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Safety profile of Trastuzumab deruxtecan in patients with advanced HER2+ breast cancer: an active pharmacovigilance study

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Abstract

Objective: To analyze the safety profile of the drug Trastuzumab deruxtecan and describe the clinical and epidemiological characteristics of patients diagnosed with advanced breast cancer as HER2 positive. **Methods:** This is a retrospective observational study, approved by the Research Ethics Committee, in which patients with HER2 positive breast cancer undergoing chemotherapy based on Trastuzumab deruxtecan were evaluated through the hospital management system, from March/2022 to March/2024, finding the adverse events presented, clinical and epidemiological data, as well as information regarding the treatment. The events presented in previous treatments were considered in order to avoid brightness bias. Causality was assessed by the Naranjo Algorithm and severity by the Common Terminology Criteria for Adverse Events methodology. **Results:** 45 patients were selected, 3 of which were excluded due to loss of follow-up. Of the group of patients analyzed, 33% did not report any complications or complaints arising from Trastuzumab deruxtecan and previous protocols. Some patients presented more than one adverse event, all of which were considered. Among the observations, the following stand out: nausea and vomiting (78.6%), followed by asthenia (46.4%), alopecia (32.1%), constipation (21.4%), mucositis (14.3%) and loss of appetite (10.7%). Regarding the causality profile, it was found that 31.5% were defined as definite and 68.5% as probable, with the majority defined as grade 1 (67.1%). **Conclusion:** The results reflect agreement with the literature regarding the profile, severity and causality of the events. It is suggested that real-life studies be conducted with a larger population and for a longer period to evaluate the long-term safety profile.

Keywords: trastuzumab deruxtecan, adverse drug events, HER2+ breast cancer, pharmacovigilance, drug safety.

Perfil de segurança do Trastuzumabe deruxtecano em pacientes com neoplasia maligna de mama HER2+ avançada: estudo de farmacovigilância ativa

Resumo

Objetivo: Analisar o perfil de segurança do medicamento Trastuzumab deruxtecano e descrever as características clínicas e epidemiológicas dos pacientes com diagnóstico de neoplasia maligna de mamas avançadas classificadas como HER2 positivo. **Métodos:** Trata-se de um estudo retrospectivo observacional, aprovado por Comitê de ética em pesquisa, no qual foram avaliados, através do sistema de gestão hospitalar, pacientes com neoplasia de mama HER2 positivo submetidos a quimioterapia à base de Trastuzumab deruxtecano, no período de março/2022 a março/2024, sendo coletados os eventos adversos apresentados, dados clínicos e epidemiológicos, bem como informações referentes ao tratamento. Os eventos observados nos tratamentos prévios foram considerados a fim de evitar viés de correlação. A causalidade foi avaliada pelo Algoritmo de Naranjo e a gravidade pela metodologia *Common Terminology Criteria for Adverse Events*. **Resultados:** Foram selecionados 45 pacientes, sendo 3 excluídos devido à perda de seguimento. Do grupo de pacientes analisados, 33% não apresentaram intercorrências e nem queixas advindas do Trastuzumab deruxtecano e protocolos anteriores. Alguns pacientes apresentaram mais de um evento adverso, sendo todos considerados. Entre os observados, destacam-se: náuseas e vômitos (78,6%), seguidas de astenia (46,4%), alopecia (32,1%), constipação (21,4%), mucosite (14,3%) e inapetência (10,7%). Quanto ao perfil de causalidade, verificou-se que 31,5% foram classificadas como definidas e 68,5% como prováveis, sendo a maioria classificada como grau 1 (67,1%), **Conclusão:** Os resultados refletem concordância com a literatura, no que diz respeito ao perfil, gravidade e causalidade dos eventos. Sugere-se a realização de estudos de vida real com população mais amplos e por um maior período a fim de avaliar o perfil de segurança a longo prazo.

Palavras-chave: trastuzumabe deruxtecano, eventos adversos a medicamentos, câncer de mama HER2+, farmacovigilância, segurança de medicamentos.

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Introduction

Globally, breast cancer is the most prevalent and has the highest mortality rate among women[1,2]. In Brazil, according to data from the National Cancer Institute (INCA) for the 2023–2025 triennium, breast cancer is the most common cancer among women after non-melanoma skin cancer[3], with approximately 74,000 new cases expected by 2025.

Among the most common subtypes of breast cancer is the one that overexpresses the human epidermal growth factor receptor 2 (HER2), accounting for approximately 15%–20% of cases. When overexpressed, this receptor stimulates cancer growth and makes the disease more aggressive[1,2].

Currently, treatments for this subtype have been extensively studied and have undergone significant advances. The first-line standard of treatment for HER2-positive metastatic breast cancer was established by the CLEOPATRA study, which demonstrated the effectiveness of dual anti-HER2 monoclonal antibody therapy—pertuzumab combined with trastuzumab—along with a taxane-based chemotherapy agent. When chemotherapy is not an option, studies suggest the use of trastuzumab emtansine (T-DM1), which can also be used as a second-line treatment if disease recurrence occurs within six months[4].

A new second-line treatment option with the drug trastuzumab deruxtecan (T-DXd) was approved by the FDA in December 2019, based on the results of the phase 2 DESTINY-Breast01 study. Subsequently, the DESTINY-Breast03 study reinforced the efficacy of T-DXd, leading to its approval in Brazil in 2021. The drug was indicated for patients previously treated with anti-HER2 therapies—whether in the metastatic, neoadjuvant, or adjuvant setting—who experienced disease recurrence during or within six months after completing treatment, with T-DM1 being the recommended subsequent option[4,5].

Trastuzumab deruxtecan is an antibody-drug conjugate (ADC), composed of a humanized monoclonal antibody linked to a potent topoisomerase I inhibitor, deruxtecan. Indicated for the treatment of solid tumors that express HER2, its mechanism of action begins with the binding of the antibody to the HER2 receptor on the surface of tumor cells, facilitating internalization of the ADC complex. Once inside the cell, the drug is released after lysosomal cleavage and inhibits topoisomerase I, leading to DNA damage and apoptosis. Additionally, the antibody can mediate antibody-dependent cellular cytotoxicity (ADCC) and block the phosphatidylinositol 3-kinase (PI3-K) signaling pathway, which is crucial for tumor cell growth and survival[6–9].

The safety of T-DXd, evaluated through the DESTINY-Breast01, DESTINY-Breast03, and Phase 1 DS8201-A-J101 studies, showed that the most commonly reported adverse events (≥20%) were decreased white blood cell count, decreased hemoglobin, decreased neutrophil count, fatigue, vomiting, alopecia, increased aspartate aminotransferase, increased alanine aminotransferase, decreased platelet count, constipation, decreased appetite, anemia, diarrhea, hypokalemia, cough, interstitial lung disease (ILD), pyrexia, and pneumonitis[9,10].

The incorporation of new drugs for oncologic treatments requires knowledge of their short-, medium-, and long-term safety profiles, mainly to enable the identification and proper management of possible adverse events. Furthermore, no data were found in the literature regarding the safety profile of T-DXd in Brazil, especially in a real-world setting, which differs from the populations typically recruited in randomized clinical trials. Such information is highly relevant to improve understanding of its use in clinical practice. Therefore, we propose this retrospective observational study to evaluate the safety data of patients treated with T-DXd at a private oncology clinic in Rio de Janeiro.

Methods

Study Design

This is a retrospective observational study in which patients diagnosed with HER2-positive breast cancer who received T-DXd-based chemotherapy as a second- or third-line treatment were monitored between March 2022 and March 2024 to determine the drug's safety profile.

Study Setting

The study was conducted in a network of private clinics internationally certified by the Quality Oncology Practice Initiative and Joint Commission International. The network comprises six units located in the state of Rio de Janeiro and is recognized as a reference center for cancer treatment.

Population

The study included patients of both sexes, aged over 18 years, diagnosed with HER2-positive metastatic malignant breast neoplasia and undergoing treatment with T-DXd at the institution. Individuals concurrently using other antineoplastic therapies were excluded to minimize confounding bias in the assessment of adverse events, as well as those whose prescribing physicians were affiliated with external institutions, due to the inability to access complete clinical data. Since consultations and tests performed by external professionals are not recorded in the institutional medical records, this limitation could introduce bias in the analysis, restricting interpretation to data from in-house multiprofessional consultations only, thereby compromising completeness.

Patient selection was carried out using a drug utilization report generated by the institutional hospital management system, which centralizes the management of pharmaceutical care across the institution on a single platform and integrates detailed information about patients' clinical histories through electronic health records. Based on this report, patients undergoing T-DXd treatment during the analysis period were identified, and their medical records were then reviewed to ensure compliance with eligibility criteria.

Data Collection

The variables analyzed included age, sex, presence of comorbidities, adverse events, start date of T-DXd use, use of supportive medications for chemotherapy, prior oncological treatments, treatment-related adverse events, and interventions, when applicable.

To ensure data reliability, epidemiological data were extracted from electronic medical records, which compile both demographic information—such as age, sex, and presence of comorbidities—and clinical history, including diagnoses, laboratory tests, treatments received, and detailed records of medical and multiprofessional consultations.

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Adverse event identification was based on two main sources. First, pharmacovigilance reports extracted from the hospital management system were analyzed; these reports document notifications submitted by the multiprofessional team. Additionally, physician progress notes and clinical pharmacy records were reviewed, which include patient-reported complaints throughout the treatment. It is worth noting that at the institution, all interventions related to the assessment and management of adverse events are documented in the electronic medical record, ensuring traceability and continuity of care.

Data Analysis

After data collection, the information was organized and tabulated in an Excel spreadsheet to facilitate visualization, analysis, and interpretation. A descriptive analysis of the clinical and epidemiological variables was carried out, with results presented as absolute and relative frequencies.

The epidemiological profile analysis included identifying and characterizing the main variables, with data on age, sex, comorbidities, and other relevant clinical conditions being analyzed and quantified.

Adverse events related to previous treatments were considered in order to avoid bias in the causality analysis during T-DXd use. Additionally, pre-existing comorbidities and the concomitant use of supportive medications were analyzed to ensure more accurate attribution of adverse events to the study drug. The analysis of variables was conducted during the period in which the patient was undergoing treatment, to allow for a temporal causality assessment. Therefore, the events were analyzed using two standardized methodologies that are integrated into the institution's routine: the Naranjo Algorithm and the Common Terminology Criteria for Adverse Events (CTCAE).

Although the Naranjo Algorithm has limitations in the oncology setting, it is widely used to assess the likelihood of adverse drug reactions and is the standard methodology employed at the institution and in this study. Through objective questions, the sum of the responses classifies the reaction into one of five probability categories: definite, probable, possible, doubtful, and conditional[11]. The concomitant use of supportive medications was considered a potential confounding factor. To mitigate this bias, these medications were classified up to level 2 of the Anatomical Therapeutic Chemical Classification System (ATC)—a method used to standardize drugs according to the organ or system they act upon, as well as their therapeutic, pharmacological, and chemical properties. These medications were taken into account during adverse event analysis in order to distinguish their association from events potentially attributed to T-DXd.

The severity of adverse events was determined using the CTCAE, a methodology widely used in oncology for the classification of adverse events and periodically updated to reflect advancements in cancer therapies. Developed by the National Cancer Institute (NCI) and the National Institutes of Health (NIH), the CTCAE employs a grading scale to categorize event severity, ranging from grade 1 (mild) to grade 5 (fatal), aiding in safer clinical decision-making[12].

Ethical Aspects

A waiver of informed consent (ICF) was requested, as this is a retrospective study involving the description of clinical data collected and stored as part of institutional routines, without any interventions. The study was approved by the research ethics committee under protocol number: 69820423.3.0000.5533.

Results

A total of 110 patients with advanced HER2+ breast cancer undergoing treatment with T-DXd were identified. After applying the eligibility criteria, 45 patients were selected, excluding those under external medical care or undergoing concomitant chemotherapy to avoid bias in adverse event analysis. Subsequently, three patients were excluded due to loss of follow-up, resulting in 42 eligible patients for the study (Table 1).

Table 1. Epidemiological profile of eligible patients undergoing treatment with Trastuzumab deruxtecan (N=42) (Rio de Janeiro/ Brazil, 2022–2024).

Variables	Total	
	n	%
Sex		
Male	1	2.4
Female	41	97.6
Age		
30 to 49 years	7	16.7
50 to 69 years	31	73.8
70 to 89 years	3	7.1
> 90 years	1	2.4
General Comorbidities		
Anxiety	2	5.4
Constipation	1	2.6
Diabetes	5	13.2
Epilepsy	1	2.6
Hypercholesterolemia	4	10.5
Hypertension	16	42.2
Hyperuricemia	1	2.6
Hypothyroidism	4	10.5
Heart failure	1	2.6
Lower back pain	1	2.6
Osteoporosis	1	2.6
Asthma	1	2.6

The analysis of the epidemiological profile revealed that the majority of patients were female (97.6%), with only 2.4% being male. The predominant age group was between 50 and 69 years (73.8%), followed by 16.7% aged 30 to 49 years, and 7.1% aged 70 to 89 years. Only 2.4% of patients were over 90 years old. Comorbidity assessment identified a total of 38 findings, noting that some patients presented more than one clinical condition. The most frequent comorbidity was hypertension (42.2%), followed by diabetes mellitus (13.2%), hypothyroidism and hypercholesterolemia, both with a prevalence of 10.5% (Table 1).

Among the 42 patients analyzed, 66.7% experienced at least one adverse event related to treatment, the most common being nausea and vomiting (78.6%), fatigue (46.4%), alopecia (32.1%), constipation (21.4%), mucositis (14.3%), and anorexia, leukopenia, and mucositis (10.7% each). No cases of interstitial lung disease (ILD) were identified in the population analyzed (Table 2).

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Table 2. Most prevalent adverse reactions in patients (n=28) treated with T-DXd and their severity and causality classifications (Rio de Janeiro/Brazil, 2022–2024).

Variables	Total	
		%
Adverse reactions		
Yes	28	66.7
No	14	33.3
Reported adverse reactions (n = 28 patients)		
Alopecia	9	32.1
Weakness	13	46.4
Elevated transaminases	1	3.6
Headache	2	7.1
Abdominal cramps	1	3.6
Constipation	6	24.1
Diarrhea	2	7.1
Dysgeusia	1	3.6
Numbness	1	3.6
Epigastric pain	2	7.1
Loss of appetite	3	10.7
Leukocytosis	1	3.6
Leukopenia	1	3.6
Mucositis	4	14.3
Nausea and vomiting	22	78.6
Thrombocytopenia	2	7.1
Itching (Pruritus)	1	3.6
Dizziness	1	3.6
Severity		
Grade 1	49	67.1
Grade 2	21	28.8
Grade 3	3	4.1
Causality		
Defined	23	31.5
Probable	50	68.5

The causality assessment of adverse reactions, conducted using the Naranjo Algorithm, revealed that most were classified as probable or definite. Of these, 31.5% were considered "definite" and 68.5% "probably related" to the drug (Table 2). Nausea and vomiting stood out, with 50% being classified as probably related, and 21.4% of alopecia and 28.6% of nausea and vomiting as definite (Table 3).

Table 4 presents the classification and frequency of patients who experienced an adverse event while using supportive medications, categorized according to the ATC level 2 classification. Among the most frequently used classes, antiemetics (A04) were the most common (71.4%), followed by corticosteroids (H02) and analgesics (N02), both used by 60.7% of patients. It is important to note that patients may use more than one supportive medication depending on their clinical needs and medical guidance. Notably, among the patients who experienced constipation (n=6), 83.3% were using antiemetics and 16.7% were using analgesics.

Regarding the severity of adverse events, most were classified as Grade 1 (67.1%), followed by Grade 2 (28.8%) and Grade 3 (4.1%). Grade 3 events represent more severe effects that may lead to hospitalization or significant disability (Table 2). The most severe types included leukocytosis and nausea and vomiting (Grade 3), while Grade 2 events included episodes of nausea and vomiting, fatigue, alopecia, abdominal cramps, epigastric pain, elevated transaminases, anorexia, and pruritus (Table 3). Additionally, 25% of the patients who experienced some type of adverse event required a dose reduction to continue treatment.

Table 3. Classification of severity and causality of each adverse event observed in patients (n=28) treated with T-DXd (Rio de Janeiro/Brazil, 2022–2024).

Variables	Severity						Causality			
	Grade 1 (n=49)		Grade 2 (n=21)		Grade 3 (n=3)		Defined		Probable	
	n	%	n	%	n	%	n	%	n	%
Alopecia	3	10.7	6	21.4	-	-	6	21.4	3	10.7
Fatigue	9	32.1	4	14.3	-	-	2	7.1	11	39.3
Headache	2	7.1	-	-	-	-	-	-	2	7.1
Elevated transaminases	-	-	1	3.6	-	-	-	-	1	3.6
Abdominal cramp	-	-	1	3.6	-	-	-	-	1	3.6
Constipation	6	21.4	-	-	-	-	-	-	6	21.4
Diarrhea	2	7.1	-	-	-	-	2	7.1	-	-
Dysgeusia	-	-	1	3.6	-	-	1	3.6	-	-
Numbness	1	3.6	-	-	-	-	-	-	1	3.6
Epigastric pain	1	3.6	1	3.6	-	-	1	3.6	1	3.6
Loss of appetite	1	3.6	1	3.6	-	-	1	3.6	2	7.1
Leukocytosis	1	3.6	-	-	1	3.6%	-	-	1	3.6
Leukopenia	1	3.6	-	-	-	-	-	-	1	3.6
Mucositis	4	14.3	-	-	-	-	1	3.6	3	10.7
Nausea and vomiting	15	53.6	5	17.9	2	7.1%	8	28.6	14	50
Thrombocytopenia	2	7.1	-	-	-	-	-	-	2	7.1
Dizziness	1	3.6	-	-	-	-	-	-	1	3.6
Pruritus	-	-	1	3.6	-	-	1	3.6	-	-

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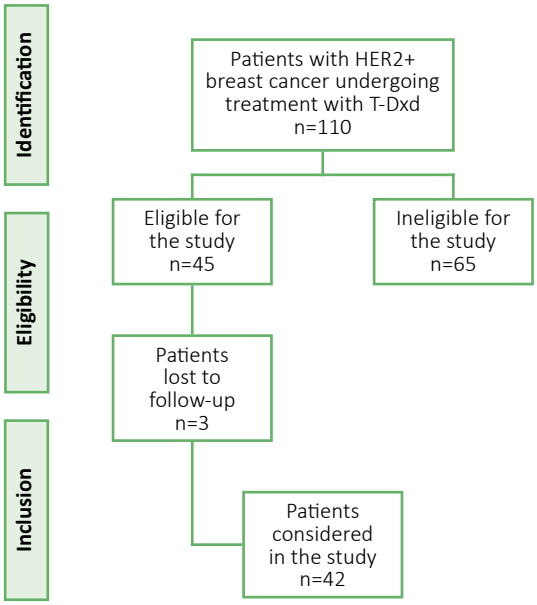
Table 4. Classification of supportive medications according to major systemic groups of the ATC classification up to the 2nd level and correlation with episodes of constipation (Rio de Janeiro/Brazil, 2022–2024).

ATC 2nd Level Classification	Total	
	n	%
A04 – Antiemetics and antinauseants	20	71.4
R06 – Antihistamines for systemic use	1	0.03
H02 – Corticosteroids for systemic use	17	60.7
N05 – Psycholeptics	1	0.03
N02 – Analgesics	17	60.7
A06 – Drugs for constipation	2	7.14
A02 – Drugs for acid-related disorders	9	32.1
A07 – Antidiarrheals. intestinal anti-inflammatory/ anti-infective agents	9	32.1
A03 – Drugs for functional gastrointestinal disorders	6	21.4
N06 – Psychoanaleptics	1	0.03
ATC Group	Constipation (n=6)	
A04	5	83.3
N02	1	16.7
Total	6	100.0

Figure 1. Flowchart of patient selection for the study (Rio de Janeiro/Brazil, 2022–2024).



Discussion

The findings of this study provide a detailed analysis of the safety profile of T-DXd in the studied population, taking into account their clinical and epidemiological characteristics. Deaths that occurred shortly after the first treatment cycle, attributed to disease progression, were not evaluated. These cases were treated as loss to follow-up, as the limited availability of data made it difficult to establish a direct correlation between the treatment and the outcome, hindering accurate causality assessment. Thus, among the patients analyzed, 66.7% experienced at least one treatment-related adverse event (Table 1), with the most frequent being nausea/vomiting (78.6%), fatigue (46.4%), and alopecia (32.1%). Notably, nausea/vomiting were among the most severe events (Grade 3) (Table 2), and 25% of patients who developed adverse events required a dose reduction.

The increase in life expectancy has significantly contributed to the rise in cancer cases in the population. In the DESTINY-Breast studies, a predominance of female patients was observed, with a mean age around 55 years[4]. Regarding the epidemiological characteristics analyzed, the profile of our sample aligns with the literature, which indicates a population mostly composed of women, especially those aged between 50 and 69 years—accounting for 73.8% of the cases. This profile is also consistent with other studies conducted in oncology referral centers, which highlight the prevalence of breast cancer among women[1].

Among the pre-existing comorbidities observed, hypertension was the most prevalent (42.2%), followed by diabetes (13.2%) and hypothyroidism (10.5%) (Table 1). These findings are consistent with other studies that have shown an association between age and comorbidities such as hypertension and diabetes. Specifically, findings by Douberin et al. (2019) indicated a prevalence of 65.2% for hypertension and 36.5% for diabetes in patients with breast cancer, while Cruz et al. (2021) reported 53.7% for hypertension and 20.9% for diabetes. These results support the strong association between breast cancer and the presence of such comorbidities, particularly in older populations[13,14].

In the DESTINY-Breast studies, the most common adverse events associated with T-DXd treatment were nausea (75.8%), fatigue (58.3%), vomiting (43.7%), and alopecia (39.9%)[4]. In the present study, 33.3% of patients did not report adverse events related to T-DXd, suggesting good tolerability to treatment in part of the population. Among those who did experience adverse events, the most frequent were nausea and vomiting (78.6%), followed by asthenia (46.4%), alopecia (32.1%), constipation (24.1%), mucositis (14.3%), and anorexia (10.7%). These results are consistent with the findings of the clinical trials, reinforcing the drug's safety profile in the study population.

Interstitial lung disease (ILD) is a significant adverse reaction associated with T-DXd, with an incidence between 10% and 14%. However, in this study, no patients had prior pulmonary comorbidities or clinical records suggesting or confirming ILD, which may indicate that the absence of predisposing factors could be associated with a lower risk of this toxicity. Nonetheless, the smaller sample size in this study compared to clinical trials can be considered a limiting factor for detecting low-incidence events, and caution is required when extrapolating these results. It is worth noting that clinical trials emphasize the importance of early diagnosis to minimize ILD severity, highlighting the need for close monitoring during T-DXd use.

Supportive medications were classified according to the ATC system, and this classification was adopted to analyze drugs prescribed for use after chemotherapy cycles, aiming to assess potential influences on adverse events and minimize bias in analyzing those associated with T-DXd. It is important to note that no causality assessment was performed using the Naranjo Algorithm in this context; correlations were based on the mechanisms of action and adverse events described in the drug label. Moreover, the institutional standard of pre-chemotherapy supportive care was not considered, as this protocol is common to all patients undergoing treatment, making differential comparative evaluation unfeasible.

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A more detailed analysis of constipation episodes, which affected 21.4% of patients, revealed a possible correlation with the use of supportive medications—especially antiemetics (A04), since 83.3% of patients who experienced constipation were concurrently using this therapeutic class. This finding suggests that constipation may be related not only to T-DXd but also to supportive medications used during chemotherapy, which have known effects on intestinal motility.

Therefore, the increased reports of constipation may indicate that the management of supportive medications should be carefully monitored, and considering alternative therapeutic strategies may be an important approach to reduce this adverse event and improve patient comfort.

The analysis performed using the Naranjo Algorithm revealed that 31.5% of the adverse reactions were classified as "definite," suggesting a possible correlation between T-DXd and the observed reactions. Meanwhile, 68.5% of the reactions were classified as "probable," indicating an association, although other factors, such as comorbidities or supportive treatments, may also be involved. Although this algorithm is a widely used and useful tool, it presents limitations that may underestimate causality in the oncology context, since it considers the rechallenge of the drug as a criterion for establishing causality, which may not be feasible due to the risk of additional adverse events[11]. In this study, the algorithm was maintained to ensure consistency and alignment with the institutional standard for analysis.

The severity analysis performed using the CTCAE methodology revealed that most events were classified as grade 1 (67.1%), suggesting mild effects that generally do not require treatment interruption. However, 28.8% were grade 2, requiring medical intervention, while only 4.1% were grade 3, indicating severe effects that may lead to hospitalization or persistent disability. This severity profile suggests that although T-DXd is generally well tolerated, continuous monitoring is essential to detect any events that may require therapeutic adjustments at an early stage.

Although the methodology used is effective for assessing toxicity, it does not clearly distinguish between adverse reactions and general adverse events, which may hinder the interpretation of findings in causality studies[12]. To minimize this bias, the analysis adopted the temporal relationship between the onset of symptoms and the administration of T-DXd. Furthermore, the subjectivity in classifying severity and the method's limitation in identifying late-onset effects could compromise result accuracy[12]. To reduce such influence, peer reviews were conducted to ensure greater agreement among evaluators, and the limitation regarding late-onset events did not affect this study, as the analysis was restricted to the treatment period.

According to data from medical records and prescription histories in the electronic health records, 25% of patients who experienced adverse events required a dose reduction to ensure treatment continuity. This figure is close to the 20.9% reported in T-DXd clinical trials, and this small difference may reflect real-world clinical practice conditions, suggesting consistency with previously published data on the drug[4].

Although the data sources used for this study are reliable—given that they come from electronic medical records—it is important to consider the possibility of underreporting of adverse events and/or the absence of documentation of some reactions as a limitation of the study. Additionally, a more robust analysis, using multiple data sources and a longer observation period, would be essential for detecting events such as interstitial lung disease and others that may have gone unidentified.

Conclusion

The results of this study contribute to the understanding of the safety profile of T-DXd in a real-world Brazilian population, supporting findings from the literature and detailing the frequency and severity of adverse events in the population analyzed. Nausea, fatigue, alopecia, and constipation were the most frequent events, with 67.1% classified as mild in severity. Causality assessment indicated that 31.5% of the observed reactions were classified as "definite" and 68.5% as "probable," reinforcing the potential temporal relationship between the use of the drug and the reported events.

In addition to validating previous findings, this study advances knowledge by correlating the occurrence of adverse events with the use of supportive medications, highlighting the importance of pharmacological strategies to minimize toxicity and optimize treatment tolerability. The need for early intervention and individualized therapeutic adjustments was also evident, with 25% of patients requiring dose reductions due to toxicity.

Given the study's limitations, future investigations using broader methodologies are recommended, including multiple data sources, larger populations, and longer follow-up periods. These approaches may provide a more robust assessment of T-DXd's safety, supporting improved management of adverse events and enhancing the quality of oncologic care.

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The authors declare no conflict of interest related to this article.

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Authors Gama LG and Cabo CJ contributed to the study design, critical review of the intellectual content, data analysis and interpretation, and manuscript writing. All authors are responsible for all aspects of the work and for ensuring the accuracy and integrity of any part of the manuscript.

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