Title

333 Changes in proteomic markers after injections of personal AV-GBM-1 dendritic cell/tumor initiating cell vaccines in a phase II trial in patients with newly diagnosed glioblastoma

Journal

Journal for ImmunoTherapy of Cancer, 9(Suppl 2)

ISSN

2051-1426

Authors

Kesari, Santosh
Bota, Daniela
Piccioni, David
et al.

Publication Date

2021-11-01

DOI

10.1136/jitc-2021-sitc2021.333

Peer reviewed

333 CHANGES IN PROTEOMIC MARKERS AFTER INJECTIONS OF PERSONAL AV-GBM-1 DENDRITIC CELL/TUMOR INITIATING CELL VACCINES IN A PHASE II TRIAL IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

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

Background Despite standard aggressive therapy, including maximum safe surgical resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ) followed by maintenance TMZ, survival is still extremely poor for patients with newly diagnosed primary glioblastoma (GBM). Adding treatment with AV-GBM-1, a personal 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 changes in blood proteomics before and after injections of AV-GBM-1.

Methods AV-GBM-1 consists of autologous DC incubated with ATA from a lysate of irradiated autologous GBM cells that had been placed in culture and incubated in serum-free medium with factors that favor the survival and proliferation of stem cells and early progenitor cells. After recovery from RT/TMZ, GBM patients were injected subcutaneously with AV-GBM-1 admixed in granulocyte-macrophage colony-stimulating factor (GM-CSF) at weeks 1, 2, 3, 8, 12, 16, 20, and 24. Blood samples obtained at baseline (week-0), just prior to the third injection (week-2) and just prior to the fourth injection (week-8), were cryopreserved and subsequently analyzed for 448 proteomic markers using quantitative, multiplex enzyme-linked immunosorbent assays (Raybiotech, Inc., Norcross, GA.). In this preliminary analysis the averages of paired samples for each time point were determined and compared using the student T-Test with a focus on differences of $p<0.01$.

Results Patients were enrolled from five sites in California, and one each in Kentucky and New Jersey. 57 patients were treated during November 2018 to October 2020. Paired samples from all three time points were available for 49 patients. After two weekly injections there were increases in thymus- and activation-regulated chemokine (TARC, CCL17), the chemotactic protein chemerin, lipocalin-2, (expressed by macrophages and epithelium in response to inflammation) and angiopoietin-1 (suppressor of vascular inflammation), and decreases in thrombospondin-5 (possibly involved in synaptogenesis in brain repair), angiotensinogen (a precursor of all angiotensin peptides), and beta-fibroblast growth factor (important in tissue repair). The increase in TARC ($p<0.0000001$) was attributed to GM-CSF; TARC had declined almost to baseline levels by week-8. The other six markers had p values between 0.0011 and 0.0087. The only marker that was still changed at week-8 was thrombospondin-5 ($p=0.023$).

Conclusions If there were humoral changes in proteins associated with Th1 and Th2 responses, these were no longer present after two weekly vaccinations. More sophisticated analyses of this data set, such as principal component analysis, may be needed to understand the effects of 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

http://dx.doi.org/10.1136/jitc-2021-SITC2021.333