Title

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Journal

Journal for ImmunoTherapy of Cancer, 9(Suppl 2)

ISSN

2051-1426

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Publication Date

2021-11-01

DOI

10.1136/jitc-2021-sitc2021.952

Peer reviewed

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

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Background Standard therapy of glioblastoma (GBM), which includes maximum safe resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ) followed by maintenance TMZ, is associated with poor overall survival (OS). Adding treatment with AV-GBM-1, a vaccine consisting of autologous dendritic cells (DC) pulsed with autologous tumor antigens (ATA) may improve OS. A multi-center phase II clinical trial was conducted to determine feasibility, safety, and efficacy of AV-GBM-1.

Methods Key eligibility criteria for tumor collection were clinical suspicion of newly diagnosed GBM and age 18 to 70 years at the time of surgery. Prior to starting RT/TMZ, key eligibility criteria for intent-to-treat-with-AV-GBM-1 enrollment were: (1) primary GBM confirmed, (2) successful GBM cell culture, (3) collection of sufficient numbers of monocytes (MC) by leukapheresis, (4) Karnofsky Performance Status 70 or greater and (5) plan to treat with concurrent RT/TMZ. AV-GBM-1 was manufactured during RT/TMZ. Interleukin-4 and granulocyte-macrophage colony stimulating factor (GM-CSF) were used to differentiate MC into DC. AV-GBM-1 consists of autologous DC incubated with ATA from the lysate of irradiated GBM cells grown in serum-free media with factors that favor the survival and proliferation of stem cells and early progenitor cells. After recovery from RT/TMZ, over six months patients received up to 8 subcutaneous injections of AV-GBM-1 admixed with 500 µg GM-CSF. The primary objective was to determine if OS was 75% or higher 14.6 months from ITT enrollment, which ended January 2020. The minimum follow-up at the time of analysis was 15.2 months. Secondary endpoints included progression-free survival (PDS) from ITT enrollment and from the first injection.

Results Success rates for cell cultures and sufficient monocyte collections were both 97%. AV-GBM-1 was manufactured for 60/60 (100%). 57 patients received 392 injections; 68% received all 8. The primary adverse events (AE) attributed to AV-GBM-1 were local injection site reactions (16%) and flu-like symptoms (10%). Progression-free survival (PFS) from ITT enrollment is 10.3 months, about 50% longer than reported in four randomized trials with comparable standard therapy arms. PFS from the first injection is 8.3 months, which is 51% and 107% longer than reported in two randomized trials with comparable standard therapy arms. OS was 72% at 12 months, but dropped to 54% at 14.6 months; median OS is 16.0 months.

Conclusions Patent-specific AV-GBM-1 was reliably manufactured and distributed for administration. AV-GBM-1 produced minimal toxicity. PFS was very encouraging but did not translate into OS, perhaps because of discontinuation of treatment after 8 months.

Trial Registration [Clinicaltrials.gov NCT03400917]

Ethics Approval Western IRB, approval number 20182582

Consent n/a

http://dx.doi.org/10.1136/jitc-2021-SITC2021.952