International Journal of Basic & Clinical Pharmacology
Pandey JRC et al. Int J Basic Clin Pharmacol. 2026 May;15(3):589-593
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20261129

Review Article

A comprehensive review of biomarker-based therapies for hormone receptor-positive and HER2-low breast cancer: clinical pharmacists' implications

Jayesh R. C. Pandey, Gajendra N. Vyas, Esha H. Dutta, Shiwani K. Shah, Hirni J. Patel*

Department of Pharmacy Practice, Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat, India

Received: 24 March 2026
Accepted: 15 April 2026

***Correspondence:**
Dr. Hirni J. Patel,
Email: hirni.patel29322@paruluniversity.ac.in

ABSTRACT

The purpose of this review is to outline the role of clinical pharmacist's in implementing precision oncology and to synthesize current evidence on biomarker-driven targeted therapies in metastatic breast cancer delivers significant regulatory approvals from 2024 to 2025. A thorough literature search was carried out using Scopus, PubMed and conference materials from the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO). Breast neoplasms, molecular targeted therapy, PIK3CA, ESR1, Trop-2, and clinical pharmacy were among the most important search terms. Phase III randomized controlled trials and recent notifications derived from the U. S. Food and Drug Administration (FDA) were top prioritized during the selection process. From empirical hormonal blockade to a important molecular taxonomy, the therapy of hormone receptor-positive, human epidermal growth factor receptor 2-negative metastatic breast cancer has changed. Management of hormone receptor-positive, HER2-negative metastatic breast cancer shows differentiated from empirical hormonal blockade to a precise molecular taxonomy. In "HER2-low" illness, which is characterized as IHC 1+ or 2+ with ISH negative, trastuzumab and deruxtecan significantly improved results. Furthermore, the approval of inavolisib, datopotamab deruxtecan, and imlunestrant in 2024–2025 marks a regulatory turning point in HR-positive illness. The pharmacists must monitor these drugs closely as they have improved progression-free survival, but they also have some side effects, such as hyperglycemia, stomatitis, and ILD. Biomarker-driven therapy is the benchmark synonym for metastatic breast carcinoma with hormone receptor positivity and low HER2 expression. Biomarker-driven therapy is the current evidence-based practice standard for metastatic hormone receptor-positive and HER2-low breast cancer. Clinical pharmacists play a crucial role in the successful implementation of these complex regimens because they must manage diagnostic stewardship, treatment sequencing, and specific adverse effects to ensure complete patient safety.

Keywords: Breast neoplasms, HER2-negative, Inavolisib, Datopotamab deruxtecan, Imlunestrant

INTRODUCTION

The management of breast cancer has undergone substantial alterations, moving from a wide morphological classification to a highly specific molecular taxonomy.

Historically, oncologists depended upon a binary evaluation of hormone receptor and HER2 status. At present this approach has expanded to incorporate actionable genomic alterations, including phosphoinositide 3-kinase (PIK3CA) and estrogen receptor 1 (ESR1) mutations, in association with quantitative evaluations of cell surface proteins such as Trop-2 and low-level HER2 expression.[1,2] The cancer pharmacist's practice has been completely re-evaluated as a result of this paradigm change. The modern clinical role embraced diagnostic stewardship, which ensures that the right biomarkers are estimated at the optimal clinical

juncture, and the management of sophisticated oral oncolytics alongside novel antibody-drug conjugates.[3,4] The three main biomarker-driven developments that have transformed clinical practice in 2024 and 2025 are outlined in this review.

HER2-LOW DISEASE: BEYOND THE BINARY

The status of human epidermal growth factor receptor 2 was definitively positive or negative for 20 years through pathology results, based on a 3+ immunohistochemical result or positive in situ hybridization fluorescence. The trastuzumab deruxtecan review challenged this binary system by showing the marked efficacy in "HER2-low" cancers, defined by IHC 1+ or 2+/ISH-negative. Since then, targeted antibody drug conjugate therapy has become an option for an estimated 55% of patients who were previously defined as "HER2-negative".[5]

MECHANISM: THE BYSTANDER EFFECT

Trastuzumab deruxtecan implements a breakable linker integrated with a membrane-permeable topoisomerase I inhibitor. The payload disperses outside from the target cell after cellular internalization, eliminating nearby tumor cells regardless of each one's degree of synthesis of HER2 receptor.

PHARMACIST CONSIDERATIONS FOR TRASTUZUMAB DERUXTECAN

Pharmacists must systematically review the core pathology report, because a generic note of a negative status is clinically inadequate. The patient's eligibility for treatment is identified by their immunohistochemistry score. Significantly, differentiating between an immunohistochemistry score of 0 and 1+ is conventionally susceptible to pathologist disagreement; therefore, pharmacists should encourage for further pathology review at high-volume centres if the initial biopsy results are indeterminate.[7] Additionally, interstitial lung disease indicates a potentially fatal class effect co-related with this agent. Pooled assessments illustrate an incidence rate of approximately 12%.[8] The pharmacist must make sure the dosage is sustained and take corticosteroids into assessment if a patient has asymptomatic Grade 1 interstitial lung disease. On the condition, the patient develops symptomatic Grade 2 interstitial lung disease, the medication must be permanently terminated, and the clinical team must begin systemic corticosteroids within a minimum dose of 1 mg/kg of prednisone. The pharmacist must make sure the dosage is maintained and take corticosteroids into consideration if a patient has asymptomatic Grade 1 interstitial lung disease.

TARGETING TROP-2: DATOPOTAMAB DERUXTECAN

Therapy attention turned to Trop-2, a transmembrane glycoprotein that has been shown to be overexpressed in more than 90% of breast tumors, after the clinical success of HER2-targeted immunoconjugates.

EFFICACY IN CLINICAL SETTINGS

Datopotamab deruxtecan considerably increased progression-free survival in pretreatment individuals with metastatic breast cancer when compared with the investigator's preferred chemotherapy, according to information from the experiment TROPION-Breast01.[11]

UNIQUE TOXICITY: STOMATITIS

Stomatitis is the most frequent adverse consequence of datopotamab dereuxtecan, with comparison to lung toxicity seen with trastuzumab deruxtecan or the diarrhea linked to sacituzumab govitecan. Pharmacists must promote for a prophylaxis protocol that includes dexamethasone oral solution 0.5 milli gram per 5 milli litre mouthwash commencing on first day of the first treatment cycle. Patient education is necessary; patients must be directed to swish and spit 10 milli litres of the solution four times daily throughout the initial 21-day cycle. The severity of the stomatitis may also be diminished by using cryotherapy with ice chips during the intravenous infusion.[12,13] Additionally, pharmacists must study treatment histories because sequential administration permit careful clinical consideration, as potential payload cross-resistance may reduce efficacy.[14] Topoisomerase I inhibitor payloads with comparable mechanistic characteristics are used by both agents. Optimal antibody–drug conjugate organizing is still being researched, however current sequencing recommendations are in line with current international guideline frameworks.

APPROACHING ENDOCRINE RESISTANCE

Noncompliance with endocrine therapy signifies an unavoidable clinical hurdle that is often driven by acquired genomic mutations. Novel treatments therapies approved for breast cancer from 2024-2025 are mentioned in Table 1.

TARGETING PIK3CA: INAVOLISIB

FDA approved inavolisib to treat metastatic breast cancer alongside PIK3CA mutations in October 2024 [15]. Differing from the older agent alpelisib, inavolisib enhances the therapeutic window by performing a dual role both an inhibitor and a degrader of the mutant PI3Kα protein [16, 17]. The triplet therapy of inavolisib, palbociclib, and fulvestrant increases the median time without disease progression to 15.0 months, as against to 7.3 months for doublet control, as indicated by the Phase III INAVO120 study.[16] Adjacent glucose monitoring is highly recommended even if inavolisib minimize incidence of hyperglycemia than alpelisib. Although inavolisib exhibits reduced rates of hyperglycemia relative to alpelisib, close glucose monitoring is strongly recommended. During first two to four weeks of therapy.

Fasting plasma glucose levels require assessment every three to seven days. If a patient's fasting plasma glucose levels steadily reach 160 mg/dL, pharmacists should think about starting metformin.[17]

TARGETING ESR1: IMLUNESTRANT

Immunestrant is an oral selective estrogen receptor of the next generation, which is engineered to target estrogen receptors harboring ESR1 mutations that accelerate resistance to aromatase inhibitors approved in September 2025.[18] In comparison with first-generation oral treatments, imlunestrant demonstrate better receptor degradation by presenting ongoing target engagement. In comparison with conventional endocrine therapy, imlunestrant monotherapy experienced an enhanced disease-free interval, in line with the EMBER-3 trial.[18]

In contrast to Elacestrant, which must be administered with food, imlunestrant's bioavailability is impaired by meal consumption.[19]

The accurate instruction that the dose be taken on an empty stomach, which is one hour before or two hours after a meal, need to be emphasized by pharmacists. To assure therapeutic efficacy, pharmacists must continue to emphasize this crucial adherence factor.[18]

The toxicity management algorithms led by pharmacists are mentioned in Table 2.

Table 1: Novel Treatments for breast cancer in the 2024-2025 regulatory period.

Generic name	Drug class	Key indication	Target biomarker	Pivotal trial	Hallmark toxicity
Inavolisib	PI3Kα inhibitor and degrader	Hormone receptor positive/Human epidermal growth factor 2-metastatic breast cancer accompanied by PIK3CA mutation (post-endocrine progression)	PIK3CA mutation	INAVO120	Hyperglycemia
Datopotamab deruxtecan	Trop-2 directed ADC	Hormone receptor positive/Human epidermal factor 2-metastatic breast cancer following previous endocrine therapy and chemotherapy	Trop-2 (broad expression)	TROPION-Breast01	Stomatitis
Imlunestrant	Oral SERD	Hormone receptor positive /Human epidermal growth factor 2-metastatic breast cancer	ESR1 mutation	EMBER-3	GI Upset/ nausea
Trastuzumab deruxtecan	HER2 directed ADC	HER2-low metastatic breast cancer	HER2 immunohistochemistry 1+ or 2+/Insitu hybridization-	DESTINY-Breast04	Interstitial lung disease

*Information gathered through clinical evidence and regulatory framework approvals.[5,11,16,18]

Table 2: Toxicity management algorithms led by pharmacists.

Toxicity	Associated agent(s)	Grade 1 (Mild) clinical action	Grade 2 (Moderate) clinical action	Critical pharmacist pearl
Hyperglycemia	Inavolisib	Implement diet/lifestyle modifications. monitor FPG.	Initiate metformin 500 mg once daily and titrate as tolerated.	Monitor fasting plasma glucose every 3-7 days during the first 2-4 weeks of therapy.[16,17]
Stomatitis	Dato-DXd	Initiate non-alcoholic mouthwash.	HOLD dose. Initiate Triamcinolone paste.	Dexamethasone oral solution 0.5 mg/5 mL prophylaxis is recommended beginning in cycle 1.[12]
ILD/pneumonitis	Primarily T-DXd; reported with Dato-DXd	HOLD dose. Consider high-resolution CT scan.	Permanently discontinue. Initiate systemic steroids.	Counsel patients to report any "new dry cough." Rechallenge is contraindicated.[8,9]
Ocular toxicity	Datopotamab Deruxtecan	Administer preservative-free artificial tears.	HOLD dose. Refer to ophthalmology.	Avoid contact lenses during therapy.[12]

Management techniques modified from accepted toxicity recommendations and clinical trial methods.[8,9,12,16,174]

DIAGNOSTIC STEWARDSHIP: THE PHARMACIST AS GATEKEEPER

Clinical pharmacists execute play a crucial role in assuring appropriate biomarker selection is arranged with therapeutic choice. Early in the etiology of the disease the PIK3CA alteration is mainly a truncal mutation. Standard practice sets up that testing via tissue or liquid biopsy in the period of metastatic clinical evaluation is adequate.[20]. On other hand, the ESR1 alteration demonstrates as an acquired resistance mutation. Testing produces the highest utility following disease progression upon aromatase inhibitor. The crucial adherence instruction that the dose be taken on an empty stomach, which is one hour before or two hours after a meal, must be emphasized by pharmacists. To assurance therapeutic efficacy, pharmacists must continue to emphasize this crucial adherence factor.[18]

REDUCING FINANCIAL TOXICITY

Although the introduction of new oral antineoplastic agents and targeted antibody drug conjugates (ADCs) has undoubtedly improved survival outcomes, these precision medicines are associated with significant costs. To mitigate this financial toxicity, the oncology pharmacist specialist plays a crucial role.[21] These methods findings manufacturer patient assistance programmes, percipiently managing strict prior authorization procedures, and educate the patient about what to expect out of pocket. By systematically eliminating these barriers, the clinical pharmacist guarantees equitable access to precise treatments and prevents administrative treatment delays.

LITERATURE REVIEW

A thorough literature review was carried out utilizing Scopus, PubMed and oncology conference proceedings from ASCO and ESMO up to December 1, 2025 to isolate a rigorous synthesis of contemporary therapeutic procedures. The primary search parameters integrated the terms breast neoplasms, molecular targeted therapy, PIK3CA, ESR1, Trop-2, and clinical pharmacy.

In order to ensure that the clinical significance remains high, phase III randomized controlled trials and FDA regulatory notifications were given prime consideration in the selection of articles.

DISCUSSION

A biomarker-driven precision strategy has replaced traditional endocrine therapy in the treatment of hormone receptor-positive (HR+) and HER2-low metastatic breast cancer. The identification of HER2-low illness and advances in our knowledge of genetic changes such PIK3CA and ESR1 mutations have improved patient outcomes and increased therapy choices.[1,2]

The conventional binary classification of HER2 status has been challenged by antibody-drug conjugates (ADCs), especially trastuzumab deruxtecan, which have shown notable efficacy in HER2-low tumors.[5] Although interstitial lung disease is still a serious safety concern that need early attention, its bystander effect increases activity in heterogeneous malignancies.[6,8,9] Additionally, stomatitis is the most frequent side effect that requires preventive care, and datopotamab deruxtecan has demonstrated increased progression-free survival in pretreated patients.[11-13]

Another significant development is the targeting of endocrine resistance. Although monitoring for hyperglycemia is still crucial, inavolisib has improved outcomes in PIK3CA-mutated illness.[16,17] Imlunestrant, a next-generation SERD, is beneficial in tumors with ESR1 mutations, but for best results, administration recommendations must be strictly followed.[18,19]

These therapeutic developments demonstrate the growing involvement of clinical pharmacists in therapy optimization, toxicity management, and diagnostic stewardship. Pharmacists are also crucial in alleviating financial toxicity and expanding access to expensive treatments.[20,21]

CONCLUSION

The breast cancer community has entered a highly specialized era. The key connecting point between highly specialized cancer research and actual patient care is the clinical pharmacist. The paradigm shift has moved away from hormonal blockade and towards highly specialized, biomarker-guided therapy with agents such as inavolisib, datopotamab deruxtecan, and imlunestrant. Pharmacists manage specific toxicities, ensure accurate biomarker testing, and manage substantial financial responsibilities. Pharmacists apply theoretical survival advantages of precision medicine to actual patient survival benefits through their knowledge and clinical attentiveness.

Thus, the clinical pharmacists are essential to the safe and efficient application of biomarker-driven therapy, which is currently the standard for HR-positive and HER2-low metastatic breast cancer.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Harbeck N, Gnant M. Breast cancer. Lancet. 2017;389(10074):1134-50.
2. Mosele F, Stefanovska B, Lusque A. Outcome and molecular landscape of patients with PIK3CA-mutated metastatic breast cancer. Ann Oncol. 2020;31(3):377-86.

3. Holle LM, Segal EM, Jeffers KD. The expanding role of the oncology pharmacist. Pharmacy (Basel). 2020;8(3):130.
4. Wang Y, McTaggart S, Haywood A. Pharmacist's role in breast cancer management: a scoping review. J Oncol Pharm Pract. 2022;28(4):890-8.
5. Modi S, Jacot W, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. N Engl J Med. 2022;387(1):9-20.
6. Ogitani Y, Hagihara K, Omate J. Bystander killing effect of DS-8201a, a novel anti-human epidermal growth factor receptor 2 antibody-drug conjugate, in tumors with HER2 heterogeneity. Cancer Sci. 2016;107(7):1039-46.
7. Fernandez AI, Liu M, Bellizzi A. Examination of low HER2 protein expression in breast cancer clinicopathologic features and interobserver concordance. Arch Pathol Lab Med. 2022;146(4):439-47.
8. Powell CA, Modi S, Iwata H. Pooled analysis of drug-related interstitial lung disease and/or pneumonitis in nine trastuzumab deruxtecan monotherapy studies. ESMO Open. 2022;7(4):100554.
9. ESMO Guidelines Committee. Multidisciplinary clinical guidelines in proactive monitoring, early diagnosis, and effective management of trastuzumab deruxtecan-induced interstitial lung disease. ESMO Open. 2023;8(6):102043.
10. Rugo HS, Bartsch R, Cortes J. QOL and updated safety of trastuzumab deruxtecan (T-DXd) in patients with HER2-low metastatic breast cancer from DESTINY-Breast04. J Clin Oncol. 2023;41(16):1018.
11. Bardia A, Jhaveri K, Im SA. Datopotamab deruxtecan vs chemotherapy for pretreated ER+, HER2- breast cancer (TROPION-Breast01). J Clin Oncol. 2024;42(17): LBA1000.
12. Meric-Bernstam F, Bardia A, Bossi P. Prophylaxis and clinical management of datopotamab deruxtecan-associated stomatitis. ESMO Open. 2024;9(1):102062.
13. Rugo HS, Seneviratne L, Beck JT. Prevention of everolimus-related stomatitis in women with hormone receptor-positive, HER2-negative metastatic breast cancer using dexamethasone mouthwash (SWISH): a single-arm phase 2 trial. Lancet Oncol. 2017;18(5):654-62.
14. Abelman RO, Spring L, Bardia A. Sequential use of antibody-drug conjugates in breast cancer. Curr Oncol Rep. 2023;25(5):451-60.
15. U.S. Food and Drug Administration. FDA approves inavolisib with palbociclib and fulvestrant for endocrine-resistant, PIK3CA-mutated, HR-positive, HER2-negative, advanced breast cancer. FDA.gov. 2024. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-inavolisib-palbociclib-and-fulvestrant-endocrine-resistant-pik3ca-mutated-hr-positive. Accessed 01 December 2025.
16. Turner NC, Jhaveri K, Kalinsky K. Inavolisib-based therapy in PIK3CA-mutated advanced breast cancer (INAVO120). N Engl J Med. 2024;391(17):1584-96.
17. Nader-Marta G, Tolaney SM, Mayer EL. Inavolisib-based triplet therapy for PIK3CA-mutated hormone receptor+/HER2- breast cancer: clinical implications and practical considerations. JCO Oncol Adv. 2024;2(1):e2500041.
18. Jhaveri KL, Neven P, Casalnuovo ML. Imlunestrant, an oral selective estrogen receptor degrader (SERD), as monotherapy and combined with abemaciclib, for patients with ER+, HER2- advanced breast cancer (ABC): results of the phase 3 EMBER-3 trial. Ann Oncol. 2024;35(2):S1-S1338.
19. Bidard FC, Kaklamani VG, Neven P. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the phase 3 EMERALD trial. J Clin Oncol. 2022;40(28):3246-56.
20. Turner NC, Swift C, Jenkins B. Circulating tumor DNA analysis to direct therapy in advanced breast cancer (plasmaMATCH): a multicentre, multicohort, open-label, phase 2a platform trial. Lancet Oncol. 2020;21(10):1296-308.
21. Desai A, Gyawali B. Financial toxicity of cancer treatment: moving the needle from multiple problems to potential solutions. JCO Oncol Pract. 2020;16(5):261-3.

Cite this article as: Pandey JRC, Vyas GN, Dutta EH, Shah SK, Patel HJ. A comprehensive review of biomarker-based therapies for hormone receptor-positive and HER2-low breast cancer: clinical pharmacists' implications. Int J Basic Clin Pharmacol 2026;15:589-93.