BACKGROUND: GBM AGILE (Glialoblastoma Adaptive, Global, Innovative Learning Environment) is a global, Phase 2/3 Response Adaptive Randomization platform trial designed to rapidly identify experimental therapies that improve overall survival and confirm efficacious experimental therapies and associated biomarker signatures to support new drug approvals and registration. It is a collaboration between academic investigators, patient organizations, health care providers, and pharmaceutical companies, as well as the National Brain Tumor Society, National Brain Tumor Network, and organizations supporting the non-profit organization, Global Coalition for Adaptive Research, to support new drug applications for newly diagnosed and recurrent GBM.

MATERIAL AND METHODS: The primary objective of GBM AGILE is to identify therapies that effectively improve overall survival in patients with newly diagnosed or recurrent GBM. Bayesian response adaptive randomization is used within subtypes of the disease to assign participants to investigational arms based on their performance. Operating under a master protocol, GBM AGILE allows multiple early phase investigational drugs from different pharmaceutical companies to be evaluated simultaneously and over time against a common control arm. Based on performance, a drug may graduate to a Stage 2 (Phase 3) within the trial, and the totality of the data can be used for a new drug application and regulatory review. New experimental therapies are reviewed on an ongoing basis, and information about promising new drugs is identified while other therapies are removed as they complete their evaluation. The master protocol trial infrastructure includes efficiencies through an adaptive trial design, shared control arm, and risk-based monitoring with enhanced reporting on complications.

RESULTS: AGILE has screened over 1000 patients studying multiple investigational treatments, and in March 2021 the Voluntary Harmonization Procedure (VHP) in April, 2021. As of June 2022, AGILE has received full and conditional approval from the US FDA in April 2019, and in Europe through the Mutual Recognition Procedure (MRP) in April 2020. GBM AGILE has screened over 1000 patients studying multiple investigational treatments. Enrollment rates are 3 to 4 times greater than traditional GBM trials, with active sites averaging 0.73 to 1 patients/month.

Currently, there are 41 sites activated in the US, 4 in Canada and 2 in Switzerland and an estimated 24 sites yet to open in Germany, France, Switzerland, Italy and Austria. In addition to the continued expansion in Europe, effort is ongoing to extend the trial to China and Australia as well. Clinical trial information: NCT03970447

P11.66.A. IMMUNE CHECKPOINT INHIBITORS RELATED PERIPHERAL NERVE DISORDERS: CLINICAL AND ELECTROPHYSIOLOGICAL PARTICULARITIES


BACKGROUND: The immune-checkpoint inhibitors (ICIs) announced a new era in cancer treatment allowing long-term survival in advanced cancers. However, immune related adverse events impose treatment limitations being one of the main challenges when dealing with ICI treated patients. Neurologic toxicities have unique presentations and can progress rapidly, requiring prompt recognition. Among them, ICI-related peripheral nerve disorders are...
highly heterogeneous, profoundly debilitating, and insufficiently explored. MATERIAL AND METHODS: We reviewed the clinical and electrodiagnostic features of a retrospective cohort of patients hospitalized in our center for ICIs related SE in order to understand if and how the use of an antiepileptic drug (AED) could affect the clinical course of SE in this setting, and we correlated electrodiagnostic findings with the presence of tumor necrosis in tumor tissue with prognosis parameters (OS and relapses number). Statistical analysis was completed with immunohistochemistry with primary antibodies for STAT 6 (IDHwt gliomas) or NAB2-STAT6 (IDH1 WT glioblastomas) and TERT promoter (glioblastomas). Statistical analysis was performed using GraphPad Prism software. RESULTS: Out of 254 patients, 78% (50/64) IDHwt hLG and 68% (129/190) IDHwt glioblastoma patients developed epilepsy during the disease course (p=0.121). Epilepsy onset before histopathological diagnosis occurred more frequently in IDHwt hLG compared to IDHwt glioblastoma patients (90% versus 60%, p<0.001), with a significantly longer median time to diagnosis (3.5 versus 1.3 months, p=0.001). Median total seizure days was also longer for IDHwt hLG patients (7.0 versus 3.0, p=0.005), and they received more often AED polytherapy (42% versus 17%, p=0.028). CONCLUSION: Although the incidence proportion of epilepsy during the entire disease course is similar, IDHwt hLG patients show a significantly higher incidence of epilepsy before diagnosis and a significantly longer median time between first seizure and diagnosis compared to IDHwt glioblastoma patients, indicating a distinct clinical course.

P11.70.A. THE YIELD OF SCREENING BRAIN MRI AMONG STAGE IV NON SMALL CELL LUNG CANCER PATIENTS

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BACKGROUND: Brain metastases are a common complication of non small cell lung cancer (NSCLC). Approximately 10 percent of newly diagnosed patients with advanced NSCLC have brain metastases. The purpose of this study was to determine whether younger patients with extensive lung cancer and extracranial metastatic disease on staging (MRI) for early screening of brain metastases can improve survival. MA-

P11.67.B. TUMOR CENTRALITY IS ASSOCIATED WITH A DECLINING OVERALL SURVIVAL IN IRRADIATED DIFFUSE GLIOMA


BACKGROUND: For diffuse glioma, tumor location is an important factor that influences symptomatology, treatment strategy and, ultimately, survival. Our previous research showed an association between overall survival (OS) and local involvement in eloquent white and grey matter areas in the left hemisphere. Moreover, our findings argue for the benefit of adding vGIF immunoglobulin to steroids as a first line treatment for different phenotypes of ICI related neurotoxicities.

CONCLUSION: Our series expand the knowledge on the clinical and electrophysiological phenotype of ICI related neurotoxicities improving their recognition in clinical practice. However, our findings argue for the benefit of adding vGIF immunoglobulin to steroids as a first line treatment for different phenotypes of ICI related neurotoxicities.