



SYSTEMIC THERAPY FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE

- For treatment of brain metastases, see [NCCN Guidelines for Central Nervous System Cancers](#).

General considerations:

- An FDA-approved biosimilar is an appropriate substitute for any recommended systemic biologic therapy in the NCCN Guidelines.
- Screen for and manage immunotherapy-related toxicities and endocrine dysfunctions (eg, hypothyroidism, adrenal insufficiency) in patients treated with immune checkpoint inhibitors. See NCCN Guidelines for Management of Immunotherapy-Related Toxicities.
- Regular cardiac monitoring for patients with current or prior use of anthracyclines or HER2-targeted therapy. See NCCN Guidelines for Survivorship: Cardiovascular Disease Risk Assessment.
- Consider scalp cooling to reduce incidence of chemotherapy-induced alopecia for patients receiving chemotherapy. Results may be less effective with anthracycline.
- When receiving taxane-containing regimen:
 - Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) may be substituted for select patients due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of albumin-bound paclitaxel should not exceed 125 mg/m².
 - Consider cryotherapy of hands and feet to decrease the risk of peripheral neuropathy.^{1,2}

For Those Receiving HER2-targeted Therapy

- Trastuzumab and hyaluronidase-oysk subcutaneous injection may be substituted for trastuzumab IV; however, dosing and administration instruction differ. Do not substitute trastuzumab and hyaluronidase-oysk for or with ado-trastuzumab emtansine or fam-trastuzumab deruxtecan-nxki.
- Pertuzumab, trastuzumab, and hyaluronidase-zzxf subcutaneous injection may be substituted for IV pertuzumab and trastuzumab; however, the dosing and administration instruction may differ.
- Patients previously treated with chemotherapy plus trastuzumab in the absence of pertuzumab in the metastatic setting may be considered for one line of therapy including both trastuzumab plus pertuzumab in combination with or without cytotoxic therapy (such as vinorelbine or taxane). Further research is needed to determine the ideal sequencing strategy for anti-HER2 therapy.

¹ Sphar BG, Bowe C, Dains JE. The impact of peripheral cooling on chemotherapy-induced peripheral neuropathy: An integrative review. J Adv Pract Oncol 2020;11:845-857.

² Hanai A, Ishiguro H, Sozu T, et al. Effects of cryotherapy on objective and subjective symptoms of paclitaxel-induced neuropathy: Prospective self-controlled trial. J Natl Cancer Inst 2018;110:141-148.

Note: All recommendations are category 2A unless otherwise indicated.