bcac breast cancer aotearoa coalition

Together we're stronger
Tangata tū pakari tonu

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20th June 2023

Re: Switching IV Herceptin® to IV Herzuma® brand of trastuzumab

Kia ora Pharmac,

The Breast Cancer Aotearoa Coalition (BCAC) is supportive of the **switch from Herceptin to Herzuma** as this product has been used safely and effectively in Australia since 2019 and in private clinics in New Zealand since at least 2020. We have repeatedly asked for the timely introduction of such a biosimilar product so that funds can be made available to fund new therapy advances.

We are pleased to see that Pharmac will **retain a stock of Herceptin** for use under exceptional circumstances if patients have a reaction to Herzuma. We are also pleased to see the introduction of the option for a **'treatment holiday'** for long-term responders to trastuzumab treatment with metastatic HER2 positive breast cancer.

However, we are deeply disappointed to see that access has not been extended to allow **retreatment with trastuzumab following progression in metastatic breast cancer**. Evidence-based treatment guidelines compiled by expert committees around the world have all recommended later line retreatment with trastuzumab, especially in the absence of other recommended treatment options. This is particularly relevant in current circumstances as New Zealand has very limited funding for other treatments recommended for later lines of therapy. It is likely that these treatments, when they are eventually funded will be a lot more expensive than trastuzumab.

Multiple guidelines recommend retreatment with trastuzumab, including those promulgated by ESMO , NCCN and New Zealand's own Advanced Breast Cancer Guidelines (Breast Cancer Special Interest Group (Breast SIG) New Zealand 2022). Indeed, trastuzumab is offered in a range of combinations throughout mBC treatment lines to fourth-line and beyond.

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New Zealanders with breast cancer do not have access to a full range of possible treatments for recurrent HER2+ breast cancer. **NCCN Guidelines (2023)** state that "Multiple lines of concurrent chemotherapy with anti-HER2 therapy (trastuzumab or a TKI (tyrosine kinase inhibitor)) offer clinical benefit for recurrent unresectable HER2+ metastatic breast cancer and have been studied in phase 2 or 3 trials. Clinical experience suggests frequent clinical benefit for such treatment" (NCCN 2023). The options as outlined by NCCN in their 2023 breast cancer guidelines are reproduced below.

SYSTEMIC THERAPY REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[k]

HR-Positive or -Negative and HER2-Positive[j,k]	
Setting	**Regimen**
First Line[l]	Pertuzumab + trastuzumab + docetaxel (Category 1, preferred)
	Pertuzumab + trastuzumab + paclitaxel (preferred)
Second Line[n]	Fam-trastuzumab deruxtecan-nxki[m] (Category 1, preferred)
Third Line	Tucatinib + trastuzumab + capecitabine[n] (Category 1, preferred)
	Ado-trastuzumab emtansine (T-DM1)[o]
Fourth Line and Beyond (optimal sequence is not known)[p]	Trastuzumab + docetaxel or vinorelbine
	Trastuzumab + paclitaxel ± carboplatin
	Capecitabine + trastuzumab or lapatinib
	Trastuzumab + lapatinib (without cytotoxic therapy)
	Trastuzumab + other chemotherapy agents[q,r]
	Neratinib + capecitabine
	Margetuximab-cmkb + chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine)
	Additional Targeted Therapy Options see BINV-Q (6)

Source: (NCCN 2023)

Amongst the options for later line treatment, the following are not funded in New Zealand: trastuzumab deruxtecan; tucatinib; lapatinib; neratinib; and margetuximab. The lack of available, funded options is therefore a concern at second, third and fourth lines of treatment.

A similar treatment algorithm is seen in the **ESMO guidelines (2021)** where second line treatments after trastuzumab/pertuzumab include TDM-1, tucatinib, and trastuzumab deruxtecan, with the latter two not funded in New Zealand.

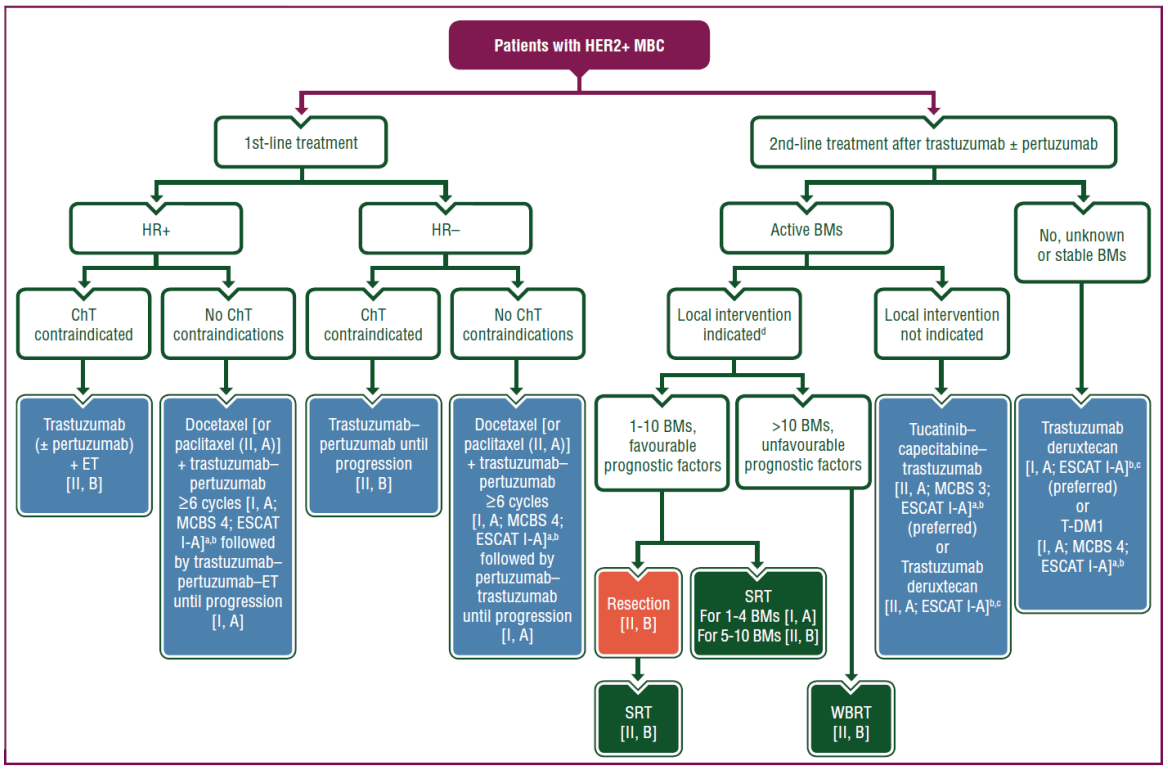


Figure 3. First- and second-line treatment of HER2-positive MBC.
Purple: general categories or stratification; red: surgery; turquoise: combination of treatments or other systemic treatments; green: RT; white: other aspects of management; blue: systemic anticancer therapy.
BM, brain metastasis; ChT, chemotherapy; CNS, central nervous system; EMA, European Medicines Agency; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; ET, endocrine therapy; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PD, progressive disease; RT, radiotherapy; SRT, stereotactic radiotherapy; T-DM1, ado-trastuzumab emtansine; WBRT, whole brain radiotherapy.
[a] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation-forms-v1.1).
[b] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[c] Not FDA approved for use in second line.
[d] Keep on current systemic therapy unless PD outside CNS.

Source: (Gennari, André et al. 2021)

At third line, the ESMO algorithm includes tucatinib, trastuzumab deruxtecan, margetuximab and lapatinib in combination with trastuzumab (Gennari, André et al. 2021), none of which are funded in New Zealand.

ESMO Guidelines state that “Continued anti-HER2-based therapy is the current clinical standard for patients with HER2-positive tumours. If other anti-HER2 therapies have been exhausted, are not considered suitable or are not available, trastuzumab beyond progression should be considered [III, A].” (Gennari, André et al. 2021).

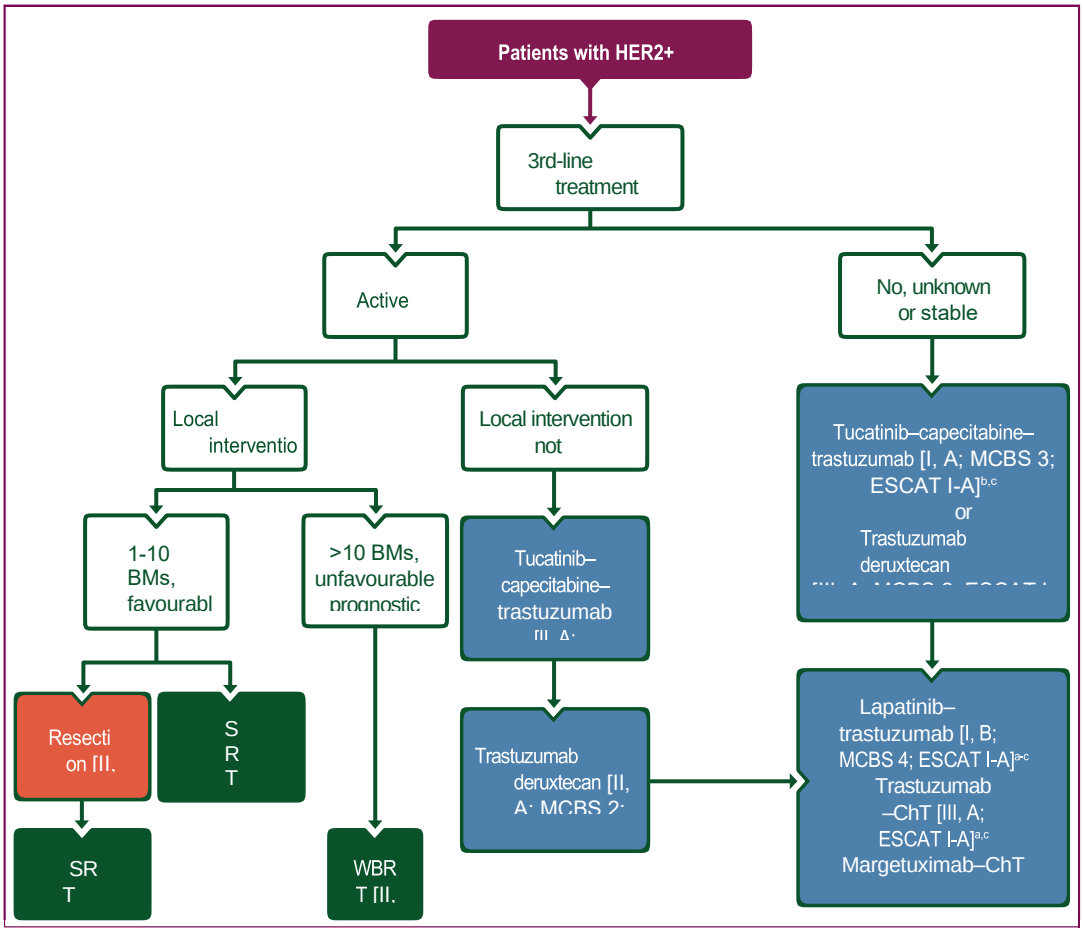


Figure 4. Third-line and beyond treatment of HER2-positive MBC.
Purple: general categories or stratification; red: surgery; turquoise: combination of treatments or other systemic treatments; green: RT; white: other aspects of management; blue: systemic anticancer therapy.
BM, brain metastasis; ChT, chemotherapy; CNS, central nervous system; EMA, European Medicines Agency; ESCAT, ESMO Scale for Clinical Actionability of Molecular Targets; FDA, Food and Drug Administration; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; MCBS, ESMO-Magnitude of Clinical Benefit Scale; PD, progressive disease; RT, radiotherapy; SRT, stereotactic radiotherapy; T-DM1, ado-trastuzumab emtansine; WBRT, whole brain radiotherapy.
[a] There are no data for any of these combinations after tucatinib- and/or trastuzumab deruxtecan-based therapy.
[b] ESMO-MCBS v1.1[93] was used to calculate scores for new therapies/indications approved by the EMA or FDA. The scores have been calculated by the ESMO-MCBS Working Group and validated by the ESMO Guidelines Committee (https://www.esmo.org/guidelines/esmo-mcbs/scale-evaluation-forms-v1.0-v1.1/scale-evaluation- forms-v1.1).
[c] ESCAT scores apply to genomic alterations only. These scores have been defined by the guideline authors and validated by the ESMO Translational Research and Precision Medicine Working Group.[89]
[d] FDA approved, not EMA approved.
[e] If not received as second-line therapy.
[f] Keep on current systemic therapy unless PD outside CNS.
[g] If not previously used, including all other drugs that are also a second-line treatment option.

Source: (Gennari, André et al. 2021)

The **New Zealand Advanced Breast Cancer Guidelines (2022)** state that trastuzumab can be administered as later line retreatment with several chemotherapy (CT) agents – consensus was 84% amongst the New Zealand expert panel, as shown below (Breast Cancer Special Interest Group (Breast SIG) New Zealand 2022).

HER2-positive ABC For later lines of therapy, trastuzumab can be administered with several CT agents, including but not limited to, vinorelbine (if not given in 1st line), taxanes (if not given in 1st line), capecitabine, liposomal anthracyclines, platinum, gemcitabine, or metronomic CM. *Trastuzumab is not Pharmac-funded (as of September 2022) for continuation beyond progression.* *Liposomal anthracyclines are Medsafe-approved but not Pharmac-funded (as of September 2022).* The decision should be individualized and take into account different toxicity profiles, previous exposure, patient preferences, and country availability.	II/A	84%

In summary, the lack of funding for trastuzumab at later lines of treatment leaves every few options for New Zealand patients with recurrent metastatic HER2+ breast cancer. This is of significant concern because of the statistics on patient survival in New Zealand compared with similar countries (Breast Cancer Foundation New Zealand 2018).

In denying patients with recurrent disease access to trastuzumab (and other more recently available treatments) for advanced HER2+ breast cancer **Pharmac is neglecting the current global standard of care, real-world evidence and the needs of patients for additional later line treatment options**. This decision is contrary to both international and local guidelines and consensus. It only serves to perpetuate our lamentable survival rates. It condemns affected New Zealand women to shortened lives compared with what they could expect in countries with similar heath care systems. This is particularly callous when a trastuzumab biosimilar is now available at a significantly reduced price.

The impact of failing to extend access to later line retreatment is likely to have a **greater effect on wāhine Māori**, given their higher rate of breast cancer diagnosis (121 per 100,000 for Māori, 89.6 per 100,000 for non-Māori for all breast cancer) and mortality (18.2 per 100,000 for Māori, 14.1 per 100,000 for non-Māori for all breast cancer) (Te Whatu Ora 2023). Survival of wāhine Māori with advanced breast cancer is lower than other ethnicities as shown in the table below (Breast Cancer Foundation New Zealand 2018; Te Whatu Ora 2023).

Table 4: Māori and other ethnicities' survival with ABC

	NZ Māori	Pacific Island	Asian	European
Median survival (months)	12.8 (9.5, 18.6)	18.5 (12.1, 23.1)	26.8 (18.3, 36.4)	15.7 (13.7, 17.3)
One-year survival	50% (41, 59)	64% (52, 73)	82% (68, 90)	57% (53, 60)
Five-year survival	5% (2, 10)	21% (13, 31)	14% (5, 29)	15% (12, 18)

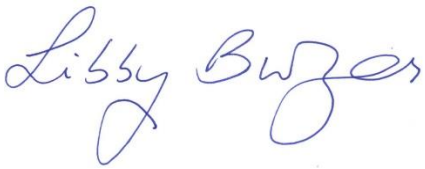
Pharmac notes in relation to a treatment holiday 'We consider this option would improve the quality of life for people who choose to pause treatment, allowing them to spend less time receiving treatment and more time engaging with their day-to-day activities, friends and whānau'. We note that this would also be the case if Pharmac were to fund **a rapidly injectable form of trastuzumab** that could be delivered subcutaneously. Treatment could involve a 10-minute injection in a doctor's clinic, closer to home and whānau for patients, providing greater access for those who find it difficult to travel to centralised cancer treatment centres. The inability to take days off work, to travel to hospitals for treatment

and to receive treatment away from whānau support tends to affect Māori and Pasifika patients more than those of other ethnicities and compounds existing inequities in access to cancer treatments.

Providing an injectable form of trastuzumab, both with and without pertuzumab, would considerably lessen the pressure on our cancer treatment centres. We agree with the statement from the Cancer Society in their recent media release in relation to this consultation '*the UK first announced funding for subcutaneous Herceptin in 2013 on the basis that it would free up specialist cancer nurses and hospital pharmacists given rising pressures on chemotherapy facilities ; minimise waste and overall drug costs because the subcutaneous form of Herceptin is given as a fixed dose not dependent on patient size or weight; is a much less invasive treatment; and has the benefit for patients of less time receiving treatment*'.

We are supportive of extension of access to patients with gastric cancer.

Nga mihi



Libby Burgess
Chair
Breast Cancer Aotearoa Coalition

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