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Adverse events reported to the National Reporting System (VigiMed) involving antineoplastic medications in Brazil

Eventos adversos notificados ao sistema nacional de notificação (VigiMed) envolvendo medicamentos antineoplásicos no Brasil

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ABSTRACT
Objective: to describe suspected adverse drug events (ADEs) involving antineoplastics reported in Brazil. **Methods:** descriptive study of reports to the VigiMed system between 01/01/2019 and 03/31/2023. **Results:** 29,656 reports involving antineoplastics were identified, most were spontaneous (85.5%) and came from health services (59.0%). Adults (48.1%) and females (63.0%) were more involved in the reports, with a large number of unreported data on age and sex. The most common antineoplastic medicines were paclitaxel (10.4%) and oxaliplatin (7.6%), with emphasis on parenteral presentations (45.1%). A reduced number of medication errors involving antineoplastics were identified (1.3%) and the Reporting Odds Ratio (0.22; 95% CI 0.21-0.23) demonstrated they were less frequent for this class than for other products. **Conclusion:** reports of ADE involving antineoplastics are frequent in Brazil, and it is important to improve safety barriers and monitor cancer patients, in addition to promoting education and engagement to improve notifications.

Keywords Antineoplastic agents; Drug-related side effects and adverse reactions; Medication errors; Adverse drug reaction reporting systems; Pharmacovigilance.

RESUMO
Objetivo: Descrever as suspeitas de eventos adversos a medicamentos (EAM) envolvendo antineoplásicos notificadas no Brasil. **Métodos:** Estudo descritivo das notificações realizadas no sistema VigiMed entre 01/01/2019 e 31/03/2023. **Resultados:** Foram identificadas 29.656 notificações envolvendo antineoplásicos, sendo que a maioria delas eram espontâneas (85,5%) e advindas de serviços de saúde (59,0%). Adultos (48,1%) do sexo feminino (63,0%) estiveram mais envolvidos nas notificações, sendo grande o número de dados não registrados sobre idade e sexo. Antineoplásicos mais frequentes foram paclitaxel (10,4%) e oxaliplatina (7,6%), com destaque para apresentações parenterais (45,1%). Identificou-se um número reduzido de erros de medicação envolvendo antineoplásicos (1,3%) e o *Reporting Odds Ratio* (0,22; $IC^{95\%}$0,21-0,23) demonstrou que estes foram menos frequentes para essa classe que para outros produtos. **Conclusão:** Notificações de EAM envolvendo antineoplásicos são frequentes no Brasil, sendo importante aprimorar barreiras de segurança e monitorar pacientes oncológicos, além de promover a educação e engajamento para qualificação da notificação.

Palavras-chave: Antineoplásicos. Efeitos colaterais e reações adversas relacionados a medicamentos. Erros de medicação. Farmacovigilância. Sistemas de notificação de reações adversas a medicamentos.

INTRODUCTION

Antineoplastics are widely used in oncology treatments, although they have a complex safety profile. These medications are characterized by high intrinsic toxicity and a narrow therapeutic range, in addition to presenting several adverse effects and drug interactions described.[1] Because they present an increased risk of causing significant harm to the patient when involved in failures in the use process, antineoplastics are classified as high-alert medications (HAM).[2,3] Further, this medication class is included in the acronym "*A-PINCH*" proposed by the World Health Organization (WHO), which lists medications that should be the target of priority actions to minimize medication-related harm.[4]

In addition, oncology is one of the specialties with many weaknesses in terms of robust clinical trials, due to the rarity of some conditions, as well as differences in staging and patients' multiple comorbidities.[5] Therefore, the continuous evaluation of the safety profile of antineoplastic medicines through pharmacovigilance studies is fundamental for risk detection, especially those based on national reporting systems, which are based on complex communication systems, records, and databases.[5]

Pharmacovigilance systems monitor the medication safety by producing information that provides alerts and enables the adoption of assertive strategies by health professionals, regulators, manufacturers, and consumers. Furthermore, knowing the profile of reports from a country, in addition to allowing comparability with other countries, can also enable the mitigation and prevention of harm resulting from adverse drug events (ADEs).[6] In this context, it is important to define that ADE comprises any harm or injury, arising from the use of medications, caused by the use or lack thereof when necessary.[7]

In Brazil, the National Health Surveillance Agency (Anvisa) is the governmental body responsible for pharmacovigilance and has, since December 2018, made the VigiMed system available as a national system for reporting suspected ADEs, which include: "adverse or harmful reactions; (...) therapeutic ineffectiveness; medication errors (...); abusive use; use for a purpose other than that indicated in the insert (off label); and intoxications."[8] Suspected ADEs can be reported to the VigiMed system by health professionals, drug registration holders, study sponsors, and also by citizens.[8] VigiMed is the adapted version of the VigiFlow system, a system offered by the World Health Organization (WHO) to the national pharmacovigilance centers of member states of the WHO Programme for International Drug Monitoring. Therefore, the data recorded in VigiMed make up, together with data sent by other countries, the global database called VigiBase.[8]

Given the complexity of antineoplastic therapies and the safety profile of these medications, reports of ADE involving these classes should receive attention. Studies that target the set of reports in national reporting systems allow reflection on the notification process and profile. Furthermore, considering that VigiMed, specifically, is a relatively new reporting system, it is important to identify possible weaknesses and opportunities for improvement. However, to the authors' knowledge, there are no studies that evaluate reports of suspected ADEs specifically involving the class of antineoplastics in the national and international scenario. Therefore, the present study aimed to describe suspected ADEs reported to the VigiMed system involving antineoplastic medications between January 2019 and March 2023.

METHODOLOGY

STUDY DESIGN

This was a descriptive retrospective study of suspected ADEs reported to the National Reporting System, VigiMed, involving antineoplastic medications. The present study was not submitted for approval by a research ethics committee because it used blinded data from a collective database.

DATA SOURCE AND COLLECTION

We used the "open data in Pharmacovigilance" regarding reports of suspected ADEs made available in the public domain by the Pharmacovigilance Management (GFARM) in partnership with the General Management of Knowledge, Innovation, and Research (GGCIP) of Anvisa in a Microsoft Excel® spreadsheet format. This file contains three tables that correspond to data relating to reports, medications, and reactions/events, respectively. The information that connects the tables is the report identification number. It is important to point out that "Suspected ADE" is the standard nomenclature adopted by Anvisa to refer to ADE reports whose information does not present a causality assessment.[9,10]

In the present study, specifically, only information on reports of suspected ADE involving antineoplastic medications between 01/01/2019 and 03/31/2023 was analyzed. To identify data involving antineoplastics, the first- and second-level codes of the Anatomical Therapeutic Chemical (ATC) system referring to this group of medications (L01) were used, available in the Anvisa database. Therefore, any report involving at least one antineoplastic was included in the analysis.

In the VigiMed system, the notifier makes a report of suspected ADE according to standardized optional or mandatory closed fields. Each report may present more than one reaction/event, and one or more antineoplastic medicines may be associated with a single report. Thus, to describe the data, three units of analysis were adopted, which correspond to the three output tables of "open data in Pharmacovigilance", namely: 1) reports of suspected ADE; 2) reactions/events; and 3) medications.

REPORTS OF SUSPECTED ADE INVOLVING ANTINEOPLASTICS

Reports of suspected ADE involving antineoplastics identified within the analyzed period (N = 29,656) were described according to the following characteristics:

- monthly number of total reports, reports containing at least one serious reaction/event, and reports containing only non-serious reactions/events;
- type of report: spontaneous report, study report, or others (reports not originating from a spontaneous report or a study);
- report entry type: healthcare services, vaccination services, pharmaceutical companies, patients or healthcare professionals;
- type of notifier: pharmacist, physician, other healthcare professional, lawyer, consumer, or other non-health professional;
- sex of the individual involved in the report: female or male;
- age range of the individual involved in the report (calculated from the date of birth informed in the report): infant (31 days to 5 years), child (6 to 12 years), adolescent (13 to 18 years), adult (19 to 64 years), or older adult (over 65 years old);
- pregnant patient: yes or no;
- lactating patient: yes or no.

In case of missing data in any of the report fields evaluated, its frequency was also described as "unreported" data.

REACTIONS/EVENTS INVOLVING ANTINEOPLASTICS

Data relating to reactions/events involving antineoplastics identified within the analyzed period (N = 85,846) were described according to the "System Organ Class" (SOC) level of the Medical Dictionary for Regulatory Activities (MedDRA) classification. The MedDRA classification is used in VigiMed to categorize reported reactions. It is a standardized and highly specific medical terminology, which was developed by the International Council for

Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), with the aim of facilitating the international sharing of regulatory information for medical products used by humans. The structural hierarchy of MedDRA terminology comprises five hierarchical levels: SOC, high level group term (HLGT), high level term (HLT), preferred term (PT), and lowest level term (LLT), in which SOC is the highest level in the hierarchy and LLT is the lowest.[11]

Reactions/events classified with the SOC "Injuries, poisonings, and procedural complications" and HLGT level "Medication errors and other product use errors and issues" were described, allowing visibility of the types of errors involving antineoplastics from their HLT classification.[11]

ANTINEOPLASTIC MEDICINES INVOLVED IN THE REPORTS

The medicines involved in reports of suspected ADE (N = 43,354) were described according to the following characteristics:

- Most frequent medicines;
- ATC code up to the 3rd level, that is, according to anatomical group and main pharmacological or therapeutic group;
- For each anatomical group and main pharmacological or therapeutic group, the most prevalent medicines were presented. We chose to describe all medicines that had a frequency greater than 10%;
- Route of administration of the medicines (parenteral *vs.* non-parenteral).

DATA ANALYSIS

Stata SE 18® software was used for data analysis. As this is a population of data, descriptive statistics were applied using measures of frequency or central tendency and dispersion according to the characteristics of the variables. A graphic description of the number of reports per month of the evaluated period was also made. Additionally, a disproportionality analysis was carried out comparing reactions referring to medication errors (reactions included in the HLGT level "Medication errors and other product use errors and issues") involving antineoplastics *versus* other products. To this end, the Reporting Odds Ratio (ROR) measure was adopted with its respective 95% confidence interval (95%CI).[12]

RESULTS

REPORTS OF SUSPECTED ADE INVOLVING ANTINEOPLASTICS

During the period analyzed, an overall total of 161,685 reports of suspected ADEs to VigiMed were identified. Among these, 29,656 were related to at least one antineoplastic medicine (18.3%). Figure 1 illustrates the number of total reports, the number of reports containing at least one serious reaction/event, and the number of reports containing only non-serious reactions/events involving antineoplastics over the months within the analyzed period. An average of 581 reports per month was found.

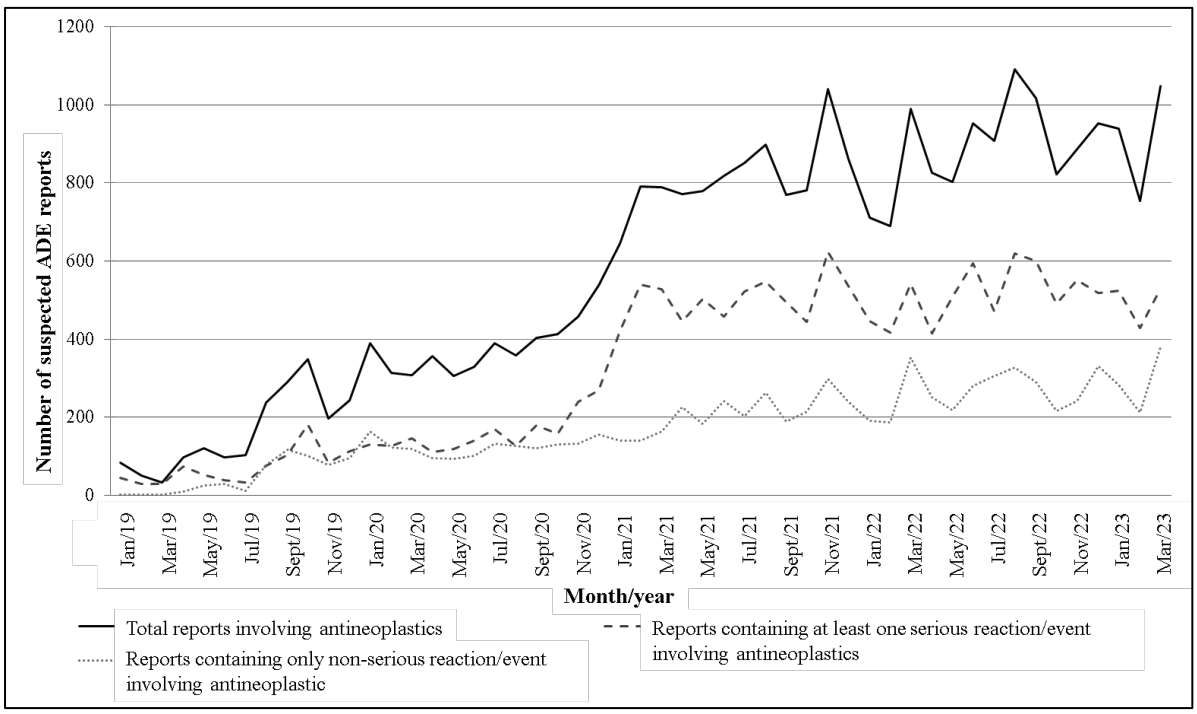

Figure 1. Total number of reports of suspected adverse drug events related to antineoplastic medications, of reports containing at least one serious reaction/event, and of reports containing only non-serious reactions/events involving antineoplastics. Brazil, January 2019 to March 2023.
Source: VigiMed, 2019-2023.

All the characteristics of reports of suspected ADE involving antineoplastics are listed in Table 1. Regarding the type of report, the majority of reports involving antineoplastics were spontaneous (85.5%) and were received from "Health Services" (59.0%; n = 17,496). Most suspected ADEs involving antineoplastics involved females (63.0%; n=18,689) and adults (48.0%; n = 14,255). Only one report involved a pregnant patient and four reports involved lactating patients. A report may contain more than one type of associated notifier, and most of them involved a "Pharmacist" as the notifier (48.0%; n = 14,767).

TABLE 1. Characteristics of reports of suspected adverse drug events involving antineoplastics (n=29,656). Brazil, January 2019 to March 2023.

Report characteristics	Absolute frequency (N)	Relative frequency (%)
Type of report		
Spontaneous	25,356	85.5
Study reports	3,529	11.9
Others	771	2.6
Type of report entry		
Health service	17,496	59.0
Pharmaceutical company	9,327	31.4
Patient/health professional	2,824	9.5
Unreported	8	0.1
Vaccination services	1	0.0
Sex of the patient involved		
Feminine	18,689	63.0
Masculine	9,835	33.2
Unreported	1,132	3.8
Age group of the patient involved		
Adults	14,255	48.0
Older adults	8,184	27.6
Unreported	6,23	21.0
Neonate/Infant	532	1,8
Adolescent	257	0.9
Children	198	0.7
Pregnant patient		
No	29,655	99.9
Yes	1	0.01
Lactating patient		
No	29,652	99.9
Yes	4	0.01
Notifier type*		
Pharmaceutical	14,767	48.0
Other healthcare professional	7,472	24.0
Consumer or other non-health professional	5,108	16.0
Doctor	3,427	11.0

* A report can contain more than one type of associated notifier.
Source: VigiMed, 2019-2023.

REACTIONS/EVENTS INVOLVING ANTINEOPLASTICS

A total of 85,846 reactions/events involving antineoplastics were reported, highlighting that a report may be associated with several different reactions/events. Table 2 lists the results relating to the system organ class (SOC) most related to reactions/events involving antineoplastics.

TABLE 2. Classification of reactions involving antineoplastics classified according to the System Organ Class (SOC) (n=85,846). Brazil, January 2019 to March 2023.

System Organ Class	Absolute frequency (N)	Relative frequency (%)
General disorders and administration site conditions	12,840	15.0
Gastrointestinal disorders	9,137	10.6
Skin and subcutaneous tissue disorders	9,066	10.6
Respiratory, thoracic and mediastinal disorders	7,934	9.2
Vascular disorders	6,434	7.5
Nervous system disorders	5,563	6.5
Blood and lymphatic system disorders	5,312	6.2
Injury, poisoning and procedural complications	4,543	5.3
Musculoskeletal and connective tissue disorders	4,223	4.9
Investigations	3,919	4.6
Neoplasms benign, malignant and unspecified	3,289	3.8
Infections and infestations	2,580	3.0
Cardiac disorders	1,857	2.2
Immune system disorders	1,856	2.2
Metabolism and nutrition disorders	1,437	1.7
Psychiatric disorders	1,435	1.7
Eye disorders	1,021	1.2
Renal and urinary disorders	714	0.8
Hepatobiliary disorders	623	0.7
Surgical and medical procedures	414	0.5
Reproductive system and breast disorders	303	0.4
Ear and labyrinth disorders	252	0.3
Product issues	193	0.2
Endocrine disorders	147	0.2
Social circumstances	123	0.1
Congenital, familial and genetic disorders	74	0.1
Pregnancy, puerperium and perinatal conditions	27	0.0
Unregistered	530	0.6
Total	**85,846**	**100**

Source: VigiMed, 2019-2023.

Injuries, poisoning, and procedural complications, which include possible medication errors, represented 5.3% of reactions (n=4,543). Of these, 1,121 were described as medication errors, in which errors related to product administration (47.1%; n = 528) were the most frequent (Table 3). According to the disproportionality analysis, errors involving antineoplastics were reported less frequently (1.3% of reactions) than errors involving non-antineoplastic products (6.0% of reactions), resulting in a ROR=0.22 (95%CI=0.21-0.23).

TABLE 3. Reactions/events involving antineoplastics classified as medication errors according to the High Level Term (HLT) (n=1,121). Brazil, January 2019 to March 2023.

HLT	Absolute frequency (N)	Relative frequency (%)
Product administration errors and problems	528	47.1
Medication errors, errors and problems using the product	314	28.0
Product prescription errors and problems	128	11.4
Product dispensing errors and problems	59	5.3
Product preparation errors and issues	39	3.5
Product transcription errors and communication issues	26	2.3
Product monitoring errors and problems	12	1.1
Product storage errors and problems	10	0.9
Errors and problems due to product confusion	4	0.4
Product selection errors and problems	1	0.1
Total	**1,121**	**100**

Source: VigiMed, 2019-2023.

ANTINEOPLASTIC MEDICINES INVOLVED IN THE REPORTS

A total of 43,354 citations of antineoplastic medicines supposedly involved in reported suspected ADEs were identified. A report may be associated with one or more medications. The antineoplastics most involved in notifications were paclitaxel (n= 4,503; 10.4%) and oxaliplatin (n= 3,282; 7.6%). There was a predominance of the parenteral (n=19,572; 45.1%) over the non-parenteral (n=2,906; 6.7%) route. The proportion between pharmacological groups and medicines with a frequency greater than 10.0% is presented in Table 4.

TABLE 4. Proportion of antineoplastic medicines involved in reports of suspected adverse drug events per chemical, pharmacological or therapeutic subgroup and most frequent medicines. Brazil, January 2019 to March 2023.

ATC	Chemical, pharmacological or therapeutic subgroup	Frequency	
		N	%
L01X	**Other antineoplastic agents**	**14,344**	**33.1**
	Oxaliplatin	3,282	22.9
	Carboplatin	2,655	18.5
L01C	**Plant alkaloids and other natural products**	**8,827**	**20.4**
	Paclitaxel	4,503	51.0
	Docetaxel	2,172	24.6
	Irinotecan	996	11.3
L01E	**Protein kinase inhibitors**	**6,288**	**14.5**
	Ribociclib	1,619	25.7
L01B	**Antimetabolites**	**5,312**	**12.3**
	Fluorouracil	1,826	34.4
	Methotrexate	1,333	25.1
	Gemcitabine	697	13.1
L01F	**Monoclonal antibodies and antibody drug conjugates**	**5,028**	**11.6**
	Cetuximab	1,099	21.85
	Rituximab	1,085	21.58
L01A	**Alkylating agents**	**1,980**	**4.6**
	Cyclophosphamide	1,218	61.50
L01D	**Cytotoxic antibiotics and related substances**	**1,582**	**3.7**
	Doxorubicin	1,283	81.0

Source: VigiMed, 2019-2023

DISCUSSION

The present study characterized the reports to the VigiMed system regarding suspected ADEs involving antineoplastics. This type of study should be encouraged because, by knowing the profile of ADEs, it is possible to act in the design and implementation of safety barriers, prevention strategies, and harm minimization involving antineoplastics, whose safety profiles are extremely complex. In addition, this study allowed to outline the national profile of suspected ADEs involving antineoplastics, allowing historical monitoring and international comparability.

The results indicated that suspected ADEs involving antineoplastics are significantly frequent, corresponding to almost a fifth of total reports. This data is coherent, given the complex safety profile of antineoplastics. Mota *et al.* also identified a relevant contribution from antineoplastics (32.1%) among the total ADE reports carried out between 2008 and 2013, in Notivisa, a system prior to VigiMed.[13] In the international scenario, only one study, which evaluated data from the National Reporting System of Portugal, demonstrated a considerable representativeness of antineoplastics and immunomodulators (25.5%) among the total reports.[14]

Furthermore, a growing trend in the number of reports was found between 2019 and 2023, without periods of significant decline. The lowest number of reports was observed in March 2019, the second month of system implementation, in which there were still instabilities and a lack of access for most notifiers, as this access was granted gradually and upon

registration of the professional/institution. At this stage, people without access to VigiMed were advised to continue to use Notivisa for ADE reports. On the other hand, the gradual increase in reports over the evaluated period may represent the notifiers' awareness of the new platform.[15]

Regarding the seriousness profile, a predominance of reports containing at least one record of suspected serious reactions/events was identified. In general, notifiers tend to underreport events considered "common", as they do not understand the relevance of this type of record.[5] In addition, the work overload in health services makes professionals prioritize the report of serious events, which must be compulsorily reported in Brazil. From the point of view of notifiers representing pharmaceutical companies, it is worth reiterating that, according to RDC 406/2020, it is mandatory to submit reports of serious reactions.[16]

As for the type of report, there was a predominance of spontaneous reports, which are the most used reporting method in Brazil today, given their low cost and high potential for evaluating signs and monitoring the safety profile of medicines. However, the success of this practice depends, above all, on the active participation of reporting agents, such as health professionals and citizens, since underreporting is still a challenge.[6]

Most reports were provided by "Health Services". This is consistent with the fact that most oncology medicines are dispensed and administered in health services with an adequate structure for infusion, monitoring, and support in case of serious and non-serious adverse events. Furthermore, in these settings, health teams can identify most ADEs associated with antineoplastics, allowing timely reports.[1] National efforts have also been made to promote pharmacovigilance practices in health services, such as the National Program of Patient Safety and its regulatory framework, which made the report of ADE mandatory.[17] The entry of reports by "Pharmaceutical Companies" also proved to be relevant, possibly reflecting the publication of RDC 406/2020, an important regulatory framework that provided for Good Pharmacovigilance Practices for Medicine Registration Holders for human use, contributing to greater participation of these agents in pharmacovigilance practices.[16]

Regarding the type of notifier, a higher rate of ADE reported by pharmacists was found compared to other professionals, as observed in other studies, including a systematic review and meta-analysis.[14,18] The presence of the pharmacist as a notifier in almost half of the reports can be attributed to organizational systems, which usually assign the responsibility for reporting ADE to the pharmacy sector. In addition, generally in patient safety centers, the pharmacist is the professional responsible for pharmacovigilance.

The frequency of females among patients involved in suspected ADEs in the present study was similar to that identified by Mota *et al.* regarding Notivisa (60.5%).[13] In this sense, the female gender has already been identified as a risk factor for the occurrence of ADE, as it is related to higher incidences of pharmacokinetic and pharmacodynamic changes, related, for example, to changes in body weight and hormonal factors.[19]

The predominance of adult and older people is because cancer is, in general, more common in these age groups. Estimates indicate that around 70% of cancer cases worldwide occur after the age of 65. Moreover, it is important to highlight that older people present pharmacokinetic and pharmacodynamic changes that predispose them to the occurrence of ADE.[20,21] However, the low completeness and quality of the description of sex and age in the reports evaluated made such analysis of individuals involved in ADE difficult. This limiting point must be taken into account in educational strategies to improve ADE reporting in the national context, especially given the relevance of analyzing the frequency of age groups and gender poorly represented in clinical trials or contexts of off-label use.[5]

In the present study, four reports of ADE involving lactating patient were identified, although lactation is not encouraged during chemotherapy, due to the risk of toxicity for the child. In addition, only one report of ADE involved a pregnant patient, which seems to reflect the caution in using antineoplastic therapies in this population.[22]

Considering the types of reactions/events recorded, there was a predominance of "General

disorders and administration site conditions". This class of SOC includes nonspecific reactions that can affect various systems and regions of the body, as well as the administration site.[11] For example, infusion reactions are common in oncological treatments, so most antineoplastics in parenteral presentations can cause this type of response. Certain medicines, such as taxanes, platinum, and immunotherapeutics, are more associated with infusion reactions, as well as the concomitant administration of two or more antineoplastics in therapeutic regimens. In general, these reactions can be prevented with the use of premedication (corticosteroids and antihistamines), and the patient must always be monitored to provide rapid treatment when necessary.[23]

The "Gastrointestinal disorders" SOC was also common, which is justifiable considering that the gastrointestinal epithelium is greatly affected by antineoplastic medicines due to the profile of rapid cell division. Gastrointestinal toxicity includes anorexia, mucositis, diarrhea, nausea, and vomiting, for example.[24] Estimates indicate that 60 to 100% of patients who receive high doses of chemotherapy experience gastrointestinal reactions at some point.[25]

"Skin and subcutaneous tissue disorders" also stood out. Skin reactions are also common in oncology due to rapid cell division. Dermatological toxicities include, for example, alopecia, hand-foot syndrome, pruritus, skin rash, and xerosis.[26] Another aspect to consider is that skin reactions are easily identified, as they are very visible, which may favor greater reporting of these events.[27]

Regarding medication errors, there was a predominance of errors occurring in the administration stage, followed by usage problems/errors, prescription errors, and dispensing errors. In the study by Ford *et al.*, over two years, the occurrence of 141 medication errors was identified in 4,572 admissions to an oncology hospital (3.0%), with a predominance of administration errors (41.0%), dispensing errors (38.0%), and prescription/transcription errors (21.0%).[28] Data from the literature estimate that the incidence of adverse events in hospitals can vary between 3.0% and 16.0%, of which around 40.0% could be prevented. Errors with antineoplastics are considered especially hazardous since these medications are among those most involved in incidents that result in severe toxicity and death.[29] In addition, it is important to highlight the need to encourage the practice of reporting this type of ADE among healthcare professionals to reduce the occurrence of similar errors.

After an analysis of disproportionality about medication errors, a lower frequency of reports of errors involving antineoplastics was observed than for other non-antineoplastic products (ROR=0.22; 95%CI=0.19-0.22). Because antineoplastics are HAM[2], it is common for healthcare institutions to adopt multiple safety barriers to protect patients, who are usually already weakened by cancer. Additionally, the fact that these medications, when in parenteral formulation, are manipulated/fractionated in a restricted environment and exclusively by pharmaceutical professionals in Brazil[30], may have a positive impact on the incidence of medication errors involving antineoplastics.

In relation to antineoplastics involved in suspected ADEs, a predominance of parenteral over non-parenteral presentations was found, although most of the data on the administration route were absent or doubtful (48.1%). The route of administration considerably changes the profile of potential ADEs caused by antineoplastics, providing essential information for analyzing the notification. To improve the completeness and adequacy of this data, it is suggested to avoid open fields for recording these variables in the reporting system and promote the qualification and recycling of notifiers. The study by Mota *et al.* identified a predominance of the intravenous route (75.3%) in Notivisa reports.[13]

As for the medicines most involved in ADEs, a result similar to that identified in the Notivisa system was observed, which included the antineoplastic medicines docetaxel (9.1%), paclitaxel (3.6%), carboplatin (1.9%) and oxaliplatin (1.9%) among the most frequent.[13] These are classic antineoplastics that are incorporated into the Unified Health System (SUS) and, therefore, are widely used in Brazil.

The main limitation of the present study is the quality of the data reported to VigiMed regarding the completeness and consistency of

the variables. Although Anvisa provides manuals and various materials for the qualification and guidance of notifiers, they still require educational activities to become able to provide adequate records. Working with a national data source with pre-determined fields also limits more detailed clinical analysis of patient's health conditions and their individual clinical profiles. On the other hand, it allows discussion about the limitations of reporting systems and the participation of notifiers in the national context.

Nonetheless, even with these limitations, the present study has high scientific relevance because, to the best of our knowledge, no studies have yet been published that evaluate reports of suspected ADEs involving antineoplastics in the national setting after the recent implementation of the VigiMed system. In this way, carrying out studies that profile the reports in this system contributes to the detection of crucial points that require adjustments to the reporting system and the qualification of reports. In addition, our findings may contribute to the prevention of harm related to the use of antineoplastic medicines.

CONCLUSION

This study demonstrated the relevance of antineoplastics among ADE reports to the VigiMed system, reinforcing the need to rigorously monitor the post-marketing safety data of these medicines. Most reports were spontaneous, containing at least one serious reaction, and received from health services, highlighting strengths and weaknesses in the context of reports that should be explored.

Therefore, our findings point to the need to monitor medication safety through indicators related to safety in their use in the real world. Such monitoring makes it possible to restructure and improve not only the reporting systems but also health practices and systems to mitigate harm, prevent it, and promote health. In addition, engagement and education initiatives must be targeted at reporting professionals, in order to achieve higher data completeness and adequacy. Other studies must be conducted, mainly to robustly evaluate the performance of the VigiMed System.

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