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CLINICAL EXPERIENCE IN ADVANCED CANCER WITH DENDRITIC CELLS LOADED WITH AUTOLOGOUS STEM CELL ANTIGENS

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Tumor initiating cells, including cancer stem cells and their early progenitors are a desirable target for cancer therapy but hard to target with chemotherapy and radiation therapy and hard to target with tumor-specificity using targeted therapies. Immunologic vaccines directed to tumor stem cells have shown promise in animal models. Our approach has been to utilize autologous tumor antigens (ATA) derived from short-term cell lines. Such cells have phenotypic markers shared with stem cells, produce tumors of the parental histology in animals and contain many non-synonymous mutations that may encode for neo-antigens. Author's early work focused on irradiated tumor cells as a tumor cell vaccine (TCV) and was associated with a 29% 5-year survival rate in patients with metastatic melanoma. Then they turned to autologous dendritic cells (DC) loaded with ATA from irradiated tumor cells (DC-ATA). 5-year survival rates of 33% were observed in patients with metastatic renal cell cancer and 50% in patients with metastatic melanoma. Next a randomized trial confirmed the superiority of the DC-ATA approach compared to TCV in metastatic melanoma with more than a doubling of median survival from 20 to 43, and a 70% reduction in the risk of death. Toxicity was minimal in all of these studies. A major limitation of these trials was that it typically took three to four months to establish successful cell lines, and only about 50% of tumor samples resulted in cell lines; in contrast, DCs were reliably derived from peripheral blood mononuclear cells. More recently they converted to using serum free media to encourage tumor-spheres that favor tumor stem cells and establish short-term cell lines in four weeks. So far this approach has been associated with greater than 90% success in various tumor types including glioblastoma, ovarian cancer, melanoma, hepatocellular cancer, sarcoma and squamous cell cancers of the neck and vulva. At the time of treatment, DC-ATA are suspended in granulocyte-macrophage colony stimulating factor and injected subcutaneously weekly for three weeks, then monthly at weeks 8, 12, 16, 20 and 24. DC-ATA. Multi-institutional phase II trials are in progress: A double-blind randomized phase II trial in patients with a primary diagnosis of stage 3 or 4 ovarian cancer and a single-arm phase II trial in patients with newly diagnosed glioblastoma that can be at least partly resected surgically. Trials are also in development for patients with metastatic melanoma and locally advanced hepatocellular cancer.

BIOGRAPHY

Robert O Dillman is Chief Medical Officer of AIVITA Biomedical. Earlier he served as Vice President of Oncology at Caladriu's Biosciences Inc. (formerly Neostem Inc.), a leading development and manufacturing partner to the cell therapy industry. From May 2014 to January 6, 2016 he also served as Member of Caladriu's Melanoma Scientific Advisory Board. He has served as the Executive Medical Director of the Hoag Hospital Institute for Research and Education, in Newport Beach, California, a position he has held since 2011.

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