bcac breast cancer aotearoa coalition

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Tangata tū pakari tonu

25th September 2024

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**BCAC response to Pharmac consultation on the proposal to list trastuzumab deruxtecan (T-DXd, Enhertu) for the treatment of advanced HER2 positive breast cancer on the Pharmaceutical Schedule**

We are supportive of Pharmac's proposal to fund T-DXd for people whose metastatic HER2 positive (HER2+) breast cancer has:

- Progressed after prior trastuzumab treatment for metastatic disease or
- Progressed within 6 months of adjuvant HER2 targeted treatment.

We also support funding for people who are receiving trastuzumab emtansine (T-DM1) at the listing date as proposed and the transitioning of those accessing T-DXd by private funding to publicly funded T-DXd.

We note remarkable benefits of T-DXd evident in the update of the Destiny-Breast03 trial presented at ASCO 2024 after median follow-up of 43 months for T-DXd and 35.4 months for T-DM1. This showed progression free survival of 29.0 months on T-DXd vs 7.2 months for T-DM1. Overall survival analysis showed superiority for T-DXd, mOS (95% CI) 52.6 months (48.7 – not evaluable) vs T-DM1 42.7 months (35.4 - not evaluable), hazard ratio 0.73. Overall survival rate at 36 months (95% CI) was 67.6% (61.3 – 73) for T-DXd vs 55.7% (49.2 – 61.7) for T-DM1 (Hamilton et al. 2024).

While the safety profile of T-DXd is likely to be manageable for most people, we are aware of some New Zealand patients who have experienced intolerable side effects on T-DXd and have subsequently switched to T-DM1.

Given the possibility of severe side effects caused by T-DXd in some patients, we submit that **those who experience unmanageable or intolerable side effects on T-DXd treatment and those who have a pre-existing condition that would exclude them from T-DXd treatment should be offered T-DM1 treatment as an alternative to T-DXd**.

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We further submit that **there is an additional group that should be included in this proposal, i.e. those whose advanced HER2+ breast cancer has previously progressed on T-DM1.**

The Destiny-Breast02 trial (André et al, 2023) tested the use of T-DXd in patients with HER2+ advanced breast cancer whose disease was refractory or resistant to T-DM1. The efficacy and safety of T-DXd were compared with treatment of physician's choice (TPC) in this population. TPC was either capecitabine plus trastuzumab or capecitabine plus lapatinib.

After median follow-up of 21.5 months in the T-DXd group and 18.6 months in the TPC group, progression free survival was found to be 17.8 months (95% CI 14·3–20·8) in the T-DXd group vs 6.9 months (5.5-8.4) with TPC, (HR 0·36 [0·28–0·45]; p<0·0001).

PFS benefit was seen in all patient sub-groups, whatever their age, hormone receptor status, whether they had previously received pertuzumab treatment, whether they had visceral disease or baseline brain metastases, whatever number of lines of previous therapy they had received and whether their ECOG score was 0 or 1.

This study provides compelling evidence of a significant benefit of T-DXd after progression on T-DM1.

We also note that Pharmac has received an application to fund Enhertu for advanced HER2-low breast cancer. In patients with HER2-low unresectable or metastatic breast cancer who had received one or two previous lines of chemotherapy, the Destiny-Breast04 trial compared PFS and OS after either T-DXd or a treatment of physician's choice (TPC). Eligible patients had to have received chemotherapy for metastatic disease or have had disease recurrence within 6 months of receiving adjuvant chemotherapy. Those with hormone receptor positive (HR+) disease had to have received at least one line of endocrine therapy. Low expression of HER2 was defined as a score of 1+ on immunohistochemical [IHC] analysis or as an IHC score of 2+ and negative results on in situ hybridization. TPC was capecitabine, eribulin, paclitaxel or nab-paclitaxel.

In the HR+ cohort PFS was 10.1 months in the T-DXd group vs 5.4 months in the TPC group (HR for progression or death 0.51, P<0.001). Overall survival was 23.9 months with T-DXd and 17.5 months for TPC (HR for death 0.64, P=0.003). Among all patients median PFS was 9.9 months in the T-DXd group vs 5.1 months for TPC (HR for progression or death 0.50, P<0.001) and OS was 23.4 months for T-DXd vs 16.8 months for TPC (HR for death = 0.64, P=0.001).

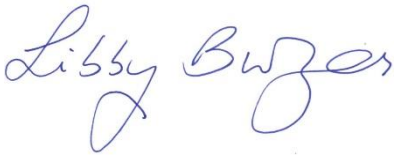
Analysis of data from Te Rèhita Mate Ūtaetae (Breast Cancer Foundation NZ National Register) shows that 38% of women with advanced cancer have HER2-low disease; of these, 31.7% are HR+ and 6.3% are HR- (Lasham et al. 2024). The researchers concluded that the potential to treat a wider spectrum of breast cancers with targeted therapies like T-DXd could transform the therapeutic landscape in NZ.

Given the impressive gains in both PFS and OS for patients, whatever the hormone receptor status of their disease, we further submit that **Pharmac should fund T-DXd for unresectable or metastatic HER2-low breast cancer with urgency**.

In summary, we support the funding proposal for T-DXd and ask that:

1. Those who experience unmanageable or intolerable side-effects on T-DXd or have a pre-existing condition that excludes them from T-DXd treatment should have funded access to T-DM1
2. The eligible group for T-DXd should be expanded to include those whose advanced HER2+ breast cancer has previously progressed on T-DM1
3. Pharmac should proceed with urgency to fund T-DXd for unresectable metastatic HER2-low breast cancer.

Ngā mihi,



Libby Burgess

BCAC Chair

**References attached to submission**

Hamilton et al. 2024, Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients (pts) with HER2+ metastatic breast cancer (mBC): Updated survival results of DESTINY-Breast03. *Journal of Clinical Oncology*, 42 (16) supp. https://doi.org/10.1200/JCO.2024.42.16_suppl.1025

André et al., 2023. Trastuzumab deruxtecan versus treatment of physician's choice in patients with HER2-positive metastatic breast cancer (DESTINY-Breast02): a randomised, open-label, multicentre, phase 3 trial, *The Lancet* Volume 401, Issue 10390, pp1773-1785. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00725-0/abstract

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