account recent advances in the molecular characterization of tumours. We set out to investigate the effect of EoR on overall survival (OS), and to develop a stratification algorithm incorporating both EoR and modern molecular markers for prognostication. HYPOTHESIS: Greater EoR is independently associated with improved OS. METHODS: We examined 190 consecutive cases of histopathologically confirmed newly-diagnosed glioblastoma who were operated upon between January 1, 2012 and December 31, 2014. Variables including age, sex, postal code, KPS, tumour location, presenting symptoms, treatment history, date of progression, date of reoperation, as well as MGMT, IDH, 1p/19q codeletion, and ATRX status were recorded. Preoperative and postoperative MRIs were reviewed and volumetric tumour burden will be analyzed and EoR will be calculated. RESULTS: Preliminary EoR calculations (n=18) show a positive correlation between EoR and OS. CONCLUSION: A correlation exists between EoR and OS, although multivariable analysis is planned to exclude potential confounders. MRI review, chart review including molecular marker analysis and EoR calculations are ongoing.

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Phase I/II Study of VAL-083 in Patients with Recurrent Glioblastoma

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Glioblastoma (GBM) is the most common brain cancer. Resistance to front-line systemic therapy with temozolomide (TMZ) is correlated with O6-methylguanine-DNA-methyltransferase (MGMT) expression. Second-line treatment with bevacizumab has not improved overall survival. Dianhydrogalactitol (VAL-083) is a bi-functional alkylating agent that has MGMT-independent cell-kill activity against GBM cell-lines and cancer stem cells in vitro. VAL-083 crosses the blood-brain barrier and showed promise against CNS tumors in prior NCI-sponsored clinical trials. The goal of this clinical trial is to determine appropriate VAL-083 dosing for advancement to Phase III trials as a new treatment for recurrent GBM. METHODS: Patients must have recurrent GBM following surgery, radiation, TMZ and bevacizumab. Phase I: Open-label, single-arm, dose-escalation study. Patients received VAL-083 on days 1,2,3 of a 21-day cycle, until reaching MTD. Phase II: Additional patients enrolled at MTD to further assess safety and outcomes. RESULTS: Phase I: 29 patients were enrolled across 9 dose cohorts (1.5-50 mg/m2/d). 40mg/m2/d was confirmed as MTD. Myelosuppression was mild; no drug-related serious adverse events were reported at doses up to 40mg/m2/d. Dose limiting G4 thrombocytopenia was observed at higher doses. Platelet nadir occurred around day 20 and resolved rapidly and spontaneously. A dose-related survival improvement was observed. Pharmacokinetic analyses show 1-2h plasma terminal half-life; average Cmax 781ng/mL at 40mg/m2/d. Phase II: 14 patients were enrolled at 40mg/m2/d. To date, safety observations in Phase II are consistent with Phase I. CONCLUSIONS: VAL-083 at 40mg/m2/d exhibits a favorable safety profile and dose-related trend toward clinically meaningful improved survival in refractory GBM patients.

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Phase II Study of Dianhydrogalactitol in Patients with MGMT-Unmethylated, Bevacizumab-Naïve Recurrent Glioblastoma

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Glioblastoma (GBM) is the most common brain cancer. Most GBM tumors have unmethylated promoter status for O6-methylguanine-DNA-methyltransferase (MGMT); a validated biomarker for MGMT protein-expression and ensuing temozolomide-resistance. Second-line treatment with bevacizumab has not improved overall survival (OS). Dianhydrogalactitol (VAL-083) is a bi-functional alkylating agent targeting N7-Guanine, thus MGMT-independently inducing interstrand cross-links, DNA double-strand breaks and cell-death in GBM cell-lines and cancer stem cells. VAL-083 is currently in Phase I/II clinical trial for recurrent GBM, post-TMZ and post-bevacizumab. In this Phase II clinical trial, the main goal is to assess the 9-month OS in MGMT-unmethylated, recurrent, bevacizumab-naive GBM. RATIONALE: The vast majority of GBM patients experience recurrent/progressive disease within a year from initial diagnosis and median survival after recurrence is 3-9 months. Chemotherapy regimens for these patients are lacking and there is a significant unmet medical need. Given VAL-083's novel alkylating mechanism, promising clinical benefit, and favorable safety profile, a trial studying VAL-083 in MGMT-unmethylated recurrent GBM is warranted. METHOD: Randomized, non-comparative biomarker-driven Phase II clinical trial in MGMT-unmethylated GBM patients at first recurrence/progression, prior to bevacizumab. 48 patients will be randomized to receive VAL-083 or "standard-of-care" salvage drug lomustine. 32 patients will receive VAL-083 40mg/m2/day on days 1,2,3 of a 21-day cycle. 16 patients will receive lomustine 90 mg/m2/day on day 1 of a 42-day cycle. Patients will be followed until death or for at least 9 months from enrollment, whichever occurs earlier. Survival will be compared to the BELOB trial for recurrent MGMT-unmethylated GBM patients treated with lomustine.

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Urban-Rural Residence and Brain Cancer Survival in Canada (1996-2008)

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Disparities in cancer survival rates have been identified for rural patients in Canada and are thought to be due to inequities in access to care. The objective was to perform the first examination of urban and rural brain cancer survival in Canada. Methods: A population-based retrospective cohort study was performed using Canadian Cancer Registry data for patients diagnosed with a primary brain cancer from 1996-2008. Seven major brain cancer histology groups used were glioblastoma, diffuse astrocytoma, glioma (not otherwise specified), oligodendroglioma, anaplastic astrocytoma, oligoastrocytic tumours, and anaplastic oligodendroglioma as categorized by the Central Brain Tumor Registry of the United States (CBTRUS). Kaplan-Meier (KM)