Title

CTIM-33. PHASE II TRIAL OF VACCINE IMMUNOTHERAPY IN PRIMARY GLIOBLASTOMA: ADJUNCTIVE AUTOLOGOUS DENDRITIC CELLS PULSED WITH LYSATE FROM IRRADIATED SELF-RENEWING AUTOLOGOUS TUMOR CELLS (AV-GBM-1)

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In primary glioblastoma (GBM), overall survival (OS) is poor despite standard aggressive therapy. Adjunctive AV-GBM-1 vaccine immunotherapy may improve OS. In this multi-institutional phase II trial, key eligibility criteria for intent-to-treat (ITT) enrollment were: (1) primary GBM, (2) age < 70 years when GBM was resected, (3) successful GBM cell culture, (4) successful monocyte collection by leukapheresis, (5) KPS > 70 post-surgery, and (6) plan to treat with concurrent RT/TMZ. Dendritic cells (DC) were differentiated from monocytes by culturing in IL-4 and granulocyte-macrophage colony stimulating factor (GM-CSF). AV-GBM-1 consisted of autologous DC incubated with autologous tumor antigens contained in the lysate of irradiated cultured GBM cells. After recovery from RT/TMZ, doses were admixed with 500 mcg GM-CSF; up to 8 doses were injected subcutaneously over 6 months. Patients were not excluded by apparent progression or pseudo-progression post RT/TMZ. OS and progression-free-survival (PFS) were calculated from ITT enrollment. The success rate was 97% for both GBM cell cultures and collection of monocytes; 60/60 vaccines were successfully manufactured. Median age was 59 years. 57 patients received 392 injections. After two weekly injections there were significant increases in plasma lipocalin-2 and angiopoietin-1, and decreases in thrombospondin-5, angiotensinogen, and beta-fibroblast growth factor. The most common adverse events attributed to AV-GBM-1 were local injection site reactions (16%) and flu-like symptoms (10%). With follow up from 15.2 to 32 months, median PFS and OS were 10.3 (8.5,11.6 95% CI) and 16.0 (13.0,21.3 95% CI) months respectively. OS was better in the 25 patients who had *methylguanine-methyltransferase (MGMT)* methylation and/or *isocitrate dehydrogenase (IDH)* mutation. Age was not independently correlated with survival. From date of first injection, OS was not increased in 14 patients who were treated with alternating electrical tumor-treating fields. CONCLUSION: feasibility, safety, and PFS were encouraging. A phase III trial is in development.

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