Improved Antiemetic Outcomes with NEPA vs (Fos)aprepitant in Patients with Breast Cancer Receiving Antibody-Drug Conjugates: A 12-Month Real-World Claims Analysis

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BACKGROUND

- Antibody–drug conjugates (ADCs) have transformed breast cancer (BC), combining the potency of chemotherapy with the precision of targeted therapy[1]. Trastuzumab emtansine (T-DM1) was the first HER2-targeting ADC, approved in 2013 for metastatic BC and in 2019 for adjuvant therapy[2]. More recently, trastuzumab deruxtecan (T-DXd, HER2-targeting) and sacituzumab govitecan (SG, TROP2-targeting), have broadened treatment options.
- Despite targeted design, ADCs remain associated with toxicities, particularly nausea and vomiting (NV). Clinical trials report any-grade nausea in up to 75% of patients treated with T-DXd and 65.6% with SG, with vomiting in 45% and 43.7%, respectively[1,3]. NV can persist for 10 days or longer, significantly impairing quality of life and leading to treatment dose adjustments with potential impact on treatment outcomes [4-7].
- International antiemetic guidelines recommend starting antiemetic prophylaxis with an NK1-receptor antagonist (NK1RA)-based regimen for newly approved ADCs. Both the 2025 NCCN and 2023 MASCC/ESMO antiemetic guidelines recommend initiating prophylaxis with an NK1RA-based regimen for ADCs such as T-DXd and SG to ensure effective NV control across treatment cycles and help maintain dose intensity throughout therapy [8,11].
- Since NV can persist for an extended period, antiemetics with extended half-lives and sustained NK1 receptor occupancy may be more effective in managing long-delayed NV (occurring >120hours).
- (Fos)netupitant, used in combination with palonosetron (NEPA), has a longer half-life and extended NK1 receptor occupancy than (Fos)Aprepitant, both of which are thought to support to its sustained long-lasting efficacy[9,10].While NV, including long-delayed nausea, is a well-established side effect, limited real-world evidence exists evaluating antiemetic outcomes over extended treatment durations. Moreover, there is a lack of comparative data on the effectiveness of different antiemetic regimens in patients receiving ADC therapy.

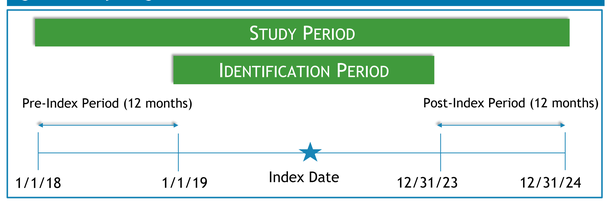
OBJECTIVE

This study examined the clinical and economic outcomes associated with antiemetic use in BC patients receiving ADCs providing real-world insights into the impact of antiemetics on patient outcomes and healthcare resource utilization.

METHODS

- This retrospective observational study used the STATinMED RWD Insights all-payer medical and pharmacy claims database, a national all-payer data source that includes commercial, Medicare, and Medicaid health plans. The study period was from January 1, 2018, through December 31, 2024.
- Eligible patients were ≥18 years, had a diagnosis of BC, and received at least one of three ADCs: T-DM1, T-DXd, or SG, between January 1, 2019, and December 31, 2023.
- The index date was defined as the earliest claim for NEPA or an (Fos)Aprepitant-based regimen. Continuous enrollment in medical and pharmacy benefits for ≥12 months before and after the index date was required.
- Cohorts were constructed based on first-line antiemetic use: NEPA versus (Fos)Aprepitant. To minimize confounding, 1:1 propensity score matching (PSM) was applied using demographic and clinical characteristics (age, sex, payer type, geographic region, comorbidities), resulting in two balanced groups of 209 patients each.
- Cohort 1 included patients treated with NEPA. Cohort 2 included patients treated with (Fos)Aprepitant, regardless of whether they also received other antiemetics such as dexamethasone or 5-HT3RAs. Cohorts were mutually exclusive based on the first antiemetic identified following ADC initiation.

Figure 1. Study Design and Observation Periods



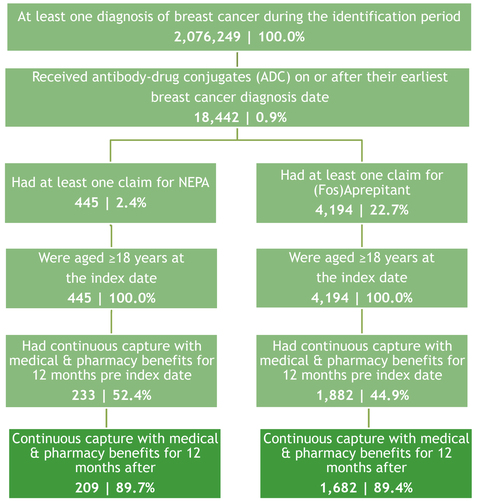
Study Outcomes

Outcomes were evaluated over a 12-month follow-up period and included:

- NV–related complications (nausea, vomiting, dehydration, IV fluid use, electrolyte imbalance)
- Nausea occurring >72 hours after treatment
- Emergency room visits and outpatient hospital services related to NV. Outpatient hospital services refer to scheduled treatments or procedures that take place in a hospital's outpatient department without inpatient admission or emergency care.
- NV-related healthcare costs, including costs from emergency room visits and outpatient hospital services.

Statistical analyses included descriptive statistics to summarize patient characteristics and outcomes, and hypothesis testing to evaluate differences between treatment cohorts. Chi-square tests were used for categorical variables, and t-tests were used for continuous variables. A two-sided p-value <0.05 was considered statistically significant.

Figure 2. Patient Selection Criteria



RESULTS

Table 1. Clinical and Economic Outcomes During the 12-Month Follow-Up Period

Outcome	NEPA (N=209)	(Fos)Aprepitant (N=209)	P-value
Complications (NV/dehydration/IV*/ electrolyte imbalance)	82.30%	90.40%	0.0154
Nausea >72h	27.80%	40.20%	0.0073
Outpatient ER visits (NV-related)	4.30%	5.70%	0.5017
Outpatient hospital services (NV related)	43.00%	69.40%	<0.0001
Mean number of outpatient hospital services	3.6	5.4	<0.0001
Mean NV-related costs (ER+outpatient hospital services)	$14,884	$30,665	<0.0001

* Intravenous fluid administration

- NEPA patients experienced significantly fewer NV-related complications than those receiving (Fos)Aprepitant–(82.3% vs 90.4%; p=0.0154). Nausea, occurring more than 72 hours after treatment, was also significantly less frequent with NEPA (27.8% vs 40.2%; p=0.0073).
- Outpatient hospital services related to NV occurred in 43.0% of NEPA patients compared with 69.4% of (Fos)Aprepitant-patients (p<0.0001). The mean number of visits was nearly three times lower with NEPA (1.7 vs 4.3; p<0.0001). NEPA patients had fewer emergency room visits compared with (Fos)Aprepitant patients (4.3% vs 5.7%; p=0.5017).
- Economic outcomes showed substantial differences. The mean NV-related cost per patient was $14,884 in the NEPA cohort compared with $30,665 in the (Fos)Aprepitant cohort (p<0.0001), representing nearly a 50% reduction.

Subgroup Analyses by ADC

- Among T-DM1 patients, outpatient hospital services were 43.6% with NEPA versus 67.3% with (Fos)Aprepitant (p=0.0009), with mean costs of $14,032 versus $28,777 (p=0.001).
- In the T-DXd subgroup, outpatient hospital services were 41.4% versus 71.6% (p=0.0002), with costs of $16,023 versus $40,179 (p<0.0001).
- In the smaller SG subgroup, outpatient hospital services were 42.86% vs 70.45% (p=0.0199), and mean costs were $14,334 vs $19,645, though the cost difference was not statistically significant (p=0.5208).

Figure 3. Outpatient Hospital Services by ADC Subgroup

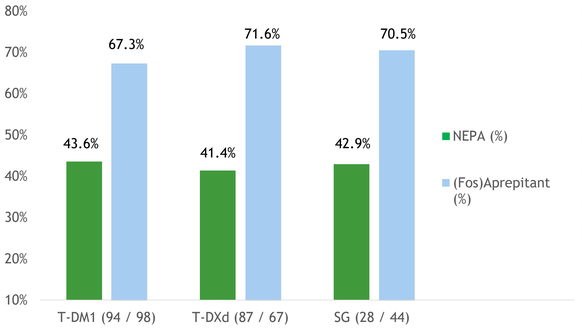
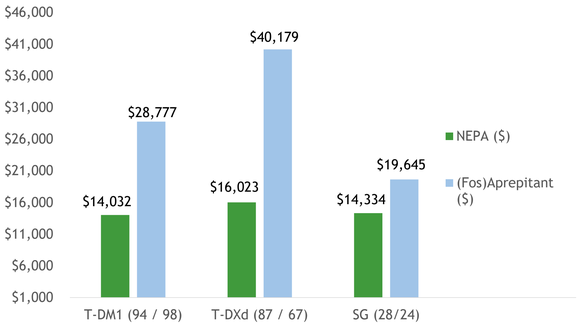


Figure 4. NV-Related Costs by ADC Subgroup



DISCUSSION

- In this real-world analysis of breast cancer patients receiving ADC therapy, NEPA was associated with better control of nausea and vomiting compared with (Fos)Aprepitant.
- Patients treated with NEPA had significantly fewer overall complications, a significantly lower incidence of persistent nausea > 72 hours, and markedly reduced outpatient hospital services. These clinical benefits translated into nearly a 50% reduction in nausea/vomiting-related healthcare costs.
- The consistency of results across ADC subgroups, particularly T-DM1 and T-DXd, strengthens confidence in the robustness of the findings. Even in the smaller SG subgroup, where statistical significance was not reached, the trend still favored NEPA.
- Together, these results indicate that NEPA provides sustained protection against nausea, reducing the clinical and economic burden with ADC-related NV.

CONCLUSIONS

- NEPA was associated with both clinical and economic benefits, including fewer nausea/vomiting-related complications, lower rates of long-delayed nausea, reduced outpatient hospital services, and nearly 50% lower costs compared with (Fos)Aprepitant in breast cancer patients treated with ADCs.
- These findings support NEPA as a preferred NK1RA-based regimen in real-world clinical practice.

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