PROSTATE CANCER

Cabazitaxel boosts post-docetaxel survival

New data on a novel microtubule inhibitor have led to the FDA approving its use for second-line treatment of metastatic castration-resistant prostate cancer. The TROPIC trial of cabazitaxel in patients with post-docetaxel progressive disease detected a 30% reduction in the risk of death and a 2.4-month increase in overall survival relative to mitoxantrone.

Docetaxel plus prednisone is standard first-line therapy for men with castration-resistant metastatic prostate cancer. For patients whose disease progresses after docetaxel, mitoxantrone is often used to alleviate symptoms and improve quality of life. This drug does not, however, prolong survival.

Johann de Bono and colleagues compared the safety and efficacy of prednisone plus either mitoxantrone or cabazitaxel in an open-label, randomized phase III trial. Participants received 10 mg of oral prednisone daily plus either 12 mg/m^2 mitoxantrone intravenously over 15–30 min (n = 377) or 25 mg/m^2 cabazitaxel intravenously over 1 h (n = 378) every 3 weeks. The cabazitaxel dose was selected in an effort to limit neutropenia. Treatment was continued for a maximum of 10 cycles (to minimize the risk of toxic cardiac effects associated with mitoxantrone).

During a median follow-up period of 12.8 months, 234 deaths occurred in the cabazitaxel group and 279 in the mitoxantrone group. Median overall survival was 15.1 months for patients who received cabazitaxel compared with 12.7 months for their mitoxantrone-treated counterparts. Progression-free survival was also superior in the cabazitaxel group (2.8 months versus 1.4 months).

Significant improvements in PSA and tumor responses were recorded in the cabazitaxel group. There was no significant difference, however, in pain or time-to-pain progression between the two groups. Patients in the cabazitaxel group completed a median of six treatment cycles compared with four for the mitoxantrone group. The main reason for discontinuation of either regimen was disease progression.

The most common severe adverse event was neutropenia, which occurred more frequently in the cabazitaxel group. Indeed, the most frequent cause of death in the cabazitaxel group was neutropenia and its clinical consequences. The researchers suggest that prophylaxis with granulocyte colony-stimulating factor, or modifying the cabazitaxel dose, could help to manage these toxic effects.

"We believe that cabazitaxel should now be standard therapy," de Bono comments. He adds "combinations with abiraterone and trials of cabazitaxel versus docetaxel in the first-line setting are now warranted."

Lisa Richards

Original article de Bono, J. S. *et al.* Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet* **376**, 1147–1154 (2010)