bcac breast cancer aotearoa coalition

Together we're stronger
Tangata tū pakari tonu

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Pharmac
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Re: pembrolizumab and triple negative breast cancer

Kia ora Jared,

I'm writing to express concern about the pace of progress with getting pembrolizumab funded for patients with both high risk early stage and metastatic (CPS>10) triple negative breast cancer (TNBC). As you are aware, BCAC applied for both these indications to be funded in November 2022. The applications were considered by CTAC in October 2023 and outcomes published in March 2024.

The metastatic use was given a medium ranking by CTAC and moved onto the Options for Investment (OFI) list while the indication for early breast cancer received only a low ranking and was not placed on that list.

We wish to bring your attention to the publication of new data from the KEYNOTE-522 trial in Annals of Oncology in February, Pusztai et al. 2024, DOI: https://doi.org/10.1016/j.annonc.2024.02.002

As summarised by the authors:

Background

The KEYNOTE-522 trial demonstrated statistically significant improvements in pathological complete response (pCR) with neoadjuvant pembrolizumab plus chemotherapy and event-free survival (EFS) with neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab in patients with high-risk, early-stage triple-negative breast cancer (TNBC). Prior studies have shown the prognostic value of the residual cancer burden (RCB) index to quantify the extent of residual disease after neoadjuvant chemotherapy. In this preplanned exploratory analysis (undertaken by Pusztai et al.), the distribution of residual cancer burden (RCB) and event free survival (EFS) within RCB categories by treatment group were reviewed.

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Patients and methods

A total of 1174 patients with stage T1c/N1-2 or T2-4/N0-2 TNBC were randomized 2 : 1 to pembrolizumab 200 mg or placebo every 3 weeks given with four cycles of paclitaxel + carboplatin, followed by four cycles of doxorubicin or epirubicin + cyclophosphamide. After surgery, patients received pembrolizumab or placebo for nine cycles or until recurrence or unacceptable toxicity. Primary endpoints are pCR and EFS. RCB is a prespecified exploratory endpoint. The association between EFS and RCB was assessed using a Cox regression model.

Results

Pembrolizumab shifted patients into lower RCB categories across the entire spectrum compared with placebo. There were more patients in the pembrolizumab group with RCB-0 (pCR), and fewer patients in the pembrolizumab group with RCB-1, RCB-2, and RCB-3. The corresponding hazard ratios (95% confidence intervals) for EFS were 0.70 (0.38-1.31), 0.92 (0.39-2.20), 0.52 (0.32-0.82), and 1.24 (0.69-2.23). The most common first EFS events were distant recurrences, with fewer in the pembrolizumab group across all RCB categories. Among patients with RCB-0/1, more than half [21/38 (55.3%)] of all events were central nervous system recurrences, with 13/22 (59.1%) in the pembrolizumab group and 8/16 (50.0%) in the placebo group.

Conclusions

Addition of pembrolizumab to chemotherapy resulted in fewer EFS events in the RCB-0, RCB-1, and RCB-2 categories, with the greatest benefit in RCB-2. These findings demonstrate that pembrolizumab not only increased pCR rates, but also improved EFS among most patients who do not have a pCR.

These further data confirm the importance of pembrolizumab as an effective treatment for those with early-stage TNBC, in addition to the metastatic indication previously considered by CTAC. Patients with early-stage TNBC urgently need access to this treatment to prevent their cancers from advancing.

We note that there are three classes of medicines recommended in international guidelines for the treatment of TNBC that remain unfunded in Aotearoa New Zealand: immunotherapies such as pembrolizumab, antibody drug conjugates such as sacituzumab govitecan and PARP inhibitors such as olaparib. Pembrolizumab was funded in Australia for metastatic TNBC in September 2023 and for early TNBC in December 2023. Sacituzumab govitecan was funded in Australia for metastatic TNBC in March 2022. Olaparib was recommended by PBAC in Australia for high-risk early-stage BRCA1/2m breast cancer in November 2023.

We ask that recently published pembrolizumab data from KEYNOTE-522 be urgently reviewed by CTAC so they can reconsider the low ranking given to this medicine for high-risk early breast cancer. This aggressive form of breast cancer threatens the lives of many women and every effort should be made to stop the disease while it remains curable. The need to fund pembrolizumab in the metastatic setting also remains urgent.

Ngā mihi

Libby Burgess

BCAC Chair

Reference:

Pusztai, L., Denkert, C., O'Shaughnessy, J., et al. 2024. Event-free survival by residual cancer burden with pembrolizumab in early-stage TNBC: exploratory analysis from KEYNOTE-522. Annals of Oncology, 35 (5), 429-436. DOI: https://doi.org/10.1016/j.annonc.2024.02.002