trastuzumab emtansine

An inadequately assessed combination of two cytotoxic drugs

Abstract

There is no consensus on second-line treatment for women with metastatic or locally advanced breast cancer overexpressing HER-2 protein in whom treatment with a taxane + trastuzumab has failed. Capecitabine is one option. Adding lapatinib does not prolong survival.

Trastuzumab emtansine (Kadcyla®, Roche) has received EU marketing authorisation for use in this setting. It consists of two covalently bound drugs: trastuzumab, a monoclonal antibody that binds to HER-2 receptors, and DM1, a cytotoxic microtubule inhibitor. DM1 is derived from maytansine, a cytotoxic drug abandoned in the 1980s because it proved to be too toxic after systemic administration.

Clinical evaluation of trastuzumab emtansine is based on an unblinded trial versus capecitabine + lapatinib in 991 patients. The use of lapatinib in all patients in the control group is questionable. An interim analysis suggested that overall survival was about 6 months longer with trastuzumab emtansine (30.9 versus 25.1 months).

In addition to the adverse effects of trastuzumab (thrombocytopenia, heart failure, etc.), trastuzumab emtansine causes frequent and potentially life-threatening hepatic toxicity, peripheral neuropathy, and urinary tract infections. Trastuzumab emtansine appears to be less toxic to the skin and mucous membranes than the capetitabine + lapatinib combination.

DM1 is metabolised by cytochrome P450 isoenzymes CYP3A4 and CYP3A5 and is also a P-glycoprotein substrate, creating a potential risk of multiple pharmacokinetic interactions.

Trastuzumab emtansine appears to be teratogenic and embryotoxic.

The international proprietary name of this drug is easily confused with trastuzumab.

In practice, it is best to at least wait for the full results of the only available comparative trial of trastuzumab emtansine before drawing conclusions about its harm-benefit balance and its possible use if it represents a real therapeutic advance.

trastuzumab emtansine

powder to be diluted for IV infusion

KADCYLA®

- 100 or 160 mg of trastuzumab emtansine per vial

cytotoxic drug; anti-HER-2 antibiotic

Indication: “(…) as a single agent (…) for the treatment of adult patients with HER2-positive, unresectable locally advanced or metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:
– received prior therapy for locally advanced or metastatic disease, or
– developed disease recurrence during or within six months of completing adjuvant therapy”. [EU marketing authorisation, centralised procedure]

In response to our request for information, Roche provided us with administrative documents and packaging items.

Quality of information from pharmaceutical companies

In response to our systematic requests

Company provided detailed information including unpublished data and packaging items.

Company provided information limited to administrative and published data.

Company provided minimal information, mainly administrative data.

Company provided no information.