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336 ADVERSE EVENTS IN A PHASE II TRIAL OF AV-GBM-1: DENDRITIC CELL VACCINE PULSED WITH LYSATE ENRICHED FOR AUTOLOGOUS TUMOR-INITIATING CELL ANTIGENS FOR PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

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Background Standard glioblastoma (GBM) therapy includes maximum safe resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ), and maintenance TMZ, but it is associated with a 2-year survival of only about 25%. Adding treatment with AV-GBM-1, a vaccine consisting of autologous dendritic cells (DC) pulsed with autologous tumor antigens (ATA) may improve survival, but it may be associated with additional toxicity. One objective of a multicenter phase II clinical trial was to identify, characterize, and enumerate treatment-emergent adverse events (TEAE) and serious AE (SAE) that occurred during AV-GBM-1 treatment.

Methods Key eligibility criteria for enrollment prior to starting RT/TMZ, were: (1) confirmation of primary GBM, (2) successful GBM cell culture, (3) collection of sufficient numbers of monocytes (MC) from leukapheresis, (4) Karnofsky Performance Status 70 or higher, and (5) planning to treat with concurrent RT/TMZ. Interleukin-4 and granulocyte-macrophage colony stimulating factor (GM-CSF) were used to differentiate DC from MC. AV-GBM-1 was manufactured while patients were being treated with RT/TMZ. Each vaccine consisted of autologous DC incubated with ATA from the lysate of irradiated GBM cells grown in serum-free media with factors that favor survival and proliferation of tumor initiating cells, i.e., tumor stem cells and early progenitor cells. Following RT/TMZ, patients were injected subcutaneously with cryopreserved AV-GBM-1 admixed with 500 µg GM-CSF at weeks 1, 2, 3, 8, 12, 16, 20 and 24. Adverse events (AE) were identified and classified per Common Terminology Criteria for Adverse Events (CTCAE v 4.03).

Results 57 patients received at least one injection of AV-GBM-1 during November 2018 to October 2020. Patients received an average of 6.9 injections; 39 (68.4%) received all 8 injections. Injections generally were well-tolerated. Only 26 AE were attributed to AV-GBM-1, 24 grade-1 and 2 grade-2, including injection site reactions (16%), flu-like symptoms (10%), and bone discomfort (7%). The most frequent TEAE were fatigue (54)%, headache (37%), seizures (33%), nausea (30%), and focal weakness (28%). The frequency of seizures is higher than reported in other GBM trials; one patient discontinued AV-GBM-1 because of seizures. There were 55 SAE reported for 29 patients, including hospitalizations for 16 episodes of seizures in 13 patients, 7 falls in 6 patients, 6 episodes of focal weakness in 4 patients, and 3 for cerebral edema.

Conclusions AV-GBM-1 was well-tolerated, but it was associated with a high frequency of TEAE and SAE. The high frequency of focal neurologic events may be secondary to local inflammation induced by AV-GBM-1.

Trial Registration ClinicalTrials.gov NCT03400917

Ethics Approval This study was approved by the Western IRB, approval number 20182582; all participants gave written informed consent before taking part

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