Kadcyla® (trastuzumab emtansine)

The first antibody drug conjugate (ADC) for the treatment of HER2-positive metastatic breast cancer

HER2-positive breast cancer: an aggressive disease

HER2-positive breast cancer occurs when breast cancer cells have too many copies of the HER2 protein. Around one in five women diagnosed with breast cancer will have HER2-positive breast cancer, which is an aggressive type of the disease and is likely to progress more quickly than cancer that is not HER2-positive.[1,2]

Currently there is no cure for HER2-positive late-stage (also called metastatic) breast cancer. In around half of women given first-line Herceptin® (trastuzumab) for metastatic disease, the treatment will stop working within 1 year, meaning they need another treatment option. Many patients may receive multiple treatments over the course of their disease in an attempt to prolong their life.[3]

Kadcyla: a new medicine with a unique mechanism of action

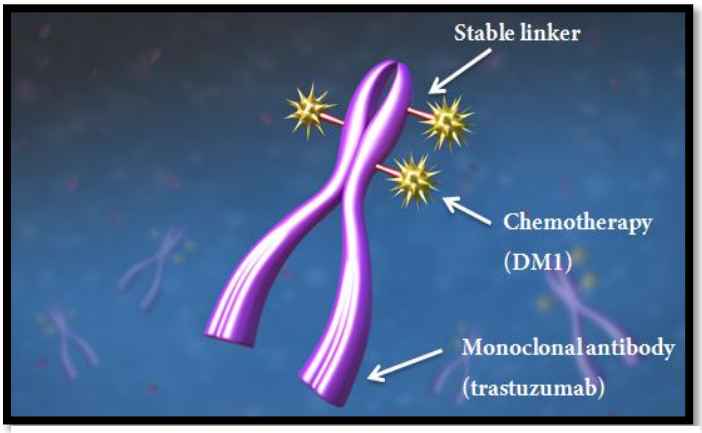

Figure 1: Structure of the ADC Kadcyla

Kadcyla is an example of a new generation of cancer drugs currently being developed, called an antibody-drug conjugate (ADC). It recognises the HER2 protein on the surface of HER2-positive cancer cells and is designed to selectively kill these cancer cells whilst minimising the effects on normal tissue. Kadcyla is made up of three parts; trastuzumab (the same active ingredient as Herceptin) and a chemotherapy called DM1 joined together by a stable linker (see figure 1). The stable linker enables the chemotherapy DM1, which is 24 to 270-fold stronger than currently used chemotherapies, to remain inactive until it enters the HER2-positive cancer cell.[4]

The trastuzumab component of Kadcyla allows it to find and bind to HER2-positive cancer cells. The trastuzumab component is then thought to block out-of-control signals that make the cancer grow, while also calling upon the body's immune system to attack the cancer cells. Kadcyla is taken up by the HER2-positive cancer cell and once it is inside the cell, the linker breaks down, releasing the DM1 which results in the destruction of the cancer cell (see figure 2).[4,5] As DM1 is released inside the cancer cell, this limits damage to nearby healthy tissue and results in fewer of the side effects patients often experience with chemotherapy, such as hair loss.[6]

Kadcyla specifically targets HER2-positive cancer cells, potentially maximising clinical benefit while minimising harmful side effects for patients.[4]

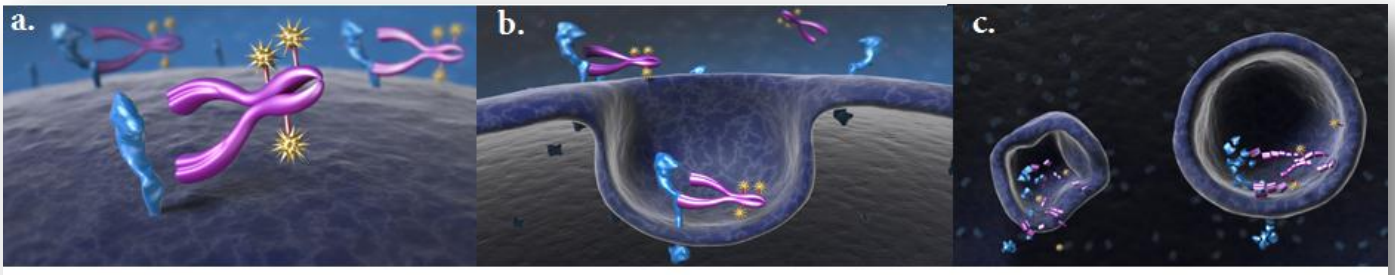

Figure 2a: The trastuzumab component of Kadcyla allows it to find and bind to HER2-positive cancer cells. Kadcyla retains the mechanism of action of trastuzumab and is thought to block out-of-control signals that make the cancer grow, while also calling upon the body's immune system to attack the cancer cells

Figure 2b: The HER2-positive cancer cell starts to take up the Kadcyla

Figure 2c: The linker breaks down, releasing the DM1 which results in the destruction of the cancer cell

Kadcyla: patient studies

A large international study called EMILIA has shown that patients who received Kadcyla survived a median of 5.8 months longer (overall survival) than those who received the combination of lapatinib and capecitabine, the current standard of care (median overall survival: 30.9 months vs. 25.1 months respectively).[7] Patients receiving Kadcyla experienced a 32 percent reduction in the risk of dying compared to people who received lapatinib and capecitabine.

Furthermore, patients who received Kadcyla lived for a median of 9.6 months without their disease getting worse (progression-free survival), compared to 6.4 months for those who took the combination of lapatinib and capecitabine which is an additional 3.2 months longer.[7] The EMILIA study also showed that patients who received Kadcyla lived 2.5 months longer without experiencing deterioration in their quality of life than those who received lapatinib plus capecitabine. Quality of life was defined as the time from when the patient started their treatment until the symptoms of their breast cancer returned – this measure is also called time to symptom progression. Importantly, patients treated with Kadcyla experienced fewer serious adverse effects than patients treated with lapatinib and capecitabine.[8]

> The EMILIA study showed that Kadcyla extended survival of patients with HER2-positive mBC by 5.8 months (overall survival; OS).[7]

How is Kadcyla administered?

Kadcyla is given as an intravenous infusion, which means that it is delivered directly into the bloodstream through a tube called a catheter or 'port' in the patient's vein. Typically, a patient would go to hospital every three weeks and have a single infusion which lasts around 30 minutes to one hour. As Kadcyla is given as a single agent, this means that patients only receive one infusion, per visit. The dose of Kadcyla is calculated according to body weight at 3.6mg per kg.[9]

Kadcyla: a new treatment option

Kadcyla has received New Zealand registration from Medsafe for the treatment of patients with HER2-positive metastatic breast cancer who have previously been treated with Herceptin and taxane chemotherapy. To be eligible for treatment with Kadcyla, patients should have either received prior treatment for their metastatic disease or developed disease recurrence during or within six months of completing treatment for early breast cancer.[9] Kadcyla has been approved by the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA) and also the Australian Therapeutic Goods Agency (TGA). It is anticipated that Kadcyla will offer an important new treatment option for patients with HER2-positive late-stage breast cancer.

References
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5. Hurvitz S, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer. J Clin Oncol: 2013; 31:1157-1163
6. Ducry L and Stump B. Antibody-drug conjugates: linking cytotoxic payloads to monoclonal antibodies. Bioconjugate Chem, 2010; 21; 5-13.
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9. Kadcyla (trastuzumab emtansine) Data Sheet. 05 August 2013

ID# 1666/TAPSNA6713/SEPT13

Kadcyla Consumer Panel

Kadcyla® (trastuzumab emtansine), 100mg and 160mg vials, is a **Prescription Medicine** used to treat patients with metastatic (spreading) breast cancer who have tumours with a large amount of the HER2 protein. **Tell your doctor if:** you have had a serious infusion-related reaction to Herceptin (trastuzumab); you have a history of heart problems; you have any breathing or lung problems; you have liver problems; you have bleeding problems; you are receiving anti-coagulant treatment (blood thinning medication); you are pregnant or breast-feeding, or plan to become pregnant or breast-feed. **Possible serious unwanted effects:** swelling of your lips, face, tongue or throat with difficulty breathing; swelling of other parts of your body such as your hands or feet; weight gain of more than 2 kilograms in 24 hours; shortness of breath, wheezing or trouble breathing; abnormal or irregular heartbeat; rash, itching or hives on the skin; flushing (warm, red) skin; pain or swelling at the site of infusion; feeling sick (nausea) or vomiting, diarrhoea; pain or discomfort (including stomach pain, back pain, chest or neck pain); fever or chills; headache; fatigue or tiredness; cough; dizziness or fainting; jaundice; dark urine; or loss of appetite. **If you experience any of the side-effects listed above, tell your doctor or nurse immediately or go to Accident and Emergency at your nearest hospital.** Other possible side effects include: getting tired more easily after light physical activity; insomnia (difficulty sleeping); weakness, soreness in muscles and/or joints; numbness or weakness of arms and legs; bleeding or bruising more easily than normal; nose bleeds; feeling dizzy, tired, looking pale; flu and/or cold like symptoms, frequent infections such as fever, severe chills, sore throat or mouth ulcers; dry mouth; taste disturbance or loss of taste; constipation, vomiting, indigestion or diarrhoea; or eye problems such as producing more tears, swollen runny eyes or conjunctivitis .

Ask your Oncologist if Kadcyla is right for you. Use strictly as directed. If symptoms continue or if you experience side effects or would like more information, please talk to your Oncologist or visit www.medsafe.govt.nz for the full Kadcyla Consumer Medicine Information.

Kadcyla is an unfunded medicine. You will need to pay for this medicine. A prescription charge and normal oncologist fees apply.

Consumer panel dated 25 September 2013 based on CMI dated 01 May 2013.
Roche Products (New Zealand) Limited, Auckland. Phone: 0800 656 464. www.roche.co.nz.