FEASIBILITY, SAFETY, AND EFFICACY OF PERSONAL VACCINES CONSISTING OF AUTOLOGOUS DENDRITIC CELLS LOADED EX VIVO WITH AUTOLOGOUS TUMOR ANTIGENS FROM SELF-RENEWING CANCER CELLS

Robert O Dillman*, Gabriel I Nistor, Hans S Keirstead. AIVITA Biomedical, Inc., Irvine, CA, USA

Background Personal therapeutic cancer vaccines consisting of autologous dendritic cells (DC) loaded ex vivo with autologous tumor antigens (ATA) derived from cells that are self-renewing in culture (cancer-initiating cells, stem cells) have been clinically tested for more than 20 years. The current study addressed feasibility, safety, and efficacy of the DC-ATA approach.

Methods ATA, as irradiated tumor cells (ITC) or ITC lysates, were derived from short-term tumor cell lines established from resected cancer tissue. Peripheral blood monocytes (MC) were collected by leukapheresis; MC were differentiated into DC by culturing with interleukin-4 and granulocyte-macrophage colony-stimulating-factor (GM-CSF). Cryopreserved doses were thawed, suspended in 500 mcg GM-CSF, and injected at weeks 1, 2, 3, 8, 12, 16, 20, and 24. Data was derived from clinical trials conducted during 2000–2023 in patients with metastatic renal, hepatocellular, and ovary cancers, melanoma, and glioblastoma (GBM). Key end-points were DC-ATA manufacturing success rates, treatment emergent adverse events (TEAE), objective response rates, progression-free survival (PFS) and overall survival (OS).

Results The success rate for establishing tumor cell lines in proprietary stem cell media was 173/178 (97.2%) including 80/82 GBM, 73/75 ovary, 17/18 liver, 3/3 other. During 2002–2023, leukapheresis procedures yielded sufficient monocytes in 218/223 patients (97.8%) including 74/74 melanoma, 72/74 GBM, 50/53 ovary, 11/11 renal cell, 8/8 hepatoma, and 3/3 other. Of 187 treated patients, no one discontinued DC-ATA because of TEAE; there were no grade 4 TEAE. Most common TEAE were mild to moderate, self-limited local injection site reactions and flu-like symptoms. There was no difference in TEAE frequency or grade in a blinded, randomized trial of DC-ATA vs MC in ovary patients. Immune responses were more favorable for DC-ATA vs ITC in metastatic melanoma, and for DC-ATA vs MC in advanced ovary cancer. During treatment there were no objective responses among 30 patients with measurable metastatic disease, but 3 (10%) had delayed, durable, complete remissions (2 renal, 1 melanoma). In GBM, PFS of 10.4 months was 50% longer than in standard treatment arms of six randomized trials. In metastatic melanoma, DC-ATA was associated with better OS compared to historical treatment with ITC vaccine (median 60 vs 20.4 months, p<0.001), and better OS compared to ITC in a randomized trial (43.4 vs 20.5 months with a 70% reduction in death p=0.0053).

Conclusions This DC-ATA approach is feasible and reproducible across tumor types, treatment is well-tolerated, and there is efficacy in some patients. Additional investigation is warranted.

Trial Registration Clinicaltrials.gov: NCT00014131, NCT00012064, NCT00436930, NCT00331526, NCT03400917

Ethics Approval All clinical studies obtained approvals from local ethics committees or institutional review boards, and all participants gave written informed consent.