EDITORIAL

Immunotherapy for Prostate Cancer

In 2011, approximately 240,890 new cases of prostate cancer are expected to be diagnosed in the United States and 33,720 men are expected to die from the disease.[1] While several treatment options are available for localized prostate cancer, until recently only a few therapeutic modalities existed for metastatic castrate resistant prostate cancer (mCRPC) patients. For these patients, the estimated median survival is 12.2 to 21.7 months.[2] In 2010, a new era in prostate cancer treatment began with the FDA approval of sipuleucel-T, cabazitaxel and abiraterone acetate.[2]

Certainly this is a new era and revival of immune therapy. Active and passive immunotherapy approaches have been explored over the years to identify additional treatment options for cancer patients, including those with prostate cancer. One approach is active cellular immunotherapy, which targets antigen presenting cells to stimulate a T cell response to tumor-associated antigens.

Sipuleucel-T is an autologous cellular immunotherapy product designed to stimulate an immune response against prostate cancer. It consists of autologous peripheral blood mononuclear cells (PBMCs), including antigen presenting cells which have been activated *in vitro*. Cells are activated with a recombinant fusion protein (PA2024) comprising prostatic acid phosphatase and granulocyte-macrophage colony-stimulating factor. A dose of sipuleucel-T is prepared from a single leukapheresis procedure is infused at approximately 2-week intervals intravenously.

In the pivotal Phase III IMPACT trial (D9902B), 512 subjects were randomized 2:1 to receive sipuleucel-T (n = 341) versus control (n = 171). Control consisted of autologous non-activated PBMCs. IMPACT was a multi-center, double-blind, controlled trial conducted in subjects with asymptomatic or minimally symptomatic mCRPC.[2]

Subjects randomized to sipuleucel-T on the IMPACT trial, had a 22% reduction in the risk of death was compared control (HR = 0.78 [95% CI: 0.61, 0.98]; p = 0.03).[2] This treatment effect was also demonstrated with an unadjusted Cox model and log rank test analysis (HR = 0.77 [95% CI: 0.61, 0.97]; p = 0.02). The median survival advantage was 4.1 months (25.8 months for sipuleucel-T subjects versus 21.7 months for control subjects). Survival probability at 36 months was 31.7% in sipuleucel-T versus 23.0% in control.

In an integrated analysis of four Phase III trials conducted in subjects with mCRPC and with androgen dependent prostate cancer, adverse events (AEs) reported at least twice as frequently in the sipuleucel-T group by ≥ 5% of subjects were chills, pyrexia, headache, myalgia, influenza-like symptoms, and hyperhidrosis. The most common AEs reported in the sipuleucel-T group at a rate ≥ 15% were chills, fatigue, pyrexia, back pain, nausea, arthralgia, and headache. These events generally occurred within 1 day of infusion, were generally of Grade 1 of Grade 2 severity, and usually resolved within 1 to 2 days, with the exception of myalgia and influenza-like illness, which generally resolved within 14 days of infusion.[3]

Immunotherapy was neglected for many years and considered "unsuitable" for prostate cancer. These data have proven otherwise and future studies will define its role in the treatment paradigm of CRPC and prostate cancer in general.

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References

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