COGNO
COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

16th COGNO ANNUAL SCIENTIFIC MEETING

Precision Targets: Personalised Care in Neuro-Oncology

Sunday 13th October – Tuesday 15th October 2024

The Langham Hotel, Melbourne, VIC, Australia

CONFERENCE BOOKLET

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2024 ASM ORGANISING COMMITTEE

- **Dr Liz Ahern, Co-Convenor** (Medical Oncologist, Monash Health)
- **Dr Andrew Gogos, Co-Convenor** (Neurosurgeon, St Vincent's Public and Private Hospitals, Melbourne)
- **Associate Professor Eng-Siew Koh** (COGNO Chair)
- **Professor Rosemary Harrup** (COGNO Deputy Chair)
- **Associate Professor Shalini Amukotuwa** (Neuro-radiologist, Monash Health)
- **Dr Joseph Sia** (Radiation Oncologist, Peter MacCallum Cancer Centre)
- **Dr Saskia Freytag** (Biostatistician / Lab Head, The Walter and Eliza Hall Institute of Medical Research)
- **Ms Marcia Fleet** (Neuro-oncology Care Coordinator, Peter MacCallum Cancer Centre)
- **Dr Vino Pillay** (Executive Officer, COGNO)

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WELCOME FROM 2024 ASM CO-CONVENORS

Dear Colleagues,

On behalf of the ASM Organising Committee, it is our pleasure to welcome you to the 16th COGNO Annual Scientific Meeting, held at The Langham Melbourne from Sunday 13th October to Tuesday 15th October 2024. This year's theme is "Precision Targets: Personalised Care in Neuro-Oncology".

We are excited to announce that in 2024, for the first time, COGNO and the Stereotactic Interest Group of Australasia (SIGA) will be hosting their meetings in conjunction, with the Australian Brain Cancer Research Alliance (ABCARA) hosting their annual Scientific Research Symposium on Sunday October 13th. Furthermore, the Brain Tumour Alliance Australia (BTAA) will also host their annual Patient Education and Information Forum on October 13th.

We have assembled a comprehensive program featuring satellite meetings and workshops, keynote presentations from international and local speakers, and sessions covering the latest developments in neuro-oncology. This meeting provides a unique opportunity for clinicians, researchers, allied health professionals and consumers to exchange ideas, share experiences, and collaborate to improve patient outcomes.

We would like to extend our gratitude to all the speakers, sponsors, and delegates for making this event possible. We look forward to welcoming you to Melbourne and engaging in a productive Annual Scientific Meeting.

Dr Liz Ahern
Co-Convenor
COGNO ASM 2024

Dr Andrew Gogos
Co-Convenor
COGNO ASM 2024

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KEYNOTE SPEAKERS

Professor Shawn Hervey-Jumper

Shawn Hervey-Jumper, MD is Professor at University of California San Francisco. He is a neurosurgeon researcher with a clinical practice focused on the surgical management of patients with brain cancer within functional areas using physiological mapping. In his research laboratory he seeks to understand the causal mechanisms of brain cancer induced neuronal circuit remodeling. His ultimate goal is to uncover molecular drivers and therapeutic targets to treat cancer induced cognitive impairments. Through these efforts Dr Hervey-Jumper has served as principal investigator for numerous therapeutic clinical trials. He's published extensively on pathways to equitable cancer care focused specifically on clinical trial enrolment for historically excluded patient populations.

Professor Erin Dunbar

Erin Dunbar, M.D., is a founding physician of the Brain Tumor Center and Director of Neuro-Oncology at Piedmont Atlanta Hospital. She specializes in the comprehensive care of brain and spine tumor patients who are battling both primary and metastatic tumors. Her team creates a medical "home for life" by maintaining a robust portfolio of promising clinical trials, novel therapies, and supportive resources to serve patients and caregivers. She is an avid clinical researcher and a collaborator with organisations, including the National Cancer Institute and other national brain tumor centers. Collectively, these efforts enable patients to receive cutting-edge care close to home. These achievements have contributed to Governor Nathan Deal repeatedly proclaiming the Piedmont Brain Tumor Center as one of three renowned brain tumor centers in Georgia. She is a passionate driver of patient-centered care through her service to advocacy forums like the Southeastern Brain Tumor Foundation and the American Brain Tumor Association, and in her service to medical associations, like the Society of Neuro-Oncology and the American Academy of Neurology. Dr. Dunbar completed fellowships in Neuro-oncology at Johns Hopkins University, in Hospice and Palliative Medicine at the Malcom Randall VA Medical Center and in Medical-oncology at the University of Florida. She enjoys outdoor activities and Atlanta United FC.

Professor Pim French

Pim French has been recruited to the Neuro-Oncological Laboratory at the Erasmus University Medical Center by the department of Neurology. Pim French works as a molecular biologist with a strong background in translational studies and in molecular screens with subsequent functional analysis of candidates. Research focuses on the identification of clinically relevant molecular subgroups and identification of genes involved in glioma initiation and/or progression using state of the art high-throughput genomic approaches. The research group has extensive collaborations with national and international research groups and works in close collaboration with the European Organisation for Research and Treatment of Cancer (PF is chair of the translational research committee of the Brain Tumor Group). There are currently around ten members working in the lab including post-docs, Ph.D. students, technicians, master students and students from HLO and MLO higher education.

INVITED SPEAKERS

Professor Antonio Di Ieva

Antonio Di Ieva is a Professor of Neurosurgery and Associate Professor of Neuroanatomy at Macquarie University (Sydney), with expertise in neuro-oncology, neurotraumatology, neuroimaging, specialising in microneurosurgery, spine surgery, and pain treatment. He operates at the Macquarie University Hospital and Nepean Hospital in Sydney. Prof Di Ieva has a main interest in neuro-oncology and skull base surgery, with 200 peer-reviewed publications and four textbooks (including the Handbook of Skull Base Surgery, Thieme, The Fractal Geometry of the Brain, Springer, the latter with the second edition published in 2024, and a Computational Neurosurgery textbook in press), awarded international neurosurgical research awards, including the 2019 John Mitchell Crouch Fellowship, the most prestigious research award of the Royal Australasian College of Surgeons, as well an Australian Research Council (ARC) Future Fellowship. Over the last 5 years, Professor Di Ieva has been granted 8 million Australian dollars for research.

He leads international and national seminars and workshops teaching neuroanatomy and neurosurgical approaches, including the first workshop on the white matter dissection technique and connectomics in Australia. He is the world leader in the field of computational neurosurgery, with expertise in the application of computational modeling and Artificial Intelligence to the study of diseases of neurological and neurosurgical relevance. He is the head of the Computational NeuroSurgery (CNS) Lab at Macquarie University, founded by him in 2018, and he is involved in trialing and patenting new surgical devices for medical use. In 2021, he established the first Computational Neurosurgery Fellowship in the world.

Professor Kate Drummond

Professor Kate Drummond AM is the Director of Neurosurgery at Royal Melbourne Hospital and Head of Central Nervous System Tumours at the VCCC Parkville Precinct. Her research and clinical interests are in the biology and management of brain tumours, with special interests in advanced surgical techniques such as awake craniotomy, quality of life for patients with brain tumours and blood and imaging biomarkers (including liquid biopsy).

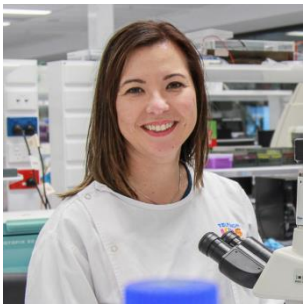
She has published over 180 peer-reviewed papers and many book chapters and has received more than $35 million in research funding. Her h-index is 41 and i10-index 96.

Professor Drummond is Co-Editor-in-Chief of the Journal of Clinical Neuroscience and on the Editorial Board of the Journal of Neurosurgery. She has served as Chief Examiner in Neurosurgery, Chair of the Women in Surgery Committee and on the Neurosurgery Surgical Education and Training Board for the Royal Australasian College of Surgeons, being awarded the RACS medal for these services. She is the President of the Asian Australasian Society of Neurosurgeons and is the 2nd Vice President (AASNS) for the World Federation of Neurosurgical Societies. She is president of the Academia Eurasiana Neurochirurgica.

She is a strong advocate for and has written and presented widely on diversity in neurosurgery. She is Chair of Pangea Global Health Education, a for-impact organisation specialising in health education in low resource settings. In 2019 she was awarded Member of the Order of Australia (AM) for

services to medicine, particularly in neuro-oncology and community health.

Associate Professor Raelene Endersby



Associate Professor Raelene Endersby holds a Cancer Council WA Research Fellowship and co-leads the Brain Tumour Research Program – part of the Telethon Kids Cancer Centre at the Telethon Kids Institute in Perth, WA. Raelene joined Telethon Kids following postdoc training at St Jude Children's Research Hospital (Memphis, USA), where she has built a translational research team that seeks to discover improved treatments for childhood brain cancers. Her team use a suite of preclinical models and techniques to understand the underlying biology of paediatric brain tumours, as well as to evaluate novel treatments, the best of which she translates to clinical trial with clinical collaborators at Perth Children's Hospital and beyond. Raelene is passionate about mentoring the next generation of scientists, performing rigorous high-quality research, and engaging diverse opinions to guide her work especially from families affected by brain cancer.

Dr Pouya Faridi

Dr. Pouya Faridi leads the Translational Antigen Discovery Laboratory and childhood cancer immunotherapy programme at the Centre for Cancer Research, Hudson Institute of Medical Research. Dr. Faridi earned his Doctor of Pharmacy (PharmD) and PhD at Shiraz University of Medical Sciences, Iran. He subsequently worked in Prof. Ruedi Aebersold's lab at the Institute for Molecular Systems Biology, ETH Zurich, before joining Monash University in 2016. His research has contributed to the development of several mass spectrometry and proteomics technologies, some of which are currently employed in cancer vaccine clinical trials. He is also the co-director of the Monash Proteomics and Metabolomics Platform. He has been awarded numerous honours, including the Victorian Cancer Agency Mid-Career Fellowship (2021), the Australian Proteomics Society Early Career Researcher Award (2019), Outstanding Mid-Career Cancer Researcher in Victoria (2020), and the Australian Melanoma Research Foundation Early Career Researcher Award (2021). Dr. Faridi holds multiple patents in antigen discovery and has published extensively in high-impact journals such as Cell, Science Immunology, Nature Communications, and Cancer Immunology Research. His work has been funded by leading organisations, including the National Health and Medical Research Council (NHMRC), Cancer Australia, the Australian Melanoma Research Foundation, the Medical Research Future Fund (MRFF), the U.S. Department of Defense (DoD), and the National Breast Cancer Foundation (NBCF).

Dr Lucy Gately

Lucy Gately is a medical oncologist with a special interest in Breast Cancer and Brain Cancer, and a strong focus on survivorship and improving quality of life during treatment and beyond. She also works with patients and their families to understand their own genetic risk for cancer, and is developing a strong research career.

Professional associations and appointments

- Editorial Board Member, The Oncology Republic
- ASPREE Cancer Endpoint Adjudicator
- Consultant Oncologist, Oncology Clinics Victoria, Cabrini Hospital
- Consultant Oncologist, Cabrini Family Cancer Clinic
- Clinical Research Fellow, Walter and Eliza Hall Institute

Professional memberships

- Cooperative Trials Group for Neuro-Oncology
- American Society of Clinical Oncology

Dr Andrew Gogos

Dr Andrew Gogos is a neurosurgeon and spine surgeon based in Melbourne.

Dr Gogos is an expert in brain tumour and cranial surgery, having completed a prestigious brain tumour fellowship at the University of California, San Francisco. He is passionate about providing individualised care using the latest technologies and minimally-invasive techniques to improve outcomes for his patients. He has a special interest in treating people with brain tumours (including gliomas, pituitary tumours, schwannoma, meningiomas and metastases), trigeminal neuralgia and Chiari malformations. In addition, Andrew is experienced in the latest minimally-invasive techniques for the treatment of spine conditions, including, sciatica, disc protrusions, spondylolisthesis and tumours. He offers a rapid second opinion and telehealth service. If you are unsure whether surgery is the right option to manage your condition, he believes getting a second opinion is the right thing to do. Dr Gogos graduated with 1st class honours from the University of Melbourne with degrees in medicine and medical science.

Professor Graeme Jackson

Professor Jackson is the Clinical Director of the Florey Institute of Neuroscience and Mental Health in Melbourne Australia and a Neurologist at Austin Health and a Professorial Fellow of the University of Melbourne. Professor Jackson's research is in advanced MR imaging and epilepsy, and the classification and understanding of malformations of cortical development. He received the prestigious American Epilepsy Society awards for clinical research in 2016 and the named Lombroso award and lecture in 2020. Additionally, he was honoured with the 2020 distinguished research award of Austin Health and the National Health and Medical Research Council of Australia achievement award for highest ranked practitioner fellow in 2008. His contributions include 43 primary data peer-reviewed scientific papers with more than 100 ISI citations. In 2021, as Chief Investigator of the Australian Epilepsy Project, Professor Jackson was successful in securing AU$30m in funding from the FRONTIERS program of the Australian Medical Research Future Fund to help transform the lives of people living with epilepsy, the largest single Federal Government investment made to epilepsy research in Australia.

Associate Professor Zarnie Lwin OAM

A/Prof Lwin (MBBS, FCP, FRACP) is a senior clinician at the Royal Brisbane and Women's Hospital and University of Queensland. She graduated in Medicine from Burma, completed her FRACP in South Africa, before specializing in Medical Oncology in Australia. She undertook a two-year clinical research fellowship in Princess Margaret Hospital, Canada and specializes in Neuro-oncology. Her other major research interests are in Health Services Research, Equity, Societal Research and Thoracic Oncology. She is Executive Editor for Neuro-oncology Practice, Co-Chair of the Society of Neuro-oncology International Outreach Committee, Deputy Chair of COGNO International Collaborative Research Subcommittee and incoming Chair of the Asian Society of Neuro-oncology inaugural Education and Outreach Committee. She has been invited as international faculty/ speaker to several international conferences and has

convened numerous scientific meetings. A/Prof Lwin is a Clinical Fellow at the Sid Faithful Brain Cancer Research Laboratory, QIMR Berghofer MRI. She has been site Principal Investigator for numerous clinical trials and has won three awards for her original research in Societal/ Health Services Research.

Associate Professor Andrew Morokoff

Associated Professor Morokoff is a consultant neurosurgeon who trained at the University of Melbourne and was awarded the Fellowship of the Royal Australasian College of Surgeons in 2005. He completed a brain tumour fellowship at the Brigham & Women's Hospital and Harvard University, Boston, USA, followed by a paediatric neurosurgery fellowship at the Necker Hospital for Children in Paris, France. He has trained extensively in Australia, Europe and the United States in the latest minimally invasive spinal surgery techniques. A/Prof Morokoff also holds a PhD in the molecular biology of brain tumours and directs an active brain cancer research program. He has published over 70 papers and is a regular invited speaker at both national and international conferences. He has received several awards, scholarships and prizes. He is a Fellow of the Royal Australasian College of Surgeons and member of the Neurosurgical Society of Australasia, The Clinical Oncological Society of Australia, The Congress of Neurological Surgeons and The European Association of Neurosurgeons. A/Prof Morokoff is an expert in brain tumour surgery, epilepsy surgery, skull base surgery, minimally invasive spine surgery and endoscopic neurosurgery. He is committed to a patient-centred approach to diagnosis and surgery and will ensure that every patient is cared for in a pleasant, effective and fully informed way.

Associate Professor Sarah Olson

Assoc Prof Sarah Olson is a fellow of the Royal Australasian College of Surgeons trained in Brisbane, Auckland and Victoria. She has an active interest in research, having completed a Masters of Philosophy in 2006.

Assoc Prof Olson operates from Mater Private Hospital Brisbane and Princess Alexandra Hospital.

Her special interests include neuro oncology and pituitary tumours, endoscopic surgery, trigeminal neuralgia and functional neurosurgery.

Professor Jennifer Philip

Jennifer Philip is the Chair of Palliative Medicine, University of Melbourne, St Vincent's Hospital and in collaboration with the Victorian Comprehensive Cancer Centre. Jennifer is a palliative care physician whose research focuses on improving access and equity to high quality care for people with advanced illness and improving the evidence base underpinning symptom management.

Associate Professor Claire Phillips

Claire Phillips is a senior radiation oncologist and Deputy Director of Radiation Oncology at the Peter MacCallum Cancer Centre. She has been a consultant radiation oncologist at Peter Mac since 2002. Claire is a subspecialist in NeuroOncology and was also a member of the Breast Unit until 2021. She served as Acting

Director of Radiation Oncology in 2018 and again from mid 2021 to late 2022. Claire's main clinical research interests are in primary and secondary brain tumours and ocular oncology. She has chaired several clinical trials through the Trans Tasman Radiation Oncology Group (TROG) and in collaboration with colleagues at the Royal Victorian Eye and Ear Hospital, conducted a world first study of radiation oncology standard fractionation for choroidal melanoma aiming to reduce toxicity and improve vision outcomes. In addition, Claire is and has been local primary investigator for numerous studies in breast cancer and brain tumours. Claire's publications span these clinical areas as well technical delivery and quality of stereotactic and ocular radiation therapy techniques and imaging in radiation therapy. In 2003, she developed Australia's first stereotactic radiotherapy for choroidal melanoma programme. Whilst Clinical Lead of the Peter Mac NeuroOncology unit, Claire initiated and lead the project that brought the Victorian Gamma Knife to Peter Mac in 2021 and is the clinical lead for the current project to bring particle therapy to Victoria.

Dr Adrian Praeger

Dr. Adrian Praeger MBBS FRACS is a highly specialised Neuro-surgeon located in Melbourne, Australia. He obtained his medical degree from the University of Melbourne in 2006. His extensive neurosurgical training was completed in various centres in Melbourne, Sydney, Canberra and Bonn, Germany. He was awarded Fellowship of the Royal Australasian College of Surgeons (FRACS) in Neurosurgery in 2020. He has been practicing at Monash Health since 2020. Dr Praeger has a subspeciality interest in glioma surgery, other cranial tumours (meningioma, metastasis, vestibular (schwannoma), trigeminal neuralgia, and spinal surgery, both for spinal tumours and degenerative conditions. Dr Praeger is active in teaching of both Neurosurgical registrars and in research. He has published in the areas of trigeminal neuralgia, spinal surgery, and cranial tumours. He is a reviewer for leading neurosurgical journals. He is a fellow of the Royal Australasian College of Surgeons. Dr Praeger holds memberships of the Neurosurgical Society of Australasia (NSA), Australian Medical Association (AMA), European Association of Neurosurgical Societies (EANS), American Association of Neurological Surgeons (AANS), AO Spine, and the North American Spine Society (NASS).

Dr Sam Roberts-Thomson

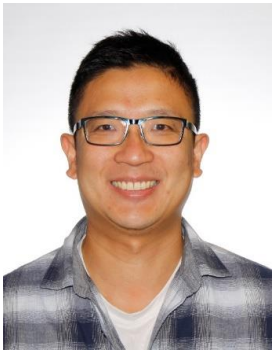
Dr Samuel Roberts-Thomson is an Anatomical Pathologist at The Royal Melbourne Hospital. His main area of interest is neuropathology, with a specific interest in adult tumours of the brain and spinal cord

Professor Daniel Trifiletti

As an international leader in radiation oncology and stereotactic radiosurgery, the research of Daniel M. Trifiletti, M.D., includes numerous clinical studies involving radiation, surgery and drug therapies in the treatment of tumors.

Dr. Trifiletti's short-term research goals focus on describing the impact of radiation on the priming of the brain tumor microenvironment. Discovering the biological underpinnings of radiation priming will allow for novel, "game-changing" cancer therapies, rapid translation to early-stage clinical trials and, ultimately, improved outcomes in patients with fatal diseases.

Dr Joseph Yang



Dr Joseph Yang is the lead clinician scientist and a research fellow for Department of Neurosurgery at the Royal Children's Hospital. His research focused on diffusion MRI-based advanced white matter modelling and tractography techniques, and translation of these advanced techniques into paediatric brain tumour and epilepsy neurosurgery practice. He has a medical doctoral background with six years of advanced neurosurgery training and completed a PhD on advanced tractography application in paediatric epilepsy surgery. He currently holds academic honorary positions at the Murdoch Children's Research Institute and the Department of Paediatrics at the Melbourne University.

ORAL ABSTRACT LISTING

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1 **Tools for studying and targeting glioma stem cell quiescence**

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2 **Systemic and local immune responses following stereotactic radiosurgery to brain metastases from HER2-amplified breast cancer**

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3 **ANZ Patterns of Care Study in Low Grade Glioma**

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4 **A customisable, modular mouse model that combines driver mutations to accurately recapitulate the diverse phenotypes of human glioblastoma**

Devlin R. Forsythe, Olivia K. Burn, Ian F. Hermans, Melanie J. McConnell

5 **Enhanced telomerase targeting in glioblastoma via augmented 6-thio-2'-deoxyguanosine**

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6 **Multi-site, prospective trial evaluating FET-PET In Glioblastoma (FIG) Study (TROG 18.06): Preliminary results of central nuclear medicine review of FET-PET biologic target volume delineation for radiation planning**

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7 **Current status and key learnings from the first year of the ongoing LUMOS-2 trial**

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8 **A randomised controlled waitlist trial of a telehealth group cognitive intervention (BRAINS-LaTCH) for people with primary brain tumour**

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9 **Importance of Carer Mastery and performance status for outcome with Glioblastoma**

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10 **Do neuro-oncology care coordinator position descriptions match the care roles staff report?**

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2 **Predominantly non-enhancing Glioblastoma may have different natural history and outcome**

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4 **Adapting a web-based intervention (RESTORE) to support self-management of cancer-related fatigue in people living with a brain tumour**

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9 **Modifying a supportive care needs screening tool for people with brain tumour**

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ORAL ABSTRACTS

1

Tools for studying and targeting glioma stem cell quiescence

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Aims: Treatment for glioblastoma involves resection and post-operative IR and chemotherapy. Unfortunately, significant populations of resistant glioma stem cells remain after treatment, these cells resist IR/chemotherapy in part because they are quiescent/slow-cycling. As glioma stem cells sit on top of the cellular hierarchy in glioblastoma, the proliferation of these cells post-therapy reconstitutes the tumour. Multiple pathways are known to regulate quiescence in healthy neural stem cells. It is unclear whether these pathways are conserved in quiescent glioma stem cells and whether these pathways are therapeutically tractable. To address these questions, we set out to implement novel 1) bioinformatic, 2) in vitro and 3) in vivo tools.

Methods: We used single-cell RNA sequencing data and trajectory inference tools to compare the gene expression changes that occur as quiescent neural stem cells and glioma stem cell leave quiescence. Secondly, we tested a number of these pathways through functional in vitro assays using patient-derived 2D glioma stem cell cultures and organoids. Thirdly, to track quiescent glioma stem cells in vivo, we generated a novel somatic cell electroporation model of brain cancer, based on combining deletion of the tumour suppressors Nfi, Pten, P53 with the G0-reporter mVenus-P27K–.

Results: We found that activation signatures of quiescent neural stem cells and glioma stem cells are largely correlated and functionally conserved. We identified pathways that could both deepen quiescence or inhibit quiescence. Our in vivo quiescence tracking model successfully distinguished between proliferating tumour cells (fluorescing red) and quiescent glioma stem cells (fluorescing green). The behaviour of these different populations during early vs late gliomagenesis, in response to temozolomide, and at the tumour core vs invasive edge revealed distinct behaviour.

Conclusions: Overall, these data reveal conservation of major signalling pathways in health and disease and suggest new therapeutic opportunities.

Theme:
Basic /Translational Science

2

Systemic and local immune responses following stereotactic radiosurgery to brain metastases from HER2-amplified breast cancer

Joseph Sia[1,2], Criselle D'Souza[1,2], Becky Castle[1,2], Yu-Kuan Huang[1,2], Han Aw Yeang[1], Rejhan Idrizi[1], Metta Jana[1], Shankar Siva[1,2], Paul Neeson[1,2], Claire Phillips[1,2]

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Aims: Brain metastases (BrMs) afflict 30-50% of HER2-amplified breast cancer (HER2-BC) patients. Stereotactic radiosurgery (SRS) is a highly effective focal treatment for BrMs, but whether it can promote anti-tumour immune responses that synergise with immunotherapy is unclear. We investigated this in blood samples from the TROG 16.02 translational substudy for HER2-BC BrMs, matched with longitudinal HER2-BC BrM samples resected from the same location in the same patient.

Methods: Blood samples from 10 patients taken pre- and 7-14 days post-SRS to intact BrMs or post-resection BrM cavities were analysed by mass and flow cytometry. One patient received pre-

operative SRS for a BrM that recurred 7 months after resection, followed by planned re-resection 8 days post-SRS. Pre- and post-SRS tumours from this patient were analysed by bulk RNAseq, multiplex immunohistochemistry (mIHC), and TCR sequencing.

Results: Monocytes, central memory CD8+ T and regulatory T cells were enriched in blood post-SRS, together with increased MHC-II expression on monocytes, conventional DCs, and myeloid MDSCs. In tumour, cell type deconvolution from RNAseq suggested an SRS-induced loss of metastatic tumour cells and enrichment of tumour-associated macrophages (TAMs) and CD4+ T cells. Antigen presentation, T cell proliferation and T cell co-stimulation gene signatures were also upregulated. mIHC corroborated CD68+ TAM and CD4+ T cell influx into tumour post-SRS. Specifically, TAMs and CD4+ T cells, but not CD8+ T cells, demonstrated spatial co-localisation post-SRS. These TAMs were lowly PD-L1 expressing, but CD4+ T cells showed increased PD-1 expression. A sizeable proportion of T cell clonotypes were retained post-SRS, and four clones demonstrated significant non-stochastic expansion.

Conclusion: Systemic and local immunological changes in this homogenous patient cohort suggest that SRS may facilitate MHC-II restricted T cell priming responses involving the monocyte-macrophage lineage and CD4+ T cells, which should be further explored.

Theme:
Basic / Translational Science; CNS Metastasis; Radiation Oncology

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3

ANZ Patterns of Care Study in Low Grade Glioma

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Aim: The management of low-grade gliomas (LGGs) is evolving with new insights into disease biology and recent clinical trials. This includes the phase III INDIGO1 study, highlighting the benefits of vorasidenib in treating residual or recurrent grade 2 IDH-mutant gliomas following surgery alone. This study aims to characterise current patterns of care for LGGs in Australia and New Zealand, particularly addressing the role of vorasidenib.

Methods: An online survey outlining three clinical scenarios was distributed to the Cooperative Trials Group for Neuro-Oncology (COGNO), New Zealand Aotearoa Neuro-Oncology Society and Neuro-Oncology Pathology group members in December 2023, with three follow-up emails.

Results: The survey response rate was 12% (50/416); 84% from Australia and 16% from New Zealand; spanning medical oncology (50%), radiation oncology (20%), pathology (26%) and neurosurgery (4%); metropolitan (94%) and regional centres (6%). Case 1 examined an IDH-mutant grade 2 glioma following gross total resection. Observation alone was recommended by 91%. Of the 70% who were familiar with the INDIGO1 study, 48% would not recommend vorasidenib. The presence of a CDKN2A/B homozygous deletion led 87% to treat as a high-grade glioma. With recurrence at 24-months and further salvage surgery, 76% recommended

adjuvant chemotherapy and radiotherapy, but if available, 64% would recommend vorasidenib. Case 2 examined an incompletely resected IDH-mutant grade 2 astrocytoma. If feasible, 36% recommended further surgery and 69% adjuvant chemotherapy and radiotherapy. After 12 months of disease stability, 56% of respondents preference vorasidenib over these existing therapies. Case 3 examined an incompletely resected, IDH-mutant grade 3 oligodendroglioma. No respondents recommended observation alone; 97% recommended radiotherapy, 94% chemotherapy (57% temozolomide), and 29% salvage surgery.

Conclusions: These findings underscore the variation in managing LGGs and highlight the challenges in applying the INDIGO1 study results to clinical practice. The COGNO community preferences vorasidenib mainly in the grade 2 intermediate-risk setting.

References: *Mellinghoff, Ingo K et al. "Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma." The New England journal of medicine vol. 389,7 (2023): 589-601. doi:10.1056/NEJMoa2304194*

Theme:
Personalised Medicine and/or Therapeutics

4

A customisable, modular mouse model that combines driver mutations to accurately recapitulate the diverse phenotypes of human glioblastoma

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Abstract: To effectively beat glioblastoma, new pre-clinical models are needed: to dissect the biology of processes like migration and therapy resistance; to understand immune suppression and immunotherapy; and to use as a model for testing in therapeutic development. We have developed a new panel of glioblastoma mouse models, which engineer well-characterised glioblastoma driver mutations into an immortalised eGFP murine astrocyte-like cell. These "GEM-CLeM" are Genetically Engineered Mouse Cell Line Models. When transplanted intra-cranially into immunocompetent mice, these lines formed tumors with the key characteristics of glioblastoma – migratory and invasive, with rapid proliferation and infiltration of suppressive immune cells. The eGFP expression allowed detection of glioblastoma cells in situ and ex vivo, and the ability to readily distinguish tumor and stromal components of the tumors. Importantly, different combinations of driver mutations led to diverse tumor phenotypes. Loss of PTEN with over-expression of mutant Ras generated tumors with 100% efficiency and the same time to tumor onset as the commonly used GL261 cell line. However, unlike GL261 tumors the PTEN-RasV12 tumors had a highly invasive edge and extensive migration, and were full of pro-tumorigenic macrophages and monocytes, with very few T-cells or dendritic cells. Together, this recapitulated the phenotype of human wildtype IDH1 glioblastoma. In contrast, the very common EGFRvIII mutant did not drive tumor formation in combination with PTEN loss. We also modelled mutant IDH glioblastoma by combining loss of p53 with overexpression of IDH1R132H. These were slow growing, densely packed tumors with extensive microglial involvement in addition to pro-tumorigenic macrophages. This GEM-CleM system combines the benefits of the traditional genetically engineered mouse models with accessible, rapid, reproducible tumor formation. The GEM-CleM lines are amenable to further genetic manipulation, so cells can be customised with other mutations to ask important biological questions in the presence of a intact tumor immune microenvironment.

Theme:
Basic / Translational Science

5

Enhanced telomerase targeting in glioblastoma via augmented 6-thio-2'-deoxyguanosine

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Aim: Cancer cells achieve replicative immortality by maintaining telomeres, protective structures located at the ends of chromosomes. Most cancers achieve this by upregulation of the enzyme telomerase. The thio-nucleoside compound 6-thio-2'deoxyguanosine (TdG) is a substrate for telomerase and is thus selectively toxic to telomerase expressing cancer cells. Recently, enzyme-X (de-identified) has been implicated in neutralizing the effect of thio-nucleosides. In this study, we examine the role of enzyme-X in modulating the efficacy of TdG in the primary brain cancer glioblastoma, which demonstrates telomerase upregulation in over 80% of cases.

Methods: A panel of telomerase dependent glioblastoma cell lines was treated with TdG to determine a range of sensitivities to TdG. Enzyme-X expression was determined for each cell line using digital PCR and correlated with TdG sensitivity. Next, CRISPR-Cas9 mediated knockout of Enzyme-X was performed in selected glioblastoma cell lines. Cell viability assays were used to determine the effect of enzyme-X knockout on TdG sensitivity. These modified cell lines were then used in murine orthotopic xenograft models in order to examine the effect of enzyme-X abrogation on TdG efficacy in vivo.

Results: A significant correlation was found between Enzyme-X expression and TdG sensitivity. Enzyme-X knockout lines showed markedly increased sensitivity to TdG compared to controls. In vivo, mice with enzyme-X knockout xenografts exhibited a survival benefit when treated with TdG versus controls.

Conclusions: Enzyme-X expression appears to be a marker of resistance to TdG in glioblastoma. Furthermore, inhibiting enzyme-X may significantly enhance the effectiveness of TdG in treating glioblastoma.

Theme:
Basic / Translational Science; Personalised Medicine and/or Therapeutics

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6

Multi-site, prospective trial evaluating FET-PET In Glioblastoma (FIG) Study (TROG 18.06): Preliminary results of central nuclear medicine review of FET-PET biologic target volume delineation for radiation planning.

Eng-Siew Koh[1, 2], Roslyn J. Francis[3, 4], Sze Ting Lee[5, 6], Eddie Lau[6, 7], Elizabeth L. Thomas[3], Angela Whitehead[8], Olivia Cook[8], Rachael Dykyj[8], Alisha Moore[8], Alana Rossi[8], Paul Thomas[9], David Pattison[9], Tim Akhurst[10], Ramin Alipour[11], Ed Hsiao[12], Geoffrey Schembri[12], Peter Lin[13], June Yap[13], Tam Ly[13], Ian Kirkwood[14], Wilson Vallat[14], Dayanethee Krishna[15], Shahroz Khan[15], Stanley Ngai[16], Chris Yu[16], Scott Beuzeville[17], Tow Chan Yeow[17], Nathaniel Barry[18], Martin A. Ebert[3, 19], Hui Gan[5, 20], Bradford A Moffat[21], Greg Fitt[7, 22], Sweet Ping Ng[23], Mark B. Pinkham[24], Dale L. Bailey[12, 25], Andrew M. Scott[5, 6]

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Background: To provide an update from the multi-site trial evaluating O-(2-[18F]-fluoroethyl)-L-tyrosine Positron Emission Tomography (FET-PET) in Glioblastoma (FIG) study and 2) assess the impact of central Nuclear Medicine physician (NMP) review of prospective FET-PET1 delineation of the biological target volume (BTV) for radiotherapy (RT) planning.

Material and Methods: Up to 210 adult GBM participants across 11 Australian sites will undergo FET-PET post-surgery/pre-chemo-RT [CRT] (FET-PET1), one month post CRT (FET-PET2) and at suspected progression (FET-PET3). Group 1 participants enter at timepoint 1 (FET-PET1 with MRI1), with Group 2 at timepoint 2. Adjuvant RT target volumes are derived per standard contrast MRI with hybrid post-hoc RT volumes then incorporating the FET-PET1 NM-derived BTV utilising MiM version 7.0. All trial sites and NMP have passed credentialling, which included three benchmarking cases involving BTV delineation.

Results: Recruitment commenced in January 2021, with 202 (n=139 Group 1 and n=63 Group 2) participants enrolled to date, with a target of 140 Group 1 participants. During trial credentialling, results demonstrated variations in FET-PET1-derived BTV in 25/72 (34.7%) - 13 minor and 12 major. Currently, 42 of 129 participant FET-PET1 with BTV delineation cases across 10 sites have undergone central review, with 8/42 (19%) requiring resubmission. Reasons for resubmission/protocol deviation included incorrect imaging sequence selection within MiM workflow (n=3), Static GTV overcontouring (n=3), dynamic volume of interest change in size/position during workflow (n=1) and static FET interpretation issues (n=1).

Conclusion: The FIG trial will complete recruitment in 2024 with analyses planned at one year post CRT completion. Despite improvements in resubmission rates compared to the credentialling phase, central review of prospective FET-PET1-derived BTV delineation remains important in ensuring protocol adherence. The FIG study is the largest prospective multi-site study of its kind addressing FET-PET's impact on adjuvant radiation planning and its role in management of pseudoprogression and prognostication.

Theme:
Clinical Trials and Trials in Progress

7

Current status and key learnings from the first year of the ongoing LUMOS-2 trial

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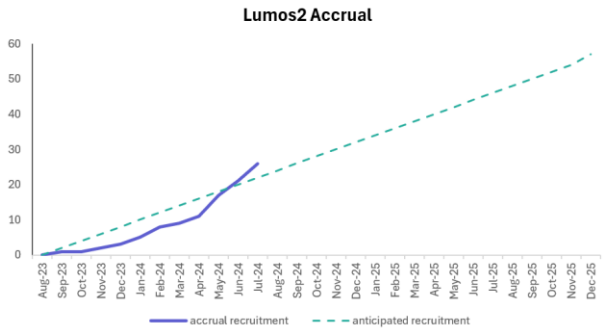
Background: IDH-mutant gliomas are the second commonest primary adult brain cancers, with limited therapeutic options at progression. LUMOS-2 is an innovative precision oncology umbrella trial for these patients, leveraging a new collaboration between COGNO, Omico and CCTG. We provide a trial-in-progress update, highlighting current activity and international expansion, and key learnings from this world-first precision brain oncology study spanning Australia and Canada.

Methods: The first year of LUMOS-2 recruitment were reviewed, including projected versus actual recruitment across Australian sites. Key learnings were synthesised by the LUMOS-2 steering committee.

Results: We confirm the feasibility of a multi-centre, national platform study requiring contemporaneous fresh tissue for comprehensive genomic profiling (CGP) at time of IDH mutant glioma progression. As of 30th July 2024, 9 of 12 Australian sites have been activated. In total, 26 participants have been enrolled, across all sites active for over 1 month. One participant is in screening and seven are currently undergoing CGP. Of the remaining 18, one had insufficient tissue and 17 had successful CGP; of these 18, 10 have commenced study treatment, two withdrew due to clinical deterioration and six are in the process of treatment assignment. Currently, we are recruiting ahead of projections (Figure 1).
To date, key operational challenges and the strategies implemented to mitigate them include:
- Optimising neurosurgical processes for optimal sample acquisition and integration with local practices for surgery across sites.
- Minimising turnaround times for tissue retrieval and transport to Omico, CGP turnaround times and report distribution/interpretation
- Refining the treatment allocation process for optimal patient allocation
- Expanding the trial to include additional treatment arms to maintain sustainability of the platform



Conclusions: LUMOS-2 has demonstrated the feasibility and appeal of conducting a neuro-oncology precision oncology study, including multiple Canadian sites in start-up and initiation of new arms across multiple countries.

Figure 1: Recruitment is ahead of schedule, with the accrual rate exceeding projections for the number of actively enrolling sites.

Theme:
Clinical Trials and Trials in Progress

8

A randomised controlled waitlist trial of a telehealth group cognitive intervention (BRAINS-LaTCH) for people with primary brain tumour

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Background: Cognitive changes are common following primary brain tumour (PBT), impacting employment, independence, relationships, and quality of life (QOL). Despite this, tailored interventions are largely unavailable in Australia. The La Trobe and Caulfield Hospital (LaTCH) cognitive rehabilitation group has demonstrated efficacy in older adults without PBT.

Aims: To examine the efficacy of LaTCH adapted for people with PBT (BRAINS-LaTCH), delivered by telehealth to increase access.

Methods: We used a Type 1 hybrid implementation design randomised controlled trial (RCT) with a waitlist control (WLC). Adults >3-months post-PBT diagnosis, and >1-month post-radiation therapy, from healthcare services and community groups across Australia were randomised to: i) Intervention [6-week group sessions; 2 hours/week] delivered over Zoom (n=3-7/group); or, ii) WLC and intervention offered at 16 weeks. Primary outcome was self-perceived cognitive function; secondary outcomes included: QOL, fatigue, mood, and objective cognition (attention, working memory, processing speed, memory, executive function). Between group differences post-intervention and 6 weeks later (maintenance) were analysed using linear mixed models.

Results: Sixty participants (M age =49.0, SD=10.4 years, 57% female, 55% high-grade) were randomised; 29 intervention group, 31 WLC. The intervention group participants reported significantly improved self-reported memory ability, satisfaction, strategy use, and strategy knowledge post-intervention compared to WLC. Effect sizes were moderate to large ($\eta p2$ range 0.06 – 0.21) and were maintained for memory ability ($t = 4.26$, $p < .001$, $\eta p2 = 0.18$), memory satisfaction ($t = 2.23$, $p = .028$, $\eta p2 = 0.18$), and memory strategy knowledge ($t = 2.92$, $p = .004$, $\eta p2 = 0.09$). There was no intervention effect on secondary outcomes.

Conclusions: Our findings indicate BRAINS-LaTCH delivered via telehealth improved memory-related outcomes in people with PBT. Benefits were maintained after the intervention was completed. Despite the lack of improvement in objectively measure cognition, this intervention should be offered to people with PBT self-reporting memory decline.

Theme:
Survivorship, Psychology, and Supportive Care

9

Importance of Carer Mastery and performance status for outcome with Glioblastoma

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Aims: Carer Mastery, defined as an individual's sense of control and effectiveness in managing care situations, is an emerging concept in neuro-oncology and intimately linked to ongoing patient performance status and outcome. Importantly this potentially may be modified through supportive care interventions. This study aims to describe the impact of objectively assessed carer mastery in patients managed for glioblastoma.

Methods and Materials: Database of consecutive patients with glioblastoma managed with radiation therapy(RT) between 2016-2019 was audited for presentation symptoms, performance status(ECOG) and carer support. An objective measure of carer mastery was provided retrospectively by two clinical teams involved in the adjuvant therapy (medical/nursing) and ranked on four-scale rating. Major endpoints were ECOG at month+6, and median overall survival(mOS). Analysis was performed to determine association with carer mastery.

Results: 182 patients were assessed with median age 62years; and 25% received Elderly(40Gy) Protocol. Personality change(23%), generalised seizure(18%), motor deficit(14%) and focal seizure(14%) were major presenting symptoms. Initially 60.4% were ECOG 0,1; and no significant change at month+6 (p=0.28). The mOS was 16.5 months(95%CI:14.5-18.5); ECOG 0-1 was associated with improved mOS at both RTstart(p<0.001) and month+6(p=0.006). Patients lived with carer in 81%, and 70% of patients had either good/excellent rating of carer mastery. Patients with carer were more likely to be discharged within 10 days of surgery. Recognised Carer Mastery (p=0.007), but not the presence of a carer (p=0.35) was associated with improved mOS. Median survival in those with poor/limited carer mastery was found to be 10.5 months (95%CI:6.7-14.2) compared to 17.9 months (95%CI:15.7-19.9) for good/excellent carer mastery(p < 0.001). Those with excellent carer mastery had a mOS of 19.8 months(95% CI:17.3-22.2).

Conclusion: Performance status and Carer Mastery were associated with clinical outcome and survival. Improving recognition through multidimensional instruments may guide the design of supportive care services to optimise future patient care.

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Theme:
Survivorship, Psychology, and Supportive Care

10

Do neuro-oncology care coordinator position descriptions match the care roles staff report?

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Background: Navigating a primary brain tumour (PBT) diagnosis often requires specialist support and care due to the unique, multifaceted and devastating impacts of the disease and its treatment. Neuro-oncology care coordination (NOCC) can mitigate these challenges by providing continuous and timely care tailored to individual needs. While NOCC is commonly based on nurse-led models of care, a lack of standardisation has created ambiguity in the roles and responsibilities of healthcare professionals (HCPs) involved in NOCC.

Aim: We aimed to compare formal position descriptions with the experiences and perceptions of HCPs involved in NOCC.

Methods: Semi-structured interviews were conducted with HCPs involved in clinical neuro-oncology care. Participants were asked about their perceptions of NOCC and asked, where possible, to provide a copy of their official position description. Interviews were transcribed verbatim and position descriptions converted to a standardised template, before undergoing qualitative thematic analysis. Necessary qualifications, key capabilities, roles and responsibilities were extracted and compared across the two datasets.

Results: We interviewed 12 HCPs from Australia and New Zealand and were provided with six position descriptions. The median interview length was 58 minutes and position descriptions varied in detail provided. Role and responsibilities were categorised into coordination, institutional, and resource-related duties. Coordination-related duties, multidisciplinary collaboration, referrals and clinical consultancy were commonly reported in interviews and position descriptions. In the interviews, almost all participants commented on their role as a key, trustworthy point of contact who provides emotional support and psychological first aid to patients and carers. However, only two position descriptions included providing psychological support as a key duty.

Conclusion: NOCC position descriptions are inconsistent across practice settings and fail to recognise the relational and emotional labour required as part of NOCC. Core duties of NOCC staff need review to ensure they reflect the components of care provided.

Theme:
Survivorship, Psychology, and Supportive Care

POSTER ABSTRACTS

1

Clinical quality indicators for an Australian Brain Cancer Registry in high-grade glioma: a retrospective analysis of neuro-oncology multidisciplinary care

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Purpose: In 2022, 58 Clinical Quality Indicators (CQI) for an Australian brain cancer registry spanning key aspects of high-grade glioma (HGG) and low-grade glioma management were developed via Delphi process [1]. Patients managed via a multidisciplinary team (MDT) setting have higher rates of concordance with MDT recommendations and treatment guidelines [2]. This study focuses on 1) adherence to MDT discussions and treatment guidelines and 2) ascertaining feasibility of MDT data extraction.

Methods and Materials: 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 management 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. Of the cases discussed in the MDT setting, further analysis was carried out to determine those that received guideline recommended therapy (GRT) and the reasons why GTR was not completed.

Results: To date, the study cohort comprised 103 patients, WHO Grade IV glioma (n=93) and Grade III (n=9) with anaplastic astrocytoma (n=6) and oligodendroglioma (n=3). Initial MDT discussions were carried out for 92/103 (89%) cases. Of those discussed, 63/92 (68%) completed GRT, 24/92 (26%) partially completed the GRT, and 5/92 (5%) of cases did not complete the GRT. The primary reasons GRT could not be completed included: disease progression (n=10/92, 10.9%), patient decision (n=9/92, 9.8%), death (n=6/92, 6.5%), change in performance status (n=1/92, 1.1%), clinical decision (n=1/92, 1.1%), other comorbidities (n=1/92, 1.1%), and a geographical move in patient care (n=1/92, 1.1%).
Regarding mode of data extraction, automation was feasible for referral to an MDT, radiotherapy (RT) details, demographics, age, and date of diagnosis. However, manual data extraction was needed for ECOG before/after initial oncology consultation, histological and/or molecular pathology, NGS testing, pre- and post-operative MRI details, extent of resection (EOR), time to RT, most oral chemotherapy details, and all MDT discussions and recommendation details.

Conclusion: Alignment of tailored data documentation and information systems will facilitate more efficient capture of HGG CQI, including referral to an MDT and MDT recommendations. Importantly, reasons for non-GRT delivery impacting outcomes were feasible but relied on manual data extraction currently. Enhanced CQI into routine automated data systems for neuro-oncology patients will enable outcomes to be compared longitudinally and benchmarked against other patient cohorts.

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Theme:
Basic / Translational Science

2

Predominantly non-enhancing Glioblastoma may have different natural history and outcome

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Aim: Patients with minimal gadolinium enhancement at initial diagnosis of glioblastoma intuitively may have different natural history. This study assesses the clinicopathological features and outcome of these non-enhancing tumours.

Methods: Consecutive patients with glioblastoma(IDHwt) managed with definitive RT60Gy/TMZ from 2016-2023 were eligible. Volumetric analysis of T1gad and T2 abnormality was performed on preoperative MRI. A non-enhancing tumour was categorized as <=1cm3 (nonENH). Neuropathological features (MGMT and presence of TERT mutations, EGFR amplification, chromosome 7gain,10loss, and CDKN2AB deletions) were analysed. Primary endpoint was median overall survival(mOS) assessed for neuropathological features.

Results: 284 consecutive patients were managed, and only 35 were nonENH(12.3%). Median T2 volume was 21cm3(9-37cm3). Histone-mutated tumours were excluded, leaving 31 patients for analysis. The mOS was 20.4 months(95%CI:17.4-23.3) compared to 18.5 months(95%CI: 16.7-20.3) for overall cohort(p=0.31). Resection extent, ECOG PS were associated with improved survival, but not MGMT(p=0.80).
Full molecular analysis was available in 80% of nonENH patients, of which 92% had TERTmut. Two patients had TERTmut only; and were progression-free at 10 and 27 months. EGFR status was available in 97%; and 50% had amplification with mOS of 20.7 and 20.4 months respectively(p=0.90).
MGMT was further analysed in nonENH with mOS of 18.5months and 21.3months for unmethylated and methylated tumours respectively(p=0.80). The mOS for unmethylated tumours in remaining 253patients was only 14.4 months, compared with nonENH of 18.5 months(p=0.02). A favourable subgroup of nonENH tumours with ECOG0,1 and subtotal/near-total resection also demonstrated equivalent outcome for MGMTmethylation (22.8 months vs 20.7 months for unmethylated tumours p=0.76).

Conclusion: This data suggests that glioblastoma with minimal enhancement as defined by <=1cm3 may have a different natural history compared to more frequent presentation with bulky enhancing mass. This is important to recognise for studies assessing future neoadjuvant approaches where patients with less enhancing tumours may be preferentially included for delayed definitive resection.

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Theme:
Radiation Oncology

3

Brain Tumours Online: Preliminary findings on usability, acceptability and feasibility of a novel digital supportive care platform for people affected by a brain tumour in Australia

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Introduction: Currently, there is no comprehensive, evidence-informed digital supportive care platform for people with a brain tumour and their carers in Australia. Based on a decade of research documenting the limited quality of life of brain tumour patients[1,2] and the need for rigorously evaluated digital interventions to support disease self-management[3,4], we co-produced Brain Tumours Online, a secure, digital supportive care platform to streamline access to educational resources, digital health tools and peer support for people affected by a brain tumour.

Aims: To present preliminary findings of the usability, acceptability and feasibility of Brain Tumours Online.

Methods: A concurrent mixed methods single-arm study design was employed, supported by bespoke implementation and evaluation plans. Quantitative and qualitative data has been collected at baseline, three and six months and at activity specific time points. The data collection methods included interviews and surveys with patients, carers and healthcare professionals, web analytics to gather objective usage data, and participant-reported outcomes measures from patients and carers to identify changes over time.

Results: 225 participants (137 patients, 61 carers, and 27 healthcare professionals) registered with Brain Tumours Online and completed all baseline surveys. Patient tumour types included 34 meningioma, 32 astrocytoma, 30 glioblastoma, 19 oligodendroglioma, 22 other. At the time of registration, 55 carers were currently providing care, and 6 were bereaved carers. Healthcare professionals included neurosurgeons, oncologists, cancer care coordinators, and allied health. Data collection will close in August 2024. We will present the preliminary data on user demographics, web-analytic patterns and qualitative feedback from participants.

Conclusions: Participation and input from patients, carers and healthcare professionals was important in this project to incorporate the needs and preferences of the users of Brain Tumours Online. They are integral for transitioning this evidence-informed digital supportive care platform to a publicly-accessible resource for people affected by a brain tumour.

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Theme:
Survivorship, Psychology, and Supportive Care

4

Adapting a web-based intervention (RESTORE) to support self-management of cancer-related fatigue in people living with a brain tumour

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Aims: Cancer-related fatigue (CRF) is a debilitating symptom commonly reported by people with a brain tumour (BT). RESTORE is an online intervention that has demonstrated preliminary efficacy in enhancing self-efficacy to self-manage CRF following primary cancer treatment. Previous evaluations of RESTORE did not include people with BT. Given the unique functional deficits experienced by people with BT, we aimed to explore the appropriateness of RESTORE to support self-management of fatigue in this population, and identify modifications required.

Methods: We conducted semi-structured interviews with people with BT, their caregivers, and healthcare professionals (HCPs) who treat them. Before the interview, participants viewed a video summarising the intervention components and accessed the intervention. Interviews explored the appropriateness of RESTORE for this population, and modifications to improve its relevance and suitability. Interviews were transcribed, coded and analysed thematically using interpretive description to devise recommendations.

Results: We interviewed 40 participants (24 people with BT, 5 caregivers, 11 HCPs). We identified four themes: 1) feedback on content; 2) feedback on format; 3) feedback on use; and, 4) barriers to engagement. These themes were linked by an overarching need for flexible and responsive tailoring to the unique needs of people with BT. We derived 32 recommended modifications from feedback to optimise RESTORE for this population.

Conclusion: Our results suggest a BT-specific version of RESTORE is desirable and would be acceptable to address fatigue self-management in this population. However, to be effective for people with BT, adaptations such as greater flexibility and tailoring of content and format are required. Based on these recommendations, we are developing a BT-specific version of RESTORE; the prototype will be presented at the conference. Barriers to engagement including digital access and literacy, caregiver burden, and awareness of the resource, will need to be addressed in the implementation of this BT-specific version of RESTORE.

Theme:
Survivorship, Psychology, and Supportive Care

5

The use and effectiveness of non-pharmacological interventions to reduce fatigue in people with primary brain tumours: a systematic review.

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Aim: People with primary brain tumour (PBT) report high levels of fatigue. This systematic review aimed to synthesise the evidence on use and effectiveness of non-pharmacological interventions for fatigue in people with PBT.

Methods: This review was prospectively registered with PROSPERO. PsycInfo, Medline, Scopus, CINAHL, and Web of Science databases were searched in August 2023 using terms related to fatigue, PBT, non-pharmacological approaches, and interventions/treatment. Randomised controlled trials (RCT) and non-randomised studies were included. A narrative synthesis approach was employed to analyse extracted information. The Cochrane Risk of Bias (RoB-2) and Risk of Bias in Non-randomised Studies of Interventions (ROBINS-I) tools were applied.

Results: We identified 18 articles; 10 RCTs, 4 single-arm studies, 3 case studies, and 1 quasi-experimental study. Interventions included exercise-based interventions (n=10), cognitive rehabilitation (n=3), education/self-help (n=2), psychological (n=1), neuromuscular stimulation (n=1), and nursing (n=1). Eight were feasibility/pilot studies and 11 had small sample sizes (N<30). Six studies (3/10 RCTs) reported a statistically significant reduction in fatigue post-intervention. Studies, including those with positive results, commonly reported fatigue as a secondary outcome, had high attrition rates, and/or were uncontrolled. Regarding risk of bias for RCTs, 2 studies had a low risk of bias, 6 'some concerns', and 2 a high risk. For non-randomised studies, 4 had a moderate risk, and 1 a high risk of bias.

Conclusions: Current evidence to suggest the effectiveness of non-pharmacological interventions for fatigue in people with PBT is limited and effective elements of these interventions could not be identified. Mixed results, small sample sizes, and high attrition rates highlight the need for a different approach to conducting non-pharmacological studies for fatigue in this population. Inherent challenges associated with conducting research in this population necessitates alternative methodologies. Innovative trial designs such as platform trial, n-of-1 studies, stated-preference studies, and tailored interventions, should be considered for future trials.
Theme:
Survivorship, Psychology, and Supportive Care

6

ACTION: A randomized phase 3 study of dordaviprone (ONC201) in patients with newly diagnosed H3 K27M-mutant diffuse glioma

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Background: H3 K27M-mutant diffuse midline glioma is a universally fatal malignancy primarily affecting children and young adults. While radiotherapy (RT) provides transient benefit, no effective systemic therapy is currently available and current standard of care is RT followed by monitoring. Dordaviprone (ONC201), a first-in-class imipridone, is an oral, blood-brain barrier penetrating, selective small molecule antagonist of dopamine receptor D2/3 (DRD2) and agonist of the mitochondrial protease ClpP. An integrated pooled analysis of five open-label trials previously demonstrated efficacy in dordaviprone-treated patients with recurrent disease. This phase 3 trial will be the first randomized, controlled study evaluating ONC201 in patients with H3 K27M-mutant disease.

Material and Methods: ACTION (NCT05580562) is a randomized, double-blind, placebo-controlled, parallel-group, international Phase 3 study of ONC201 in patients with newly diagnosed H3 K27M-mutant diffuse glioma. Patients who have completed standard frontline radiotherapy will be randomized 1:1:1 to receive placebo, once-weekly dordaviprone, or twice-weekly dordaviprone on two consecutive days. Primary efficacy endpoints are overall survival (OS) and progression-free survival (PFS) in all participants; PFS will be assessed by response assessment in neuro-oncology-high grade glioma by blind independent central review. Other objectives include assessments of safety, additional efficacy endpoints, clinical benefit, quality of life, pharmacokinetics, biomarkers, and healthcare resource utilization. Eligible patients will have histologically confirmed H3 K27M-mutant diffuse glioma, a Karnofsky/Lansky performance status ≥70, and completed first-line radiotherapy. Eligibility will not be restricted based on age; however, patients must be ≥10 kg at time of randomization. Patients with a primary spinal tumor, diffuse intrinsic pontine glioma, leptomeningeal disease, or cerebrospinal fluid dissemination are not eligible. ACTION is currently enrolling globally, with sites in North America, Europe, and Asia-Pacific.

Theme:
Clinical Trials and Trials in Progress

7

Caring for the Carer: Optimising an Online Intervention for Carers of People with Brain Tumour

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Aim: Assess the acceptability and usability of the Caring for the Carer online intervention.

Methods: Semi-structured interviews were conducted by phone and videocall from May 2022 to November 2023 with health professionals working with people with brain cancer; and carers of someone with brain tumour. Interviews were transcribed and analysed by participant group using inductive thematic analysis. Specific website changes suggested by participants were summarised descriptively.

Results: Interviews were completed with 16 carers and 15 clinicians, aged 37-77 years old for carers; 31-57 clinicians, and gender 3:10 M:F for carers, 3:12 clinicians. Main themes from the clinician perspective were: online intervention information was comprehensive and widely applicable; the intervention addresses a gap, complementing what clinicians provide; stress and time may affect carer use of the intervention; and, ideally carers are offered the intervention after the initial shock of diagnosis. These themes were echoed by carers who expressed feeling overwhelmed, as well as wishing they had known about the intervention sooner. Themes generated from Carer interviews highlighted: the uniqueness of each person's experiences with brain tumour; reflections on how the intervention caters for individual circumstance and the unpredictable nature of brain tumour; provides valuable guidance (and "permission") on how to communicate with health professionals; and, provides a sense of 'not being alone'. General feedback from both clinician and carer has guided further refinement of the intervention.

Conclusions: The intervention is a comprehensive and useful tool that supports a carer to prepare for caring for someone with a brain tumour. Day-to-day carer stress may limit the time carers have to engage with the intervention. Quantitative evaluation data is currently being analysed and will complement the current findings. Meanwhile, clinician and carer feedback is being incorporated before making the intervention publicly available.

Theme:
Survivorship, Psychology, and Supportive Care

8

Ephrin A5: a key modulator of the astrocytic cell lineage in glioblastoma

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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. 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. Spatial and single cell analysis of patient tumours revealed that ephrin A5 is overexpressed in recurrent disease and is associated with the astrocytic-like (AC-like) cell state which is distinct from the EphA3 expressing MES- like cell state.

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.

Theme:
Basis and Translational research

9

Modifying a supportive care needs screening tool for people with brain tumour

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Introduction: People with brain tumour (PwBT) experience a range of symptoms and needs. As part of the Brain cancer Rehabilitation, Assessment, Interventions for survivorship Needs (BRAINS) program, we are implementing a clinical pathway that incorporates screening and management of unmet needs in PwBT using an online portal (ADAPT BRAINS). The 9-item Supportive Care Need Survey (SCNS-ST9) has been used to identify unmet needs of adults with cancer, although its acceptability among PwBT has not yet been assessed.

Aim: To assess the face and content validity of the SCNS-ST9 for PwBT.

Methods: Semi-structured, cognitive walkthrough interviews were conducted with PwBT, their caregivers, and healthcare professionals (HCPs) who treat them. Participants reviewed the SCNS-ST9 and discussed the acceptability, relevance, and comprehension of the content and language. Interviews were analysed using interpretive description.

Results: We interviewed fourteen PwBT, four caregivers, and seven HCPs. One item was easy to understand and relevant. Suggestions to the wording for eight out of the nine other items included: a) using language that reflects a brain tumour diagnosis (e.g., brain tumours 'progress' not 'spread'); b) modifying language perceived to be sensitive (e.g., 'changes in sexual relationships' amended to 'changes in your relationships'); and, c) simplifying language (e.g., 'as soon as feasible' was changed to 'as soon as possible'). Feedback suggested modifications to the response options were needed as they were difficult to understand and apply. Participants recommended simplifying the instrument instructions by using plain language and being concise.
Conclusions: It is essential that instrument instructions, items, and response options for patient measures are easily understood. Based on our results, the instructions, items, and response options for the SCNS-ST9 were revised and implemented in the ADAPT BRAINS portal. Simplifying language will improve accessibility of screening for PwBT to identify unmet needs and inform the provision of appropriate supportive care.

Theme:
Survivorship, Psychology, and Supportive Care

10

IPAX-2: Phase 1 safety and dose finding study of [131I]IPA plus standard of care in patients with newly diagnosed glioblastoma

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Aim: 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 LAT1/2, which are the target for the small-molecule amino acid derivative, 4-L-[131I] iodo-phenylalanine ([131I]IPA). Previous studies of [123I]IPA as a SPECT tracer have shown retention in glioma tissue, high metabolic stability, and uptake by >85% of gliomas. Preliminary efficacy and safety results from a phase 1 study of [131I]IPA + external radiation therapy in patients with recurrent GBM are promising. The objective of IPAX-2 is to evaluate the safety and tolerability of [131I]IPA in patients newly diagnosed with GBM.

Methods: IPAX-2 is a phase 1, multicenter, open label, single arm, parallel group, dose finding study to evaluate the safety of ascending radioactive dose levels of [131I]IPA + best standard of care in newly diagnosed patients with GBM. Eligible patients (n=12) will be 18-65 years of age with histologically confirmed intracranial GBM following surgial resection; no prior systemic therapy or radiation for GBM; a Karnofsky Performance Status ≥70; a plan to begin chemoradiation 3-6 weeks after surgical resection with Stupp regimen; have adequate organ function; and have adequate tissue samples previously archived. Four cohorts will encompass a 3+3 dose escalation, beginning at 2 doses of 3 GBq each. Primary outcome measures are the incidence rate and severity of dose-limiting toxicities, and the safety, tolerability, and recommended phase 2 dose. 18F-FET PET will be used for pre- and post-treatment evaluations.
Results: This study is ongoing and currently enrolling patients; no results are available at the time of abstract submission.

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

Disclosures: Telix Pharmaceuticals is the sponsor of this study.
ClinicalTrials.govID NCT05450744

Theme:
Clinical Trials and Trials in Progress; Radiation Oncology

11

The Impact of Tumour Volumes as a Clinical Biomarker in Brain Tumours Trials: Data from the Intellance-2 study

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Aim: 3D tumour volumes are emerging as an clinical biomarker in recurrent glioblastoma patients.1 Using the Intellance 2 study, we confirm their importance in recurrent glioblastoma trials.

Methods: A total of 260 patients were randomized to Depatux-M, Depatux-M with temozolomide, or control treatment (lomustine/temozolomide). Manual segmentation of MRIs was performed. Statistics analyses (SPSS Version 29.0) included Kaplan-Meier survival analysis and Cox regression analyses, Fishers' exact test and Pearson's correlation.

Results: MRI scans and data from 240/260 (92%) patients were available. In the control arm, survival of patients were compared in cohorts using increments of 10 ml between groups. A significant difference was seen across the 6 groups (log rank $p<0.001$) with a threshold found for those below or above 20 ml (309 vs 164 days, $p<0.001$).
We undertook a similar analysis in the Depatux-M treatment groups. Again, a threshold was found

for those below or above 20 ml (356 vs 187 days, p<0.001). In addition, a second threshold was found at 40 ml.
A final combined analysis of all patients was then undertaken. Clinical and statistically significant differences (Figure 1) were seen between the 0-20 vs 20.01- 40 ml groups (321 vs 216 days, p<0.001) and between the 20.1-40ml vs the 40+ groups (216 vs 150 days, p<0.001). Regarding PFS (Figure 1), a significant difference was observed between the 20.1-40 ml and the 40+ ml groups (62 vs. 56 days, p=0.005). However, the comparison of PFS between the 0-20 ml and the 20.01-40 ml groups did not reach statistical significance (100 vs. 62 days, p=0.411).
A comparison of 3D vs 2D was undertaken and 3D volumetric measurements were superior (data to be shown in full presentation)

Conclusions: 3D tumour volumes are an important prognostic biomarker in recurrent glioblastoma and should be further investigated for use in future clinical trials.

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Theme:
Clinical Trials and Trials in Progress; Imaging; Personalised Medicine and/or Therapeutics

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12

BEACON: A supporting and guiding light through a brain tumour journey

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Background: Brain cancer is the sixth leading cause of cancer burden in Australia, impacting physical, cognitive, and psychosocial wellbeing1. While clinical trials have traditionally focussed on improvements in survival, brain cancer consumers have highlighted a need to focus on patient-centred care2. Despite the medical and research community recognising that patients experience substantial morbidity and see this as an area of unmet need3,4, patients' opportunity to report morbidity related issues is currently limited and this compromises their ability to receive appropriate support.

Methods: The BEACON registry is a prospective, non-interventional registry. It aims to systematically collect consumer-entered data on patient-reported outcomes (PRO) and the lived experience of patients with brain tumours. Data captured will include key domains, such as cancer diagnosis and detail, treatment history, supports required, and Quality of life and Symptoms using validated tools, such as EORTC-QLQ-C30 and EORTC-QLQ-BN20. By supporting patients to register themselves, independently manage consent for data use, track their symptoms and their severity over time, and to readily access downloadable summaries of any data entered, BEACON will better engage and inform patients in their cancer journey and support and enhance their interactions with the medical system. Unique research opportunities will be created by linking the PRO data in BEACON with the clinical data in the BRAIN registry5 and tissue-related data in the BioBRAIN registry. BEACON will also support PRO collection included as part of any future registry-based clinical trials. As such, BEACON will establish a unique resource, complementing existing data collection and translational research efforts, beginning to address the unmet needs highlighted by brain cancer consumers while also supporting ongoing research efforts by the medical community. BEACON is well advanced in development and will be launched in Q1 2025.

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Theme:
Clinical Trials and Trials in Progress; Survivorship, Psychology, and Supportive Care

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13

Exploring molecular alterations in long-term survivors of glioblastoma: a focus on MGMT methylation

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Background: Approximately 13.7% of all patients diagnosed with glioblastoma survive longer than 2 years1, corresponding to twice the median survival. These patients, deemed long-term survivors (LTS)2,3, are often younger, have improved performance status at diagnosis, and undergo total tumour resection4-7. Currently, there are no hallmark molecular features unique to LTS and thus predicting long-term survival at the time of diagnosis remains difficult. Here, we explore the molecular alterations present in glioblastoma LTS, with a particular focus on MGMT methylation.

Methods: Patients diagnosed with glioblastoma from 1/1/2006 to 31/12/2016 were identified from pathological databases at St Vincent's Hospital Melbourne. Patients alive at 24 months post diagnosis were defined as LTS, whilst those who survived less than 24 months post diagnosis were defined as shorter term survivors (STS). Only patients with sufficient tissue available for molecular testing who underwent maximal resection followed by combined multimodal therapy at the time of initial diagnosis were included. MGMT methylation testing was performed using methylation sensitive-high resolution melting method, optimised to detect methylation down to 5%. 56 patients were required to obtain 80% power to detect a difference in the frequency of MGMT methylation of 35% to 75%. Where possible, tumour samples also underwent next generation sequencing at The Alfred Hospital.

Results: 73 patients were identified. 60% were male with median age 59 years. 41 patients (56%) were deemed LTS, with median overall survival (mOS) of 37.9months, and 32 patients (44%) were deemed STS, with mOS of 16.4months. Both cohorts were similar with respect to median age, gender and tumour location. Compared to STS, LTS were significantly more likely to be MGMT methylated (LTS vs STS: 80% vs 28%, $p<0.0001$).

Conclusion: When accounting for treatment and age, MGMT methylation is a predictor for long-term survival over 2 years. Exploratory analyses of further molecular markers is pending.

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Theme:
Pathology and Genomics

14

Understanding Grade-4 glioma in young adults: patterns of care and predictive and prognostic factors in the molecular era

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Aim: Whilst grade-4 glioma is the most common primary brain cancer, diagnoses in young adults (age<40yrs) remains rare. As such, literature is scarce. Here, we describe the clinicopathologic features, treatment patterns and survival outcomes of young adults with grade-4 glioma (Y-G4G) in a registry cohort.

Methods: Consecutive patients registered in the Brain tumour Registry Australia INnovation and translation (BRAIN) database were identified. Patients aged 18-40yrs with a diagnosis of Grade-4 glioma were included. Demographics, clinicopathological features and survival outcomes were analysed. Comparison of outcomes between groups based on molecular differences was performed.

Results: Between 1/1/2019 and 28/2/2024, 80 Y-G4G patients were identified. Median age was 33yrs with majority being male (60%) and ECOG 0-1 (80%). All patients underwent surgery with 25 (31%) achieving macroscopic resection, 41 (51%) achieving subtotal/partial resection and 10 (12%) having biopsy only, as estimated by surgeon

alone (25%), MRI within 48 hours (49%) or both (14%). Extent of resection was unknown for 4 patients (5%). 50 patients (62%) were IDH-wildtype. MGMT methylation was found in 24 of 54 tested (44%) (Table 1). 71 (89%) patients commenced Stupp protocol [1], with median PFS and OS of 13m and 20m respectively. In the remaining 9 patients, 3 had temozolomide alone (due to previous radiotherapy for a low-grade glioma), 5 had rapid disease progression or poor ECOG, and 1 was lost to follow-up. At diagnosis, only presence of IDH mutation was predictive of improved PFS (IDH wildtype vs mutant: 8.5m vs 24.8m; HR0.38, p=0.020) and OS (IDH wildtype vs mutant: 17.7m vs NR; HR 0.30, p=0.038) (Figure 1).

Conclusions: A minority of Y-G4G undergo biopsy only or do not progress to Stupp protocol post-surgery. With treatment, survival outcomes appear improved compared to age-unselected populations, with IDH mutations being prognostic amongst Y-G4G in a real-world population. Further exploration of genomic markers unique to this population is underway.

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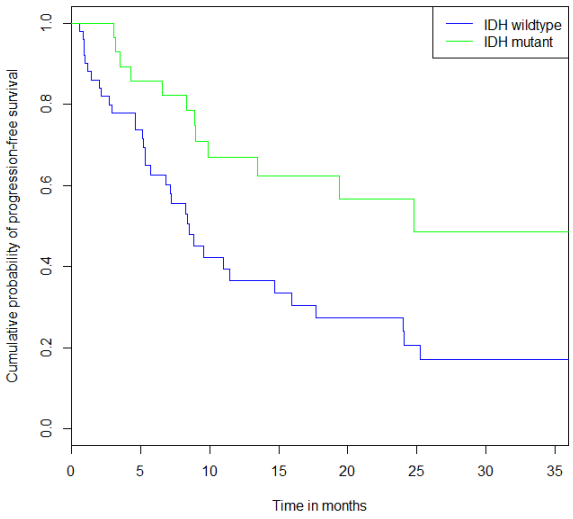
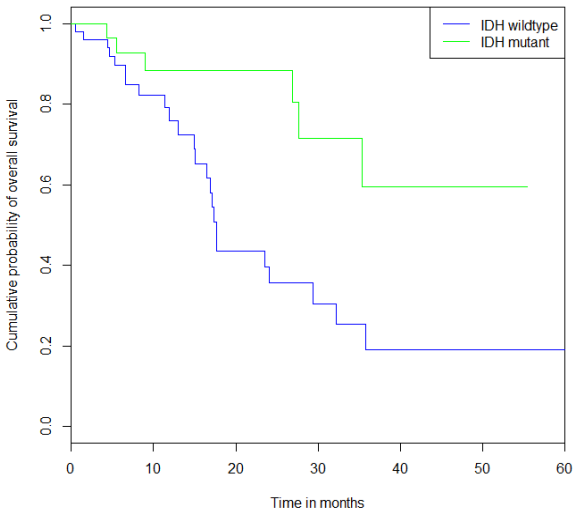
Table 1: Molecular characteristics of patients with Y-G4G

Molecular biomarker		Total N=80
IDH	Mutant	29 (37%)
	Wild-type	50 (63%)
ATRX	Retained/present/positive/ wildtype	43 (61%)
	Absent/Lost/Negative/ mutant	27 (39%)
	Missing	10
MGMT	Methylated	24 (44%)
	Unmethylated	30 (56%)
	Missing	26
1p19q	Codeleted	6 (19%)
	Non-codeleted	26 (81%)
	Missing	48
TERT promoter	Mutant	13 (52%)
	Wild-type	12 (48%)
	Missing	55
CDKN2A	Homozygous	9 (38%)
	Heterozygous	4 (17%)
	Intact	11 (4%)
	Missing	56

Figure 1: Cumulative probability of progression-free survival (left) and overall survival (right) for Y-G4G patients with IDH-wildtype versus IDH-mutant disease.





Theme:
Adolescent and Young Adult, Paediatric and Rare CNS Tumours

15

Update on the BRAIN registry: continuing to generate real-world evidence in neuro-oncology

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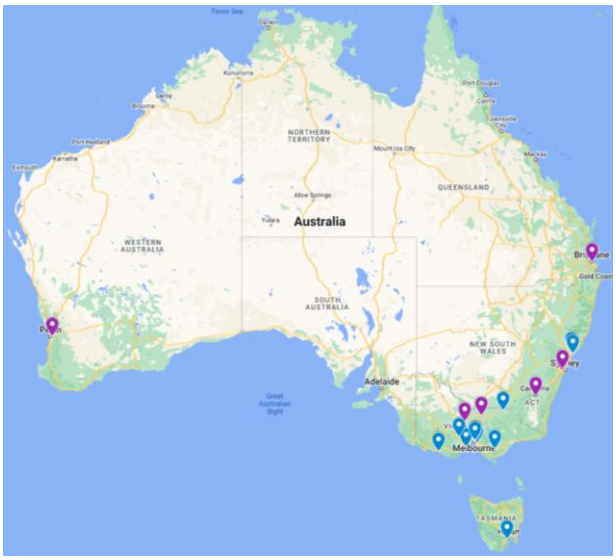
Background: The multi-site BRAIN (Brain tumour Registry Australia: INnovation and translation) registry collects real-world data on patients diagnosed with brain tumours, commencing at diagnosis, including recurrence and treatment data, and capturing death data (see Fig 2). It builds on a substantial initial database at Royal Melbourne Hospital, was activated in February 2021 and continues to receive major funding support from The Brain Cancer Centre. Here we provide an update from the last 12 months.

Results: Eight new sites have been added (including four awaiting lead site ethics approval) with BRAIN now collecting data on patients treated at 20 sites across NSW, Victoria and Tasmania (see Fig 1), including four private and ten regional institutions. Approximately 700 new patients have been added, bringing the total number of patients in BRAIN to 8619. Major updates to the dataset include the addition of detailed genomic/ sequencing data. The establishment of a link with the Victorian Births Deaths and Marriages providing updated death data at 6-monthly intervals has improved the accuracy of our survival data and similar interstate datalinks are being pursued. Output continues to increase with a further three multi-site and seven single-site projects having been approved by the BRAIN steering committee. In total, 20 projects are now supported by BRAIN. There have been three publications1-3, including two arising from BRAINs pioneering registry-based randomised trial, EX-TEM; as well as seven poster presentations and three oral presentations at local and international conferences.

Conclusion: The BRAIN registry is a unique research-enabled infrastructure that continues to add new sites, expand data items and critical linkages, and to enable a diverse array of output. By facilitating collaboration and research efficiency in neuro-oncology, BRAIN will ensure every patient's experience informs research and improves care.

Figure 1: Dot map of BRAIN sites (blue) and additional EX-TEM sites (purple)



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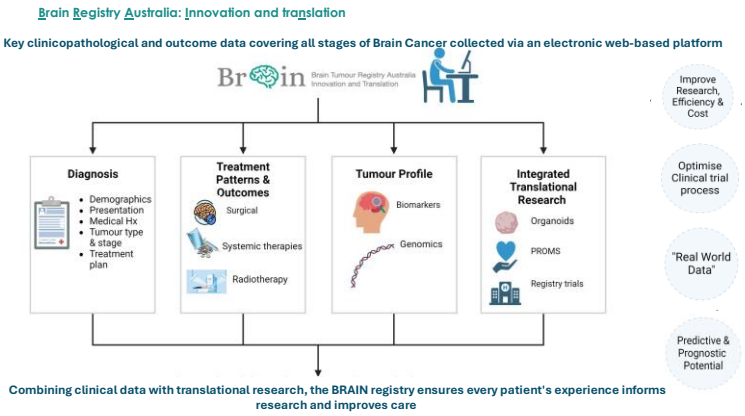

Figure 2:

Theme:
Clinical Trials and Trials in Progress

16

Novel aptamer-drug conjugates successfully deliver drug payloads illustrating therapeutic potential against glioblastoma

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Background: The limited success of current treatment options for glioblastoma, an aggressive brain cancer with poor survivability, can be attributed to the blood-brain barrier (BBB). This barrier primarily prevents entry of most therapeutic drugs to treat brain cancers thus, a novel targeted therapeutic capable of crossing the BBB for drug delivery is essential. Aptamers, or chemical antibodies, are small single-stranded nucleotide sequences that can not only specifically and selectively bind to desired cell membrane targets but can be modified as drug delivery vehicles for therapeutic purposes. We have previously generated a bifunctional aptamer-drug conjugate by combining the transferrin receptor (TfR) and epithelial cell adhesion molecule (EpCAM) aptamers together and intercalated the chemotherapeutic doxorubicin (DOX) for treatment of brain metastases (1). This aptamer-DOX conjugate, termed TEPP-DOX, was successfully able to deliver drug payloads across an in vitro and in vivo BBB to EpCAM positive brain metastases, reducing metastatic spread and tumourigenicity.

Aims: For the first time, we aim to assess the therapeutic efficacy of bifunctional aptamer-DOX conjugates in treating glioblastoma in vitro.

Methods: Firstly, the binding affinity of two bifunctional aptamer-DOX candidates against the TfR was determined by flow cytometry and internalisation rate into glioblastoma cells observed through confocal microscopy. Lastly, DOX and aptamer-DOX cytotoxicity towards glioblastoma was assessed by performing a MTS assay on cell monolayers, and a trypan-blue exclusion assay on 3D tumours.

Results: A moderate binding affinity and specificity was observed by both candidates towards the glioblastoma cells, including internalisation. Upon 72 hours post-treatment, the half inhibitory concentration calculated for the aptamer-DOX conjugates showed similar therapeutic efficacy within the high nanomolar to low micromolar ranges for glioblastoma cells and tumours, respectively compared with DOX alone.

Conclusions: These findings, therefore, demonstrate the potential aptamer-drug delivery vehicles have as a targeted therapeutic candidate for future studies.

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Theme:
Personalised Medicine and/or Therapeutics

17

A Legacy of Hope: Understanding the Experiences of Next of Kin Who Have Supported a Loved One with Brain Cancer to Donate Their Brain Post-Mortem

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Abstract: Post-mortem brain donation provides insight into pathogenesis as well as spatial and temporal heterogeneity beyond what a surgical biopsy can afford. Post-mortem biobanking programs are increasing in number. Therefore, it is imperative that clinical research teams understand the human experience associated with brain donation protocols to ensure benefit is maximised and harm minimised.
We interviewed 27 next-of-kin (NOK) following the death of their loved one and subsequent donation to the Mark Hughes Foundation (MHF) Biobank and 13 NOK at the time of consent. A thematic analysis based on the work of Braun and Clark was carried out on the transcribed, qualitative interviews and the identified themes presented with a narrative synthesis. Themes included; 1: "We were just doing it, that's it!" – Brain donation is a decision grounded in altruism and pragmatism, 2: "I didn't feel helpless" – supporting donors is a source of comfort, pride and empowerment, 3: "His death has had some sort of purpose" – Brain donation can provide meaning for suffering and tragedy and 4: "I can still remember the zipping up of the bag" – perceptions of procedures and processes. These themes represent that brain donation can be an instinctive decision grounded in pragmatism, which provides a sense of comfort while assisting in making meaning for loved ones. We also obtained insight into areas in need of improvement, for example the process for removal of the donor in the event of a home death and the role of the body bag.
Our data indicate that supporting a loved one to donate their brain can be a positive experience providing a source of hope, empowerment, and purpose. Data indicating areas for consideration will be utilised to improve delivery of the program for future donors and their loved ones.

Theme:
Survivorship, Psychology, and Supportive Care

18

Characterising the Views of Health Care Providers Consenting Brain Cancer Patients to Post-Mortem Brain Donation Programs

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Abstract: While invaluable for brain cancer research, post-mortem brain biobanking presents unique ethical, psychosocial and logistical considerations. Often coupled with conversations relating to mortality or end-of-life care, obtaining informed consent can be a delicate and highly personalised process requiring trust among the patient, their loved ones and health care providers (HCPs). There is a growing evidence base detailing the positive psychosocial impact of post-mortem brain donation for donors and their loved ones with existing data reflecting the comfort and empowerment afforded by such programs. Despite this, recent data suggests that while HCPs see value in cancer biobanks, some are concerned that discussions relating to post-mortem research may harm doctor-patient relationships or cause undue distress to the donor or their family. These data are scarce and further work is needed to characterise the views of HCPs towards post-mortem brain donation to ensure optimal and comprehensive informed consent processes and a continuity of support for patients and loved ones engaging in these research programs.
Our aim is to characterise the perceptions and experiences of health care providers who may engage with or may be exposed to post-mortem brain donation programs in the context of primary brain cancer. Using a national, online, survey we will characterise opportunities for engagement, obstacles to participation and identify

disincentives or misconceptions that may impact the ways in which HCPs interact with those who consent to brain donation programs.
Data collection instruments are in the final stages of development and we expect to invite participation from the clinical community in late 2024. Our hope is that the insights afforded by this study will enable integration of brain donation programs into clinical palliative practice – providing the dual benefit of maximising psychological benefit for the brain cancer population and ensuring the ongoing provision of invaluable biospecimens for research.

Theme:
Survivorship, Psychology, and Supportive Care

19

Coordination of care in the context of primary brain tumours: healthcare professionals' exploration of the unspoken impact and clinical implications

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Aim: People with primary brain tumours (PwBT) and their families experience high distress and face challenges navigating their disease and treatment, the healthcare system, and/or survivorship. Quality care coordination enables continuous, timely care according to the individual care needs of PwBT. We aimed to explore healthcare professionals' (HCPs) practices and perceptions about neuro-oncology care coordination (NOCC).

Methods: We conducted a qualitative study using semi-structured interviews via videoconferencing. Participants were HCPs providing neuro-oncology care. Interviews were audio-recorded and transcribed verbatim. Data were analysed thematically using interpretive description, following the Consolidated Criteria for Reporting Qualitative Research.

Results: We interviewed 12 HCPs from Australia and New Zealand between June and November 2023. The median interview duration was 58 minutes. Participants had a median of 13 years of experience in neuro-oncology across medical, nursing, and allied health disciplines. NOCC models were not standardised. We identified five themes related to NOCC: 1) Vulnerable and complex PwBT and families: PBT is a unique cancer generating pervasive, multifaceted disabilities; 2) Tailored coordination: Shaping and tailoring NOCC is in the best interests of PwBT and families; 3) Going the extra mile: Care needs warrant proactive support, which is often unfunded to mitigate crisis; 4) Emotionally demanding: HCPs manage emotional weight with limited support; and 5) Barriers to effective care: Limited resources impact HCPs' capacity to deliver the optimal standard of care.

Conclusion: PwBT experience a unique and complex set of care needs requiring specialist skills and knowledge beyond general oncology care coordination. NOCC encompasses continuous coordination of multidisciplinary care to optimise functional living for PwBT. Given the complexity of

the NOCC role, better support infrastructure with training and resources for HCPs is needed to retain HCPs and prevent burnout. These findings will inform further research to identify support, training and resource needs for HCPs and implement appropriate interventions.

Theme:
Survivorship, Psychology, and Supportive Care; Other

20

What constitutes optimal care coordination for primary brain tumours and how do we assess it in Australia: a Delphi consensus study

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Aim: People with primary brain tumours (PwBT) and their caregivers experience diverse issues across physical, cognitive, behavioural, and psychosocial domains. These impacts can create barriers to seeking care and support. While care coordination (CC) is a critical process to achieve high-quality care for PwBT, a framework of optimal CC to guide clinical practice is lacking. We aimed to develop a consensus framework and assessable indicators for the delivery of optimal CC for PwBT.

Methods: A two-phase, modified Delphi process was conducted from June 2023 to April 2024. In Phase 1, a preliminary framework of 4 domains and 140 items was identified from a scoping review and expert stakeholder advisory group (n=14) discussion. In Phase 2, multidisciplinary panel members (n=40) with expertise in clinical management and support for PwBT indicated the level of agreement (defined as ≥80% agreement and a median score of ≥4) on proposed items using a 5-point Likert scale against consensus criteria in a 2-round iterative Delphi survey. The expert stakeholder advisory group met to finalise components and indicators based on panel consensus findings.

Results: Consensus was achieved for 97 of 140 items across four domains of CC (definition, objective, components and indicators). A further 33 items approached consensus following the two survey rounds. Panel opinions about what indicates quality CC varied, especially for items related to performance indicators of governance/system (ranging between 48-79% agreement). The expert stakeholder panel finalised the inclusion of an additional six items based on qualitative feedback from panellists, producing a final list of 136 items (Table 1).

Conclusions: We defined a novel framework of CC specific to PwBT. This presents consensus

definition and objectives for optimal CC and a comprehensive list of components and indicators of quality CC. This provides a useful template for developing models of CC in the Australian clinical context.

Table 1. Final items achieving consensus criteria for inclusion across domains of CC (n=136)

Domain	# Items (n)
Definition of CC	1
Objectives of CC	12
Components of optimal CC	81
Communication	16
Assessment	22
Support	13
Referral	5
Information	7
Tools that facilitate coordination	7
Carer recognition, assessment and support	11
Indicators of quality CC	42
Person-centred indicators Patient/carer reported outcomes	25
HCP reported outcomes	6
Performance indicators of system/governance	11

Abbreviations. CC=care coordination; HCP=healthcare professionals

Theme:
Survivorship, Psychology, and Supportive Care

21

Liquid biopsy of ctDNA in glioma shows promise for clinical utility

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Aim: Liquid biopsy based on circulating tumor DNA (ctDNA) is a novel tool in clinical oncology to assess prognosis, tumor burden and treatment resistance. Despite significant progress seen in other cancers, ctDNA analysis in glioma has been limited by low levels of circulating DNA and poor sensitivity. In this study, we report the use of digital droplet PCR and a novel next generation sequencing technique on longitudinal blood samples in glioma patients.

Methods: In a prospectively collected cohort of gliomas, including patients from a novel Phase 0 trial of an IDH1 inhibitor, we analysed plasma samples from 10 patients with tumor tissue available from at least two operations. Circulating cell free DNA was extracted from the plasma and analysed with AVENIO, a custom panel and ddPCR.

Results: We found glioma associated mutations in 93% of plasma samples including common drivers such as EGFR amplification. Concordance between plasma and tissue was 52%, with 25% of mutations detected in the plasma only, suggesting ctDNA may complement tissue biopsy in providing a complete genomic characterisation of a tumor and overcome the spatial heterogeneity encountered on biopsy. Mutations in the mismatch repair genes (MMR) were most frequently detected following temozolomide treatment and were observed prior to their appearance in tissue at the time of progression. IDH mutations could be detected in >90% of plasma samples in patients harbouring tumours with that mutation.

Conclusion: We show that novel sequencing techniques can detect low concentrations of glioma ctDNA and show potential clinical utility in diagnosis, monitoring, early detection of chemo-resistance and genomic personalised profiling.

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Theme:
Basic/translational science; Pathology and genomics; Personalised medicine and/or therapeutics

22

Radiomic models to predict survival and IDH mutation in glioma patients: impact of delineation accuracy

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Introduction: The aim of this study was (1) to build radiomic models to predict overall survival (OS) at 6 months and IDH mutation status for individuals with glioma using pre-operative MRI; and (2) to evaluate the impact of delineation errors on model performance.

Methods: Patients with glioma were identified from our institutional database. 5, 11 and 117 patients with WHO grade 2, 3 and 4 gliomas, respectively, were included in the OS model, majority IDH wildtype. 28, 22 and 110 patients with grade 2, 3 and 4, respectively, were included in the IDH model, 46 IDH mutated and 115 wildtype. Image pre-processing included resampling, intensity normalization (z-score), and wavelet transformation. Tumour segmentation was performed manually using FLAIR sequences, yielding the reference "undistorted" volumes. Radiomics feature extraction was computed using in-house MATLAB software. Features were selected using ANOVA and Chi2 statistical methods, followed by recursive elimination. Two models were trained and validated to predict OS and IDH. Next, new volumes were created with intentional delineation errors based on systematic uniform contractions up to 5mm and expansions up to 10mm on the original. New models were trained and validated based on the new datasets. 10-fold cross validation was used to validate the models.

Results: Using the original 'undistorted' volumes, the ROC AUC values for the training dataset were 0.880 for OS and 0.975 for IDH. Using the altered volumes, ROC AUC decreased by < 0.020 for OS and this difference was not statistically significant. For IDH, delineation changes more than 4 mm decreased ROC AUC by more than 0.050 and this was statistically significant.

Conclusions: Radiomic models using pre-operative MRI can predict 6-month OS and IDH mutation status. OS prediction was mostly independent of delineation errors within the tested range, however IDH prediction accuracy decreased with increasing delineation errors.

Theme:
Imaging; Survivorship, Psychology, and Supportive Care; Radiation Oncology

23

Establishment of the ACT Brain Cancer Biobank and Observations from Glioma Cell Line Expansion

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Aim: A major challenge in the brain cancer field is development of efficacious therapies, which requires drug discovery research considering glioma genotype diversity. Thus, the Canberra Brain Cancer Collaborative (CBCC), an interdisciplinary team of researchers at the Australian National University (ANU) and clinicians from The Canberra Hospital (TCH), established the ACT Brain Cancer Biobank (ABCB) in 2022. We aim to integrate data collected from all consented patients (e.g. treatments, outcomes, glioma subtype and grade) into the National Brain Cancer Registry. Moreover, we aim to generate patient-derived material, including primary glioma stem cell (GSC) lines to share with all Australian

researchers through Brain Cancer Biobanking Australia.

Methods: Between June 2022 and July 2024, we collected data, including patient identifiers (age/sex), disease duration, and molecular markers (IDH, ATRX, EGFR, GFAP, Ki 67, 1p/19co-deletion, and MGMT promoter status), from tissue samples obtained with patient consent at surgery. Additionally, the tissue samples were cultured to assess the potential for successful cell line expansion.

Results: We recruited 43 consenting patients, collected 23 tumour samples, and successfully established 13 GSC lines. As expected, the most common glioma subtype was glioblastoma (19 patients), followed by oligodendroglioma (3 patients), and astrocytoma (1 patient). Cell lines were successfully expanded for 61% of all gliomas: 12 glioblastoma and 1 oligodendroglioma. Although material for explant organoid cultures was collected from the low-grade glioma (LGG) subtypes, the finite nature of this resource necessitates investigation of alternative protocols for generating primary LGG lines for inclusion in the national biobank.

Conclusion: ABCB's establishment is enabling continued collection of diverse glioma genotypes, for integration of data from Canberra region patients into the National Brain Cancer Registry and increased availability of primary glioma lines for researchers nationwide. Thus, we are providing a critical resource for drug discovery and the advancement of effective brain cancer therapies.

Theme:
Pathology and Genomics

24

Role of FET-PET in assessing enhancing changes after radiosurgery to differentiate between tumour progression and radionecrosis

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Aim: Primary outcome to prospectively determine the sensitivity of 18-FET PET and MRI respectively in diagnosing tumour recurrence (progressive disease, PD) and radiation necrosis (RN). Secondary outcomes included assessing the correlation of growth rate and baseline size of lesion on MRI with 18F-FET-PET metabolic parameters (SUVmax, SUVmean, mean and maximum tumour-to-background ratio (TBR)).

Methods: Prospective single arm study 2019-2021, patients with ≥1 brain metastasis treated with GK SRS or linac SRT who met RANO-BM criteria for progression. • Median time from treatment to FET/MRI 15 months. Median follow up after FET/MRI 25 months.• Imaging performed on Siemens Biograph PET/MRI scanner. 3T MRI 3D T1W, T1W+Gd, T2, T2 FLAIR, DSC and DCE sequences, 200 MBq FET, dynamic images captured q5-40 mins; SUV/TBR max, SUV/TBR mean. Independent assessors for MRI and PET, categorical diagnosis. • Final outcome determined by serial MRI ≥6 months or histological confirmation. Performance of the rate of size change on MRI, size of lesion, and nuclear medicine parameters (SUVmax, SUVmean, TBRmax, TBRmean) as predictors of final classification of RN and PD was assessed using ROC curve analyses.

Results: Total 47 lesions analysed, 31 lesions were RN and 16 lesions were PD as obtained either by tissue diagnosis from surgical resection and/or results of clinical/ radiological follow up. MRI and FET-PET were concordant with the final outcome

of PD or RN on 22 occasions but were both discordant with the final outcome on 7 occasions.

Conclusions: MRI demonstrated 74% concordance in this single arm prospective study. FET-PET parameters alone were not reliable discriminators without MRI in this cohort. Reliable identification of progressive disease remains a significant problem and the utility of FET PET is yet evolving, with impacts of technical variability and performance variation between certain tumour histologies to address in future studies.

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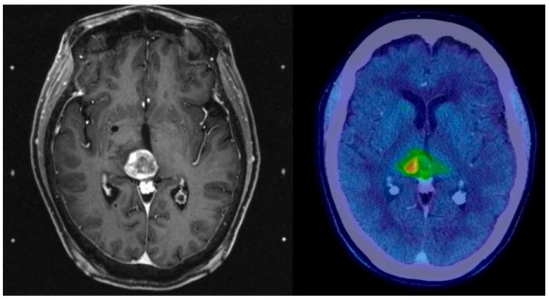

Fig 1. Solitary pineal brain metastasis, evolving changes 2 years following 25 Gy in 5# GK SRS FET-PET localises lateral component of PD - salvage GK SRS 16 Gy. Images courtesy of Pinkham M1,3,6

	PD (n=16)	RN (n=31)	Overall (n=47)
MRI+ (concordant)	7 (44%)	28 (90%)	35 (74%)
FET+ (concordant)	9 (56%)	18 (58%)	27 (57%)
MRI+ FET-	2 (13%)	11 (35%)	13 (28%)
MRI- FET+	4 (25%)	1 (3%)	5 (11%)
MRI+ FET+	5 (31%)	17 (55%)	22 (47%)
MRI- FET-	5 (31%)	2 (6%)	7 (15%)

Histology	n	FET+ for RN	FET+ for PD
NSCLC	13	6/10 (60%)	1/3 (33%)
Breast cancer	12	6/9 (67%)	3/3 (100%)
Melanoma	10	4/8 (50%)	0/2
Colorectal cancer	4	0/1	3/3 (100%)
Other	8	1/3 (33%)	2/5 (40%)

Table 1. Comparing FET-PET and MRI to final outcome. Courtesy of Pinkham M 1,3,6.

Theme:
CNS Metastasis; Clinical Trials and Trials in Progress; Imaging; Radiation Oncology

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Exploring the role of androgen receptor signaling in glioblastoma in an orthotopic animal model

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Objective: Glioblastoma frequently express androgen receptors (AR). We explored AR expression in glioma to investigate whether disrupting AR signaling with readily available blood-brain-barrier penetrant drugs could improve treatment for this deadly disease.

Methods: Low- and high-grade glioma samples were stained for AR by immunohistochemistry. AR expression was correlated to grade and sex. AR expression was characterized in conventional cell lines and patient derived xenografts by immunoblot. Localization of AR and the influence of dihydrotestosterone (DHT) and anti-androgens in glioblastoma cell line U251 were determined by immunofluorescence at timepoints from 15 mins to 24 hours and immunoblot at 24 hours. An orthotopic AR-positive patient-derived model (RN1) was used to test the efficacy of seviteronel, a blood-brain-barrier penetrant anti-androgen.

Results: Two thirds of glioblastoma biopsy samples were positive for AR expression by IHC (n=25/39). AR expression correlated with increasing tumor grade ($p<0.05$) but was similar between sexes ($p=0.94$). High AR expression was seen in U251, U87 and RN1, and low expression in murine line GL261 and patient-derived WK1. Anti-androgens enzalutamide and seviteronel prevented DHT-induced nuclear translocation of AR. Of the examined timepoints by immunofluorescence, these effects were maximal at 24 hours. Seviteronel inhibited nuclear translocation to a lesser extent than enzalutamide. Immunoblot of cell lysates collected 24 hours after treatment showed a similar pattern. In the intracranial mouse model, seviteronel significantly improved survival compared to vehicle (n=12, 36.0 vs 27.5 days, $p=0.03$), and demonstrated reduced Ki67 expression in tumors at the endpoint (68.9% vs 85.0%, $p<0.001$). Combining seviteronel with temozolomide or radiotherapy did not extend survival compared to either treatment alone.

Conclusions: Targeting AR signaling with blood-brain-barrier penetrant anti-androgens may represent a promising biomarker-directed therapeutic strategy. The role or AR signaling in glioblastoma is being further investigated through affinity-purification mass spectrometry analysis

and CUT&RUN sequencing of AR positive glioblastoma cells.

Theme:
Basic / Translational Science

26

'What is this brain's story?': Healthcare professionals' management of brain tumour related personality and behaviour changes

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Background: Management of brain tumour related personality and behaviour changes (BTrPBc) is complex. Contributing factors include tumour location, treatment side effects, and psychological adjustment to the diagnosis. Whilst clinicians' roles should include providing support and management for personality and behaviour changes, scant research has focused on management of BTrPBc.

Aim: We aimed to explore how neuro-oncology healthcare professionals manage personality and behaviour changes in adults with a primary brain tumour.

Method: An interpretive description approach was taken, with semi-structured interviews conducted with healthcare professionals practicing in neuro-oncology across Australia. Interview recordings were transcribed and analysed using thematic analysis.

Results: Twenty-two interdisciplinary healthcare professionals practicing in neuro-oncology participated in interviews with a median duration of 34 minutes (range 17 - 57 minutes). Four key themes were developed. The first, "Building trusting relationships," included sub-themes 'Involving and supporting carers,' and 'Respecting patients' autonomy and confidentiality.' The second theme, "What is this brain's story?", incorporated the sub-theme 'Sharing care.' The third theme, "Brief Intervention", encompassed the sub-themes 'Information provision' and 'That's the tumour talking.' Lastly, "Targeted Intervention," includes the sub-themes 'Modifying environments and managing cognitive resources,' 'Acceptance of personality changes,' and 'Enriching the relationship'.
Healthcare professionals recognised the need to build trusting relationships with patients and carers to be able to discuss sensitive or difficult experiences including personality changes. Healthcare professionals emphasised involving carers in patient care and ensuring carers have their own support. Finally, participants highlighted the importance of providing information about causes and contributing factors to BTrPBc and possible impacts on functioning.

Conclusion: Our results provide insight into the diverse support healthcare professionals provide for the management of BTrPBc. Our data point to the potential for a stepped care approach to managing BTrPBc, however further testing in clinical practice is required.

Theme:
Survivorship, Psychology, and Supportive Care

27

Rapid processing and biobanking of resected brain tumour tissue to generate brain tumour explant organoids for preclinical studies

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Aim: Brain tumour heterogeneity presents a major obstacle to identifying effective treatments. A solution is using patient-derived brain tumour explant organoids (GBOs) to predict a patient's response to therapy however generation is time-consuming, costly, and technically challenging. We overcame these limitations by improving the tissue processing workflow and established a patient biobank covering the spectrum of brain tumour heterogeneity for preclinical drug screening.

Methods: We improved an existing protocol to generate GBOs, implementing semi-automated tissue processing, filtration for size-specific isolation, and immediate cryopreservation of tissue pieces post-processing. The GBOs generated were used to compare effects of novel idronoxil-conjugated benzopyran compounds (NX786, NX904) against Bortezomib (100% cell death reference), with GBO size and propidium iodide intensity readouts of growth and death respectively.

Results: Our improved method permitted tissue processing 16 hours post-surgery, expediated tissue processing from 6 to less than 1.5 hours, and tissue cryopreservation facilitated long-term off-the-shelf preclinical GBO analysis. We established a biobank of 24 GBOs from 33 samples (11 males and 13 females) with primary (n=13, GBO Yield (GY)>90%) and recurrent (n=5, GY>90%) glioblastomas, high-grade gliomas (HGG, n=2, GY≤50%), and low-grade gliomas (LGG, n=2 with GY>90%, n=2 with GY≤50%). NX786 and NX904 reduced GBO growth (≥50%) in all primary glioblastoma and one (of two) recurrent glioblastoma GBOs with milder effects in LGG GBOs. Three (of five) primary glioblastoma, both recurrent glioblastomas, and one (of two) LGG GBOs exhibited significant cell death (>60%) in response to NX904, whereas NX786 mediated its effects by inducing senescence.

Conclusions: We provide a new method for efficient processing and cryopreservation of brain tumour tissue, enabling capture of more patient samples across Australia. This allows establishment of a central brain cancer biobank of patient-derived tumour tissue pieces representative of inter-patient brain tumour heterogeneity and is a

valuable resource for preclinical targeted drug screening.

Theme:
Basic / Translational Science

28

Building the bridge to life with brain cancer: leveling up to a national brain cancer consumer resource

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Background: Resources for people with brain tumours (PwBT) traditionally focused on medical and symptom management needs, in the early phases of this challenging diagnosis. Recently, survivorship resources whether as books or online resources, have been developed to target living a good life with a brain tumour diagnosis. The Building the Bridge to Life with Brain Cancer (BTB) resource was developed in 2019 as a Victorian survivorship and self-management resource for PwBT. Since then, there has been interest in extending the resource to meet a national audience. In 2023, funding was secured to update the BTB resource for wider distribution.

Methods: The Project team circulated a call out for feedback and recommendations for BTB to be updated. Phone, video call and in-person consultations were held with neuro-oncology healthcare professionals (HCPs), BRAINS Research Group and Community agencies involved with support for PwBT. Consultations were conducted over 18 months and focused on resource use, identified gaps in the current resource, and recommended additions to content and relevant state-based resources. The project team prioritised feedback and worked with the original design team to create BTB Edition 2024.

Results: Consultations were conducted with 14 HCPs working in neuro-oncology and four community advocacy organisations across all states/territories in Australia. Consultations were conducted over 18 months. The information collated from feedback identified content additions for fertility preservation, aged care support, carer services, palliative care and expansion of state-based support services and resources. The project team prioritised content and design recommendations and worked with the original design team to create BTB Edition 2024, in hard copy and online versions.

Conclusion: The wide consultation process for Building the Bridge to Life with Brain Cancer has ensured a relevant and actionable resource suitable for a national audience, targeting survivorship and self-management for PwBT and their families.

Theme:
Survivorship, Psychology, and Supportive Care

29

Comprehensive Molecular Profiling In CNS Cancers To Inform Post-Operative Management In Routine Neuro-oncology Practice: A Single Centre Experience

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Aims: Molecular profiling for genetic and methylation characteristics is crucial for diagnosing, prognosticating and accessing clinical trials in CNS tumours. Broader variant capture through comprehensive molecular profiling (CMP) using extended next-generation sequencing (NGS) panels and genome-wide methylation assays may improve patient care, however routine implementation remains underreported. We present our centre's experience and clinical benefit from utilising CMP prospectively with targeted NGS and RNA fusion capture, and genome-wide methylation profiling after surgery of CNS tumours between 1st May 2023 and 31st July 2024.

Methods: Eligible patients had primary CNS cancer with adequate tumour tissue from recent surgery (at diagnosis or first recurrence), who may be suitable for systemic therapy. Verbal consent was obtained for CMP in addition to standard diagnostic workup. CMP comprised tissue-based targeted NGS with RNA fusion capture (Oncomine Precision Assay [OPA] or TruSight Oncology 500 [TSO500]) ± methylation profiling (Illumina 850k EPIC Methylation Array).

Results: 103 patients had CMP with a median age 47 years (range: 17 – 76), 73 (70.9%) were male and 57 (55.3%) had glioblastoma. 86 (83.5%) patients had CMP at diagnosis. Median turnaround time was 33, 29 and 44 days for OPA, TSO500, and methylation profiling, respectively. 84 of 102 (82.4%) patients who had NGS had actionable variants (conferring biomarker-eligibility for trials, off-label therapy or drug access program [DAP]). 3 patients were recruited to trials due to CMP results. CMP changed the diagnosis in 2 patients, including a 19M from glioblastoma to germinoma who received curative intent chemotherapy.

Conclusions: Routine CMP is feasible at diagnosis or recurrence with clinically meaningful TAT and enhances diagnostic accuracy and therapy options in a subset of patients. Despite numerous actionable findings, targeted therapy uptake is likely to be curtailed by trial and DAP accessibility, though follow-up data remains immature to estimate true rate of drug access.

Theme:
Clinical Trials and Trials in Progress; Pathology and Genomics; Personalised Medicine and/or Therapeutics

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"We're all just kind of on this weird journey… this is my story": The cognitive journey of people with brain tumour

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Introduction: Cognitive impairment affects up to 90% of brain tumour survivors. Cancer-related cognitive impairment significantly burdens individuals, impeding participation in activities of daily living, driving, working, and impacting familial, social, and professional roles. However, there is limited research exploring the impact of cognitive changes for people with primary brain tumour (PBT). While the domains impacted on objective assessment are well established, the subjective experience of cognitive impairment for people with PBT has received little attention.

Aim: We aimed to explore the lived experience of cognitive changes for people with PBT by examining the most common and impactful cognitive impairments, coping strategies used, and availability and perceived usefulness of cognitive support services.

Method: Using a phenomenological qualitative design, we conducted semi-structured interviews with 17 participants (Mdn=50 years, range 32-71 years, 77% female), diagnosed with PBT (65% high grade glioma). Participants were one to 14 years

(Mdn=3 years) post-diagnosis. Qualitative accounts were audio-recorded, transcribed, and analysed using thematic analysis.

Results: The lived experience of people with PBT was permeated by an overarching theme, 'the cognitive journey of PBT is dynamic and nuanced'. This formed the foundation for six interlinked subthemes, namely: (1) 'varying contexts and their impact on cognition', (2) 'cognitive trajectories are variable', (3) 'impairments in cognitive and related functions are variable', (4) 'perceptions towards cognitive abilities are dynamic', (5) 'impacts of cognition on survivors' lives are variable', and (6) 'access to cognitive support is variable'.

Conclusion: Our results highlight the diverse and nuanced nature of the cognitive journey for individuals with PBT, enriching existing research with firsthand narratives. These findings emphasise the necessity of personalised tailored interventions delivered over time to address fluctuating cognitive challenges. Integrating a standardised model of care for cognition and education for survivors about varied experiences and modifiable factors are essential components of survivorship care.

Theme:
Survivorship, Psychology, and Supportive Care.

31

Ancillary diagnostic testing in newly diagnosed WHO CNS Grade 4 Glioblastoma: a 5-year audit at Sunshine Coast University Hospital (SCUH)

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Introduction: Ancillary diagnostic testing is increasingly important for accurate diagnosis, prognostication and treatment selection in diffuse, adult-type high-grade glioma as per 2021 World Health Organisation Central Nervous System Tumours classification[1]. We assessed the rates of immunohistochemistry (IHC) and molecular testing for newly diagnosed glioblastoma, with reference to European Association of Neuro-Oncology (EANO) guidelines[2].

Methods: A quality assurance audit was undertaken of patients diagnosed with presumed glioblastoma and treated with adjuvant therapy at SCUH between January 2020 – June 2024. Patients were identified through electronic medical records.
Histopathological reports were reviewed to determine the rates of ancillary diagnostic testing.

Results: 86 patients were identified; 79% underwent surgical resection. 84 patients had biopsy or surgery through the Royal Brisbane and Women's Hospital, a tertiary neuro-oncology referral centre. Over the study period, IHC testing for IDH1/2, ATRX and p53 was 100%. MGMT promoter hypermethylation testing increased from 35% to >90% (see Figure 1). BRAF V600E IHC and H3K27M IHC were requested in 4 and 1 patients, respectively. Targeted glioma panel (which includes IDH) and comprehensive genomic profiling by next generation sequencing (NGS) were requested in 20 and 2 patients, respectively. 2 patients were found to be IDH mutant on NGS, leading to revision of their diagnosis to Grade 4 astrocytoma. In general, BRAF V600E IHC testing was reserved for patients with epithelioid glioblastoma whilst targeted glioma panel was requested for patients with diagnostic uncertainty, particularly in younger patients.

Conclusions: At our centre, histopathological reporting of presumed glioblastoma is centralised, with high concordance of local practice with

2021 WHO CNS Classification and EANO guidelines for key diagnostic testing criteria. Since MGMT promoter hypermethylation testing became MBS reimbursed, testing rates are near 100%. BRAF V600E IHC, H3K27M IHC and targeted glioma NGS panels are only selectively utilised; increased utilisation may potentially impact patient management.

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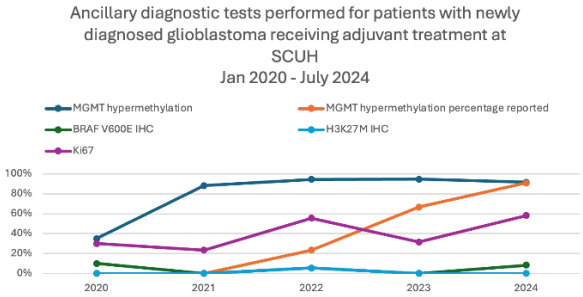
Figure 1.



Theme:
Pathology and Genomics