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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи.** Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html. В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე, დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემავსებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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ROLE OF NEOADJUVANT THERAPY FOR PATIENTS WITH GASTRIC CANCER: MULTIDISCIPLINARY HOSPITAL WITH ONCOLOGY CENTER

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Abstract.

Purpose: To compare the efficacy and safety of doublet (capecitabine + cisplatin) and triplet (capecitabine + cisplatin + docetaxel) neoadjuvant chemotherapy (NACT) regimens in patients with locally advanced gastric cancer at a regional oncology center in Kazakhstan.

Methods: A prospective stratified randomized study included 107 patients with locally advanced gastric cancer. Patients were stratified by age, tumor location, and histological type/differentiation grade and then randomized in a 1:1 ratio to receive either capecitabine plus cisplatin or capecitabine plus cisplatin plus docetaxel. Tumor response was assessed using RECIST 1.1, pathological response was assessed in resected specimens, and toxicity was graded according to CTCAE v5.0.

Results: The triplet regimen was associated with numerically higher rates of radiological partial response according to RECIST 1.1 (68.0% vs. 59.3%, $p=0.423$) and radical surgery among patients with partial response (91.7% vs. 78.1%, $p=0.172$). Pathological response was assessed in 58 patients who underwent radical gastrectomy. Pathological complete response (ypT0N0/TRG 1a) was observed in 2 patients in the triplet group and in none of the patients in the doublet group (0% vs. 6.1%, $p=0.501$). Favorable pathological regression (TRG 1a–1b) was more frequent after triplet therapy than after doublet therapy (24.2% vs. 12.0%, $p=0.320$). Grade III–IV neutropenia was more frequent in the triplet group (24.5% vs. 9.3%, $p=0.041$).

Conclusions: The triplet regimen showed a numerical efficacy advantage but was associated with increased hematologic toxicity, requiring careful monitoring. Treatment personalization based on histology and comorbidities is critical. Limitations: Small sample size, lack of survival data, and the need for multicenter validation.

Key words. Gastric cancer, neoadjuvant chemotherapy, gastrectomy, multidisciplinary hospital.

Introduction.

Gastric cancer (GC) ranks fifth in global cancer incidence and fifth in cancer-related mortality, accounting for approximately 968,800 new cases and 660,200 deaths worldwide in 2022 [1]. Despite diagnostic and therapeutic advancements, prognosis remains unfavorable in advanced disease, particularly in stage III–IV gastric cancer [2]. In Kazakhstan, delayed diagnosis remains an important clinical and organizational challenge, contributing to a high proportion of advanced-stage cases and limited access to curative surgery [3]. These findings underscore

the need for effective neoadjuvant or perioperative treatment strategies aimed at reducing tumor burden, controlling micrometastatic disease, and improving the probability of radical surgery [4,5].

Modern systemic treatment approaches for locally advanced gastric and gastro-oesophageal junction adenocarcinoma commonly combine fluoropyrimidines with platinum agents, with docetaxel-containing triplet regimens used in selected patients with adequate performance status [2,4]. Capecitabine, an oral prodrug of 5-fluorouracil, has been widely used in combination with platinum agents in gastric and gastro-oesophageal cancer because it provides an oral fluoropyrimidine alternative to continuous-infusion 5-fluorouracil [6,7]. Evidence from perioperative and neoadjuvant studies supports the role of systemic chemotherapy in improving tumor downstaging and surgical outcomes in selected patients with locally advanced gastric or gastro-oesophageal junction adenocarcinoma [4,5,8,9]. However, adding taxanes such as docetaxel may increase hematologic toxicity, including clinically relevant neutropenia, and therefore requires careful patient selection and toxicity monitoring [4,8,9].

In CIS countries, including Kazakhstan, the implementation of modern neoadjuvant chemotherapy protocols remains challenging because regional evidence is limited, treatment tolerance may vary in routine clinical practice, and access to multidisciplinary decision-making and toxicity monitoring is not uniform. Therefore, local prospective data comparing feasible doublet and triplet regimens are clinically relevant for adapting international evidence to regional oncology practice.

Research Objective: To evaluate the short-term outcomes of two NACT regimens (Xeloda + cisplatin vs. Xeloda + cisplatin + docetaxel) in patients with locally advanced gastric cancer. The study focuses on comparing tumor regression rates, resectability, and toxicity profiles to determine the optimal treatment approach in a regional oncology center setting.

Novelty. This work provides a comparative analysis of doublet (capecitabine + cisplatin) and triplet (with a taxane) regimens in resource-limited settings, which is critical for low- and middle-income countries (LMICs). The findings may facilitate the adaptation of international guidelines (NCCN, ESMO) to local clinical practices.

Materials and Methods.

Patient Population: A prospective study with stratified randomization included 107 patients with histologically confirmed locally advanced gastric cancer (GC) treated at

the State Communal Enterprise on the Right of Economic Management “City Multidisciplinary Hospital with Oncology Center” of the Healthcare Department of Shymkent City between 2018 and 2023. Inclusion criteria were as follows: age 18–75 years, histologically confirmed gastric tumor, clinical stage T3–4N0–3M0 according to the 8th edition of the TNM classification [10], and no contraindications to chemotherapy. Exclusion criteria included distant metastases, severe comorbidities, including NYHA class III–IV heart failure and CKD stages 4–5, and patient refusal. Patient recruitment was initiated only after approval of the study protocol by the local ethics committee, and all participants provided written informed consent before inclusion.

Randomization and Sample Size: After eligibility confirmation and written informed consent, patients were stratified according to clinically relevant baseline factors: age (<60 vs. ≥60 years), tumor location (proximal/cardioesophageal junction vs. body/distal stomach), and histological type/differentiation grade (poorly differentiated/signet-ring cell/scirrhous carcinoma vs. other adenocarcinoma types). Within each stratum, patients were randomized in a 1:1 ratio to Group 1 or Group 2 using a computer-generated random sequence with permuted blocks. Allocation was concealed until patient inclusion by using sequentially numbered sealed envelopes prepared by an investigator not involved in treatment assignment or outcome assessment.

The sample size was calculated for the primary short-term efficacy endpoint, defined as objective radiological response according to RECIST 1.1. Based on previously published data and institutional expectations, the objective response rate was assumed to be approximately 45% for the doublet regimen and 72% for the triplet regimen. To detect this difference with a two-sided α level of 0.05 and 80% statistical power, at least 51 patients per group were required. Considering possible dropouts and incomplete response assessment, the target sample size was set at approximately 106–110 patients. Finally, 107 patients were included and randomized: 54 patients to Group 1 and 53 patients to Group 2.

Clinical Outcomes:

Of 107 patients, 66 (61.7%) were male and 41 (38.3%) female. Mean age: 58.4±9.2 years (range: 38–73). TNM staging was challenging due to difficulties in assessing the exact number of affected lymph nodes and tumor invasion into adjacent organs. Inclusion was based on T3–4 status and absence of distant metastases. After stratified randomization, patients were assigned to two treatment groups:

- Group 1 (n=54): Two cycles of NACT with capecitabine + cisplatin (capecitabine 2000 mg/m²/day orally, days 1–14; cisplatin 80 mg/m² IV, day 1; 21-day cycle).
- Group 2 (n=53): Two cycles of NACT with capecitabine + cisplatin + docetaxel (capecitabine 2000 mg/m²/day orally, days 1–14; cisplatin 75 mg/m² IV, day 1; docetaxel 75 mg/m² IV, day 1; 21-day cycle).

Diagnostic Workup. All patients underwent:

1. Clinical and laboratory tests: Karnofsky Performance Status (KPS), complete blood count (CBC), blood biochemistry (creatinine, AST, ALT).

2. Imaging:

- Esophagogastroduodenoscopy (EGD) with biopsy.
- Contrast-enhanced CT of the abdomen and chest.
- Ultrasound of the liver and lymph nodes.

3. Histopathology: Tumor verification and differentiation grade (WHO, 2019).

Data Analysis:

Data analysis was performed according to the two predefined neoadjuvant chemotherapy groups: Group 1 received capecitabine plus cisplatin, whereas Group 2 received capecitabine plus cisplatin plus docetaxel. The primary short-term efficacy endpoints were radiological tumor response according to RECIST 1.1 and the rate of radical surgery after neoadjuvant chemotherapy. Safety endpoints included chemotherapy-related toxicity graded according to CTCAE v5.0 and 30-day postoperative complications (Clavien-Dindo grade ≥2) among patients who underwent radical gastrectomy. Postoperative complications were summarized descriptively; due to the small number of events, inferential comparisons between the two NACT groups were not performed. Categorical variables were compared using the χ^2 test or Fisher’s exact test, as appropriate. Continuous variables were summarized as mean ± standard deviation and compared using Student’s t-test or the Mann–Whitney U test depending on distribution. A two-sided p-value <0.05 was considered statistically significant.

Clinical Presentation.

Predominant symptoms at admission (see Figure 1 and Table 1) included non-specific manifestations: weight loss (95.3%), general weakness (88.8%), and persistent epigastric pain (43.9%). Occult bleeding (Hb <100 g/L) was detected in 18 patients (16.8%).

Tumor Location and Histology. Proximal tumors predominated, with 27.1% located at the cardioesophageal junction and 32.7% in the gastric body. Histologically, poorly differentiated adenocarcinoma was the most common subtype (42.1%), followed by signet-ring cell carcinoma (14.0%) and scirrhous carcinoma (7.5%) (Figure 2).

Efficacy and Toxicity Assessment. Treatment response was evaluated 4 weeks after the second NACT cycle using RECIST 1.1 criteria [11]: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). Toxicity was graded according to CTCAE v5.0 [12].

In patients who underwent radical gastrectomy after neoadjuvant chemotherapy, pathological response was additionally assessed in resected specimens. Pathological complete response was defined as the absence of viable residual tumor cells in the primary tumor and regional lymph nodes (ypT0N0). Tumor regression grade (TRG) was assessed according to the Becker classification [13]: TRG 1a, no residual tumor; TRG 1b, <10% residual tumor cells; TRG 2, 10–50% residual tumor cells; and TRG 3, >50% residual tumor cells. Favorable pathological regression was defined as TRG 1a–1b.

Statistical analysis was performed using SPSS 26.0.

Results and Discussion.

Neoadjuvant Therapy Efficacy. After two NACT cycles, RECIST 1.1 assessments showed numerically higher

radiological partial response in Group 2, although the difference did not reach statistical significance (Table 2).

- Group 1 (capecitabine + cisplatin): Partial response (PR) in 32 patients (59.3%), stable disease (SD) in 11 (20.4%), and progression (PD) in 11 (20.4%).

- Group 2 (capecitabine + cisplatin + docetaxel): PR in 68.0% (n=36), SD in 15.1% (n=8), and PD in 16.9% (n=9).

No radiological complete responses according to RECIST 1.1 were observed in either group. Among patients with poorly differentiated adenocarcinoma (n=45), PR rates tended to be lower than in patients with moderately differentiated tumors (55.6% vs. 76.9%), which is consistent with the generally lower chemosensitivity of aggressive histological variants.

Addition of Docetaxel to NACT. The inclusion of docetaxel in the NACT regimen was associated with an 8.7% higher radiological partial response rate (68.0% vs. 59.3%, $p=0.423$). Although this difference did not reach statistical significance, the direction of the effect is consistent with evidence from docetaxel-containing perioperative and neoadjuvant regimens, including FLOT4-AIO and DCX/DCC-based studies [4, 8, 9]. Importantly, the absence of complete response in the RECIST 1.1 assessment should be interpreted as the absence of radiological complete response rather than as evidence of absent pathological regression. In the pathological analysis of resected specimens, pCR was uncommon and was observed only in the triplet group (0% vs. 6.1%). Favorable pathological regression according to Becker TRG 1a–1b was also numerically more frequent in the triplet group than in the doublet group (24.2% vs. 12.0%), although this difference did not reach statistical significance. These findings suggest that the addition of docetaxel may deepen tumor regression in a subset of patients, but the overall rate of complete pathological response remained limited. This may be partly explained by the high proportion of poorly differentiated tumors in the cohort, which are generally associated with lower sensitivity to cytotoxic chemotherapy.

Surgical Outcomes.

Of 68 patients with PR (32 in Group 1, 36 in Group 2), 58 (85.3%)

underwent radical gastrectomy with D2 lymphadenectomy. Group 2 exhibited a numerically higher radical surgery rate among patients with partial response: 33/36 (91.7%) vs. 25/32 (78.1%) in Group 1 ($p=0.172$). Mean intraoperative blood loss was 450 ± 120 mL, and operation duration averaged 3.8 ± 0.9 hours. Postoperative complications of Clavien-Dindo grade ≥ 2 occurred in 12 of 58 patients (20.7%), including anastomotic leakage (n=4, 6.9%), pneumonia (n=5, 8.6%), and wound infection (n=3, 5.2%). The complication rate was comparable between the doublet and triplet groups (Group 1: 5/25, 20.0% vs. Group 2: 7/33, 21.2%, $p=0.908$), suggesting that the addition of docetaxel did not substantially increase the risk of major surgical complications.

Toxicity Profile. Toxicity graded per CTCAE v5.0 (Table 3) revealed higher hematologic toxicity in Group 2: grade III–IV neutropenia was more frequent in the triplet group than in Group 1 (24.5% [n=13] vs. 9.3% [n=5]; $p=0.041$). Non-hematologic toxicity, including hand-foot syndrome and diarrhea, was comparable between groups and was consistent with the known toxicity profile of capecitabine-containing platinum regimens [6,7].

Comparison with Prior Studies. Our findings align with recent research trends:

1. Triplet Regimen Efficacy: The radiological PR rate in Group 2 (68.0%) is consistent with the range reported for docetaxel-containing perioperative or neoadjuvant regimens in locally advanced gastric and gastro-oesophageal junction adenocarcinoma [4, 8, 9]. Direct comparison with published trials should be made cautiously because treatment regimens, number of cycles, staging procedures, pathological response criteria, and patient selection differed substantially across studies.

2. Toxicity: The higher rate of grade III–IV neutropenia in Group 2 (24.5% vs. 9.3%, $p=0.041$) is consistent with the known hematologic toxicity profile of docetaxel-containing regimens [4, 8, 9]. Notably, no febrile neutropenia was observed, which may be related to careful monitoring and supportive treatment, including G-CSF when clinically indicated.

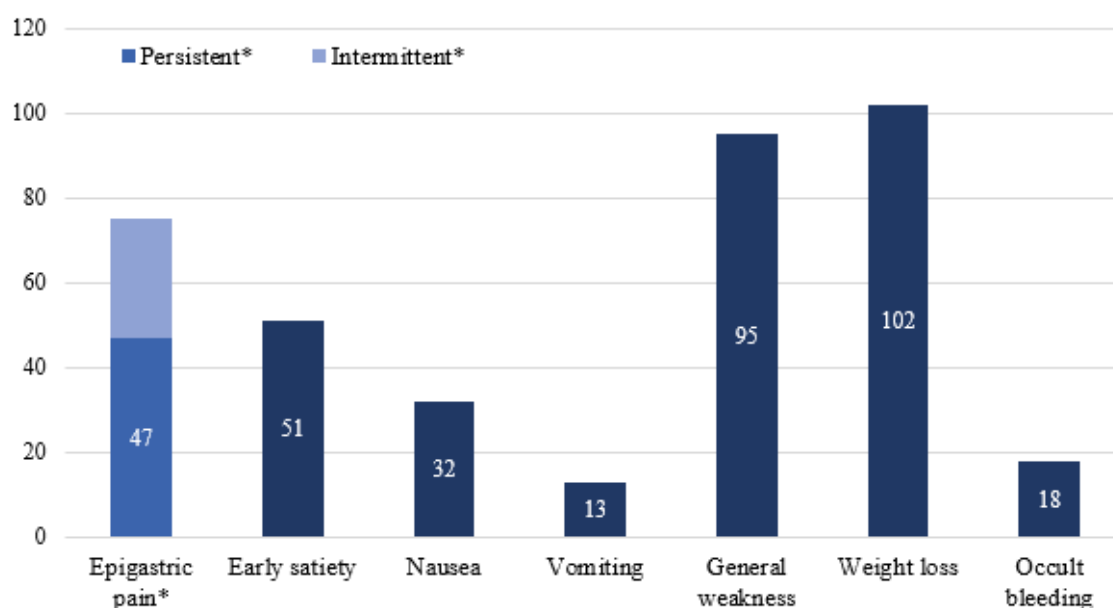


Figure 1. Clinical Symptoms at Initial Presentation (n=107): Absolute Values.

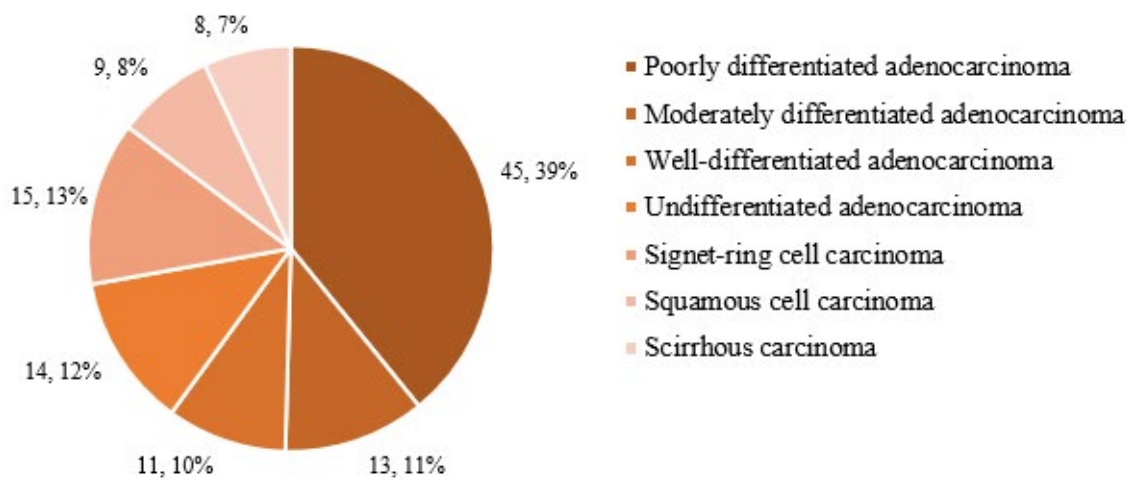


Figure 2. Histological Characteristics of Tumors (n=107): Absolute Values and Proportions.

Table 1. Clinical Symptoms at Initial Presentation (n=107).

Symptom	Proportion, %
Epigastric pain:	70.1
- Intermittent	26.2
- Persistent	43.9
Early satiety	47.7
Nausea	29.9
Vomiting	12.1
General weakness	88.8
Weight loss	95.3
Occult bleeding	16.8

Table 2. Treatment Response After 2 NACT Cycles.

Parameter	Group 1 (n=54)	Group 2 (n=53)	p-value
Partial Response (PR)	32 (59.3%)	36 (68.0%)	0.423
Stable Disease (SD)	11 (20.4%)	8 (15.1%)	0.614
Progressive Disease (PD)	11 (20.4%)	9 (16.9%)	0.805

Table 3. NACT Toxicity (n=107).

Complication	Group 1 (n=54)	Group 2 (n=53)	p-value
Hematologic:			
- Grade III–IV Neutropenia	5 (9.3%)	13 (24.5%)	0.041*
- Grade II Anemia	8 (14.8%)	10 (18.9%)	0.614
Non-Hematologic:			
- Hand-foot syndrome	10 (18.5%)	12 (22.6%)	0.639
- Grade III Diarrhea	6 (11.1%)	7 (13.2%)	0.776

*Statistically significant ($p < 0.05$).

3. Resectability: The radical surgery rate in our cohort should be interpreted in the context of strict patient selection, exclusion of distant metastases, and the single-center design of the study. Although the triplet group showed a numerically higher radical surgery rate among patients with radiological partial response, this difference did not reach statistical significance.

Pathological Response.

Pathological response was evaluated in resected specimens from 58 patients who underwent radical gastrectomy with D2 lymphadenectomy after neoadjuvant chemotherapy: 25 patients

in Group 1 and 33 patients in Group 2. Pathological complete response (ypT0N0/TRG 1a) was not observed in the doublet group and was observed in 2 patients in the triplet group (0% vs. 6.1%, $p=0.501$). Favorable pathological regression, defined as TRG 1a–1b, was observed in 3 patients in Group 1 and 8 patients in Group 2 (12.0% vs. 24.2%, $p=0.320$). Partial pathological regression corresponding to TRG 2 was found in 9 patients in Group 1 and 13 patients in Group 2 (36.0% vs. 39.4%). Poor or absent pathological regression corresponding to TRG 3 remained relatively common: 13 patients in Group

1 and 12 patients in Group 2 (52.0% vs. 36.4%). Thus, the triplet regimen was associated with a numerically higher rate of pathological complete response and favorable tumor regression, although the difference in favorable TRG response did not reach statistical significance. These findings suggest that the addition of docetaxel may deepen tumor regression in a subset of patients, but the overall rate of complete pathological response remained limited, possibly due to the high proportion of poorly differentiated tumors in the cohort.

Conclusion.

The triplet NACT regimen (capecitabine + cisplatin + docetaxel) was associated with numerically higher radiological partial response, radical surgery, pathological complete response, and favorable pathological regression rates compared with doublet therapy; however, these efficacy differences did not reach statistical significance in the present single-center cohort. At the same time, the triplet regimen was associated with a significantly higher incidence of grade III–IV neutropenia, requiring vigilant monitoring and supportive care. These findings support a personalized approach to NACT selection based on tumor histology, patient comorbidities, and expected toxicity risk. Future studies with larger multicenter cohorts and long-term survival endpoints are needed to clarify whether the observed numerical advantages translate into improved overall and recurrence-free survival.

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Author Contributions.

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Saburov Alisher, Kemelbekov Kanatzhan, Saburova Saidakhon, and Abdurakhmanov Babur. The first draft of the manuscript was written by Arybzhonov Dauranbek and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability.

The datasets generated and analyzed during the current study are not publicly available due to patient confidentiality but are available from the corresponding author upon reasonable request.

Declarations.

Ethics Approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Clinical Scientific Review Committee and Institutional Review Board of the South Kazakhstan Medical Academy before the initiation of patient recruitment (Approval No.10/12/014, dated 10 December 2018).

Consent to Participate.

Informed consent was obtained from all individual participants included in the study.

Conflict of interest.

The authors declare no competing interests.

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რეზიუმე

მიზანი: კვლევის მიზანი იყო ორმაგი რეჟიმის (კაპეციტაბინი + ცისპლატინი) და სამმაგი რეჟიმის (კაპეციტაბინი + ცისპლატინი + დოცეტაქსელი) ნეოადიუვანტური ქიმიოთერაპიის (NACT) ეფექტურობისა და უსაფრთხოების შედარება ადგილობრივად გავრცელებული კუჭის კიბოს მქონე პაციენტებში ყაზახეთის რეგიონული ონკოლოგიური ცენტრის პირობებში.

მეთოდები: პროსპექტულ სტრატეგიცირებულ რანდომიზებულ კვლევაში ჩართული იყო ადგილობრივად გავრცელებული კუჭის კიბოს მქონე 107 პაციენტი. პაციენტები სტრატეგიცირდნენ ასაკის, სიმსივნის ლოკალიზაციისა და ჰისტოლოგიური ტიპის/დიფერენცირების ხარისხის მიხედვით, რის შემდეგაც 1:1 თანაფარდობით რანდომიზებულნი იყვნენ ორ ჯგუფად: კაპეციტაბინი + ცისპლატინი ან კაპეციტაბინი + ცისპლატინი + დოცეტაქსელი. სიმსივნის პასუხი შეფასდა RECIST 1.1 კრიტერიუმებით, პათოლოგიური პასუხი — რეზეცირებულ პრეპარატებში, ხოლო ტოქსიკურობა — CTCAE v5.0 კრიტერიუმების მიხედვით.

შედეგები: სამმაგი რეჟიმი ასოცირებული იყო RECIST 1.1-ის მიხედვით რადიოლოგიური ნაწილობრივი პასუხის რიცხოვრივად უფრო მაღალ მაჩვენებელთან (68.0% vs. 59.3%, $p=0.423$) და ნაწილობრივი პასუხის მქონე პაციენტებში რადიკალური ოპერაციის უფრო მაღალ სიხშირესთან (91.7% vs. 78.1%, $p=0.172$). პათოლოგიური პასუხი შეფასდა 58 პაციენტში, რომლებსაც ჩატარდათ რადიკალური გასტრექტომია. სრული პათოლოგიური

პასუხი (ypT0N0/TRG 1a) არ გამოვლენილა ორმაგი რეჟიმის ჯგუფში და დაფიქსირდა სამმაგი რეჟიმის ჯგუფის 2 პაციენტში (0% vs. 6.1%, $p=0.501$). ხელსაყრელი პათოლოგიური რეგრესია (TRG 1a–1b) უფრო ხშირად აღინიშნა სამმაგი თერაპიის შემდეგ, ვიდრე ორმაგი თერაპიის შემდეგ (24.2% vs. 12.0%, $p=0.320$). III–IV ხარისხის ნეიტროპენია უფრო ხშირი იყო სამმაგი რეჟიმის ჯგუფში (24.5% vs. 9.3%, $p=0.041$).

დასკვნები: სამმაგმა რეჟიმმა აჩვენა ეფექტურობის რიცხოვრივი უპირატესობა, თუმცა ასოცირებული იყო ჰემატოლოგიური ტოქსიკურობის მატებასთან, რაც საჭიროებს ყურადღებით მონიტორინგს. მკურნალობის პერსონალიზაცია ჰისტოლოგიური მახასიათებლებისა და თანმხლები დაავადებების გათვალისწინებით კრიტიკულად მნიშვნელოვანია. კვლევის შეზღუდვებია მცირე შერჩევა, გადარჩენადობის მონაცემების არარსებობა და მულტიცენტრული ვალიდაციის საჭიროება.

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