Media Release

Medical audiences

Neoadjuvant treatment key to unlocking benefits of PBS-listed *Kadcyla*® (trastuzumab emtansine) in the adjuvant setting

- **Based on the results of the KATHERINE study, showing a reduced risk of disease recurrence by 50%, Kadcyla® (trastuzumab emtansine) is now available on the Pharmaceutical Benefits Scheme (PBS) for the adjuvant (after surgery) treatment of patients with HER2-positive early breast cancer (eBC) who have residual invasive disease after neoadjuvant (before surgery) taxane and trastuzumab-based treatment.**[1]
- **Under Australian guidelines, neoadjuvant therapy is a recommended approach for the treatment of early breast cancer and is a prerequisite for the use of Kadcyla under its new PBS indication.** [2]
- **The multidisciplinary team, including surgeons, alongside medical oncologists, play an increasingly important role in providing neoadjuvant (before surgery) therapy and ensuring patients have effective treatment options in the long term.**[2,3]

SYDNEY, <1 APRIL 2020> - Kadcyla is now listed on the Pharmaceutical Benefits Scheme (PBS) from April 1, 2020, for the adjuvant treatment of patients with HER2-positive early breast cancer (eBC) who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

In the adjuvant setting, Kadcyla was found to have reduced disease recurrence by 50% (HR=0.50, 95% CI 0.39-0.64; p<0.001) in patients with HER2-positive early breast cancer, who had residual invasive disease following neoadjuvant taxane and trastuzumab-based treatment.[1]

Australian guidelines recommend that treatment of early breast cancer be provided by a multidisciplinary team, consisting of at least a surgeon, medical oncologist, radiation oncologist, radiologist and nurse, to ensure optimal patient outcomes.[2,3]

Associate Professor Elisabeth Elder, specialist breast surgeon and head of research at the Westmead Breast Cancer Institute said: “As a surgeon and a member of the multidisciplinary team, the shared goal is to provide the patient with optimal treatment options and ultimately maximise success in eliminating the disease. Neoadjuvant therapy is a key part of ensuring that patients are not losing further treatment options like adjuvant Kadcyla.”

As surgeons are often the first point of contact for breast cancer patients along the treatment journey, they play an important role in identifying patients who would benefit from neoadjuvant therapy.[4]

Breast surgeon and Vice President of BreastSurgANZ, Dr. Melanie Walker further highlighted the

advantages of neoadjuvant treatment in helping to improve patient outcomes by offering additional treatment options in the adjuvant setting.[2]

"Neoadjuvant therapy can act as an *in vivo* model of disease that is important prognostically for assessing tumour response to treatment and allowing adaptation in post-surgery treatment to maximise patient outcomes. It is no longer simply a tool for improving surgical outcomes but a crucial part of the optimal treatment pathway," said Dr. Walker.[2]

According to international guidelines, neoadjuvant treatment should be considered for all appropriate patients, especially those with HER2-positive and triple-negative breast cancer, as part of optimal treatment planning.[2,5,6]

According to medical oncologist, Dr Richard de Boer, from St Vincent's Private Hospital Melbourne, "The changing algorithm of treatment in early breast cancer means we can offer patients with HER2-positive breast cancer better treatment options that can reduce the risk of disease recurrence – which is a significant cause of anxiety for breast cancer patients."[7]

Breast cancer is the most common cancer affecting Australian women– with 1 in 7 women being diagnosed with breast cancer by the age of 85.[8] In 2020, it is estimated that around 20,000 women and 170 men will be diagnosed with breast cancer.[8]

HER2-positive breast cancer is characterised by the over-expression of the HER2 protein, which causes uncontrolled growth in cancer cells.[4,9] HER2-positive cancer accounts for approximately 15-20% of breast cancer cases and is associated with a more aggressive form of the disease.[9,10]

Roche Australia Managing Director Stuart Knight said the company is committed to helping patients gain access to the most innovative treatment options.

"I congratulate the Federal Government on expediting the PBS listing of Kadcyla," Mr Knight said.

"Roche has a long heritage of innovation in breast cancer cancer, and I'm delighted that eligible patients now have an additional option for the adjuvant treatment of HER2-positive early breast cancer."

About Kadcyla®

Kadcyla® is a human epidermal growth factor receptor-2 (HER2) targeted antibody-drug conjugate (ADC) designed to deliver anti-cancer emtansine directly inside HER2-positive breast cancer cells, attaching to the HER2 protein in order to stop the growth and spread of cancer cells.[10,11] Kadcyla is made up of two substances; trastuzumab, a monoclonal antibody, and emtansine, a cytotoxic agent.[11]

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Please review Product Information before prescribing, available at
www.roche-australia.com/productinfo/kadcyla
KADCYLA is listed on the PBS for HER2-positive early and metastatic breast cancer.
Refer to PBS Schedule for full authority information.

IMPORTANT INFORMATION ABOUT KADCYLA[1,2]

MINIMUM PRODUCT INFORMATION
Kadcyla® (*trastuzumab emtansine, rch*)

Indications: ***Early Breast Cancer (EBC):*** Kadcyla, as a single agent, is indicated for the adjuvant treatment of patients with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment. ***Metastatic Breast Cancer (MBC):*** Kadcyla, as a single agent, is indicated for the treatment of patients with HER2-positive metastatic (Stage IV) breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either: 1) received prior therapy for metastatic disease, or 2) developed disease recurrence during or within six months of completing adjuvant therapy.

WARNING: Do not substitute Kadcyla for or with trastuzumab.
In order to prevent medication errors, check the vial labels to ensure the medicine being prepared and administered is Kadcyla (trastuzumab emtansine) and not trastuzumab.

Dosage and Administration: HER2+ tumour status: IHC3+ or ISH ratio ≥ 2.0. Recommended dose is 3.6 mg/kg every 3 weeks as an IV infusion (over 90 min). Observe patients during infusion and for at least 90 min following the initial dose. If prior infusions are well tolerated, subsequent infusions may be administered over 30 min and patients observed during the infusion and for at least 30 min following. The infusion rate of Kadcyla should be slowed or interrupted if the patient develops infusion-related symptoms. Discontinue Kadcyla for life-threatening infusion reactions. ***Dose modifications:*** Management of symptomatic adverse events may require temporary interruption, dose reduction, or treatment discontinuation of Kadcyla as per dose modification guidelines provided in full prescribing information. The Kadcyla dose should not be re-escalated after a dose reduction is made.

Contraindications and Precautions: contraindicated in patients with known hypersensitivity to Kadcyla or any of its excipients. Patients must have confirmed HER2+ tumour status. ***Pulmonary toxicity:*** interstitial lung disease (ILD) including pneumonitis, some leading to acute respiratory distress syndrome or fatal outcome, have been reported. Permanently discontinue in patients diagnosed with ILD or pneumonitis, except in EBC patients with radiation pneumonitis where Kadcyla should be permanently discontinued for ≥ Grade 3 or for Grade 2 not responding to standard treatment. Patients with dyspnoea at rest due to complications of advanced malignancy, co-morbidities, and receiving concurrent pulmonary radiation therapy may be at increased risk of pulmonary events. ***Hepatotoxicity:*** hepatotoxicity, liver failure and death have occurred in patients treated with Kadcyla. Monitor hepatic function (serum transaminases and bilirubin) prior to initiation and prior to each Kadcyla dose. Reduce the dose or discontinue as appropriate (refer to dose modification guidelines in prescribing information). Serious hepatobiliary disorders, including nodular regenerative hyperplasia (NRH) of the liver and some with fatal outcome due to drug-induced liver injury have been observed. NRH should be considered in all patients with clinical symptoms of portal hypertension and/or cirrhosis-like pattern on liver CT scan but with normal transaminases and no other manifestations of cirrhosis. Permanently discontinue treatment upon diagnosis of NRH. ***Left ventricular dysfunction:*** Kadcyla may lead to reductions in LVEF. Symptomatic CHF is a potential risk. Assess LVEF prior to initiation and at regular intervals during treatment (e.g. every 3 months). Monitor and reduce dose or discontinue as appropriate (refer to dose modification guidelines in prescribing information). ***Infusion-related reactions (IRR):*** treatment is not recommended in patients who permanently discontinued trastuzumab due to

an IRR. Treatment should be interrupted in patients with severe IRR and permanently discontinued in the event of a life threatening IRR. ***Hypersensitivity reactions:*** observe closely for hypersensitivity reactions, especially during first infusion. Medications to treat serious anaphylactic like reactions, as well as emergency equipment, should be available for immediate use. ***Haemorrhage:*** bleeding events with a fatal outcome have been observed. Severe cases of haemorrhagic events, including CNS haemorrhage have been reported. Monitor patients with thrombocytopenia and patients on anti-coagulant treatment closely. ***Thrombocytopenia:*** Platelet counts should be monitored prior to each dose. If platelet count decreases to ≥ Grade 3, do not administer Kadcyla until platelet counts recover to Grade 1. ***Neurotoxicity:*** treatment should be temporarily discontinued in patients experiencing Grade 3 or 4 peripheral neuropathy until symptoms resolve or improve to ≤ Grade 2. ***Extravasation:*** the infusion site should be closely monitored for possible subcutaneous infiltration during administration. ***Pregnancy Category D***: treatment is not recommended for pregnant women. Use effective contraception during treatment, and for at least 7 months after last dose. If a patient becomes pregnant while being treated with Kadcyla or within 7 months following the last dose of Kadcyla, immediately report exposure to the Roche Drug Safety Department by one of the following methods: Email: australia.drug_safety@roche.com; Fax: 02 9971 7401; Phone:02 9454 9444 or mail to Level 8, 30-34 Hickson Road, Sydney NSW 2000. Additional information will be requested during a Kadcyla-exposed pregnancy and the first year of the infant's life, this will enable Roche to better understand the safety of Kadcyla and to provide appropriate information to Health Authorities, Healthcare Providers and patients. Discontinue breastfeeding prior to starting treatment, nursing may begin again 7 months after last dose.

Adverse Effects: thrombocytopenia, anaemia, neutropenia, left ventricular dysfunction, dry eye, increased lacrimation, blurred vision, conjunctivitis, nausea, constipation, vomiting, diarrhoea, abdominal pain, dry mouth, stomatitis, dyspepsia, fatigue, pyrexia, asthenia, chills, peripheral oedema, hepatic failure, nodular regenerative hyperplasia, portal hypertension, drug hypersensitivity, urinary tract infection, infusion related reaction, radiation pneumonitis, increased transaminases, increased blood alkaline phosphatase, increased blood bilirubin, hypokalaemia, musculoskeletal pain, arthralgia, myalgia, headache, peripheral neuropathy, dizziness, dysgeusia, insomnia, epistaxis, cough, dyspnoea, pneumonitis, rash, pruritis, haemorrhage, hypertension.

Full Product Information available from Roche Products Pty Limited
(www.roche-australia.com/productinfo/kadcyla).

Disclosure

A/Prof. Elisabeth Elder, Dr. Melanie Walker and Dr. Richard de Boer and have received no honorarium or compensation for involvement in this announcement. The opinions presented by A/Prof. Elder, Dr. Walker and Dr. de Boer are their own. A/Prof. Elder, Dr. Walker and Dr. de Boer have been briefed by Roche and Weber Shandwick on the approved use of this product and the requirements of Medicines Australia's Code of Conduct. Dr de Boer has previously received honoraria from Roche for participating in advisory boards, speaking at educational meetings and has received reimbursement for travel to medical meetings.

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HER2-positive breast cancer

HER2 is a protein found on the surface of cancer cells that causes uncontrolled cell growth.[4] Tumours with high levels of these receptors are referred to as HER2-positive, which accounts for around 15-20% of breast cancers.[4,9] HER2-positive breast cancers are associated with a particularly aggressive form of the disease with high-grade tumours, increased growth rates and decreased rates of disease-free and overall survival.[10,13] HER2-positive breast cancer may be treated using chemotherapy and targeted therapy such as trastuzumab.[4]

About the KATHERINE study

KATHERINE is an international, multi-centre, two-arm, randomised, open-label, phase III study.[1] The KATHERINE study evaluates the efficacy and safety of Kadcyla versus trastuzumab as an adjuvant therapy in people with HER2-positive eBC who have pathological invasive residual disease in the breast and/or axillary lymph nodes following neoadjuvant therapy that included taxane and trastuzumab-based treatment.[1] The primary endpoint of the study is invasive disease-free survival (iDFS), which in this study is defined as the time from randomisation until the date of recurrence or death from any cause. Second primary non-breast cancer was used as a secondary end point alongside disease-free survival, overall survival, distant recurrence-free survival, and safety. Results of the KATHERINE study showed that Kadcyla significantly reduced the risk of invasive breast cancer recurrence or death from any cause by 50% (HR=0.50, 95% CI 0.39-0.64, p<0.001) compared to trastuzumab as an adjuvant treatment in people with HER2-positive eBC who have residual invasive disease after neoadjuvant taxane and trastuzumab -based treatment.[1] At three years, 88.3% of people treated with Kadcyla did not experience an invasive-disease event compared to 77.0% treated with Herceptin, an absolute improvement of 11.3%.[1] The safety profile of Kadcyla was consistent with that observed in previous studies, with the most commonly reported Grade 3 and higher adverse events being decreased platelet counts and hypertension.[1]

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology,

immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the tenth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

For medical enquiries relating to Kadcyla please contact australia.medinfo@roche.com or call 1800 233 950.

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