CAPhO RESEARCH COMMUNITY OF PRACTICE

Guidance for Canadian Breast Cancer Practice

National Consensus Recommendations for the Systemic Treatment of Patients with HER2+ Breast Cancer — Early and Metastatic Settings

2025 UPDATE

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Research Community of Practice Virtual Session
Wednesday, September 23, 2026 · 12:00 PM PT

Kumar A, Jerzak KJ, Gelmon KA, et al. Curr. Oncol. 2026, 33, 200.

BACKGROUND

What is the REAL Alliance?

Research Excellence, Active Leadership Canadian Breast Cancer Alliance — a standing nucleus committee of multidisciplinary, clinical-academic oncologists and specialists from across Canada, formed in partnership with Breast Cancer Canada.

"Because when research meets the real world, we save lives."

Why it matters to pharmacy practice

- National, standardized recommendations — one framework across provinces and territories
- Built through structured expert consensus, not a single institution's opinion
- Updated yearly as trial evidence evolves

Dec 2023

Alliance formed, in partnership with Breast Cancer Canada

≥75%

Agreement threshold for a modified-Delphi consensus recommendation

13 + 3

Voting panel: 13 medical oncologists + surgical & radiation oncologists, 1 pharmacist, 1 patient advocate

Source: realalliance.ca

CONTEXT

Building on the 2024 Original Guidance

UPDATED

2024 — ORIGINAL GUIDANCE

Curr. Oncol. 2024, 31(11), 6536–6567

First national consensus recommendations for HER2+ early and metastatic breast cancer.

2025 — THIS UPDATE

Curr. Oncol. 2026, 33, 200

Same REAL Alliance author team. Re-voted using a modified Delphi process on new 2025 trial evidence.

New 2025 evidence that reshaped the recommendations

DESTINY-Breast05

Adjuvant escalation, high-risk residual disease

DESTINY-Breast09

First-line metastatic, T-DXd + pertuzumab

DESTINY-Breast11

Neoadjuvant escalation, higher-risk early BC

PATINA

Maintenance CDK4/6i in triple-positive disease

APHINITY (10-yr)

Long-term adjuvant OS benefit confirmed

HER2CLIMB-05

Maintenance tucatinib, first-line metastatic

Treatment by Stage at Diagnosis

cT1a/b	**Low-risk, node-negative**	Surgery first, then adjuvant treatment based on pathologic stage.	**Strong**
pT1 N0	**Small tumour, node-negative**	Adjuvant paclitaxel + trastuzumab × 12 weeks, then trastuzumab monotherapy × 9 months.	**Strong**
≥cT2 / cN+	**Higher-risk, node-positive**	Neoadjuvant trastuzumab + pertuzumab + chemotherapy (taxane preferred) is the standard of care.	**Strong**
Residual	**Residual disease post-neoadjuvant**	Escalate adjuvant therapy — T-DM1 for standard risk, T-DXd for high-risk disease (pending Health Canada approval).	**Strong**
HR+/N+	**Hormone-receptor-positive**	Consider extended adjuvant neratinib × 1 year after trastuzumab-based therapy to reduce recurrence.	**Moderate**

Table 1, REAL Alliance 2025 Update

EARLY BREAST CANCER

What Changed in 2025

APHINITY — 10-YEAR FOLLOW-UP

89.8% → 91.6%

10-year overall survival with adjuvant pertuzumab added to trastuzumab (21% relative risk reduction in node-positive disease). Confirms Rec. 6.

DESTINY-BREAST11 (NEOADJUVANT)

67.3% vs. 56.3%

pCR with neoadjuvant T-DXd → THP vs. standard ddAC → THP in higher-risk disease. New option under Rec. 5(b) — pending Health Canada approval.

Pharmacist takeaway

- Two ADCs now sit in the early-disease escalation pathway — T-DM1 (standard-risk residual disease) and T-DXd (high-risk residual disease, pending approval). Confirm which criteria apply before dispensing.
- T-DXd carries a distinct ILD/pneumonitis monitoring profile versus T-DM1 — build this into counselling and toxicity-monitoring protocols now, ahead of approval.
- Until Health Canada approves DESTINY-Breast05/11-based options, continue current approved standards of care.

APHINITY 10-yr (ESMO 2025); DESTINY-Breast11 (ESMO 2025)

Treatment by Line of Therapy

Relapse	**On disease relapse**	Repeat biopsy in all patients whose disease relapses on or after adjuvant treatment.	**Strong**
1L	**De novo or late relapse (>6 mo)**	Trastuzumab + pertuzumab + taxane, then trastuzumab + pertuzumab ± endocrine maintenance — current standard of care.	**Strong**
2L	**Progressed on 1L HER2-directed tx**	T-DXd is the standard of care if not previously used, in the absence of contraindications.	**Strong**
3L	**Progressed after ≥2 HER2-directed tx**	Tucatinib + capecitabine + trastuzumab (preferred); T-DM1 or chemo + HER2-directed antibody in select cases.	**Strong**
4L+	**Progressed after ≥3 HER2-directed tx**	Continue HER2-directed therapy: chemo + trastuzumab, T-DM1, neratinib ± capecitabine, or lapatinib + capecitabine.	**Moderate**

Table 2, REAL Alliance 2025 Update

METASTATIC BREAST CANCER

What Changed in 2025

DESTINY-Breast09

+14 months

median PFS, T-DXd + pertuzumab vs. THP (CLEOPATRA regimen) in the first-line setting.

A treatment option under shared decision-making — THP remains the preferred first-line regimen pending mature OS data.

PATINA

+15.2 months

median PFS adding maintenance palbociclib + endocrine therapy after THP induction, in triple-positive (HR+/HER2+) disease.

Can be considered for fit, motivated triple-positive patients after discussing benefits/risks.

HER2CLIMB-05

24.9 vs 16.3 mo

median PFS adding maintenance tucatinib to first-line HP maintenance therapy.

Presented at SABCS 2025 — just prior to publication; watch for incorporation into future updates.

DESTINY-Breast09, PATINA (ESMO/SABCS 2024–2025), HER2CLIMB-05 (SABCS 2025)

Screening, First-Line, and Sequencing

Screen	CNS screening	Essential for symptomatic patients; consider in asymptomatic patients at baseline and at disease progression.	Strong
Care	Multidisciplinary care	Radiology, radiation oncology, neurosurgery, medical oncology, and supportive care — standard for all brain-met patients.	Strong
1L	Active/progressive systemic disease + treated brain mets	Trastuzumab + pertuzumab + taxane is the current first-line standard.	Strong
1L	Treated or active (untreated) brain mets	T-DXd + pertuzumab is the preferred first-line systemic option (pending Health Canada approval).	Moderate
2L	Progressed on 1L therapy	T-DXd, or tucatinib + capecitabine + trastuzumab, for stable or active brain metastases.	Strong

Table 3, REAL Alliance 2025 Update

BRAIN METASTASES

CNS-Active T-DXd, and Takeaways for Practice

Why T-DXd moved to the front line for CNS disease

- DESTINY-Breast09: in the ~6% of patients with CNS metastases, T-DXd + pertuzumab reached a median PFS of 31.8 months vs. 9.5 months with THP (HR 0.30).
- DESTINY-Breast12: 17.3-month median PFS and 71.7% intracranial response rate in a dedicated brain-metastasis cohort.
- HER2CLIMB: tucatinib + capecitabine + trastuzumab cut risk of intracranial progression/death by 68% — remains the key alternative when T-DXd isn't preferred or has been used.

Key takeaways for pharmacy practice

- T-DXd is now embedded across all three settings — early, metastatic, and CNS disease. Expect more patients on it, sooner.
- ILD/pneumonitis monitoring, antiemetic prophylaxis, and dose-modification protocols need to be practice-ready ahead of Health Canada approval.
- Several 2025 options (T-DXd-THP neoadjuvant, T-DXd escalation, T-DXd + pertuzumab 1L/CNS) are pending approval — continue current standards until each is approved.
- Repeat biopsy at relapse and multidisciplinary review remain constant across every setting.