

Breast Cancer Guidance

The American Society of Clinical Oncology offers the following clinical guidance on treatment alternatives during shortages of antineoplastic agents. Decisions should be based on specific goals of the therapy where evidence-based medicine has shown survival outcomes and life-extending benefits in both early and advanced stages. For more information on ASCO's general principles during drug shortages, please visit ASCO's [Clinical Guidance page](#). For further consideration of ethical guidance, please visit ASCO's [Ethical Principles and Implementation Strategies page](#).

Disclaimer: Disease site-specific guidance for clinical management during drug shortages is provided by the American Society of Clinical Oncology, Inc. ("ASCO") for voluntary, informational use in the context of limited carboplatin or cisplatin availability. This and other guidance on ASCO's website (together "Guidance") is not a comprehensive or definitive guide to treatment options. New evidence may emerge between the time information is developed and when it is published or read and should only be used in conjunction with independent professional medical judgement. Guidance is based on expert opinion of the [Drug Shortages Advisory Group](#) and non-systematic review of relevant literature. It is not medical or pharmacologic advice and is not intended as a statement of the standard of care. ASCO does not endorse third-party drugs, devices, services, or therapies and assumes no responsibility for any harm arising from or related to the use of this information. Use of the information is subject to the complete ASCO website [Terms of Use](#).

General Principles for Breast Cancer

1. Clinical factors that may influence the incremental benefit of a drug for a given patient with breast cancer include nodal status, stage, age, comorbidities, response to prior therapy, and the availability of alternative treatment options.
2. Carboplatin/Cisplatin has **no role** in the treatment of hormone receptor-positive HER2-negative breast cancer in the curative setting.
3. Carboplatin/Cisplatin has a **limited role** in the non-curative setting for all subtypes of breast cancer during national shortage given available alternatives.
4. The incremental benefit of cytotoxic chemotherapy is greater in patients with early-stage triple-negative breast cancer (TNBC) compared to those with early-stage HER2+ breast cancer, for which efficacious alternatives exist.
5. Clinical trials remain an important option for any line of therapy for both early and late-stage breast cancer that may provide a platinum-free alternative approach.

Early-Stage Triple Negative Breast Cancer

1. For the treatment of stage II-III triple-negative breast cancer, the Keynote-522 (KN-522) carboplatin-containing regimen is the recommended standard of care in the neoadjuvant setting.¹ **However, the incremental benefit of carboplatin in KN-522 is unknown.**
2. For the KN-522 regimen of preoperative pembrolizumab, carboplatin, and paclitaxel, followed by preoperative pembrolizumab, cyclophosphamide, and doxorubicin or epirubicin, the standard dose of weekly carboplatin is an AUC of 1.5, but dose modification to an AUC 1 is acceptable for resource allocation.

- a. Notably, in KN-522, median weeks of carboplatin was 11.1 (2.0 -26.1 weeks) and median number of administrations was 12 (3.0 -12.0 administrations), with 9.3% discontinuing carboplatin-based therapy during neoadjuvant treatment.¹
3. When carboplatin is limited or unavailable, consider the following modifications to KN522:
 - a. Platinum may be started at a modified dose AUC of 1 (weekly)—preferred—or 4 (q3 weeks). See general principle 3.
 - b. Start with Adriamycin and cyclophosphamide (AC)/pembrolizumab to be followed by paclitaxel and pembrolizumab with or without carboplatin.
 - i. Personalize the addition of platinum to taxane/pembrolizumab based on clinical response to AC/pembrolizumab. Consider prioritizing platinum for patients whose tumors have not responded well to AC/pembrolizumab.
 - ii. As always, for patients who do not receive carboplatin and who do not have a pathologic complete response, discuss available clinical trials and/or approved agents for residual disease including adjuvant capecitabine and olaparib (pathogenic BRCA1 or BRCA2 variants).
 - c. Starting taxane and pembrolizumab without platinum may be an acceptable strategy for patients with node-negative disease, older patients, and others with significant comorbidities or in settings where no platinum agent is available.²
 - i. In the I-SPY³ and GEPARNUEVO⁴ trials immune checkpoint inhibitors were used with taxane / anthracycline chemotherapy without carboplatin and both showed similar improvement in pCR rate as KN-522 and the GEPARNUEVO trial also demonstrated improved iDFS.
 - ii. For patients whose tumors are not responding well to neoadjuvant AC/pembrolizumab and when carboplatin is not available, the substitution of carboplatin with weekly cisplatin (25 mg/m²) combined with paclitaxel and continued pembrolizumab can be considered.^{5,6} Implement recommended cardio-oncology prevention strategies to maximize patient safety.⁷

Early Stage HER2+ Breast Cancer

1. For the treatment of HER2+ breast cancer, the carboplatin-containing regimen of docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) is one recommended standard of care for preoperative/adjuvant therapy.⁸ However, **the incremental benefit of carboplatin in TCHP is unknown.**
2. For the TCHP regimen: **AUC of 5 is acceptable for resource allocation.**
3. When carboplatin is not available, consider the following alternatives:
 - a. Treatment with Adriamycin and cyclophosphamide followed by paclitaxel, trastuzumab, and pertuzumab (AC-THP) is a guideline-based, platinum-sparing regimen alternative for patients. Implement recommended cardio-oncology prevention strategies to maximize patient safety.
 - b. Consider omitting carboplatin from TCHP, as data from the metastatic setting offers evidence that carboplatin **does not add a significant benefit.**⁹ Salvage options are available in the adjuvant setting for residual disease (i.e., additional chemotherapy, trastuzumab emtansine(T-DM1)); and ongoing de-escalation trials lend legitimacy to this approach.⁹
 - i. Treat with neoadjuvant THP x 12-16 weeks (paclitaxel) or 4-6 cycles (docetaxel).
 - ii. Patients with residual disease should be treated with T-DM1 for 14 cycles.

- iii. AC x 4 can be considered in patients with high-risk disease who have received 12 weeks of THP with residual disease.
- c. As always, patients with clinical stage I tumors should have their axilla evaluated by ultrasound with or without MRI as indicated. Neoadjuvant or adjuvant paclitaxel/trastuzumab is acceptable therapy for stage I disease.

References

1. Schmid P, Cortes J, Pusztai L, et al: Pembrolizumab for Early Triple-Negative Breast Cancer. *New England Journal of Medicine* 382:810-821, 2020
2. Gupta S, Nair N, Hawaldar R, et al: Abstract GS5-01: Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A phase III randomized controlled trial. *Cancer Research* 83:GS5-01, 2023
3. Nanda R, Liu MC, Yau C, Shatsky R, Pusztai L, Wallace A, Chien AJ, Forero-Torres A, Ellis E, Han H, Clark A. Effect of pembrolizumab plus neoadjuvant chemotherapy on pathologic complete response in women with early-stage breast cancer: an analysis of the ongoing phase 2 adaptively randomized I-SPY2 trial. *JAMA oncology*. 2020 May 1;6(5):676-84.
4. Loibl S, Schneeweiss A, Huober J, Braun M, Rey J, Blohmer JU, Furlanetto J, Zahm DM, Hanusch C, Thomalla J, Jackisch C. Neoadjuvant durvalumab improves survival in early triple-negative breast cancer independent of pathological complete response. *Annals of Oncology*. 2022 Nov 1;33(11):1149-58.
5. Vidra R, Nemes A, Vidrean A, et al: Pathological complete response following cisplatin or carboplatin-based neoadjuvant chemotherapy for triple-negative breast cancer: A systematic review and meta-analysis. *Exp Ther Med* 23:91, 2022
6. Silver DP, Richardson AL, Eklund AC, et al: Efficacy of neoadjuvant Cisplatin in triple-negative breast cancer. *J Clin Oncol* 28:1145-53, 2010
7. Armenian SH, Lacchetti C, Barac A, et al: Prevention and Monitoring of Cardiac Dysfunction in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline. *Journal of Clinical Oncology* 35:893-911, 2016
8. Schneeweiss A, Chia S, Hickish T, et al: Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). *Annals of Oncology* 24:2278-2284, 2013
9. Mamounas EP, Untch M, Mano MS, et al: Adjuvant T-DM1 versus trastuzumab in patients with residual invasive disease after neoadjuvant therapy for HER2-positive breast cancer: subgroup analyses from KATHERINE. *Ann Oncol* 32:1005-1014, 2021