565 LEUKAPHERESIS TO OBTAIN MONOCYTES TO PRODUCE DENDRITIC CELLS FOR MANUFACTURING AV-OVA-1 PERSONAL VACCINES IN A RANDOMIZED PHASE II TRIAL IN PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER

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Background Despite standard therapy, which includes chemotherapy and aggressive surgical debulking, relative 5-year survival for newly diagnosed advanced epithelial ovarian cancer is only 30%. AV-OVA-1 is a personal vaccine consisting of autologous dendritic cells (DC) loaded ex vivo with autologous tumor antigens (ATA) from a lysate of irradiated tumor cells from short-term cell culture. After completion of primary chemotherapy, immunization with DC-ATA may improve survival. A multi-center, 2:1 double-blind randomized phase 2 clinical trial was designed to compare treatment with AV-OVA-1 to autologous monocytes (MC). One objective was to determine the feasibility of collecting sufficient MC from which to generate DC for pulsing with ATA from ovarian cancer tumor-initiating cells (TIC) to produce DC-ATA.

Methods Peripheral blood mononuclear cells (PBMC) 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® Cell Separation System (Terumo, Lakewood, CO.). If fewer than 450 million viable MC were available for cryopreservation, 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, then aliquoted into individual doses.

Results Patients were enrolled from five sites in California and one in Colorado. PBMC were collected between December 2017 and April 2021. 47/50 patients (94%) had a successful PBMC collection, but four required a second procedure. An average of 1.90 billion monocytes (range 0.527 to 16.6 billion) were collected with an average of 1.55 billion monocytes cryopreserved (range 0.249 to 3.80), which subsequently could be thawed and differentiated into DC. For 29 patients treated with DC-ATA, an average of 648 million viable MC (range 336 to 1120) were differentiated into an average of 410 million DC (range 171 to 892) for incubation with ATA, which yielded an average of 78.6 million DC-ATA (range 16.0 to 270). This resulted in an average of 8.1 million DC-ATA cells per dose (range 2.0 to 27).

Conclusions Leukapheresis procedures reliably resulted in collection of sufficient numbers of monocytes to generate DC and large batches of personal AV-OVA-1 vaccines.

Trial Registration Clinicaltrials. gov NCT00331526

Ethics Approval This study was approved by the Western IRB, approval number 20171661; all participants gave written informed consent before taking part

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