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Oncology

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Update

The NCCN Guidelines® for Breast Cancer have been updated to Version 3.2026

The recommendation for recurrent unresectable or stage IV disease for hormone receptor (HR)-negative and human epidermal growth factor receptor 2 (HER2)-negative (triple-negative breast cancer; TNBC) has been updated.

- **Sacituzumab govitecan-hziy is recommended as an NCCN Category 1, preferred option for 1L metastatic TNBC PD-L1 CPS <10 and no germline *BRCA1/2* PV**
- **Sacituzumab govitecan-hziy + pembrolizumab is recommended as an NCCN Category 1, preferred option for 1L metastatic TNBC for patients with PD-L1 CPS ≥10 regardless of germline *BRCA1/2* PV status**

Sacituzumab govitecan-hziy also remains an NCCN Category 1, preferred option for 2L metastatic TNBC.

The use of sacituzumab govitecan-hziy ± pembrolizumab in patients with previously untreated, locally advanced unresectable or metastatic triple-negative breast cancer is investigational. Sacituzumab govitecan-hziy is not approved for this use and the efficacy and safety for this use have not been established.

Table 1. NCCN Guidelines recommended cytotoxic regimens for recurrent unresectable (local or regional) or stage IV (M1) disease[a]

HR-negative and HER2-negative (TNBC)		
Setting	**Subtype/biomarker**	**Regimen**
First line	PD-L1 CPS ≥10[b] regardless of germline *BRCA1/2* PV status[c]	Chemotherapy (albumin-bound paclitaxel, carboplatin/gemcitabine, or paclitaxel) + pembrolizumab[d] (Category 1, preferred)
		Sacituzumab govitecan-hziy[e] + pembrolizumab[d] (Category 1, preferred)
	PD-L1 CPS <10[b] and no germline *BRCA1/2* PV[c]	Sacituzumab govitecan-hziy (Category 1, preferred)[e,f]
		Datopotamab deruxtecan-dlnk (Category 1, preferred)
		Systemic chemotherapy
	PD-L1 CPS <10[b] and germline *BRCA1/2* PV[c]	PARPi (olaparib or talazoparib) (Category 1, preferred)
		Platinum (carboplatin or cisplatin) (Category 1, preferred)
Second line	Germline *BRCA1/2* PV[c]	PARPi (Category 1, preferred)
	Any	Sacituzumab govitecan-hziy[e,f] (Category 1, preferred)
		Systemic chemotherapy or targeted agents
	No germline *BRCA1/2* PV[c] and HER2 (*ERBB2*) IHC 1+ or 2+/ISH negative[g]	Fam-trastuzumab deruxtecan-nxki[h] (other recommended)
Third line and beyond	Biomarker positive (ie, MSI-H, *NTRK1/2/3* and *RET* gene fusions, TMB-H)	Targeted agents and emerging biomarker options
	Any	Systemic chemotherapy

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Note: All recommendations are category 2A unless otherwise indicated. Category 2A indicates that based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate. Category 1 indicates that based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.

The National Comprehensive Cancer Network® (NCCN®) recommendations differ from the sacituzumab govitecan-hziy (TRODELVY®) Prescribing Information.

[a]For treatment of brain metastases, see NCCN Guidelines for Central Nervous System Cancers.
[b]Programmed death ligand 1 (PD-L1) expression is assessed using 22C3 antibody. Threshold for positivity combined positive score (CPS) ≥10.
[c]Assess for germline *BRCA1/2* PVs in all patients with recurrent or metastatic breast cancer to identify candidates for PARPi therapy.
[d]While available data are in the first-line setting, this regimen can be used for second and subsequent lines of therapy if programmed cell death protein 1 (PD-1)/PD-L1 inhibitor therapy has not been previously used. If there is disease progression while on a PD-1/PD-L1 inhibitor, there are no data to support an additional line of therapy with another PD-1/PD-L1 inhibitor. [e]See NCCN Guidelines for Hematopoietic Growth Factors.
[f]Sacituzumab govitecan-hziy may be considered for second or later line if not used in a previous line of therapy.
[g]See NCCN Guidelines for Breast Cancer: Principles of HER2 Testing (BINV-A). The distinction between HER2 (*ERBB2*) test results of IHC 0/absent membrane staining, IHC 0+/with membrane staining (faint, partial membrane staining in ≤10%), IHC 1+, or 2+/ISH negative is currently clinically relevant for therapy selection.
[h]Fam-trastuzumab deruxtecan-nxki may be considered in a later line for HER2 (*ERBB2*) IHC 1+ or 2+/ISH negative, if not used in second line or may be considered first-line therapy when disease has progressed during or within 6 months after completing adjuvant chemotherapy. Fam-trastuzumab deruxtecan-nxki is associated with interstitial lung disease (ILD)/pneumonitis. Regular monitoring for this serious side effect is recommended. For patients with a history of ILD/pneumonitis, there are no data on managing safety or toxicity of this drug in a trial.

1L, first line; 2L, second line; *BRCA*, breast cancer gene; *BRCA1/2*, breast cancer gene 1/2; CPS, combined positive score; *ERBB2*, erb-b2 receptor tyrosine kinase 2 gene; FDA, US Food and Drug Administration; HER2, human epidermal growth factor receptor 2; HER2–, human epidermal growth factor receptor 2–negative; HR–, hormone receptor–negative; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; MSI-H, microsatellite instability-high; mTNBC, metastatic triple-negative breast cancer; NCCN, National Comprehensive Cancer Network; *NTRK1/2/3*, neutrophic tyrosine receptor kinase genes; PARP, poly (ADP-ribose) polymerase; PARPi, poly (ADP-ribose) polymerase inhibitors; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PV, pathogenic variant; *RET*, rearranged during transfection gene; TMB-H, tumor mutational burden-high.

APPROVED INDICATIONS

Sacituzumab govitecan-hziy (TRODELVY®) is indicated for the treatment of adult patients with

- Unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

TRODELVY® can cause severe, life-threatening, or fatal neutropenia. Withhold TRODELVY® for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Primary prophylaxis with G-CSF is recommended for all patients at increased risk of febrile neutropenia. Initiate anti-infective treatment in patients with febrile neutropenia without delay.

TRODELVY® can cause severe diarrhea. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY® until resolved to ≤ Grade 1 and reduce subsequent doses.

CONTRAINDICATIONS

Severe hypersensitivity reaction to TRODELVY®.

WARNINGS AND PRECAUTIONS

- Hypersensitivity and Infusion-Related Reactions: Hypersensitivity reactions including severe anaphylactic reactions have been observed. Monitor patients for infusion-related reactions. Permanently discontinue TRODELVY® if severe or life-threatening reactions occur.
- Nausea/Vomiting: Use antiemetic preventive treatment and withhold TRODELVY® for patients with Grade 3 nausea or Grade 3-4 vomiting at the time of scheduled treatment.
- Patients with Reduced UGT1A1 Activity: Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia following initiation of TRODELVY® treatment.
- Embryo-Fetal Toxicity: TRODELVY® can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 25%) (including laboratory abnormalities) were decreased leukocyte count, decreased neutrophil count, decreased hemoglobin, diarrhea, nausea, decreased lymphocyte count, fatigue, alopecia, constipation, increased glucose, decreased albumin, vomiting, decreased appetite, decreased creatinine clearance, increased alkaline phosphatase, decreased magnesium, decreased potassium, and decreased sodium.

Please see the full Prescribing Information for additional safety information.

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