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

K.C. Shih, M.R. Patel, N. Butowski, G.S. Falchook, S.H. Kizilbash, J.A. Bacha, D.M. Brown, A. Steino, R. Schwartz, S. Kanekal, L.M. Lopez, H.A. Burris, III
asteino@delmarpharma.com

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

B.J. O'Brien, J.A. Bacha, D.M. Brown, A. Steino, R. Schwartz, S.Kanekal, L.M. Lopez, M.Penas-Prado
asteino@delmarpharma.com

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)

J. Ross[1], Q. Shi, Y. Yuan, F.G. Davis
[1]University of Alberta, Edmonton, AB
jmross1@ualberta.ca

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)

survival estimates and Cox Proportional Hazards Regression were performed, adjusting for sex, histology, age group, region, and urban-rural residence. Rural residence was defined using Statistics Canada's "Rural and Small Town" definition of living in a region with a population of less than 10,000 people. Results: No significant difference between urban and rural residence was identified in crude KM survival estimates. Though not significant, 5-year survival was generally better among rural residents than urban residents, except for rural residents with anaplastic astrocytoma. There remained no significant difference for Cox hazard ratios after adjustment for age, sex, or region. Conclusions: This is the first study to examine the effect of urban-rural residence on brain cancer survival. No significant differences for any histology were found, indicating equitable access to care for brain cancer patients in Canada, regardless of their location of residence.

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Analysis of Glioblastoma Physical Characteristics in Patients Benefiting from Tumor Treating Electric Fields Therapy

P.P. San[1], J. Timmons, E. Lok, K.D. Swanson, E.T. Wong
[1]Harvard Medical School/Beth Israel Deaconess Medical Center
ewong@bidmc.harvard.edu psan@bidmc.harvard.edu

Tumor treating electric fields (TTFields) are an established treatment for glioblastoma patients. But the anatomical and physical characteristics of the brain and tumor contributing to treatment efficacy are unknown. We contoured gross tumor volume (GTV) using ScanIP and measured tumor size according to the RANO criteria on 5 patients with recurrent glioblastomas who benefited from TTFields (cohort 1) and 5 who did not (cohort 2). Tumor surface area and geometric centroid distance (GCD) from the bilateral ventricles were computed. Wilcoxon rank sum test was used to compare these physical parameters between the two cohorts. The results showed that the respective median GTV was 11.6cm3 and 38.1cm3 (P=0.0591), while the respective median GCD was 5.0cm and 5.3cm (P=0.6761), in cohort 1 and 2. The tumor size had a median of 8.2cm2 in cohort 1, as compared to a median of 53.9cm2 in cohort 2 (P=0.0591). The surface area had a median of 56.2cm2 in cohort 1, as compared to a median of 214.0cm2 in cohort 2 (P=0.4034). After removing an outlier from cohort 1 and another from cohort 2, the respective median GTV was 9.7cm3 and 41.3cm3 (P=0.1003), and the respective median surface area was 46.5cm2 and 236.0cm2 (P=0.0304). The respective median surface area/GCD was 13.3cm and 38.9cm (P=0.0304) and the respective median GTV/GCD was 2.7cm2 and 8.5cm2 (P=0.0304). The data suggest that the ratio of surface area/GCD and GTV/GCD, which are proportional to the tissue capacitance, may be an important parameter for optimizing TTFields efficacy in the treatment of glioblastoma.

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Is Conventional and Perfusion MRI Useful in Predicting Histopathology Defined Percentage of Recurrence in High Grade Gliomas

T.B. Nguye, University of Ottawa, Ottawa, ON
thnguyen@toh.on.ca

New enhancing lesions after surgery and chemoradiation for high grade glioma commonly contain variable proportions of tumor recurrence (TR), tissue necrosis and treatment related changes. Our purpose is to determine whether the pattern of contrast enhancement and perfusion MR parameters correlate with the percentage of TR in these lesions. Methods: We prospectively enrolled 30 patients with high grade gliomas who presented with a new enhancing lesion suspicious for tumor recurrence. Each patient underwent conventional MRI with DCE and DSC perfusion MRI. The pattern of enhancement was classified by a blinded neuroradiologist in 5 different categories (solid, focal nodular, peripheral rim, hazy, punctate). A hot spot region-of-interest analysis was performed for each parametric map (Ktrans, AUC, Vp, corrected CBV). TR percentage was defined histopathologically. The lesions were categorized into predominant TR (=tumor>70%), predominant treatment related changes (T=<35%) and mixed lesions (35 %< T=<70%). Differences between the groups were assessed via Kruskal-Wallis and Mann-Whitney U tests. Results: There were 32 lesions (4 predominantly treatment related lesions,5 mixed lesions,23 predominant tumor recurrence). There is no significant difference in the enhancement pattern between the three groups (p=0.18).Statistically significant difference was only seen for corrected CBV between the three groups (p=0.01), mainly between the mixed and predominant tumor groups. The rest of the perfusion parameters did not show a statistically significant difference between the groups(p>0.05). Conclusion: Corrected CBV might be useful in predicting the proportion of tumor recurrence in post-treatment high grade gliomas.

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Impact of Functional Magnetic Resonance Imaging on Clinical Decision Making and Outcomes in Patients with Low Grade Gliomas

E. Kosteniuk[1], J.C. Lau, J.F. Megyesi
[1]School of Medicine and Dentistry, University of Western Ontario, London, ON
skosteniuk2018@meds.uwo.ca

This study aims to evaluate the impact of preoperative functional magnetic resonance imaging (fMRI) on low grade glioma (LGG) patients' outcomes and surgical planning. Methods In this retrospective matched cohort study of a single surgeon's patients, we are comparing two groups of LGG patients (WHO grade II) based on exposure to fMRI. Sixteen LGG patients who underwent fMRI were selected, and 32 control (non-fMRI exposed) patients are being selected through propensity score matching from a pool of 764 brain tumour patients. To assess the impact of fMRI data on clinicians' decision making process, neurosurgeons within a single centre are completing questionnaires regarding treatment options for each LGG fMRI patient based on clinical data and structural imaging before and after fMRI. Results Within the group of 16 LGG patients who have undergone fMRI studies over a 12-year period, most patients presented with seizures (81 percent), and most lesions were left-sided (81 percent) and frontal (75 percent). Patients underwent either craniotomy (50 percent), stereotactic biopsy (25 percent) or nonsurgically management (25 percent). In surgical patients, between presurgical assessment and eight week post-surgical follow-up, mean modified Rankin scale improved from 1.80 (sd 0.79) to 1.50 (sd 0.97). In our cohort, 5-year