New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Cabazitaxel

Approved indication: metastatic prostate cancer
Jevtana (Sanofi-Aventis)
concentrate containing 60 mg/1.5 mL for dilution
Australian Medicines Handbook section 14.1.6

Androgen ablation is the usual treatment for metastatic prostate cancer, but the disease becomes refractory to hormone treatment. The patient is then offered chemotherapy with drugs such as mitoxantrone or docetaxel.

The first taxanes were derived from the Pacific yew tree. Cabazitaxel is derived from the needles of the European yew tree. It was found to have antitumour activity which included an effect in cells which were poorly responsive to docetaxel.

After dilution, cabazitaxel is given intravenously over one hour. PVC containers and polyurethane infusion sets should not be used. The recommended regimen is an infusion every three weeks, adjusted according to toxicity. As cabazitaxel is extensively metabolised by the liver, it is not recommended for patients with liver impairment. The metabolism involves cytochrome P450 3A4. While there is a potential for interactions with inducers and inhibitors of this enzyme, drug interaction studies are yet to be reported.

The main study of cabazitaxel was an open-label trial of 755 patients with metastatic prostate cancer that had progressed despite treatment with docetaxel. These men were randomised to receive cycles of treatment with cabazitaxel or mitoxantrone, in addition to daily doses of 10 mg prednisone or prednisolone. The median number of treatment cycles was six with cabazitaxel and four with mitoxantrone. Median progression-free survival was 2.8 months with cabazitaxel and 1.4 months with mitoxantrone. Approximately 61% of the cabazitaxel group and 74% of the mitoxantrone group died during the study. Median overall survival was 15.1 months with cabazitaxel and 12.7 months with mitoxantrone.[1]

More than 80% of the patients treated with cabazitaxel developed severe or life-threatening neutropenia, compared with 58% of the mitoxantrone group. While 1% of the men given mitoxantrone developed febrile neutropenia, it occurred in 8% of the cabazitaxel group. Anaemia and thrombocytopenia were also more frequent with cabazitaxel.[1]

Frequent non-haematological adverse effects of cabazitaxel included diarrhoea (47%), fatigue (37%), nausea (34%), vomiting (23%), haematuria (17%) and peripheral neuropathy (14%). Adverse effects were more frequent with cabazitaxel and resulted in 18.3% of patients stopping treatment compared with 8.4% of the mitoxantrone group.[1] As hypersensitivity reactions can occur, patients need intravenous antihistamines and corticosteroids before each infusion. It is important that patients are kept well hydrated as there is a risk of renal failure. Arrhythmias have also been reported.

While the 30% reduction in the risk of death is statistically significant, the absolute gain in survival is a few weeks. This comes with the increased risk of dying from adverse effects. Cabazitaxel also had no advantage over mitoxantrone in its effect on the patients' pain.[1] Further research is needed to investigate the patients' quality of life and whether lower doses of cabazitaxel would produce the same benefits with less toxicity.

T T manufacturer provided additional useful information

REFERENCE *†A

1. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet 2010;376:1147-54.

The T-score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2011;34:26–7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu).

A At the time the comment was prepared, information about this drug was available on the website of the Therapeutic Goods Administration (www.tga.gov.au/industry/pm-auspar.htm)