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Safety of the First- and Second-Line Metastatic Triple-Negative Breast Cancer Chemotherapy: A Retrospective Study

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ABSTRACT

INTRODUCTION. Breast cancer (BC) ranks as second most lethal cancer type among female population. Triple-negative breast cancer (TNBC) is one of the most aggressive and treatment-resistant molecular biological subtypes. The metastatic form of triple-negative breast cancer (mTNBC) presents an urgent challenge in breast cancer therapy, since the treatment effectiveness depends on multiple factors. Analysis and assessment of adverse chemotherapy reactions is essential for high-quality medical care.

AIM. This study aimed to assess the risks of adverse drug reactions and the severity of their consequences during mTNBC chemotherapy in order to develop management and prevention strategies for these reactions.

MATERIALS AND METHODS. The methods included content analysis of scientific publications, regulations, Russian national standards of BC medical care in adults, clinical recommendations for adult BC therapy and a retrospective analysis of primary medical records covering 120 BC patients at Astrakhan Regional Clinical Oncological Dispensary over 2023-2024.

RESULTS. The study established therapeutic strategies of the first- (doxorubicin + cyclophosphamide, docetaxel) and second-line drug therapy (paclitaxel + carboplatin, eribulin) for mTNBC. Established adverse drug reactions that occur after administration include febrile neutropenia, cardiotoxicity, peripheral neuropathy, drug resistance, nausea, and vomiting. The highest risk category for the two lines of therapy was assigned to febrile neutropenia, the lowest – to nausea and vomiting.

CONCLUSIONS. The incidence and profile of adverse drug reactions vary significantly depending on chemotherapy protocols and lines used in patients with mTNBC. Hematological toxicity being predominant for each of the protocols, anthracycline-cyclophosphamide strategy bears the highest risk of adverse drug reactions. Eribulin and docetaxel monotherapies are the safest options. The study results can serve as a basis for improving and optimizing mTNBC chemotherapy.

Keywords: adverse drug reaction; chemotherapy; triple-negative breast cancer; breast cancer; metastatic form; febrile neutropenia; peripheral neuropathies; nausea; vomiting; doxorubicin; cyclophosphamide; docetaxel; paclitaxel; carboplatin; eribulin

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Безопасность первой и второй линий химиотерапии метастатического трижды негативного рака молочной железы: ретроспективное исследование

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РЕЗЮМЕ

ВВЕДЕНИЕ. Рак молочной железы (РМЖ) занимает второе место в структуре смертности среди женского населения. Трижды негативный РМЖ считается одним из наиболее агрессивных по течению и трудно поддающимся терапии молекулярно-биологическим подтипом заболевания. Терапия метастатической формы трижды негативного РМЖ представляет собой актуальную проблему ввиду влияния многих факторов на эффективность лечения. Анализ и оценка нежелательных реакций химиотерапии пациентов являются ключевыми элементами обеспечения качества лекарственной помощи.

ЦЕЛЬ. Оценка рисков возникновения нежелательных реакций и тяжести их последствий при химиотерапии метастатической формы трижды негативного рака молочной железы для обоснования стратегий управления и предупреждения данных нежелательных реакций.

МАТЕРИАЛЫ И МЕТОДЫ. Использованы: метод контент-анализа научных публикаций, нормативных актов, национальных стандартов медицинской помощи взрослым при РМЖ, клинических рекомендаций терапии РМЖ взрослым; ретроспективный анализ первичной медицинской документации 120 пациентов с метастатической формой трижды негативного рака молочной железы, проходивших лечение в государственном бюджетном учреждении здравоохранения Астраханской области «Областной клинический онкологический диспансер» за 2023–2024 гг.

РЕЗУЛЬТАТЫ. Установлены терапевтические стратегии первой (доксорубин + циклофосфамид, доцетаксел) и второй (паклитаксел + карбоплатин, эрибулин) линий лекарственной терапии метастатической формы трижды негативного РМЖ. Выявлены нежелательные реакции, возникающие при их назначении: фебрильная нейтропения, кардиотоксичность, периферическая нейропатия, лекарственная устойчивость, тошнота и рвота. В категорию наиболее высокого риска для двух линий терапии был отнесен риск развития фебрильной нейтропии, наиболее низкого – проявление тошноты и рвоты.

ВЫВОДЫ. Частота развития и профиль нежелательных реакций существенно варьируют в зависимости от применяемых схем и линий химиотерапии пациентов с метастатической формой трижды негативного РМЖ. При доминировании проявлений гематологической токсичности при назначении каждого из режимов стратегия «антрациклин – циклофосфамид» относится к повышенной категории риска возникновения нежелательных реакций. Наиболее безопасными для пациентов являются монорежимы эрибулина и доцетаксела. Результаты исследования могут быть основой для усовершенствования и оптимизации лекарственной терапии метастатической формы трижды негативного РМЖ.

Ключевые слова: нежелательные реакции; химиотерапия; трижды негативный рак молочной железы; рак молочной железы; метастатическая форма; фебрильная нейтропения; периферические нейропатии; тошнота; рвота; доксорубин; циклофосфамид; доцетаксел; паклитаксел; карбоплатин; эрибулин

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INTRODUCTION

In the Russian Federation, breast cancer (BC) is the leading type of cancer (22.5%) and mortality cause (15.9%) in women [1]. Its most aggressive subtype, triple-negative breast cancer, accounts for 15–25% of all registered BC cases and is characterized by a high level of metastasis, young age of onset, and resistance to hormone therapy and chemotherapy [2]. Metastatic triple-negative breast cancer (mTNBC) is a pressing problem due to the lack of standardized therapeutic strategies, molecular heterogeneity of the tumor, high mortality, and low patient survival [3].

The standard first-line chemotherapy for mTNBC includes anthracyclines and taxanes; the second line combines regimens using platinum drugs or eribulin monotherapy. Applicability of these chemotherapy regimens is limited by pronounced systemic, cardiac, neurological, dermatological, and gastrointestinal toxicity, leading to dose reduction and/or patient dropout from chemotherapy [4]. As a result, the disease prognosis deteriorates: a 15% reduction of chemotherapy dose intensity in mTNBC reduces the median overall survival to 18.64% [5]. Monitoring adverse drug reactions (ADRs) to the prescribed chemotherapy regimens is a key step in developing strategies to prevent treatment discontinuation and improve patient compliance.

The aim of the study is to assess the risks of adverse drug reactions and the severity of their after-effects in patients receiving chemotherapy for metastatic triple-negative breast cancer in order to justify strategies for managing and preventing these reactions.

Objectives:

1. To identify the most common chemotherapy regimens for mTNBC exemplified by cases from Astrakhan Regional Clinical Oncology Dispensary.

2. To determine the main ADRs, their occurrence rate, and the severity of after-effects for the identified chemotherapy regimens based on an analysis of research publications.

3. To develop a risk matrix for the analyzed chemotherapy regimens in mTNBC.

MATERIALS AND METHODS

The study comprised three stages.

Stage 1. To study the structure of chemotherapy regimens prescribed in mTNBC patients, a retrospective analysis of original medical records of 120 patients with BC treated at Astrakhan Regional Clinical Oncology Dispensary was conducted for the period of 2023–2024.

Inclusion criteria: female sex; stage IV cancer, with lymph node and distant metastases ($>N_0$, $>M_0$); lack of expression of the estrogen, progesterone, and human epidermal growth factor receptor 2 (HER 2) in the neoplasm; age >18 years. Exclusion criteria: male sex, cancer stage I–III, no lymph node or distant metastases (N_0 , M_0); expression of estrogen, progesterone, and HER 2 receptors in the neoplasm; age <18 years.

Stage 2. To determine the main ADRs, their rate of occurrence, and the severity of after-effects upon administration of the established therapeutic strategies, we used content analysis of research publications (a total of 30). The literature search was conducted in the PubMed and eLIBRARY.RU databases over the period 2005–2025 using the following keywords: triple-negative breast cancer, metastatic subtype, anthracyclines, cyclophosphamide, taxanes, platinum drugs, eribulin, adverse drug reactions, and resistance. We also analyzed applicable laws, Russian national standards of medical care for adults with breast cancer¹, and clinical practice guidelines for the treatment of breast cancer in adults².

Stage 3. Developing a risk matrix using the methods stipulated by GOST-R 58771-2019 Risk management. Risk assessment technologies. The identified risks were ranked: 1) by probability of occurrence: very likely (4 points), likely (3 points), unlikely (2 points), slightly likely (1 point); 2) by severity of ADR after-effects: critical (4 points), significant (3 points),

¹ Order of the Ministry of Health of the Russian Federation of June 2, 2022, No. 376n “On the Approval of Standards for Medical Care for Adults with Breast Cancer”.

² Breast cancer. Clinical practice guidelines. Ministry of Health of the Russian Federation; 2021.

considerable (2 points), insignificant (1 point). Evidence shows that for each treatment regimen, a T ratio was established, which refers to the class interval boundary of the disorder probability. The present study uses variable T values for each type of toxicity to standardize the assessment of risks associated with chemotherapy strategies.

RESULTS AND DISCUSSION

Stage 1

Analysis of primary documentation for 120 women with BC allowed identifying a group of 20 patients (16.6%) with mTNBC. Of these, 13 (64.3%) were newly diagnosed cases, while seven patients (35.7%) had progressive disease. Patients in this cohort were distributed across two therapy lines and four treatment regimens (*Table 1*).

In the study sample, first-line therapy most often included anthracycline-cyclophosphamide strategy compared to docetaxel monotherapy: 45% (9 patients) versus 25% (5 patients), respectively. Second-line therapy showed no significant difference: both paclitaxel 80 mg/m² intravenously (IV) + carboplatin AUC2 V once weekly until disease progression or unacceptable toxicity, and eribulin 1.4 mg/m² V on Day 1 and 8 every 3 weeks were prescribed with a frequency of 15% (3 patients per regimen).

In addition to the regimens used at Astrakhan Regional Clinical Oncology Dispensary, clinical guidelines for the studied BC type include the following chemotherapy strategies³: paclitaxel + albumin 260 mg/m² IV every 3 weeks until progression or unacceptable toxicity; paclitaxel 90 mg/m² IV on Day 1, 8, and 15 + bevacizumab 10 mg/kg IV on Day 1 and 15 every 28 days or 15 mg/kg every 21 days until progression or unacceptable toxicity; docetaxel 75 mg/m² IV + bevacizumab 15 mg/kg IV every 3 weeks until progression or unacceptable toxicity; (paclitaxel + albumin) 100 mg/m² IV on Day 1, 8, and 15 + atezolizumab 840 mg IV on Day 1 and 15 every 4 weeks, or 1,200 mg IV every 3 weeks, or 1,680 mg IV on every 4 weeks, etc.

Stage 2

Neutropenia

One of the most common ADRs induced by chemotherapy is neutropenia, a life-threatening condition characterized by fever (body temperature ≥ 38.3 °C persisting for several hours), with neutrophil counts <500 cells/ μ L. Grade 3 and 4 neutropenia, referred to as febrile neutropenia, is directly associated with medications employed in chemotherapy as well as individual risk factors [12]. The incidence of febrile neutropenia depending on regimens administered for mTNBC is presented in *Table S1* (published on the journal's website⁴).

Table 1. The structure of prescribing therapeutic regimens in patients with metastatic triple-negative breast cancer, n=20 (as per medical records)

Therapy line	Chemotherapy protocol	Prescription frequency	
		%	pers.
First line	Anthracycline-cyclophosphamide (doxorubicin 60 mg/m ² intravenously (IV) + cyclophosphamide 600 mg/m ² IV every 3 weeks)	45	9
	Docetaxel 75 mg/m ² IV every 3 weeks	25	5
Second line	Paclitaxel 80 mg/m ² IV + carboplatin AUC2 IV once weekly; until progression or unacceptable toxicity	15	3
	Eribulin 1.4 mg/m ² IV on Day 1 and 8 every 3 weeks	15	3

The table was prepared by the authors using their own data

³ Breast cancer. Clinical practice guidelines. Ministry of Health of the Russian Federation. 2021.

⁴ <https://doi.org/10.30895/2312-7821-2026-14-1-66-77-tabl>

The analyzed chemotherapy regimens were classified into three risk groups based on the probability of febrile neutropenia (in decimal fractions): low risk (1 point): $0.0 < T \leq 0.10$; intermediate risk (2 points): $0.1 < T \leq 0.20$; high risk (3 points): $T > 0.20$ (Table 2).

As a result of the study, all four drug therapy regimens for mTNBC were classified as high-risk and required primary prevention of febrile neutropenia and inpatient monitoring.

Cardiovascular complications

Another serious side effect of chemotherapy is its cardiotoxicity, which manifests as cardiac arrhythmia, myocardial contractility disorder, arterial hypotension or hypertension, myocardial ischemia, pulmonary hypertension, and heart valve damage. The main risk factors include chemotherapy regimen and dose intensity, individual patient characteristics, and previous anthracycline therapy (Table S2

and S3 published on the journal's website⁵) [13–16].

The studied chemotherapy regimens were classified into four risk groups (as a decimal quantity) depending on the probability of cardiovascular complications: zero risk (1 point) 0.00 – eribulin monotherapy; low risk (2 points) $0.01 < T \leq 0.05$; intermediate risk (3 points) $0.06 < T \leq 0.10$ – paclitaxel + carboplatin regimen and docetaxel monotherapy; high risk (4 points) $T > 0.2$ – doxorubicin + cyclophosphamide (Table 3) [15, 16].

Neurotoxicity

Neurotoxicity is a common complication of chemotherapy, primarily manifesting as peripheral neuropathy in up to 40% of cases, and less commonly as central neuropathy (in up to 5% of the cases). Among the cytotoxic agents, the highest neurotoxicity was demonstrated by anthracyclines, taxanes, platinum-based drugs, and vinca alkaloids; targeted agents in-

Table 2. Risk assessment of febrile neutropenia depending on the applied chemotherapy protocols in patients with metastatic triple-negative breast cancer

Therapy line	Chemotherapy protocol	Probability of occurrence		Qualitative approach to preventing adverse drug reactions
		points	decimal fraction	
High	Anthracycline-cyclophosphamide (doxorubicin 60 mg/m ² intravenously (IV) + cyclophosphamide 600 mg/m ² IV every 3 weeks)	3	0.81	Primary prevention of febrile neutropenia is advisable; treatment is carried out in a 24-hour hospital
	Docetaxel 75 mg/m ² IV every 3 weeks		0.75	
	Eribulin 1.4 mg/m ² IV on Day 1 and 8 every 3 weeks		0.63	
	Paclitaxel 80 mg/m ² IV + carboplatin AUC2 IV once weekly		0.59	
Intermediate	Atezolizumab + albumin-bound paclitaxel: atezolizumab 840 mg IV every 2 weeks (Day 1 and 15 of the cycle), albumin-bound paclitaxel 100 mg/m ² on Day 1, 8, and 15, respectively	2	0.18	Secondary prevention of febrile neutropenia is advisable; therapy is carried out in a 24-hour hospital
	Docetaxel 75 mg/m ² IV + bevacizumab 15 mg/kg IV every 3 weeks		0.11	
Low	Albumin-bound paclitaxel 150 mg/m ² IV once weekly	1	0.09	Febrile neutropenia prevention is not feasible; outpatient treatment or a day patient treatment possible
	Albumin-bound paclitaxel 100 mg/m ² IV once weekly		0.05	
	Albumin-bound paclitaxel 300 mg/m ² IV once weekly		0.05	

The table was adapted by the authors from [6–11]

⁵ <https://doi.org/10.30895/2312-7821-2026-14-1-66-77-tabl>

Table 3. Risk assessment of cardiovascular complications depending on the chemotherapy protocols in patients with metastatic triple-negative breast cancer

Risk classification by probability of occurrence	Chemotherapy protocol	Disorder	Probability of occurrence		Qualitative approach to prevention
			points	decimal fraction	
High	Anthracycline–cyclophosphamide (doxorubicin 60 mg/m ² intravenously (IV) on Day 1 + cyclophosphamide 600 mg/m ² IV on Day 1 every 3 weeks)	Chronic heart failure	4	0.21	As preventive measures, therapy with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, alpha- and beta-blockers, statins are indicated
Intermediate	Paclitaxel 80 mg/m ² IV + carboplatin AUC2 IV once weekly	Myocardial ischemia	2	0.10	Risk assessment and comparison in drug prevention
Intermediate	Docetaxel 75 mg/m ² IV every 3 weeks	Chronic heart failure	2	0.08	Risk assessment and comparison in drug prevention
Zero	Eribulin 1.4 mg/m ² IV on Day 1 and 8 every 3 weeks	No	1	0	Monitoring the patient's condition as a preventive measure

The table was adapted by the authors from [13–16]

cluded protein tyrosine kinase inhibitors and BRAF inhibitors (see *Table S4* published on the journal's website)⁶ [17–25].

The studied chemotherapeutic regimens were classified into four risk groups (in decimal fractions) according to the possible occurrence of peripheral neuropathy: low-risk regimens (2 points) $0.05 < T \leq 0.20$ included eribulin monotherapy regimen; intermediate risk $0.2 < T \leq 0.5$ (3 points) – docetaxel monotherapy; high risk $T > 0.5$ (4 points) – doxorubicin + cyclophosphamide, paclitaxel + carboplatin.

Chemotherapy resistance

Chemotherapy resistance in mTNBC is defined as disease progression occurring within 3 months upon administering the last dose of cytotoxic agents, or while receiving chemotherapy. This can be attributed to the mechanism of action of anticancer drugs, individual patient characteristics, genetic heterogeneity of the neoplasm, and dysregulation of the cell cycle and apoptosis (see *Table S5* published on the journal's website)⁷ [26, 27].

Tumor cell cultures is an effective method used to study drug resistance mechanisms. Due to the lack of *in vitro* drug resistance studies specifically for mTNBC and BC, with similar tumor cell structure and the non-specificity

of the studied regimens for determining the rate of resistance development, we analyzed the results of a study by T.A. d'Amato et al. [28]. An analysis of cell proliferation and chemotherapy resistance in 3,042 cultured samples of non-small cell lung cancer revealed high resistance to carboplatin in 68% (1,056/1,565) of cultures; to cisplatin in 63% (1,409/2,227); to doxorubicin in 75% (1,101/1,471); to etoposide in 63% (1581/2505), to gemcitabine in 72% (549/823), to vinorelbine in 42% (603/1444), to docetaxel in 52% (273/521), to paclitaxel in 40% (689/1706), and to topotecan in 31% (280/896) [28].

Drug resistance is also defined as disease progression in patients receiving chemotherapy. In a study conducted in 2018–2020 at A.I. Kryzhanovsky Krasnoyarsk Regional Dispensary, 40 patients with metastatic BC received eribulin monotherapy at a dose of 1.4 mg/m² on Day 1 and 8 of a 21-day cycle. The average patient age was 57.1 years (ranging 34 to 72). Initial neoplasm stages were as follows: (55%) stage II, 16 (40%) stage III, and 2 (5%) stage IV. All patients had received an average of three prior lines of drug therapy: taxane regimens – 60%, anthracyclines – 100%, platinum-based drugs – 35%, anti-metabolites – 50%. Disease progression was

⁶ <https://doi.org/10.30895/2312-7821-2026-14-1-66-77-tabl>

⁷ <https://doi.org/10.30895/2312-7821-2026-14-1-66-77-tabl>

observed in 82.5% of patients, with one fatal case recorded [29].

Based on the probability of drug resistance, mTNBC chemotherapy regimens are divided into five groups: zero risk, $T \leq 0.05$ (0 points); low risk, $0.05 < T \leq 0.2$ (1 point); intermediate risk, $0.2 < T \leq 0.5$ (2 points); high risk, $0.5 < T \leq 0.8$ (3 points); very high risk, $0.8 < T \leq 1.0$ (4 points). Our analysis classified chemotherapy regimens employed at Astrakhan Regional Clinical Oncology Dispensary in the following way: three regimens were ranked as very high-risk (doxorubicin + cyclophosphamide, paclitaxel + carboplatin, and docetaxel monotherapy), and one regimen (eribulin monotherapy) was ranked as very high-risk.

Gastrointestinal complications

Adverse drug reactions induced by chemotherapy also include gastrointestinal disorders – nausea and vomiting. Each drug used for chemotherapy has its own emetogenic potential, i.e. the risk of inducing vomiting in patients; emetogenicity level of antitumor drugs is indicated in *Table S6* (published on the journal's website)⁸ [30].

Based on emetogenic potential, chemotherapy regimens are divided into four risk groups: zero risk, ≤ 0.10 (1 point); low risk, $0.10 < T \leq 0.30$ (2 points); intermediate risk, $0.3 < T \leq 0.9$ (3 points); high risk, $0.9 \leq T$ (4 points). Among the chemotherapy regimens for mTNBC employed at Astrakhan Regional Clinical Oncology Dispensary, two were classified as low-risk regimens (docetaxel monotherapy, eribulin monotherapy), one as an intermediate-risk regimen (paclitaxel + carboplatin), and one as a high-risk regimen (doxorubicin + cyclophosphamide).

Stage 3

To analyze the severity of adverse drug reactions observed in patients with mTNBC, all ADRs were categorized into the following risk groups: 1 – risk of febrile neutropenia, 2 – chronic heart failure, 3 – myocardial ischemia,

4 – peripheral neuropathy, 5 – drug resistance, and 6 – nausea and vomiting.

Based on the severity of after-effects, four categories were identified (in accordance with GOST R 58771-2019):

1) critical risk (4 points), a life-threatening condition for the patient; risk groups 1 and 3 were assigned to this category;

2) substantial risk (3 points), a complication that may result in disability; risk groups 2 and 4 were assigned to this category;

3) significant risk (2 points), an ADR that reduces the patient's median relapse-free survival by at least 50%; risk group 5 was assigned to this category;

4) minor risk (1 point), an ADR that worsens the patient's quality of life but does not pose a threat to life, causes no disability, and does not shorten the patient's median relapse-free survival; risk group 6 was assigned to this category.

Based on the probability of ADRs, the risk groups were categorized as follows: highly probable (4 points), probable (3 points), unlikely (2 points), slightly probable (1 point). For each chemotherapy regimen employed at Astrakhan Regional Clinical Oncology Dispensary, we compiled a risk matrix (*Figures 1, 2*).

Our analysis showed that the parameters of the studied risks vary significantly depending on the chemotherapy line: combined first-line regimen of anthracycline–cyclophosphamide is characterized by a high ADR rate, while the paclitaxel + carboplatin strategy administered as the second line is associated with a high risk of peripheral neuropathy. The monoregimens with docetaxel and eribulin had a safer profile, although eribulin strategy was associated with a higher risk of drug resistance. Hematological toxicity (febrile neutropenia) was common to all prescribed chemotherapy regimens.

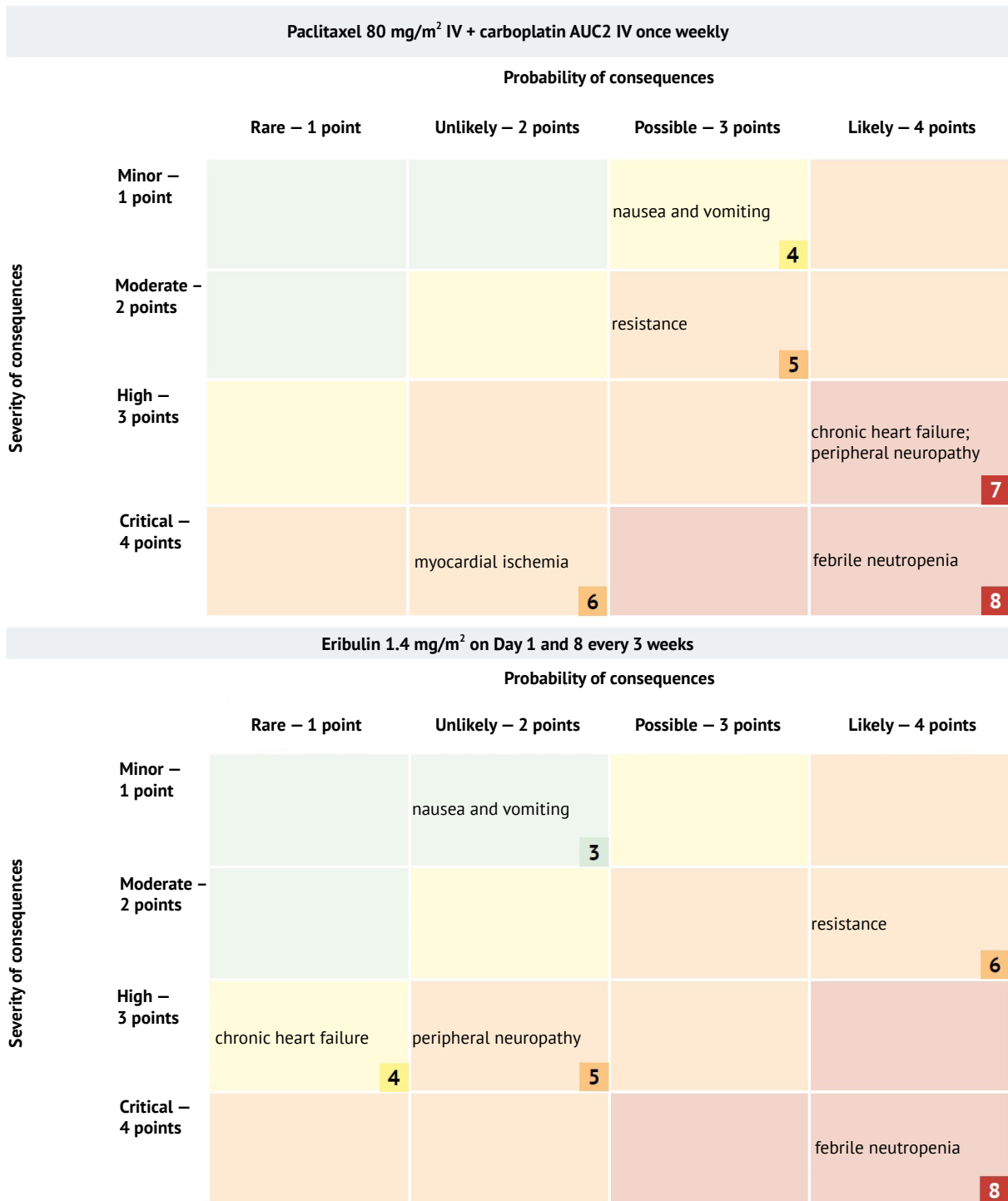
A promising avenue for future research is the development of management strategies for high- and medium-risk groups in patients with mTNBC. These strategies should focus

⁸ <https://doi.org/10.30895/2312-7821-2026-14-1-66-77-tabl>



The figure was prepared by the authors using their own data

Figure 1. Risk matrix of the first-line therapy protocols of metastatic triple-negative breast cancer. The total risk (points) is indicated in the bottom right corner of the cells. 7–8 points, severe risk (red); 5–6 points, moderate risk (orange); 4 points, low risk (yellow); 2–3 points, very low risk (light green)



The figure was prepared by the authors using their own data

Figure 2. Risk matrix of the second-line therapy protocols of metastatic triple-negative breast cancer. The total risk (points) is indicated in the bottom right corner of the cells. 7–8 points, severe risk (red); 5–6 points, moderate risk (orange); 4 points, low risk (yellow); 2–3 points, very low risk (light green)

on innovative approaches, optimizing drug therapy with preventive regimens, introducing innovative strategies, and implementing personalized medicine.

A limitation of the study is the use of literature evidence on the safety and efficacy of the analyzed chemotherapy regimens to calculate the rate and severity of ADRs. Since data are constantly updated, ongoing monitoring is necessary for correct application to real-world clinical practice. Furthermore, the first stage of the study was conducted with a small sample size, while the risk matrix was developed for a limited number of regimens.

CONCLUSIONS

1. The study found that in real-world clinical practice, in most cases patients with mTNBC receive a two-line chemotherapy combination of anthracycline–cyclophosphamide (doxorubicin 60 mg/m² IV + cyclophosphamide 600 mg/m² IV every 3 weeks). Less commonly prescribed regimens include: paclitaxel 80 mg/m² IV + carboplatin AUC2, and eribulin monotherapy (eribulin 1.4 mg/m² IV on Day 1 and 8, repeated every 3 weeks).

2. The most common adverse ADRs associated with the analyzed chemotherapy regimens were identified as follows:

1) Anthracycline–cyclophosphamide regimen: febrile neutropenia → drug resistance → peripheral neuropathy → cardiovascular complications.

2) Docetaxel monotherapy: febrile neutropenia → drug resistance → peripheral neuropathy → nausea and vomiting → cardiovascular complications.

3) Paclitaxel + carboplatin AUC2: drug resistance → peripheral neuropathy → febrile neutropenia → nausea and vomiting → cardiovascular complications.

4) Eribulin monotherapy: drug resistance → febrile neutropenia → peripheral neuropathy → nausea and vomiting.

3. Based on the severity of their after-effects in mTNBC chemotherapy, all ADRs were categorized into the following risk groups: the risk of febrile neutropenia, chronic heart failure, myocardial ischemia, peripheral neuropathy, drug resistance, and nausea/vomiting. The study revealed that the parameters of the studied risks differ significantly depending on the line of chemotherapy. The most widely prescribed first-line strategy, anthracycline–cyclophosphamide, is associated with a high rate of adverse drug reactions. Administration of platinum-based therapy (paclitaxel + carboplatin) as a second line carries a risk of peripheral neuropathy. The monotherapy strategies with docetaxel and eribulin show a safer profile; however, the eribulin monoregimen is associated with a higher risk of drug resistance. Hematological toxicity (febrile neutropenia) is typical for all prescribed chemotherapy regimens (the combined risk score for severity and probability of occurrence was 8 points for all regimens).

4. The safest chemotherapy strategy is the docetaxel monoregimen. This therapy outperforms the anthracycline–cyclophosphamide regimen across a range of indicators: febrile neutropenia (75% vs. 81%), cardiovascular complications (8% vs. 21%), peripheral neuropathy (41% vs. 65%), drug resistance (52% vs. 75%), and nausea/vomiting (10% vs. 90%). In case of docetaxel protocol, the risk of developing peripheral neuropathy and drug resistance is lower than in case of combined chemotherapy regimen with paclitaxel + carboplatin or in case of eribulin monotherapy.

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