Treatments for metastatic castrate-resistant prostate cancer
Adams E

Record Status
This is a bibliographic record of a published health technology assessment from a member of INAHTA. No evaluation of the quality of this assessment has been made for the HTA database.

Citation

Authors' objectives
The National Program Director for Oncology requested assistance from the VHA Office of Patient Care Services (OPCS) in determining the effectiveness and provision of newly FDA-approved sipuleucel-T (PROVENGE®, Dendreon Corporation) for treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer (CRPC).

The VA Technology Assessment Program (VATAP) was charged with gathering the best available evidence from research to support deliberations of a Clinical Expert Panel assembled as part of VA's National Medical Technology Assessment Protocol (NMTAP). The NMTAP provides unbiased, evidence-based advice and recommendations for clinical use of new technologies in VA. The essential role of the Clinical Expert Panel in this process was to provide guidance for use of sipuleucel-T in VA based on the best available evidence, clinical expertise and judgment.

Authors' conclusions
At present there is no cure for metastatic CRPC, and until recently, treatment options were largely palliative. Trial results, which showed that docetaxel/prednisone offers a median survival advantage of an additional 2.4 months as well as palliation of symptoms and quality of life improvement over best standards of care, have given men with metastatic CRPC a new therapeutic option using docetaxel as the standard of care. Identifying additional first-line and second-line therapies that will, first, increase overall survival, and, second, improve quality of life is an active area of investigation. These options include new docetaxel-combination first-line therapies, other new first-line agents, and new post-docetaxel second-line therapies.

Both sipuleucel-T and cabazitaxel have been FDA approved. In the case of sipuleucel-T, FDA approved its use for the treatment of asymptomatic or minimally symptomatic metastatic CRPC. However, sipuleucel-T was administered before chemotherapy, including docetaxel, in a majority of patients. Cabazitaxel has been studied and approved for use in patients with metastatic CRPC previously treated with docetaxel regimens.

Sipuleucel-T resulted in a median survival advantage of 4.1 months with a 3-year survival rate of 31.7% compared with 23.0% receiving placebo. Survival was improved for patients who had an antibody titre of more than 400 against PA2024 or prostatic acid phosphotase (PAP) at any time after baseline (P<0.001), but not for those who had T-cell proliferation responses to PA2024 or PAP measured at week 6. However, sipuleucel-T offered no evidence of a measurable antitumor effect.

The limited clinical trial results for cabazitaxel show that it offers a median survival advantage of 15.1 months compared with 12.7 months with mitoxantrone (Hazard Rate 0.70; 95% CI 0.59, 0.83; p<0.0001). While both agents show a modest risk-benefit profile, new therapies are needed that confer a greater survival advantage.

For now, access to sipuleucel-T will be limited to a subset of the Phase III trial sites, none of which are VA sites. Manufacturing capacity is expected to increase over time. In the future, VA will need to consider both in-house and fee basis leukapheresis capability, organizational and logistical support and their associated costs when providing Veterans with the best access to this option. Sanofi-Aventis is expected to begin marketing cabazitaxel at the end of June 2010. Information regarding treatment costs for sipuleucel-T is provided by the manufacturer in addition to the costs of ongoing supportive care by health care providers. Payers will need to address coverage for this treatment in light of the limited treatment options available to men with metastatic CRPC and in identifying the optimal candidates for whom such treatment would most benefit.

Several new agents are being evaluated Phase III trials listed in Table 5. Access to many novel therapies through clinical trials should be encouraged.