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## LEUKAPHERESIS TO OBTAIN MONOCYTES TO PRODUCE DENDRITIC CELLS IN MANUFACTURING OF PERSONAL AUTOLOGOUS AV-GBM-1 VACCINES IN A PHASE II TRIAL IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA

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**Background** For patients with newly diagnosed primary glioblastoma (GBM), maximum safe surgical resection, concurrent radiation therapy and temozolomide chemotherapy (RT/TMZ) followed by maintenance TMZ results in a 2-year survival of only 25%. 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 the feasibility of collecting sufficient monocytes (MC) from which to generate DC for pulsing with ATA from GBM tumor-initiating cells (TIC).

**Methods** Peripheral blood mononuclear cells were collected by leukapheresis per local standard operating procedures, then shipped by overnight courier to the AIVITA laboratory in Irvine, CA. The product was enriched for MC using the Elutra<sup>®</sup> Cell Separation System (Terumo, Lakewood, CO.). If fewer than 450 million MC were collected, an additional leukapheresis was allowed. MC were cryopreserved in liquid nitrogen and subsequently thawed and incubated in media containing granulocyte-macrophage colony-stimulating factor and interleukin-4 to differentiate MC into DC. Batches of patient-specific AV-GBM-1 were produced by incubating autologous DC with a lysate of irradiated TICs and aliquoted into individual doses.

**Results** Patients enrolled from five sites in California, one in Kentucky and one in New Jersey. 65 patients underwent 77 leukapheresis procedures between September 2018 and February 2020; 54 underwent a single pheresis, 10 two phereses, and 1 three (all unsuccessful). The average time from surgical resection to first pheresis was 26 days (range 6 to 90; 64/65 within 51 days). 63/65 (97%) had sufficient MC collected, 53/65 (82%) from a single leukapheresis; 10 required a second procedure. The interval from surgery to first pheresis was the same for those for whom MC collections were satisfactory after one pheresis compared to those who required more than one. The success rate for MC collection for East-coast sites was 14/15 versus 52/62 for West-coast sites ( $p=0.68$ ); so, longer shipping distance was not an issue. 60 patients who enrolled with intent-to-treat had an average of 1.7 billion monocytes cryopreserved, which were subsequently thawed and differentiated into DC. An average of 750 million DC were incubated with ATA for the final DC-ATA product.

**Conclusions** Leukapheresis procedures reliably resulted in collection of sufficient numbers of monocytes to generate DC and large batches of personal AV-GBM-1 vaccines. Success after a single leukapheresis was not related to the interval from surgery to pheresis procedure, or distance from the processing site.

**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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