TUMOR COLLECTION AND ESTABLISHMENT OF TUMOR-INITIATING CELL CULTURES TO SERVE AS THE ANTIGEN SOURCE FOR AV-OVA-1 DENDRITIC CELL VACCINES FOR PATIENTS WITH NEWLY DIAGNOSED ADVANCED OVARIAN CANCER

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Background With 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 cells from a short-term cell culture. After completion of primary chemotherapy, immunization with DC-ATA may improve survival. A multicenter, 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 fresh ovary cancer and establishing cell cultures to serve as the ATA source.

Methods Tumor samples were obtained during surgical debulking of patients with stage 3 or 4 ovary epithelial cancer. Fresh tumor was placed in media and shipped via transport kit per overnight courier to AIVITA where a cell suspension was placed into culture and incubated in serum-free medium with factors that favor survival and proliferation of stem cells and early progenitor cells, i.e., tumor initiating cells (TICS). The objective was to harvest a minimum of 1 million cells within 28 days, and preferably 10 million cells or more.

Results Patients were enrolled from five sites in California and one in Colorado. Tumors were collected between December 2017 and April 2021. 92 patients consented for tumor collection, but 12 were not malignant ovary, 4 withdrew consent, 3 had insufficient tissue to send, 1 had wrong stage; so, 72 malignant epithelial ovary tumors were placed into culture. 70/72 (97.2%) resulted in a successful cell culture; one could not be grown, one was contaminated. Of tumors submitted for patients who were subsequently randomized, 47/56 (84%) were in culture for 28 days or less, 4 (7%) were in culture for 29 to 35 days, and the remaining 5 were cultured 51, 52, 57, 62, and 67 days. All 56 cultures yielded at least 1 million cells; 48/56 (86%) yielded more than 10 million cells. The average number of irradiated cells per culture was 59.7 million (range 1.1 to 135 million); the median was 65.6 million (interquartile range 22.4 to 96.8 million).

Conclusions Self-renewing ovary TIC cultures were reliably and rapidly established for use as the antigen source for personal DC-ATA 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.