potential as imaging biomarkers using our minimally-invasive, optimised 12F-MMP-2- 9 MRI biosensor. Thereby, facilitating the prompt provision of personalised adjuvant therapy.

**MBRS-50. PEROXIREDOXIN1 IS A THERAPEUTIC TARGET IN GROUP-3 MEDULLOBLASTOMA**

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Group-3 medulloblastoma (MBL) is highly resistant to irradiation (IR) and chemotherapy and has the worst prognosis. Hence, there is an urgent need to elucidate targets that sensitize these tumors to chemotherapy and IR. Employing standard assays for viability and sensitization to IR, we identified PRDX1 as a therapeutic target in Group-3 MBL. Specifically, targeting PRDX1 RNAi or inhibition of PRDX1 by Adenanthin led to IR and sensitization to IR of Group-3 MBL cells. We rescued sensitization of Daoy and UW228 cells by hyperoxic expression of PRDX1. PRDX1 knockdown caused oxidative DNA damage and induced apoptosis. We concluded that IR-DNA damage, and oxidative stress in tumour microarray. Whole genome sequencing identified pathways/genes that were dysregulated with PRDX1 inhibition or silencing. Our in vivo studies in mice employing flank/orthotopic tumors from patient derived xenografts (PDX) MBL cells confirmed our findings. Animals with tumors in which PRDX1 was targeted by RNAi or Adenanthin (using mini osmotic pumps) showed decreased tumor burden and increased survival when compared to controls. Since, Adenanthin does not cross the blood brain barrier (BBB) we used HAV6 peptide to transiently disrupt the BBB and deliver Adenanthin to the tumor. Immunohistochemistry confirmed that targeting PRDX1 resulted in increased oxidative DNA damage, apoptosis and decreased proliferation. In summary, we have validated PRDX1 as a therapeutic target in group-3 MBL, identified Adenanthin as a SMO inhibitor and a chemo-prodrug of PRDX1 and confirmed the role of HAV peptide (in the transient modulation of BBB permeability) in an orthotopic model of group-3 MBL.

**MBRS-51. SINGLE CELL TRANSCRIPTOMIC ANALYSIS DEFINES DISCRETE SUBPOPULATIONS IN SHH-DRIVEN MEDULLOBLASTOMAS THAT ARE DIFFERENTIALLY AFFECTED BY VISMODEGIB**

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The use of SMO inhibitors for SHH-subtype medulloblastoma has been both promising and problematic. The SMO inhibitor vismodegib met safety and efficacy criteria to be FDA-approved for the treatment of basal cell carcinoma. In medulloblastoma, however, vismodegib therapy has been complicated by the emergence of resistance during treatment. We hypothesized that resistance is driven by a subset of cells with medulloblastomas that relapse despite MATH1 promoter (using MATH1 promoter) together with the Luciferase gene (under the control of Cyclin-B2 promoter) in a background TP53+/-, thus generating Medulloblastoma. Chemotherapeutic drugs for high-risk MB together with AA7.1 were tested in combination on medullospheres showing an impair in vivo, in xenografted studies, we showed tumour inhibition at both the primary and metastatic sites together with immunomodulatory effects. Altogether these results are of importance for future targeted therapies of high risk metastatic MB.

**MBRS-52. TARGETING PRUNE-1 IN A GEMM OF METASTATIC MEDULLOBLASTOMA: A POTENTIAL ROUTE OF INHIBITION FOR NEW FUTURE THERAPIES**

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Genetic modifications during development of paediatric Group 3 Medulloblastoma (MB, Group) are responsible for its highly metastatic properties and poor patient survival outcomes. We found PRUNE-1 to be highly expressed in metastatic MB, which is characterised by TGF-β signalling activation and OX2 expression. The molecular mechanism was identified underlying the metastatic dissemination of those PRUNE-1-driven MB, Group-1, 2, Group-3 MBL, cells confirm that PRUNE-1 acts as a metastatic sponger, activating PRUNE-1 targets that have specific anti-metastatic effects. Altogether these results are of importance for future targeted therapies of high risk metastatic MB.
NOW ENROLLING
Phase 2b study of IGV-001 in patients with newly diagnosed glioblastoma (NCT04485949)

OBJECTIVES
- PRIMARY OBJECTIVE: Progression-free survival
- SECONDARY OBJECTIVE: Overall survival
- SAFETY OBJECTIVE: Safety and tolerability

CRITERIA
Key Inclusion Criteria
- Patients who take part in the trial must:
  - Have newly diagnosed glioblastoma
  - Be 18 to 70 years of age
  - Have a KPS score ≥70 (unable to work but able to care for themselves overall)

Key Exclusion Criteria
- Patients are not allowed to participate in the trial if they have:
  - A tumor that is on both sides of the brain
  - Had previous surgery or anticancer treatment for glioblastoma
  - Glioblastoma that came back
  - Another cancer while having glioblastoma or within the last 3 years that is not cured
  - A weakened immune system (example: HIV, HBV, HCV) or an autoimmune disorder (example: Crohn's disease)
  - Heart disease or history of heart issues

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clinicaltrials.gov/ct2/show/NCT04485949

*Additional criteria apply. Please refer to protocol 14379-201 for full inclusion and exclusion criteria. †Patients can participate if they had some skin cancers, superficial bladder cancer (cancer that was only on the surface of the lining of the bladder), or carcinoma in situ (cancer that had not spread) of the cervix or breast that had been cured.

HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus; IGF-1R, insulin-like growth factor 1 receptor; KPS, Karnofsky Performance Scale; RT, radiotherapy; SOC, standard of care; TMZ, temozolomide.

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