Management of castration resistant prostate cancer

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CRPC is typically defined by 3 consecutive PSA rises over nadir in the context of castrate levels of serum testosterone, with or without evidence of clinical or radiologic progression. Secondary hormonal manipulations may alter PSA in approximately 30–40%, but currently no evidence exists that these therapeutic options result in improved survival. In 2004, docetaxel plus prednisone replaced mitoxantrone plus prednisone as the standard of care for first-line chemotherapeutic treatment of metastatic CRPC. When compared with mitoxantrone, docetaxel showed improved rates of response in terms of pain, serum PSA level and quality of life. The TAX 327 study also showed that median survival was superior in patients who received docetaxel plus prednisone every 3 weeks compared with patients who received mitoxantrone plus prednisone (19.2 months vs 16.3 months, respectively). Mitoxantrone in combination with prednisone has been shown to reduce pain and improve the quality of life of patients but does not improve survival and should only be used for palliative benefit. Zoledronic acid (a potent IV bisphosphonate given every 3–4 weeks) has been shown to reduce skeletal complications.

Novel therapeutics: Sipuleucel-T is an autologous dendritic cell-based vaccine designed to stimulate T cell immunity against prostatic acid phosphatase (PAP). A placebo-controlled phase III trial in 512 patients with asymptomatic metastatic CRPC showed that the overall survival of patients treated with sipuleucel-T was significantly greater than those treated with placebo, 25.8 and 21.7 months respectively. Cabazitaxel is a novel taxane thought to be efficacious in patients with chemoresistant disease. Recently, results from a randomized phase three clinical trial called TROPIC, comparing cabazitaxel plus prednisone vs mitoxantrone plus prednisone in patients with CRPC previously treated with docetaxel. Patients receiving cabazitaxel demonstrated a statistically significantly longer OS compared to MP (hazard ratio 0.70; 95% CI, 0.59, 0.83; p<0.0001). These results have recently led the FDA to approve cabazitaxel with prednisone in patients with metastatic CRPC who have received prior docetaxel and thus is currently the only FDA approved option for this patient cohort.

More recent unpublished results demonstrated that denosumab, a rank ligand inhibitor, was effective in reducing skeletal complications in metastatic CRPC when compared to zoledronic acid. Abiraterone, a potent CYP 17 inhibitor, demonstrated a significant improvement in overall survival in CRPC patients progressing after docetaxel.

In conclusion, progress in the management of CRPC has the potential to significantly improve patient survival and well being.

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