New drugs

Pertuzumab

Approved indication: metastatic breast cancer
Perjeta (Roche)
vials containing 30 mg/mL for infusion
Australian Medicines Handbook section 14.2.1

The human epidermal growth factor receptor 2 (HER2) is overexpressed in up to 30% of people with breast cancer. This leads to an aggressive phenotype which is associated with reduced survival. Adding an anti-HER2 antibody, such as trastuzumab, to chemotherapy has been found to improve prognosis.

Pertuzumab is another humanised monoclonal antibody specific for HER2. It inhibits dimerization of HER2 with other HER receptors on the cell surface and blocks intracellular signalling. This results in cell growth arrest, apoptosis and cell-mediated cytotoxicity. Because pertuzumab binds to a different epitope, it can be used to complement trastuzumab treatment.

In a phase III trial (CLEOPATRA) in patients with HER2-positive metastatic breast cancer, intravenous pertuzumab or placebo was added to trastuzumab plus docetaxel. Pertuzumab significantly prolonged progression-free survival by 6.1 months compared to placebo (Table).[1] In an interim analysis, more patients had died in the placebo group than in the pertuzumab group.[2]

The most common adverse events with pertuzumab, trastuzumab and docetaxel included diarrhoea (66.8% of patients), alopecia (60.9%), neutropenia (52.8%), nausea (42.3%), fatigue (37.6%), rash (33.7%), decreased appetite (29.2%), mucosal inflammation (27.8%) and asthenia (26%). Febrile neutropenia was also reported and was more common with pertuzumab than with placebo (13.8% vs 7.6%). Severe febrile neutropenia (grade 3 or more) was more frequent in Asian patients, particularly those receiving pertuzumab compared to placebo (26% vs 12%).[1]

Some patients died as a result of adverse events – the proportion of deaths was similar with pertuzumab and placebo (2% vs 3%). Febrile neutropenia and infections were the most common cause of death.[2]

Like other drugs that block HER2, pertuzumab can cause heart failure. For this reason, patients with a left ventricular ejection fraction of less than 50% were excluded from the CLEOPATRA trial. The addition of pertuzumab to trastuzumab did not appear to increase left ventricular systolic dysfunction compared to placebo (4.4% vs 8.3%).[1] Left ventricular ejection fraction needs to be assessed before and regularly during treatment. If it is low (<40%) or has declined from baseline (40–45% and ≥10% below baseline), consider discontinuing or withholding pertuzumab and trastuzumab.

Pertuzumab is given as a slow intravenous infusion over one hour every three weeks. Infusion and hypersensitivity reactions have occurred so patients should be monitored during and after the infusion. Pertuzumab is cleared by catabolism and has an elimination half-life of 17 days.

In studies on monkeys, pertuzumab was toxic to unborn offspring. It has therefore been classified as a category D pregnancy drug and should be avoided in pregnancy. Because IgG is secreted in breast milk, pertuzumab could also be transferred to a nursing infant.

In combination with trastuzumab plus docetaxel, pertuzumab appears to extend progression-free survival of people with HER2-positive metastatic breast cancer. However patients must have a positive HER2 tumour status to receive treatment. Pertuzumab is specifically indicated for those who have not previously received anti-HER2 therapy or chemotherapy for metastatic disease.

T manufacturer provided the product information

REFERENCES *

1. Baselga J, Cortés J, Kim SB, Im SA, Hegg R, Im YH, et al; CLEOPATRA Study Group. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012;366:109-19.
2. Swain SM, Kim SB, Cortés J, Ro J, Semiglazov V, Campone M, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. Lancet Oncol 2013;14:461-71.

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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.

Table **The efficacy of pertuzumab in patients with HER2-positive metastatic breast cancer[1,2]**

	Pertuzumab + trastuzumab + docetaxel	Placebo + trastuzumab + docetaxel
Number of patients	400	404
Progression-free survival‡	18.5 months	12.4 months
Deaths at interim analysis§	113	154

‡ defined as the time from randomisation to first radiographic evidence of disease progression, or death within 18 weeks of last tumour assessment
§ performed one year after the efficacy analysis

NEW DRUGS

The Transparency 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).