Abstract

BACKGROUND: Cabazitaxel is a novel tubulin-binding taxane drug with antitumour activity in docetaxel-resistant cancers. We aimed to compare the efficacy and safety of cabazitaxel plus prednisone with those of mitoxantrone plus prednisone in men with metastatic castration-resistant prostate cancer with progressive disease after docetaxel-based treatment.

METHODS: We undertook an open-label randomised phase 3 trial in men with metastatic castration-resistant prostate cancer who had received previous hormone therapy, but whose disease had progressed during or after treatment with a docetaxel-containing regimen. Participants were treated with 10 mg oral prednisone daily, and were randomly assigned to receive either 12 mg/m² mitoxantrone intravenously over 15-30 min or 25 mg/m² cabazitaxel intravenously over 1 h every 3 weeks. The random allocation schedule was computer-generated; patients and treating physicians were not masked to treatment allocation, but the study team was masked to the data analysis. The primary endpoint was overall survival. Secondary endpoints included progression-free survival and safety. Analysis was by intention to treat. This study is registered at ClinicalTrials.gov, NCT00417079.

FINDINGS: 755 men were allocated to treatment groups (377 mitoxantrone, 378 cabazitaxel) and were included in the intention-to-treat analysis. At the cutoff for the final analysis (Sept 25, 2009), median survival was 15·1 months (95% CI 14·1-16·3) in the cabazitaxel group and 12·7 months (11·6-13·7) in the mitoxantrone group. The hazard ratio for death of men treated with cabazitaxel compared with those taking mitoxantrone was 0·70 (95% CI 0·59-0·83, p<0·0001). Median progression-free survival was 2·8 months (95% CI 2·4-3·0) in the cabazitaxel group and 1·4 months (1·4-1·7) in the mitoxantrone group (HR 0·74, 0·64-0·86, p<0·0001). The most common clinically significant grade 3 or higher adverse events were neutropenia (cabazitaxel, 303 [82%] patients vs mitoxantrone, 215 [58%]) and diarrhoea (23 [6%] vs one [<1%]). 28 (8%) patients in the cabazitaxel group and five (1%) in the mitoxantrone group had febrile neutropenia.

INTERPRETATION: Treatment with cabazitaxel plus prednisone has important clinical antitumour activity, improving overall survival in patients with metastatic castration-resistant prostate cancer whose disease has progressed during or after docetaxel-based therapy.

FUNDING: Sanofi-Aventis.

Comment in

Words of wisdom. Re: Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant
prostate cancer progressing after docetaxel treatment: a randomized open-label trial.  [Eur Urol. 2011]
Cabazitaxel for castration-resistant prostate cancer.  [Lancet. 2011]
Prostate cancer: Cabazitaxel boosts post-docetaxel survival.  [Nat Rev Urol. 2010]
Cabazitaxel in prostate cancer: stretching a string.  [Lancet. 2010]
Words of wisdom. Re: Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial.  [Eur Urol. 2011]
Improved survival in second-line advanced prostate cancer treated with cabazitaxel.  [Nat Rev Clin Oncol. 2010]
Cabazitaxel for castration-resistant prostate cancer.  [Lancet. 2011]

PMID: 20888992 [PubMed - indexed for MEDLINE]