leuko-, lympho- and thrombocytopenia during temozolomide RCT with OS (36 vs. 54, 37 vs. 54 and 36 vs. 57 weeks, respectively; all p-values <0.05). In male patients there was also a trend for this unfavorable effect. Additionally, severe cytopenia correlated with reduced temozolomide dose exposure during RCT (all p-values <0.05 in total cohort) and reduced dose exposure was independently associated with worse OS (p-values <0.05 in the total and female cohort). CONCLUSION: Our data confirm that women are at higher risk for treatment-induced cytopenia during RCT which is associated with a significant decrease in OS. From our data, it appears plausible that reduced temozolomide dose exposure during RCT is at least in part responsible for this finding. Immunosuppression of patients with severe cytopenia may be an independent contributor to adverse outcome.

P14.12 GYRIFORM INFILTRATION AS IMAGING BIOMARKER FOR ADULT DIFFUSE ASTROCYTIC GLIOMA, IDH WILDTYPE, WITH MOLECULAR FEATURES OF GLIOBLASTOMA

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BACKGROUND: Diffuse astrocytic gliomas, IDH wildtype, with molecular features of glioblastoma (molecular glioblastomas) are associated with a poor prognosis. We previously found that these tumors frequently display gyriform infiltration, defined as areas of elective cortical hypersignal on MRI FLAIR sequence. The objective of the present study was to assess the diagnostic value of gyriform infiltration as an imaging marker for these tumors. MATERIAL AND METHODS: MRI scans from 430 patients with newly diagnosed glioma (molecular glioblastoma n = 31, IDH wildtype glioblastoma n = 298, IDH-mutant astrocytoma n = 50, IDH-mutant and 1p19q codeleted oligodendroglioma n= 51) were evaluated for the presence of a gyriform infiltration by 2 independent reviewers. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the performance of the presence of a gyriform infiltration for identifying molecular glioblastoma. RESULTS: A gyriform infiltration was observed in 16/31 (52%) patients with a molecular glioblastoma, 40/298 (13%) patients with an IDH-wildtype glioblastoma but in none of the patients with an IDH-mutant astrocytomas or an IDH-mutant and 1p19q codeleted oligodendroglioma. Among the 56 patients with a gyriform infiltration, 54 patients had an IDH wildtype pTERT mutant glioma and 2 an IDH wildtype pTERT wildtype glioma. Interrater agreement was good (κ= 0.68, $P < 0.001$). Specificity, sensitivity, PPV and NPV of the presence of a gyriform infiltration for the diagnosis of molecular glioblastoma were 90%, 29%, 52% and 96% and for the diagnosis of an IDHwt pTERT mutant glioma were 97%, 15%, 96% and 20%. The presence of a gyriform infiltration was associated with a worse prognosis in the entire cohort (13.6 months vs 29.3 months, $P = .001$). CONCLUSION: Gyriform infiltration is a specific imaging marker of molecular glioblastomas and IDH wildtype pTERT mutant diffuse gliomas.

P14.13 SEVERE HEMATOLOGICAL TOXICITY DURING CHEMORADIATION FOR GLIOBLASTOMA: IDENTIFICATION OF CLINICAL AND PHARMACOLOGICAL RISK FACTORS AND CONSEQUENCES FOR THE INDIVIDUAL PATIENT

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BACKGROUND: Besides early tumour progression, standard first-line radiation with concurrent and adjuvant temozolomide in de novo glioblastoma patients is abrogated frequently by severe haematological toxicity. This leads to treatment delays with unknown effect on efficacy and to more hospital visits with increased disease burden. In the present study, we identified clinical and pharmacological risk factors for temozolomide induced severe hematological toxicity. Furthermore, we describe the burden of toxicity for patients and evaluate the effect of severe toxicity on prognosis. METHODS: A retrospective cohort study of adult patients with a histological confirmed glioblastoma (n=363), treated with standard treatment regimen at the Brain Tumor Center Amsterdam between 2000 and -2020. Severe haematological toxicity was defined as a CTCAE (version 5.0) grade ≥3. We used Pearson Chi-Square test to analyze differences in patient characteristics between the groups (no vs. severe toxicity) and paired samples T- Test to analyze fluctuations in cell counts. Univariate and multivariate logistic regression were used to identify patient- and treatment characteristics associated with severe hematological toxicity. Cox Proportional Hazards models were used to estimate Hazard Ratio's for the association between survival and severe hematological toxicity. RESULTS: Female gender (OR 8.05, 95%CI 2.96–21.89, p<0.001) and older age (age > 70 years; OR 2.44, 95%CI 1.12–5.31, p=0.025) were independent risk factors for severe toxicity. Concurrent and adjuvant temozolomide was discontinued in respectively 56% and 35% of the patients. In general, patients with severe hematological toxicity had a treatment delay of 22 ± 48 days. Of all patients with severe hematological toxicity during chemoradiation, 96% developed toxicity after ≥4 weeks of treatment (p<0.001). Females who received highest temozolomide-doses (4th quartile) had a longer survival than females with low cumulative temozolomide doses (1st quartile). Patients, who developed severe toxicity had much more hospital visits (20; range 12–26), and were admitted more frequently to the hospital. Severe haematological toxicity was not related to survival (HR 1.04; 95%CI 0.74–1.45). CONCLUSION: Female gender and age >70 years are risk factors for severe hematological toxicity. Severe hematological toxicity relates to temozolomide exposure and results in a significant treatment burden for patients. Low temozolomide exposure results in decreased survival. Patient tailored therapy may result in better treatment outcomes.

P14.14 ADJUVANT TREATMENT VERSUS INITIAL OBSERVATION IN NEWLY DIAGNOSED WHO GRADE II AND GRADE III OLIGODENDROGLIOMA: REAL-LIFE DATA FROM TWO ACADEMIC, TERTIARY CARE CENTERS IN AUSTRIA

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BACKGROUND: Oligodendrogliomas are rare, slow-growing brain tumors with a survival prognosis of >10 years. Although adjuvant radiochemotherapy has been shown to prolong survival, aggressive treatment comes at the cost of increased toxicity. Systematic data on the optimal timing of adjuvant treatment in oligodendroglioma are lacking. MATERIAL AND METHODS: Patients treated for a newly diagnosed IDH-mutated, 1p/19q-codeleted oligodendroglioma (WHO grades II/III) in 2000 - 2018 at the Medical University of Vienna or the Kepler University Hospital Linz (Austria) were included in this retrospective study. Adjuvant treatment was defined as radiotherapy (RT), chemotherapy (CHT) or radio-chemotherapy (R-CHT) within 6 months after resection in the absence of progression. "Wait and see" was defined as regular follow up with magnetic resonance imaging and treatment at progression. RESULTS: 185 patients were identified, comprising 123/185 (66.5%) WHO grade II and 62/185 (33.5%) WHO grade III oligodendrogliomas. Median age at diagnosis was 42 years (range: 20–82). Gross total resection (GTR) could be achieved in 77/178 (42.3%) evaluable patients. Adjuvant treatment was applied in 63/185 (38.2%) patients, of whom 43/63 (68.3%) underwent R-CHT, 9/63 (14.3%) CHT only and 11/63 (17.5%) RT only. 43/52 (82.7%) received temozolomide-based treatment, 1/52 (1.9%) procarbazine, lomustine and vincristine (PCV), 1/52 dacarbazine/fotemustine and in 7/52 (13.5%) patients, no data on used regimens was available. Adjuvant treatment was more frequently applied in WHO grade 3 tumors (p<0.001), while there was no association of adjuvant treatment with extent of resection (p=0.24). Patients after GTR who underwent adjuvant therapy presented with longer progression-free survival (PFS) compared to patients initially managed with observation (median: 150 months, 95%CI: 100 - not reached (n.r.) vs. median: 101 months, 95%CI: 73.2–115; p=0.053). In non-GTR tumors, patients with adjuvant

therapy presented with a significantly longer median PFS of 107.5 months (95%CI: 62.8-n.r.) as compared to patients initially managed with observation (45.3 months, 95%CI: 41.2–78.8; p=0.025). CONCLUSION: The application of adjuvant therapy was associated with favorable PFS in patients who underwent resection of newly diagnosed oligodendroglioma in this retrospective study. Prospective clinical trials should investigate the risks and benefits of adjuvant treatment versus initial observation in patients with oligodendroglioma.

P14.17 CONVENTIONAL MRI CRITERIA DIFFERENTIATE TRUE TUMOUR PROGRESSION FROM TREATMENT-INDUCED EFFECTS IN IRRADIATED WHO GRADE 3 AND 4 GLIOMAS

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BACKGROUND: Post-treatment radiological deterioration of patients with an irradiated high-grade (WHO grade 3 and 4) glioma (HGG) may be the result of true progressive disease (PD) or treatment-induced effects (TIE). Differentiation between these two entities is of great importance, but remains a diagnostic challenge. This study assesses the diagnostic value of conventional MRI characteristics to differentiate PD from TIE in treated HGGs. MATERIAL AND METHODS: In this single-centre, retrospective cohort study, we included adult patients with a HGG, who were treated with radiotherapy and subsequently developed a new or increasing contrast-enhancing lesion on conventional follow-up MRI. TIE and PD were defined radiologically as stable/decreased for a minimum of six weeks or progressive according to the RANO criteria, and histologically as predominantly TIE without viable tumour or PD. Demographic and clinical data were retrieved. Twenty-one preselected MRI characteristics of the progressive lesions were assessed by two neuroradiologists. The statistical analysis included logistic regression to develop a) a full multivariable model b) a diagnostic model with model reduction, and a Cohen's Kappa interrater reliability coefficient. RESULTS: 210 patients (median age 61, IQR=54–68, 189 males) with 284 lesions were included, of which 141 (50%) had PD. Median time to PD was 2 (0.7–6.1) and to TIE 0.9 (0.7–3.5) months after RT. In multivariable modelling and after model reduction, the following determinants were significant diagnostic factors: Radiation dose (Odds ratio (OR)=0.68, p=0.017), longer time since radiotherapy (OR=3.56, p<0.0005), certain enhancement patterns (soap bubble enhancement: OR=2.63, p=0.003), isointense apparent diffusion coefficient-signal (OR=2.11, p=0.036), development of multiple new lesions (OR=1.68, p=0.088) and increased marginal enhancement (OR=2.04, p=0.027). ORs of >1 indicate higher odds of PD. The Hosmer & Lemeshow test showed a good calibration (p=0.947) and the area under the ROC-curve was 0.722 (95%-CI=0.66–0.78). Interrater reliability analysis between neuroradiologists revealed moderate to near-perfect agreement for the significantly predictive items, but poor agreement for others. CONCLUSION: In patients with irradiated high-grade gliomas, several characteristics from conventional MRI are significant predictors for the discrimination between true progression and treatment-induced effects. Interrater reliability for these characteristics was variable. Conventional MRI characteristics from this study should be incorporated into a multimodal diagnostic model that includes advanced imaging techniques.

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P14.18 PATIENT AND PUBLIC INVOLVEMENT TO DEFINE PATIENT-CENTRED OUTCOMES FROM NATIONAL CANCER DATASETS

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BACKGROUND: GlioCova uses linked national cancer data on all 51 000 adult patients with a primary brain tumour in England (2013 - 2018) to understand patterns of care, treatment, and outcomes in patients with glioma (http://wwwf.imperial.ac.uk/blog/gliocova/). A key aim is the use of patient and carer input in defining patient-centered outcomes. We have held multiple Patient & Public Involvement (PPI) sessions with patients and carergivers and data analysts to understand what patient and caregivers want to know about brain tumours. MATERIAL AND METHOD: We used a modified Delphi method. The online PPI sessions (Zoom) consisted of two presentations, open discussions, and Q&As. We made the sessions as interactive as possible by using Mentimeter and an interactive online white board (Explain Everything). Pre-reading material was circulated via email. Attendees (6–14 per session) covered a wide range of ages (30–75), diagnoses (GBM, recurrent gliomas, low grade gliomas, ependymoma); patients, caregivers, neuro-oncology staff, data analysts and basic scientists. Work was conducted in line with the INVOLVE PPI guidance. RESULTS: We identified four questions that were of interest to patients and had correlates in the data:

Ø Potential symptoms experienced 3-months pre-diagnosis;

Ø Side effects, 3-months post-diagnosis;

Ø The survival following different treatments (i.e., surgery only, radiotherapy only);

Ø Demographics of patients who finished/ did not finish 6 cycles of temozolomide;

Patients and caregivers were also interested in the impact of diet, quality of life, social life, and exercise. However, these data cannot be answered using the current national data. CONCLUSION: Our PPI work has helped us to identify and prioritise questions to ask of the data. Ongoing PPI work will provide a wider perspective and identify knowledge gaps for future research. Patients and caregivers report feeling empowered, being part of a team, feeling like they had given something back and done something meaningful for the research community and other patients. Patients and caregivers also felt that they had an enriched understanding of the data that is collected. As this process is an iterative process, we will hold more PPI sessions to identify and prioritise topics to analyse.

** are brain tumour patients and caregivers*

P14.19 REGORAFENIB IN RECURRENT GLIOBLASTOMA PATIENTS: A LARGE REAL-LIFE EXPERIENCE

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BACKGROUND: Regorafenib (REG), an oral multikinase inhibitor of angiogenic, stromal, and oncogenic receptor tyrosine kinases showed encouraging benefit in recurrent GBM patients enrolled in the randomized, phase 2 REGOMA trial. We investigated the clinical outcome and safety of REG in a real-life population of recurrent glioblastoma patients treated at Veneto Institute of Oncology as off-label use. MATERIAL AND METHODS: Patients receiving REG at Veneto Institute of Oncology (Padua, Italy) were entered prospectively on a clinical database. Data were retrospectively analyzed. The primary endpoints of the study were overall survival (OS) and safety. The major inclusion criteria were: histologically confirmed diagnosis of GBM, disease progression as defined by RANO criteria after surgery followed by radiochemotherapy with temozolomide, ECOG PS ≤ 2; PTS with ≥ 2 prior lines of therapy were excluded. According to original schedule, patients received REG 160 mg once daily for the first 3 weeks of each 4-week cycle until disease progression, death, unacceptable toxicity, or consent withdrawal. Kaplan-Meier method was used to estimate the survival curves, RANO criteria for radiological assessment, CTCAE v5.0 for drug related adverse events. RESULTS: From February 2018 to September 2020, 54 consecutive patients were treated with REG and enrolled in this study: median age was 56, ECOG PS 0–1 in 91% of patients, MGMTmet in 53%, second surgery at the time of relapse were performed in 30% of enrolled patient, 41% of patients underwent steroids at baseline. At the time of analysis, median follow-up was 11.1 ms, 30 PTS (56%) had died and 50 PTS (93%) had progressed. Median OS was 10.2 ms (95%CI, 6.4–13.9), 12m-OS was 43%; median PFS was 2.3ms (95%CI, 1.3–3.3) and 6m-PFS was 18%. All patients were evaluable for response: disease control rate (DCR) was 46.3%; stable disease was reported in 38.8% and partial response in 7.4%. Age, MGMT status and corticosteroid use at baseline were not statistically significant on multivariate analysis for OS. Grade 3 drug-related adverse events (AEs) occurred in 10 patients (18%) and the most frequent were hand-foot skin reaction, asthenia and increased lipase and transaminases; 1 PT (2%) reported a grade 4 AE (rash maculo-papular). AEs led to REG dose reductions in 37% of patients and, it was permanently discontinued in 5%. No death was considered to be drug-related. CONCLUSION: We reported a large, mono-institutional "real world" experience of REG in recurrent glioblastoma patients. Overall, results are close to those reported in REGOMA trial although, we showed a longer OS. Toxicity was moderate and manageable. Encouraging clinical benefits of REG in recurrent GBM population were confirmed.

P14.20 QUALITY OF LIFE OF PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA DURING TTFIELDS THERAPY IN ROUTINE CLINICAL CARE: FIRST RESULTS OF THE TIGER STUDY

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