobe University, Australia.
[2] Olivia Newton John Cancer & Wellness Centre, Austin Health, Victoria, Australia.
[3] School of Applied Psychology, Griffith Centre for Mental Health, & Menzies Health Institute Queensland, Griffith University, Australia
[4] Centre for Medical Psychology & Evidence-based Decision-making (CeMPED), The University of Sydney, Sydney, Australia
[5] The Psycho-oncology Co-operative Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, Australia

Introduction: Up to 90% of brain cancer survivors will experience cognitive deficits following diagnosis and treatment. These deficits can impact upon relationships, the possibility of return to employment, and quality of life. One potential intervention is a memory strategies group program, LaTCH. LaTCH has demonstrated efficacy in improving subjective memory and emotional wellbeing in a range of populations and settings. We are conducting a hybrid-implementation, waitlist randomised controlled trial (RCT) to determine feasibility and efficacy of LaTCH for brain cancer survivors

Aim: To report baseline characteristics of participants enrolled in the LaTCH RCT.

Method: RCT recruitment and data collection are ongoing (planned sample size N=70). The 6-week intervention is delivered via zoom, facilitated by two neuropsychologists, and with groups of 4-6 brain cancer survivors. Primary outcomes include subjective change in memory contentment, perceived memory ability, memory strategy knowledge and use, perceived cognitive ability, quality of life, and fatigue levels. Baseline characteristics are reported descriptively for the study cohort.

Results: As of September 2023, 61 people have been screened and 59 recruited. Baseline characteristics participants include: *M*age =49.6 (*SD*=10.3, range: 30-71), 27 male. Participants are located across Australia, with most from Queensland (34%) or Victoria (32%). Higher-grade tumours were most common (glioblastomas -27%, anaplastic astrocytomas -20%). Participants report reduced memory satisfaction and ability at baseline. Objective verbal memory assessment at baseline identified reduced learning and a decreased ability to retrieve information after a delay. The most prevalent participant memory goals relate to retrieving names effectively, prospective memory for appointments and taking medications, and remembering conversations.

Conclusions: The strong uptake of participation suggests an unmet need for memory management options post diagnosis and acceptability of the RCT. Baseline demographics indicate that those with higher grade tumours have a similar propensity to seek intervention as those with lower grade diagnoses.

Theme
Survivorship, Psychology, and Supportive Care

38

Exploring approaches to neuro-oncology care coordination in Australia: A scoping review

Megan Jeon[1], Joanne Shaw[1], Sharon He[1], Hannah Banks[1], Thomas Carlick[1], Mona Faris[1], Rachel Campbell[1], Brian Kelly[2], Eng-Siew Koh[3], Georgia BK Halkett[4], Dianne Legge[5], Tamara Ownsworth[6], Raymond J. Chan[7], Mark Pinkham[8], Ursula M. Sansom-Daly[9-11], Haryana M Dhillon[1]

[1] Psycho-oncology Cooperative Research Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney, Sydney, Australia
[2] Centre for Resources Health and Safety, Faculty of Health and Medicine, University of Newcastle (UON), Callaghan, Australia
[3] Liverpool Cancer Centre, Liverpool Hospital, South Western Sydney Local Health District, Sydney, Australia
[4] Curtin School of Nursing/Curtin Health Innovation Research institute (CHIRI), Curtin University, Perth, Australia
[5] Oliva Newton-John Cancer and Wellness Centre, Austin Hospital, Heidelberg, Australia
[6] The Hopkins Centre, School of Applied Psychology, Griffith University, QLD, Australia,
[7] Caring Futures Institute, College of Nursing and Health Sciences, Flinders University, Bedford, Australia
[8] Royal Brisbane and Womens Hospital, Herston, QLD, Australia
[9] Behavioural Sciences Unit, School of Clinical Medicine, Discipline of Paediatrics, UNSW Medicine & Health, University of New South Wales, Kensington, Australia
[10] Kids Cancer Centre, Sydney Children's Hospital, Randwick, Sydney, Australia
[11] Sydney Youth Cancer Service, Nelune Comprehensive Cancer Centre, Prince of Wales Hospital, Randwick, Sydney, Australia

Aim: People with brain tumour (PwBT) and informal caregivers face challenges navigating the disease, healthcare system, treatment, and/or survivorship. Care coordination (CC) is a comprehensive approach to achieving continuous, timely care according to individual needs of PwBT. Access to CC is inconsistent across Australian healthcare settings and optimal models of CC for brain tumour populations are unclear. Within the **B**rain Cancer **R**ehabilitation, **A**ssessment, **I**nterventions for Survivorship **N**eeds (BRAINS) program, we aimed to explore approaches to neuro-oncology CC to identify components of models of optimal CC for PwBT and informal caregivers.

Methods: We conducted a narrative scoping review of empirical research studies, clinical guidelines and reports, and educational resources for healthcare professionals (HCPs) related to the framework and/or implementation of neuro-oncology CC.

Results: From 1163 identified titles, 30 eligible reports focussed on neuro-oncology CC were reviewed (13 addressed CC interventions, 9 narrative were reports, 5 CC/navigator position descriptions, and 3 clinical guidelines). Most reports described nurse-led models of care within single tertiary care centres in metropolitan settings: nurses acting as primary contact, educator, and liaison, screening patient/carer distress and providing referrals, similar to the position descriptions. Clinical guidelines emphasise healthcare system navigation and access to medical care in CC. Facilitators of CC included availability of HCP dedicated to CC; HCPs' competency, or opportunities to upskill in relationship-based and communication skills; and improved access to resources, such as checklists or protocols. Barriers to CC included funding instability and limited access to CC staff outside hospital care. Notably, the reports reviewed did not reflect factors known to be of importance in neuro-oncology care.

Conclusions: Current literature on neuro-oncology CC largely comprised descriptions of nurse/coordinator-led models of care. Guidelines reflecting unique challenges of neuro-oncology care were lacking. Further research is required to understand approaches to CC in Australia and HCP training and support needs.

Theme
Survivorship, Psychology, and Supportive Care; Other (models of care)

39

Using computer adaptive testing to assess Quality of Life in Cancer clinical trials

Brendan Mulhern[1], Tim Luckett[1] and Carrie-Anne Ng[1]
[1] University of Technology Sydney

Abstract

Patient Quality of Life (QoL) in cancer clinical trials is generally assessed using fixed form Patient Reported Outcome Measures (PROMs) such as the EORTC QLQ-C30 and the FACT-G. The advantage of fixed form PROMs is that they provide comparable scores across the key domains of QoL both internally (within a trial) and externally (for example with published data). However, fixed form instruments are a potential burden for patients, and certain items or domains may not be relevant.
In response to these issues, Computer Adaptive Testing (CAT) instruments for use in the assessment of QoL have been developed. CAT instruments include 'banks' of items that have been calibrated using psychometric approaches. This generates flexible instruments that can iteratively deliver a targeted set of items to patients

based on their previous responses, with all patients still scored on the same scale.
The most well-known CAT based instruments are the Patient Reported Outcome Measurement System (PROMIS) item banks. There are also CAT versions of the symptom and functional domains included in the EORTC QLQ-C30.
The use of these CAT instruments in cancer clinical trials is limited, partly due to lack of knowledge about their development, use, and advantages and disadvantages. Therefore, the aim of this presentation is to introduce CAT approaches to the COGNO membership.
The presentation will include an overview of the approaches, and how they can practically be implemented in trials. The advantages presented will include the potential to reduce patient burden whilst increasing measurement precision. Disadvantages presented will include practical considerations such as the complexity of programming CAT within trial data collection software, and the lack of knowledge about how to implement CAT, and interpret the data. Other disadvantages discussed will be the lack of comparability with other trial data. Solutions to these issues will be discussed.

Theme
Survivorship, Psychology, and Supportive Care; Other

40

Challenges In NF2-related Schwannomatosis Treated With Stereotactic Radiosurgery

Molly Reynolds[1], Katrina Morris[1,2,3]

[1] Faculty of Medicine, University of Sydney, Camperdown, Australia
[2] Department Of Neurology, Concord Repatriation General Hospital, Concord, Australia
[3] Neurofibromatosis Clinic, Department of Clinical Genetics, Royal North Shore Hospital, St Leonards, Australia

Introduction: The estimated risk of secondary malignancy of schwannomatosis-NF2 treated with radiotherapy is contentious in recent cohort reports (1,2). Bin-Alamer et al (2023) in their stereotactic radiosurgery (SRS) cohort (median 59 month follow up) observed no malignant transformation. However, 27 of the 60 patients developed post-SRS progression requiring operative management (resection or shunting), an outcome which may be seen as malignant progression. Evans et al (2023) compare radiotherapy treatment of UK national schwannomatosis-NF2 care, demonstrating a risk of malignant transformation/malignant progression in 5% of patients overall (vs <1% in non irradiated NF2 patients).

Case Presentation: We present two cases with deteriorating quality of life subsequent to SRS. Our first patient presented with a growing cerebellopontine angle tumour complex despite previous surgery. Following SRS, tumour expansion was observed but restrained with glucocorticoids. Six months post SRS however, was noted to develop papilloedema with progressive loss of vision requiring acetazolamide, recurrent therapeutic drainage and optic nerve fenestration to prevent further deterioration. CSF protein was elevated at over 1.2g for several months. Our second patient had fractionated radiotherapy for control of a large trigeminal schwannoma. At 12 months follow up the patient continues to have intractable trigeminal neuralgia and has developed intrusive trigeminal autonomic dysfunction with unremitting lacrimation and rhinorrhoea.

Discussion: These cases demonstrate the challenges in managing patients with NF2 with radiotherapy. Tumour responses are less robust and risk of adverse events, including hearing deterioration following vestibular schwannoma SRS, appears higher in NF2. This, in addition to the potential longer term malignancy risks of radiotherapy, needs consideration when planning treatment in this cohort who may require more extensive follow up and symptom management. Further research is required to establish the reasons for malignant progression in schwannomatosis-NF2 post SRS.

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Theme
Survivorship, Psychology, and Supportive Care; Therapeutics in Clinical Care

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42

A retrospective state-wide audit of elderly glioblastoma patient outcomes following long course chemoradiotherapy after neurosurgical intervention in Tasmania

Jim Weston[1], Nova Thani[1], Richard Foster[2], Patrick Dyer[3], and Rosemary Harrup[4,5]

[1] Department of Neurosurgery, Royal Hobart Hospital, Hobart, Tasmania, Australia
[2] Northern Cancer Service, North West Regional Hospital, Burnie, Tasmania, Australia
[3] Northern Cancer service, Launceston General Hospital, Launceston, Tasmania, Australia
[4] Cancer & Blood Services, Royal Hobart Hospital, Hobart, Tasmania, Australia
[5] Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia

Aims: The standard of care post-neurosurgical intervention for glioblastoma (GBM) is long-course chemoradiotherapy (LC-CRT), first described by Stupp[1,2]. There is limited evidence addressing the safety and efficacy of LC-CRT in elderly patients with GBM [3,4,5]. We performed a retrospective audit to identify outcomes for older GBM patients receiving LC-CRT in Tasmania.

Methods: Patients aged 65-75 years who underwent neurosurgical intervention with a histological diagnosis of GBM, followed by LC-CRT between January 1 2020 and December 31 2022 were included. Demographic data, performance status (PS), neurosurgical intervention, isocitrate dehydrogenase (IDH), and O(6)-Methylguanine DNA methyltransferase (MGMT) statuses were collected. Patient outcomes assessed included living situation, partnership, toxic effects, ability to complete LC-CRT, toxicities, median progression free (mPFS) and median overall survival (mOS).

Results: 23 elderly Tasmanian GBM patients (74% males), median age 70.1 (65-75) years, 96% living at home, 70% partnered, and 78% in outer regional/remote/rural location using Australian Standard Geographic Classification were identified. PS was 1 for all patients. Neurosurgical intervention was biopsy (9%), debulking (48%), and gross-total-resection (43%), with MGMT statuses of methylated (26%), unmethylated (56%), and unknown (18%). The Common Terminology Criteria for Adverse Events Version 5.0 was used to assess toxicity. Adverse events during LC-CRT were Grade 1, 56%, Grade 2, 35%, and Grade 3, 9% (hyperglycaemia n=2) with no Grade 4 toxicities. All patients completed part-1 LC-CRT with one patient ceasing temozolomide. Part-2 adjuvant temozolomide (minimum 6 cycles) was completed (35%), incomplete (43%), and not commenced (22%). mPFS and mOS were 6.9 and 9.9 months respectively with 34.3% alive at 12 months. Re-resection rate was 13%.

Conclusions: This statewide audit provides evidence that post-surgical LC-CRT can be safely delivered to a selected, predominantly rural elderly GBM population with mainly low grade toxicities and 100% delivery rates with mPFS and mOS not dissimilar to a younger population[1].

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Theme
Therapeutics in Clinical Care

43

Use and impact of single agent bevacizumab for recurrent glioblastoma: a real-world study

Lucy Gately[1,12], Matthew Loft[1,6], Sam Smith[1,2], Katharine Drummond[3,4], Mark Rosenthal[5], Anthony Dowling[2,6], Claire Phillips[7], Simone Reeves[8], Iwan Bennett[9], David Campbell[10], Robert Campbell[11] and Peter Gibbs[1]

[1] Personalised Oncology Division, The Walter and Eliza Hall Institute of Medial Research, Parkville, VIC, Australia
[2] Department of Medical Oncology, St Vincent's Hospital Melbourne, VIC, Australia
[3] Department of Neurosurgery, Royal Melbourne Hospital, Parkville, VIC, Australia
[4] Department of Surgery, University of Melbourne, Parkville, VIC, Australia
[5] Department of Medical Oncology, Royal Melbourne Hospital, Melbourne, VIC, Australia.
[6] Department of Medicine, University of Melbourne, Melbourne, VIC, Australia

[7] *Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*
[8] *Ballarat Austin Radiation Oncology Centre, Ballarat, VIC, Australia*
[9] *Department of Neurosurgery, The Alfred, Melbourne, VIC, Australia*
[10] *Department of Medical Oncology, University Hospital Geelong, Barwon Health, Geelong, VIC, Australia*
[11] *Bendigo Health, Bendigo, VIC, Australia*
[12] *Department of Medical Oncology, Alfred Health, Melbourne VIC*

Aims: Beyond the Stupp protocol, there are limited effective therapies for recurrent glioblastoma. Bevacizumab, a VEGF-inhibitor, achieved PBS listing in 2019, despite a lack of strong evidence supporting its use as a single agent. Here we report an Australian experience of salvage therapy for glioblastoma.

Methods: Patients diagnosed with glioblastoma between 1st January 2016 and 31st December 2022, who were treated with salvage bevacizumab, were identified at 11 sites contributing data to the BRAIN (Brain tumour Registry Australia INnovation and translation) registry. Clinicopathologic characteristics, treatment, progression free survival (PFS) and overall survival (OS) outcomes were analysed.

Results: Of 625 glioblastoma patients identified, 145 (23%) received systemic therapy following initial treatment. Of these, 126 received bevacizumab at any time, 116 (92%) at first recurrence and 121 (96%) after 2019 PBS listing. Of those receiving bevacizumab, median age was 59 years (range 22-81), 61% were male and 81% had good performance status (ECOG 0-1). Median bevacizumab duration was 4.0 months, with 65% ceasing due to progressive disease. 6-month PFS was 49% (median PFS 5.5 months), 6-month OS was 66% (median OS 8.2 months), with similar outcomes for bevacizumab at 1st and 2nd recurrence (Figure 1). When used at first recurrence, bevacizumab was associated with longer PFS versus lomustine (median PFS 6.0 vs 2.8 months, HR 2.8, 95%CI 1.17-6.53, *p*=0.020), but not longer OS (median OS 8.2 vs 5.7 months, HR 1.58, 95%CI 0.76-3.30) (Figure 2).

Conclusion: This study shows most patients with glioblastoma don't receive systemic therapy at recurrence. Of those appropriate for treatment, a sizeable and increasing proportion receive bevacizumab, the majority on first or second recurrence. Almost half are progression free at six months, supporting evidence for potential benefit, with data collection ongoing.

Theme
Therapeutics in Clinical Care

Figure 1. PFS bevacizumab in 1st versus 2nd recurrence

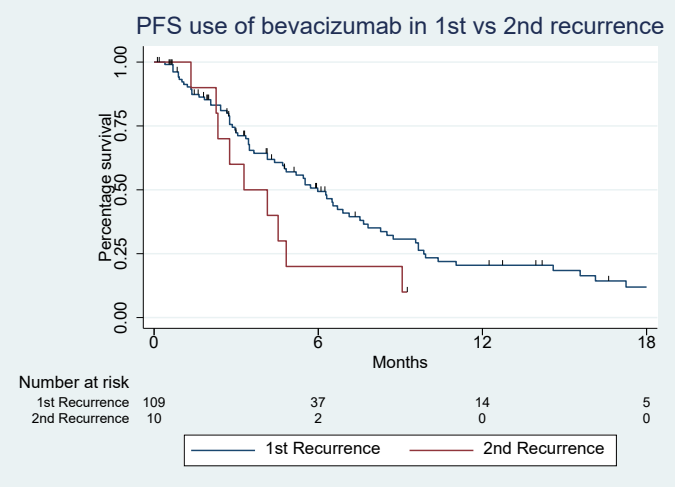

Figure 2. PFS (A) and OS (B) for bevacizumab vs lomustine in 1st recurrence