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Authors

Duma, Christopher
Bota, Daniela
Hsu, Frank
[et al.](#)

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TUMOR COLLECTION AND ESTABLISHMENT OF TUMOR-INITIATING CELL CULTURES AS ANTIGEN SOURCE FOR AV-GBM-1 DENDRITIC CELL VACCINES FOR A PHASE II TRIAL IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

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¹Christopher Duma, ²Daniela Bota*, ²Frank Hsu, ³David Piccioni, ⁴Renato LaRocca, ⁵Santosh Kesari, ⁶Mehrdad Abedi, ³Jose Carrillo, ⁷Robert Aiken, ²Xiao-Tang Kong, ²Thomas Taylor, ⁸Candace Hsieh, ⁸Gabriel Nistor, ⁸Robert Dillman. ¹NeuroScience Institute, Newport Beach, CA, USA; ²University of California Irvine, Orange, CA, USA; ³University of California San Diego, San Diego, CA, USA; ⁴Norton Cancer Institute, Louisville, KY, USA; ⁵John Wayne Cancer Institute, Santa Monica, CA, USA; ⁶University of California Davis, Sacramento, CA, USA; ⁷Rutgers Cancer Center, New Brunswick, NJ, USA; ⁸AIVITA Biomedical Inc., Irvine, CA, USA

Background Despite standard aggressive therapy (maximum safe surgical resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ), then maintenance TMZ), 2-year survival is only about 25% for patients with newly diagnosed primary glioblastoma (GBM). Adding AV-GBM-1, a vaccine consisting of autologous dendritic cells (DC) pulsed with autologous tumor antigens (ATA) may improve survival. One objective of a multi-center phase II clinical trial was to determine the feasibility of collecting fresh GBM and establishing short-term cell cultures of GBM tumor-initiating cells (TIC) to serve as ATA source.

Methods Key eligibility criteria for tumor collection were (1) clinical suspicion of new primary GBM, (2) age 18 to 70 years (3) tentative agreement to undergo a leukapheresis procedure after recovery from surgery, and (4) tentative plans for RT/TMZ. Fresh tumor was placed in media and shipped in a transport kit by overnight courier to AIVITA where a cell suspension was placed in culture and incubated in serum-free medium with factors that favor survival and proliferation of TICS (stem cells and early progenitor cells). The intent was to produce a patient-specific DC-ATA vaccine by incubating a lysate of irradiated TICs with autologous DC for subsequent subcutaneous injection.

Results Patients were enrolled from five sites in California, one in Kentucky and one in New Jersey. Tumors were collected between August 2018 and January 2020. 106 patients consented for tumor collection, but 15 were not GBM, 4 had insufficient tissue to send, 2 patients withdrew consent, 4 were ineligible because of age, and 1 was ineligible because of autoimmune disease. Of the 80 GBM tumors that were placed into culture, 7 were discontinued because of patient withdrawal. 71/73 (97%) resulted in a successful cell culture; two were unsuccessful because of contamination. 60/71 subsequently consented for intent-to-treat; 46/60 (77%) had cells in culture for 28 days or less, 11 were in culture for 30 to 35 days, and the remaining 3 were cultured 46, 54, and 55 days. The average number of cells per culture at the time of irradiation was 14.0 million (range 0.78 to 63.3 million). 58/60 (97%) yielded more than 1 million TICs for irradiation for the tumor cell lysate; 36/60 (60%) had more than 10 million cells irradiated. 57 patients were subsequently treated with AV-GBM-1 after recovery from RT/TMZ.

Conclusions Self-renewing GBM TIC cultures can be reliably and rapidly established for use as the antigen source for personal DC-ATA vaccines.

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