Canada is unknown. We compared cohorts between 2 regional Canadian Cancer Centres for differences in patient factors, treatments, and outcomes. Methods Cohorts were constructed by a hybrid of retrospective chart review and prospective data collection consisting of all consecutive cases eligible for standard treatment. Demographics, pathology, treatment, and outcome data were obtained. Results The two cohorts (Winnipeg n=80 and Calgary n=103) were similar in terms of median age (57 and 56), percent male (62.5% and 63.1%), percent with good performance status (93.8% vs 85.4%) and extent of resection (gross total/sub-total/biopsy: 17.5%/66.3%/16.3% in Winnipeg and 7.8%/ 68.9%/23.3% in Calgary). Of patients with known MGMT promoter methylation status 28% were methylated in Winnipeg and 58% were methylated in Calgary. Greater than 6 cycles of chemotherapy was given to 42.5% of patients in Winnipeg and 28.1% in Calgary. The most common second line therapies differed: carboplatin and tamoxifen (31.3%) in Winnipeg; low dose temozolomide (26.2%) in Calgary. Significant poor prognostic factors for survival in the combined cohort included age (HR 1.02), extent of resection (sub-total HR 1.7; biopsy HR 8.9) and location (Calgary HR 1.17). Conclusion Comparison of cohorts from different parts of Canada can provide interesting descriptions of patterns of practice. These patterns may be useful in determining opportunities for quality improvement and clinical trial development.

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Glioblastoma multiforme in elderly and non-elderly patients in Newfoundland and Labrador: A province-wide six-year analysis.

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Glioblastoma multiforme (GBM) is a devastating and generally incurable malignancy, with increasing incidence in elderly patients. Although advances in adjuvant chemoradiotherapy have shown promise in improving survival, the benefit of these therapies in elderly patients remains unclear. In this population-based retrospective study, we compared treatment patterns and outcomes in elderly (defined as age 65 or older) and non-elderly patients diagnosed with GBM in Newfoundland and Labrador. During 2006-2012, one-hundred-and-thirty-eight patients received a pathological diagnosis of GBM. Median age at diagnosis was 62.5 years (range 20-85) and 56(40.5%) were age 65 or older. Elderly patients were more likely to present with a performance status of ECOG 3 or greater ($p < 0.01$) and to undergo stereotactic biopsy rather than surgical resection ($p = 0.04$), and less likely to receive adjuvant temozolamide chemotherapy ($p < 0.001$). Presence of gross neurological defects and treatment with radiation therapy did not differ between elderly and non-elderly patients. Median survival was 245(CI[95%] 165-269] days for elderly patients versus 342(CI[95%] 274-440] days for non-elderly patients ($p < 0.01$). In Cox multivariate analysis, chemotherapy was associated with improved survival in elderly patients after adjusting for functional status and extent of resection ($p < 0.001$) and was the strongest predictor of overall survival across patients in both age groups ($p < 0.001$). Despite receiving less aggressive surgery and chemotherapy, elderly patients showed evidence of improved survival with adjuvant temozolamide. These data support the growing body of evidence that adjuvant chemoradiotherapy may be beneficial in selected elderly patients with GBM.

SCIENTIFIC POSTER VIEWING

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SP1

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RXFP1 promotes temozolomide (TMZ) chemoresistance in brain cancer

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Current treatments for Glioblastoma (GB), the most aggressive form of primary brain cancer, include surgery, radiation and chemotherapy. TMZ is the most commonly used alkylating agent for GB treatment, but chemoresistance to TMZ is frequently an unsatisfactory treatment outcome. Relaxin Family Peptide Receptor 1 (RXFP1) mediates RLN2-induced cell migration and tissue invasion in many cancer entities including brain cancer. We have discovered RXFP1 expression in GB cells and tissues, but not in normal astrocytes. Down-regulation of RXFP1 in primary GB cells suppressed cell survival, cell invasiveness and induced cell death via a caspase3/7 mediated apoptosis pathway. Importantly, RXFP1- activation enhanced cell survival in primary GB cells treated with TMZ. To elucidate the mechanisms of RXFP1-mediated chemoresistance in GB cells, we identified the RXFP1-mediated up-regulation of anti-apoptotic proteins. In addition, several DNA repair proteins and Base Excision Repair (BER) members were regulated upon RXFP1 activation. Our results suggest that RXFP1 promotes TMZ chemoresistance by enhancing BER function and by suppressing apoptosis, thus, protecting primary GB cells from TMZ-induced DNA damage.

SP2

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Chloroquine inhibits the malignant phenotype of glioblastoma in vitro

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Introduction: Glioblastoma (GBM) are characterized by enhanced migration and invasion abilities inherent to massive brain infiltration and hence abridged surgical resection. Together with their recognized treatment non-compliance, responses to standard therapy are invariably transient and recurrence is thus inevitable. Transforming Growth Factor-beta (TGF-b) is over-expressed and correlates with tumour aggressiveness. This cytokine heavily promotes invasion, proliferation as well as radioresistance of the tumour cells. We have already observed that treatment with chloroquine, a well-known antimalarial drug, produced important reduction in secretion of two TGF-b isoforms, TGF-b1 and 2. Objective. Our objective was to assert the efficiency of chloroquine as to abrogate GBM invasion, proliferation and radioresistance. Results: In immortalized GBM cell lines (U-373 MG et U-87 MG) as well as in primary cultures from GBM patients, TGF-b inhibition halved glioma invasion measured in Matrigel-coated transwell invasion assays. Cell cycle analysis, immunofluorescence (against Ki-67 and cleaved caspase 3) as well as proliferation assays also show a 50% inhibition of the cell proliferation correlated with increases of apoptosis. Chloroquine treatment also radiosensitizes GBM cells as shown by an accumulation in the G2/M phase and increased cell death analyzed by flow cytometry. Discussion. We will confirm the radiosensitization effect of chloroquine with DNA damage analysis with TUNEL assays and gamma-H2AX immunofluorescence. Conclusion: These promising results suggest that using chloroquine to inhibit TGF-b might be an compelling therapeutic strategy and could benefit GBM afflicted patients.

SP3

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Characterization of the chemoresistance profiles of malignant gliomas- A step towards a predictive individualized treatment

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It is now a cliché to introduce malignant gliomas as aggressive tumours that remain incurable, despite decades of research. Median survival of patients bearing GBM remains 15 months with the current standard of care. Chemoresistance represents a significant problem, and only a subset of treated patients respond to chemotherapy. Among the chemoresistance mechanisms, the ABC transporters, expressed at the cell membrane of glial cancer cells as well as at the BBB and BTB, represents a clear impediment to chemotherapy efficacy. These efflux pumps purge the chemotherapeutic agents out of the cancer cells and out of the CNS. The overexpression of these proteins could also explain the emergence of resistance. We thereby undertook the analysis of the expression profile of MDR1, MRP1, MRP3 and BCRP, in a population of 122 GBM patients locally operated and treated, and to study this expression as a clinical surrogate for chemotherapy response at first and second-line treatment, as well as survival. As recent studies have demonstrated that these ABC transporter proteins display an avidity to uptake standard chemotherapeutic agents such as doxorubicin, etoposide, and vincristine as substrates, as well as the new class of small inhibitors of the tyrosine kinase receptor such as Imatinib, Elortinib, and Gefitinib, the relevance of conducting an extensive characterization of their expression profiles is all too obvious. Results will be compared to the expression in normal samples (n=10) obtained through the Douglas Hospital, Montreal.

SP4

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PRDX1 as a radiosensitization target in ATRT

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Purpose/Objective: Atypical teratoid rhabdoid tumors (ATRTs) are rare central nervous system tumors occurring exclusively in infants and children. Radiation is an important component of treatment. The overall prognosis of ATRTs is extremely poor with median survival of 10-18mths from the time of diagnosis. Peroxiredoxin 1(PRDX1) is a thiol-dependent antioxidant enzyme that is over-expressed in multiple cancers. PRDX1 is also a cancer biomarker with over expression indicating advanced disease, increased angiogenesis, metastasis and poor outcome in several cancers. Down regulation of PRDX1 has been shown to have radio-sensitizing effects in lung cancer and other tumors. We investigated role of PRDX1 as a radio-sensitization target in ATRT. Methods: Gene expression analysis was done to find out the expression levels of PRDX1 in ATRT. We used siRNA transfection to knock down PRDX1 expression in primary ATRT cell lines BT-PA1 and BT-12/BT-16. A small molecule inhibitor (Adenanthin) was used to inhibit the activity of PRDX1. An MTS assay was used to evaluate radio-resistance after irradiation. The protein expressions were analyzed with immunoblotting. Results: PRDX1 is over expressed in ATRT cells similar to Group-3 Medulloblastoma cells. This was confirmed by both gene expression profiling and protein levels. Down regulation of PRDX1 by siRNA sensitizes ATRT cells to irradiation. Adenanthin inhibition of PRDX1 also caused similar radio-sensitization comparable to siRNA knockdown. Conclusions: PRDX1 plays a role in radio-resistance in ATRT tumors. Adenanthin is a selective PRDX1 inhibitor. Further in vitro/ in vivo studies are required to validate PRDX1 as a potential radio-sensitization target in ATRT tumors.