MATERIAL AND METHODS: This prospective, monocentric study included adult BC patients with suspected LM (clinical and/or radiological signs). CSF samples from 1–3 lumbar puncture(s) were analyzed: protein level, conventional cytology (60 drops), and CTC detection with the CellSearch® system (60 drops, first lumbar puncture only). Sensitivity (Se) and specificity (Sp) were calculated, using the results of the conventional cytology as the gold-standard. RESULTS: Forty-nine eligible patients were included (Jan 2017-Jan 2020): median age 51.8, 95.9% women, 20.4% HER2+ BC, 93.8% previously diagnosed with metastatic BC, 89.8% with clinical symptoms. Among them, 40 were evaluable (CTC detection failure: n=8, eligibility criteria failure: n=1). Median sample volume was 3.0 mL for conventional cytology samples (median time to analysis: 22min) and 3.3 mL for CTC samples. Of the 40 evaluable patients, 18 had a positive cytology (on CSF sample n=°1/n°2: n=16/n=2) and were therefore diagnosed with LM using the gold-standard method. Protein level was elevated in 88.2% of these patients, compared with 45.1% of patients with negative CSF cytology (p=0.005). CTCs were detected in these 18 patients (median 5824 CTCs, range 93-45052). CTCs were also detected in 5/22 patients with a negative cytology (median 2 CTCs, range 1–44). Among them, one patient (44 CTCs) was diagnosed with a cytologically-proven LM 9 months later, while there was no further argument for LM in the other 4 patients' history (1–3 CTC), who died of the extra-cerebral disease after a median time of 5.2 months (range 0.9–25.9). The detection of at least one CTC in CSF was associated with a Se of 100.0% (IC95% 82.4–100) and a Spe of 77.3% (IC95% 64.3–90.3) for the diagnosis of LM. CONCLUSION: CTCs were detected with the CellSearch® system in all patients diagnosed with a cytologically-proven LM, as well as in a few patients without a cytological confirmation of LM. The prognosis of these patients with CSF cytology$^-$/CTCs$^+$ needs to be further investigated in a larger cohort.

P14.06 RADIOMICS FOR THE NON-INVASIVE DETERMINATION OF THE BRAF MUTATIONAL STATUS IN PATIENTS WITH MELANOMA BRAIN METASTASES

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BACKGROUND: The BRAF V600E mutation is present in approximately 50% of patients with melanoma and is an important prerequisite for a response to targeted therapies such as BRAF inhibitors. In the majority of patients, the BRAF mutational status is based on the analysis of tissue samples from the extracranial primary tumor only. Since the extracranial and intracranial BRAF mutational status may be discrepant, the additional information on the BRAF mutational status of melanoma brain metastases would be of clinical value, e.g., for the prediction of response to targeted therapies. Here, we evaluated the potential of structural MRI radiomics for the determination of the intracranial BRAF mutational status in patients with melanoma brain metastases. MATERIAL AND METHODS: Fifty-nine patients with melanoma brain metastases from two university hospitals (group 1, 45 patients; group 2, 14 patients) underwent surgery with subsequent genetic analysis of the brain metastases tissue to determine the BRAF mutational status. All patients underwent structural MRI preoperatively. Areas of contrast enhancement were manually segmented and analyzed. Group 1 was used for model training and validation, group 2 for model testing. After image preprocessing, 1,316 radiomics features were extracted using the open-source PyRadiomics package. A test-retest analysis was performed to identify robust features prior to feature selection. Finally, the best performing radiomics model was applied to the test data (group 2). Diagnostic performances were evaluated using receiver operating characteristic (ROC) analyses. RESULTS: Twenty-two patients (49%) in group 1, and 6 patients (43%) in group 2 had an intrametastatic BRAF V600E mutation. Using a six parameter radiomics signature, a linear support vector machine classifier yielded an average area under the ROC curve (AUC) of 0.87 (accuracy, 85%; sensitivity, 78%; specificity, 91%) for prediction of the BRAF mutational status in the training data (group 1). Finally, the classifier achieved an AUC of 0.85 (accuracy, 86%; sensitivity, 83%; specificity, 88%) in the test data (group 2). CONCLUSION: The developed radiomics classifier allows a non-invasive prediction of the intracranial BRAF V600E mutational status in patients with melanoma brain metastases and may be of value for treatment decisions.

P14.09 BORTEM-17: A PHASE IB/II SINGLE-ARM, CONTROL NON-RANDOMIZED, MULTICENTRE, OPEN LABEL CLINICAL TRIAL FOR RECURRENT GLIOBLASTOMA WITH UNMETHYLATED MGMT PROMOTER (NCT03643549)

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BACKGROUND: Glioblastoma (GBM) is the most malignant primary brain tumor in adults where median survival in unselected patients is approximately 10 months. There is no standard treatment for patients who progress on temozolomide and patients are best treated within investigational clinical protocols. Patients harbouring tumours with functional O^6 methylguanine DNA methyltransferase (*MGMT*) DNA repair enzyme have particularly poor prognosis with median overall survival of 12.7 months, compared to 21.7 months for patients with hypermethylated MGMT promoter. The pre-clinical studies have shown that Bortezomib depletes the MGMT enzyme, restoring the tumour´s susceptibility to Temozolomide, if the chemotherapy is administered in the precise schedule when the MGMT enzyme is depleted. Additionally, Bortezomib shows an antitumour effect by blocking autophagy flux. Based on the promising pre-clinical results, a non-randomized, open label phase IB/II clinical trial was designed. The primary endpoints include assessment of safety of Bortezomib administered with Temozolomide for phase IB and median progression free survival, overall survival as well as progression free rate at 6 months. MATERIAL AND METHODS: Recurrent glioblastoma patients with unmethylated MGMT promotor, progressing at least 12 weeks after completion of postoperative radiotherapy, with adequate organ function, performance status Karnofsky 70 or better and radiologically measurable lesions are screened for study inclusion. The experimental treatment consists of Bortezomib 1.3mg/m^2 administered IV on days 1, 4, 7, during each 4-week chemotherapy cycle with per oral Temozolomide at 200mg/m^2 5 days/week every 4 weeks starting on day 3. Study group will be compared to historical controls on conventional management. The sample size was calculated to 63 patients, ten of them were included in the phase IB. RESULTS: The phase IB of the trial was completed in 2019 and the combination of Temozolomide and Bortezomib was shown to be safe and well tolerated. Until April 2021 a total number of 23 patients were included into the trial. The patients are treated at 4 different referral university hospitals in Norway. A clinical treatment benefit with both radiological tumor volume response and stable disease were observed. The patient inclusion in the trial is delayed due COVID-19. The majority of observed side effects are mild or moderate. The grade 3 or 4 adverse effects included thrombocytopenia, ataxia, muscle weakness, delirium and hyperglycemia. Patients that progressed under the treatment received another line of therapy according to the institutional practice. CONCLUSION: A combination of Bortezomib and Temozolomide administered in a defined time sequence to achieve sensitization of glioblastoma to alkylating agent is safe and feasible and may represent a novel treatment option for patients with this devastating disease.

P14.11 SEVERE TREATMENT-INDUCED MYELOSUPPRESSION IS MORE FREQUENT IN FEMALE MALIGNANT GLIOMA PATIENTS AND ASSOCIATED WITH REDUCED OVERALL SURVIVAL

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BACKGROUND: An association of treatment-related myelotoxicity with female gender has been previously suggested. However, a systematic analysis of the prognostic relevance of radiochemotherapy-related cytopenia involving the different blood cell lineages is lacking. MATERIAL AND METHODS: We retrospectively analyzed cytopenia during temozolomide-based concomitant radiochemotherapy (RCT) in 493 glioma patients. Histological grading, molecular pathology, surgical procedures and median overall survival (OS) were recorded. The extent of cytopenia was correlated with gender and outcome. RESULTS: Treatment-induced severe cytopenia (leuko-, lympho-, neutro- and thrombocytopenia) occurred much more often in female than in male glioma patients (40.8 vs. 13.9%, p-value <0.0001). In female patients with IDH-wildtype high-grade astrocytomas there was a negative correlation of severe