Canada's Drug Agency
L'Agence des médicaments du Canada

Neoadjuvant Pertuzumab for HER2-positive Breast Cancer

FMEC Responses to Questions from the Drug Programs

Table 1: Response Summary

Drug program implementation questions	Clinical expert response (Clinical Experts Acting as Guest Specialists for FMEC)	FMEC Response
Relevant comparators		
Neoadjuvant pertuzumab-trastuzumab was previously reviewed in 2015 (Neosphere) and 2022 (PEONY), both of which compared pertuzumab-trastuzumab-docetaxel against trastuzumab-docetaxel. The new evidence consists of retrospective studies. One of the studies compared neoadjuvant pertuzumab-trastuzumab-chemotherapy against trastuzumab-chemotherapy, which is an appropriate comparator.	This is a general comment from the drug programs to inform FMEC deliberations.	FMEC acknowledges this information.
Considerations for initiation of therapy		
Are patients treated with neoadjuvant pertuzumab-trastuzumab eligible for pertuzumab-trastuzumab in the metastatic setting?	The clinical experts stated that patients would be eligible in the metastatic setting if disease-free interval was greater than or equal to 6 months.	FMEC agrees with the clinical experts.
Considerations for discontinuation of therapy		
The request is for pertuzumab-trastuzumab use in the neoadjuvant setting only. Can FMEC define the appropriate number of cycles of neoadjuvant pertuzumab-trastuzumab?	The clinical experts recommend 4 to 6 cycles for neoadjuvant pertuzumab-trastuzumab into any neoadjuvant regimen that contains trastuzumab, depending on the chemotherapy backbone and timing of surgery. In the case of unforeseen delays in surgery, it may be reasonable to administer up to 2 additional cycles. The clinical experts also mentioned that due to delays, if only a single antibody is given prior to surgery, it would be trastuzumab alone.	FMEC notes that if the patient is receiving FEC-D chemotherapy as part of the neoadjuvant regimen, only 3 cycles of pertuzumab and trastuzumab would be given in conjunction with docetaxel. FMEC notes that there is no evidence to support giving more than 6 cycles of pertuzumab. Trastuzumab could be given alone if surgery is delayed.
Considerations for prescribing of therapy		
Pertuzumab is given as a loading dose 840mg followed by 420mg every 21 days.	This is a general comment from the drug programs to inform FMEC deliberations.	FMEC acknowledges this information.

Trastuzumab loading dose of 8mg/kg followed by 6mg/kg every 21 days (or 4mg/kg loading dose followed by 2mg/kg weekly).		
Can pertuzumab be given with biosimilar trastuzumab?	The clinical experts agreed that pertuzumab can be given with biosimilar trastuzumab, as this is already done in the advanced disease setting.	FMEC agrees with the clinical experts. FMEC also notes that biosimilar trastuzumab is being used in the neoadjuvant setting.
What chemotherapy regimens should be given with pertuzumab-trastuzumab?	All three clinical experts agreed that there are many chemotherapy regimens that can be given, such as any currently available neoadjuvant trastuzumab-based regimen. One of the clinical experts specified a few examples: docetaxel/carboplatin (x6), AC-T, FEC-D, paclitaxel, and docetaxel.	FMEC agrees with the clinical experts.
Generalizability		
Should patients currently on neoadjuvant trastuzumab-chemotherapy be switched to neoadjuvant pertuzumab-trastuzumab-chemotherapy?	The clinical experts agreed that on a time-limited basis, these patients should be switched to neoadjuvant pertuzumab-trastuzumab if the treating physician thinks it is clinically appropriate.	FMEC agrees with the clinical experts
System and economic issues		
T-DM1 is administered as adjuvant treatment of patients with HER2-positive early-stage breast cancer who have pathologic residual disease after pre-operative systemic treatment. If there is no pathologic residual disease after pre-operative systemic treatment, trastuzumab is administered as adjuvant treatment. There is potential for cost-savings and reduced patient toxicities in the adjuvant setting if the use of neoadjuvant pertuzumab-trastuzumab leads to a higher pathologic complete response, which may allow for increased use of adjuvant trastuzumab over adjuvant trastuzumab emtansine	This is a general comment from the drug programs to inform FMEC deliberations.	FMEC acknowledges this information.
Confidential prices exist for pertuzumab, trastuzumab, and trastuzumab biosimilar.	This is a general comment from the drug programs to inform FMEC deliberations.	FMEC acknowledges this information.

AC-T = doxorubicin-cyclophosphamide with a taxane-based therapy (docetaxel, paclitaxel); FEC-D = Fluorouracil, Epirubicin, Cyclophosphamide with Docetaxel; T-DM1 = Trastuzumab emtansine