Immunotherapy for the Treatment of Advanced Prostate Cancer

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Abstract

Sipuleucel-T is an autologous active cellular immunotherapy designed to stimulate an immune response to prostate cancer. It is FDA approved for the treatment of men with asymptomatic or minimally symptomatic castrate resistant prostate cancer, based on prolongation of overall survival. Sipuleucel-T is manufactured by culturing a patient's peripheral blood mononuclear cells, including antigen presenting cells, with a recombinant protein comprising a tumor-associated antigen (prostatic acid phosphatase) and granulocyte-macrophage colony stimulating factor. Treatment consists of 3 infusions at approximately 2-week intervals, resulting in a prime-boost pattern of immune activation, with a robust antigen-specific cellular and humoral immune response. Specifically, antigen presenting cells are activated after culture with the recombinant protein, as evidenced by an increase in CD54 expression in the first dose at Week 0, that is further upregulated in subsequent doses at Week 2 and Week 4. Activated APC-associated cytokines and chemokines are produced in the media during manufacture of sipuleucel-T, and activated T-cell-associated cytokines are detected in the media of the second and third products. Antigen-specific T-cell proliferative and IFN gamma ELISPOT memory responses are evident after administration of the first sipuleucel-T dose. There are correlations between product parameters as well as peripheral immune responses and overall survival. Adverse events are generally mild to moderate and resolve within 2 days. As the first autologous cellular immunotherapy to demonstrate a survival benefit, sipuleucel-T is an important new treatment for men with asymptomatic or minimally symptomatic castrate resistant prostate cancer.