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Application of the ATC/DDD Method for Estimation of Consumption of Antineoplastic Medicines during Systemic Anticancer Therapy (SACT) in Kazakhstan

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Abstract

The rapidly growing global burden of cancer is characterized by an increase in incidence and a decrease in mortality. In addition, the development of new innovative treatments has significantly increased the life expectancy of patients. As a result, the consumption of antineoplastic medicines is increasing. Monitoring and research into the consumption of antineoplastic medicines purchased from the budget of the Republic of Kazakhstan in order to improve the quality of their use. The study was done in two phases. In the first, antineoplastic medicines consumption was analyzed using the World Health Organization recommended Anatomical Therapeutic Chemical and Defined Daily Dose methodology. Data on drug purchases for 2017-2019 was used to calculate and analyze consumption. In the second stage, the results were evaluated and compared with clinical protocols used in the Republic of Kazakhstan for the period 2019-2024 for the validity of use in various oncological diseases. Despite a wider range of oncological drugs purchased in Kazakhstan, only 54% of drugs with Anatomical Therapeutic Chemical classification code 'L01' and 31% with Anatomical Therapeutic Chemical classification code 'L02' correspond to the World Health Organization list. In the structure of consumption of oncological drugs with Anatomical Therapeutic Chemical classification code 'L01', the leading pharmacological groups were 'L01E Protein kinase inhibitors' and 'L01B Antimetabolites' with consumption rates of 0.213 and 0.212 DID, respectively. 'L01D Cytotoxic antibiotics and related substances' was the least consumed group at 1.15%. In the Anatomical Therapeutic Chemical code 'L02' structure, the top oncological drugs were from the groups 'L02BA Antiestrogens', 'L02BG Enzyme inhibitors' and 'L02AE Gonadotropin-releasing hormone analogues', with shares of 39%, 31% and 25% respectively. A comparison of national clinical recommendations with international guidelines revealed discrepancies. The analysis of antineoplastic medicines consumption using the international Anatomical Therapeutic Chemical classification system and the Defined Daily Dose methodology revealed trends and dynamics in the consumption of these drugs, providing an opportunity to increase the efficiency of pharmaceutical supply optimization in oncology to include adherence to evidence-based guidelines such as European Society for Medical Oncology, National Comprehensive Cancer Network, National Institute for Health and Care Excellence, thus improving patient access to medicines.

Keywords: Anatomical Therapeutic Chemical, Defined Daily Dose, Kazakhstan, antineoplastic medicines, systemic anti-cancer therapy, drug management.

1. Introduction

According to the International Agency for Research on Cancer, there were approximately 20 million new cancer cases and 9.7 million cancer deaths in 2022 [1]. Experts predict more than 35 million new cancer cases by 2050, which represents a 77% increase compared to the number of cases in 2022 [2].

Similarly, in the Republic of Kazakhstan, the incidence of cancer is rising. In 2019, there were 186 326 cancer patients under dynamic observation in Kazakhstan, 52.5% of whom had survived for five years or more [3]. According to the National Cancer Institute of the USA, national cancer treatment expenditures amounted to $208.9 billion in 2020. This cost is expected to rise in the coming years as the population ages and the number of people diagnosed with cancer increases. Additionally, the increase in cost will likely be driven by the adoption of novel and more expensive therapies as the new standard of care [4]. According to estimation by experts, the global economic burden of cancer from 2020 to 2050 will amount to $25.2 trillion, which is equivalent to an annual tax of 0.55% on the global gross domestic product [5].

Undoubtedly, the rise in cancer incidence, the decline in mortality, and the development of new innovative treatment regimens lead to an increased consumption of antineoplastic medicines. Advancements in medical science, particularly the shift towards new cancer treatments, have significantly increased patient life expectancy. Despite the tremendous progress in cancer chemotherapy, the side effects associated with this therapy remain a serious problem [6]. Cardiotoxicity is the most common side effect of anticancer therapy. Therefore, the increased life expectancy due to cancer therapy can be negated by an increased mortality rate from heart problems as a side effect. Cardiotoxicity can occur at any stage of pharmacological treatment, with symptoms ranging from mild myocardial dysfunction to persistent heart failure and death [6-11]. Additionally, renal toxicity is a significant side effect associated with novel immunotherapy regimens. Nephrotoxicity may also be the result of prolonged survival achieved through extended lines of therapy and combinations of different drugs. According to several studies, many researchers state that nephrotoxicity is caused by primary cancer-specific treatments, including classic chemotherapeutic drugs, targeted therapy, and immunotherapy [12-15]. All the factors mentioned above underscore the importance of assessing the consumption of antineoplastic medicines to improve the quality of their use.

In February 2009, the Government of the Republic of Kazakhstan decided to create the company "SK-Pharmacy" in the structure of JSC "National Welfare Fund" Samruk-Kazyna". The Single Distributor system was created to provide medicines to the population within the guaranteed volume of free medical care, increase the sustainability and competitiveness of the pharmaceutical industry of the Republic of Kazakhstan, and develop the pharmaceutical industry by consolidating public procurement of medicines [16]. Every year the Ministry of Health of the Republic of Kazakhstan approves the list of medicines reimbursed at the expense of the state budget and purchased by the Single Distributor.

This study evaluates the consumption of antineoplastic medicines procured by the Single Distributor within the guaranteed volume of free medical care (GVFMC) framework. It employs the World Health Organization recommended ATC/DDD methodology (Anatomical Therapeutic Chemical classification, Defined Daily Dose) to elucidate the structure and compare the consumption of antineoplastic medicines in Kazakhstan during 2017-2019.

2. Materials and methods

This study was conducted as part of the state assignment of the Ministry of Health of the Republic of Kazakhstan, titled "Methodological Support for Healthcare Reform", and within a grant from the Ministry of Education and Science of the Republic of Kazakhstan "Development of an Effective Program for the Prevention and Treatment of Cardiovascular Complications in Liver Cancer Patients During Chemotherapy Using Modern Innovative Technologies" (Individual registration number AP14870224). This publication follows SQUIRE reporting guidelines [17].

The first stage of this study was to analyze the consumption of antineoplastic medicines according to the ATC/DDD methodology recommended by World Health Organization (WHO) [18,19]. The calculation and subsequent analysis of consumption were based on data pertaining to the quantity of drugs purchased by those reimbursed by budgetary funds over the course of the three-year period spanning 2017 to 2019.

This data was provided by the Department of Drug Policy of the Ministry of Health of the Republic of Kazakhstan. The analysis included antineoplastic medicines with ATC codes "L01 Antineoplastic agents" and "L02 Hormonal antineoplastic agents."

The ATC/DDD methodology was developed to provide statistical data on drug consumption and to conduct comparative analyses at an international level using a unified tool.

DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults, serving as a technical unit of use.

For calculating the consumption of antineoplastic medicines, the DID indicator was used. DID indicator is defined as the number of DDDs per 1000 inhabitants per day. The calculation of drug consumption adjusted for population size was performed using the following formula:

$$\text{DID} = \frac{\text{DDD}_s \times 1000}{\text{population size} \times 365 \text{ (number of days in a year)}}$$

Information on DDD values was obtained from the website of the WHO Collaborating Centre for Drug Statistics Methodology [20]. It's important to note that this assessment considers only those drugs that have been assigned ATC codes and DDD values.

The population data for the country during the study period were obtained from the annual statistical compilations "Basic Socio-Economic Indicators of the Republic of Kazakhstan," published on the website of the Committee on Statistics of the Ministry of National Economy of the Republic of Kazakhstan [21].

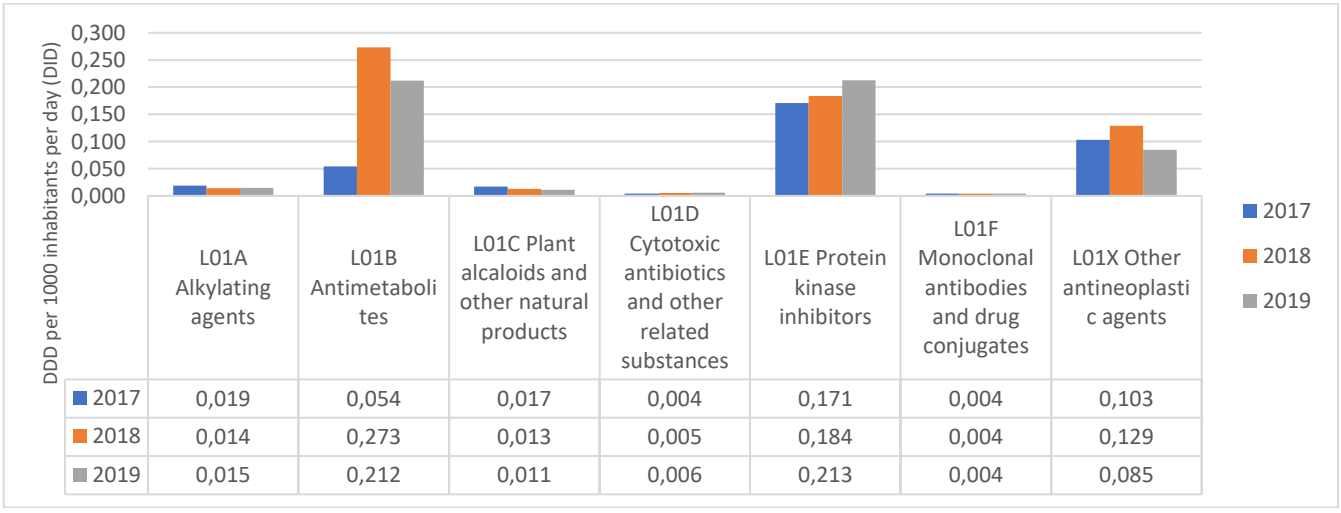
In the second stage of this study, the results obtained on the consumption of antineoplastic medicines were evaluated and compared with clinical protocols (recommendations) used in the Republic of Kazakhstan in the period 2019-2024 on the validity of use in various oncologic diseases [22].

Limitations

Pharmaceutical products with completed ATC codes (all ATC values), but without DDD, were calculated based on dosage unit measurements (DUM - dosage of the 1 measurement unit). In the list of drugs purchased by the Single Distributor from 2017 to 2019, there were a total of 357 positions of antineoplastic medicines with ATC codes L01 and L02, which constituted 13,1% of the total procurement list. Among them, L02 "Hormonal antineoplastic agents" had 73 positions, accounting for 20,5%, and all positions had established DDD values. From the group L01 "Antineoplastic agents", there were 284 positions, accounting for 79.5%, with no established DDD values for any of the positions.

3. Results

Based on the analysis of drug procurement by the Single Distributor from 2017 to 2019, in 2017, a total of 737 drug positions were purchased, in 2018 – 1164, and in 2019 – 812. Of the 737 drug positions purchased in 2017, drugs of group "L01 Antineoplastic agent" accounted for 69 positions (9%), and of group "L02" – 19 positions (2.6%). Among the 1164 drug positions purchased in 2018, antineoplastic medicines of group "L01" comprised 110 positions (9%), and of group "L02" – 36 positions (3%). Out of the 812 drug positions purchased in 2019, antineoplastic medicines of group "L01" constituted 105 positions (13%), and of group "L02" – 18 positions (2%).



	L01A Alkylating agents	L01B Antimetabolites	L01C Plant alcaloids and other natural products	L01D Cytotoxic antibiotics and other related substances	L01E Protein kinase inhibitors	L01F Monoclonal antibodies and drug conjugates	L01X Other antineoplastic agents
2017	0,019	0,054	0,017	0,004	0,171	0,004	0,103
2018	0,014	0,273	0,013	0,005	0,184	0,004	0,129
2019	0,015	0,212	0,011	0,006	0,213	0,004	0,085

Figure 1 – Consumption of 'L01 Antineoplastic agents' purchased under the GVFMC from 2017 to 2019, by pharmacological groups

In the period from 2017 to 2019, the consumption of 'L01 Antineoplastic agents' and 'L02 Antineoplastic hormonal agents' in Kazakhstan increased significantly. According to the data, the actual consumption of cancer treatment drugs in 2017 was 0.36 DID, which increased to 0.61 DID in 2018 and 0.55 DID in 2019. In the consumption structure of the 'L01' group in 2019, the pharmacological groups 'L01E Protein kinase inhibitors' and 'L01B Antimetabolites' were the leaders, with consumption rates of 0.213 and 0.212 DID, respectively.

Table 1 – Number of DUM per 1000 population per day for drugs in group L01 without DDD

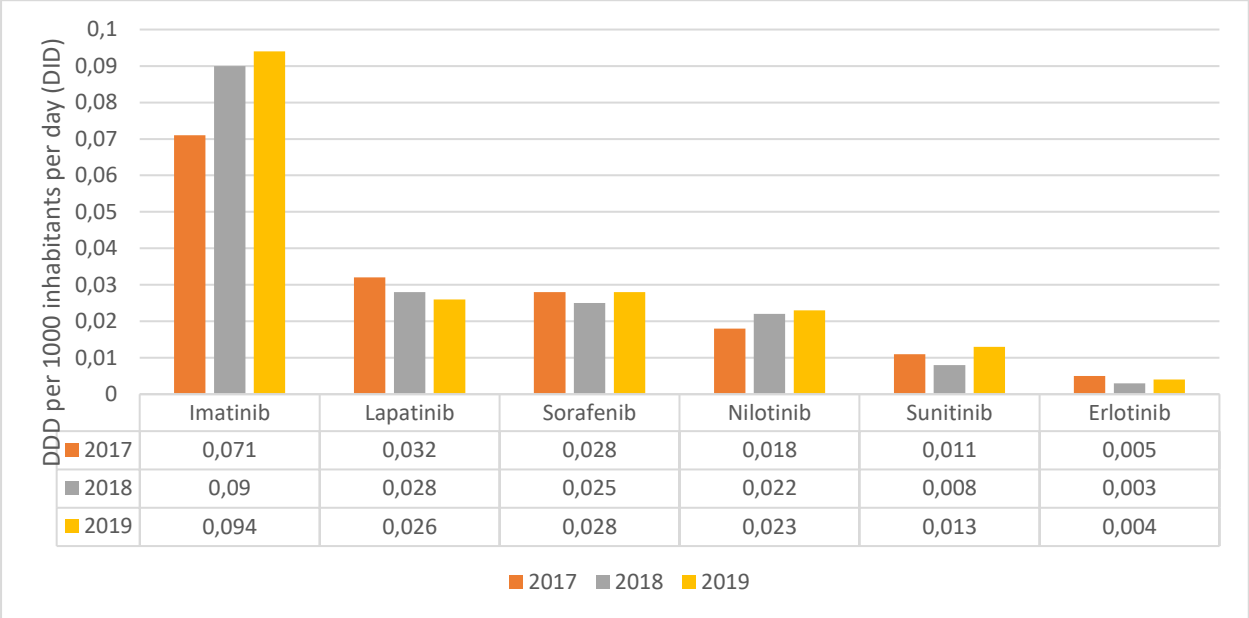
International Nonproprietary Names (INN) (L01)	**2017**	**2018**	**2019**	**General consumption rate**
Hydroxycarbamide	0.094	0.119	0.072	0.286
Imatinib	0.071	0.090	0.094	0.255
Methotrexate	0.017	0.143	0.081	0.242
Capecitabine	0.020	0.077	0.081	0.178
Lapatinib	0.032	0.028	0.026	0.086
Sorafenib	0.028	0.025	0.028	0.081
Tegafur	0.007	0.032	0.029	0.069
Nilotinib	0.018	0.022	0,023	0.064
Cyclophosphamide	0.015	0.010	0,011	0.037
Sunitinib	0.011	0.008	0,013	0.032
Mercaptopurine		0.013	0.011	0.024
Cisplatin	0.004	0.006	0.006	0.016
Docetaxel	0.005	0.005	0.005	0.016
Gemcitabine	0.004	0.004	0.005	0.013
Erlotinib	0.005	0.003	0.004	0.012
Cytarabine	0.005	0.003	0.004	0.012
Paclitaxel	0.004	0.004	0.004	0.011
Gefitinib	0.003	0.002	0.005	0.011
Oxaliplatin	0.003	0.003	0.003	0.009
Pazopanib	0.002	0.003	0.004	0.008
Doxorubicin	0.002	0.002	0.004	0.008
Temozolomide	0.001	0.002	0.002	0.006
Irinotecan	0.002	0.002	0.001	0.005
Dasatinib		0.002	0.003	0.005
Bortezomib	0.002	0.001	0.002	0.005
Vinorelbine	0.002	0.002	0.001	0.005
Dacarbazine	0.002	0.001	0.001	0.004
Epirubicin	0.001	0.002	0.001	0.004
Etoposide	0.004			0.004
Trastuzumab	0.001	0.001	0.001	0.004
Everolimus	0.001	0.001	0.002	0.004
Bevacizumab	0.001	0.001	0.001	0.003
Regorafenib			0.003	0.003

Continuation of Table 1

International Nonproprietary Names (INN) (L01)	**2017**	**2018**	**2019**	**General consumption rate**
Ifosfamide	0.001	0.001	0.001	0.003
Cetuximab	0.001	0.001	0.001	0.003
Vemurafenib			0.003	0.003
Dabrafenib			0.002	0.002
Rituximab	0.001	0.001	0.001	0.002
Pemetrexed	0.001	0.001	0.001	0.002
Daunorubicin	0.001	0.001	0.001	0.002
Carboplatin			0.0015	0.0015
Ibrutinib			0.0014	0.0014
Fludarabine	0.0003	0.0003	0.0002	0.0008
Pegylated Doxorubicin	0.0002	0.0004	0.0002	0.0008
Crizotinib			0.0006	0.0006
L-Asparaginase	0.0001	0.0001	0.0003	0.0005
Axitinib			0.0004	0.0004
Trabectedin	0.0001	0.0001	0.0001	0.0004
Decitabine	0.00008	0.00010	0.00012	0.00031
Mitoxantrone	0.00010	0.00005	0.00009	0.00024
Brentuximab Vedotin		0.00006	0.00011	0.00018
Ceritinib			0,00018	0.00018
Pegaspargase	0.00003	0.00002	0.00011	0.00016
Nintedanib			0.00009	0.00009
Pertuzumab			0.00008	0.00008
Transtuzumab Emtansine			0.00006	0.00006
Pembrolizumab			0.00004	0.00004
Brentuximab	0.00004			0.00004
Vinblastine		0.00003		0.00003
Cabazitaxel	0.00001	0.00001	0.00001	0.00002
Obinutuzumab			0.000002	0.000002

The least consumed drugs in the period 2017 to 2019 were from the groups 'L01D Cytotoxic antibiotics and related compounds' and 'L01F Monoclonal antibodies and drug conjugates' (Figure 1). The calculation of positions without established DDD values in the L01 group "Antineoplastic agents" was performed based on the indicator "Number of DUM per 1000 population per day" (Table 1).

In terms of consumption share in 2019, the leading antineoplastic medicines were from groups "L01E Protein kinase inhibitors" and "L01B Antimetabolites" accounting for 38.9% and 38.8% of consumption, respectively. Following these were "L01A Alkylating Agents," comprising 2.7% (0,015 DID) of total consumption, "L01C Plant Alkaloids and Natural Products" at 2% (0,01 DID), and "L01D Cytotoxic Antibiotics and Related Compounds" at 1.15%.



	Imatinib	Lapatinib	Sorafenib	Nilotinib	Sunitinib	Erlotinib
2017	0,071	0,032	0,028	0,018	0,011	0,005
2018	0,09	0,028	0,025	0,022	0,008	0,003
2019	0,094	0,026	0,028	0,023	0,013	0,004

Figure 2 – Consumption of "L01E Protein kinase inhibitors" from 2017 to 2019 (DDD per 1000 inhabitants per day (DID)

Among the drugs in the "L01E Protein kinase inhibitors" group, Imatinib was the most consumed 0.09 DID, followed by Lapatinib, Sorafenib, Nilotinib and Sutinib, with consumption rates of 0.026, 0.028, and 0.023 DID, respectively (Figure 2). In 2018-2019, there was a significant increase in the consumption of Imatinib.

Among the drugs in the "L01B Antimetabolites" group, Methotrexate was the most consumed, followed by Cytarabine, Capecitabine, Gemcitabine, and Tegafur. In 2018, there was a significant increase in the consumption of Methotrexate and Capecitabine. However, in 2019, the consumption pattern changed significantly, with Capecitabine consumption decreasing by 86.3% and Methotrexate consumption decreasing by 15.4%. Despite this decrease, Methotrexate remained the leading drug in 2019, with a consumption rate of 1,.16 DID. The least consumed drugs in this group in 2019 were Capecitabine, Gemcitabine, and Tegafur, with consumption rates of 0.08, 0.07, and 0.03 DID, respectively (Figure 3).

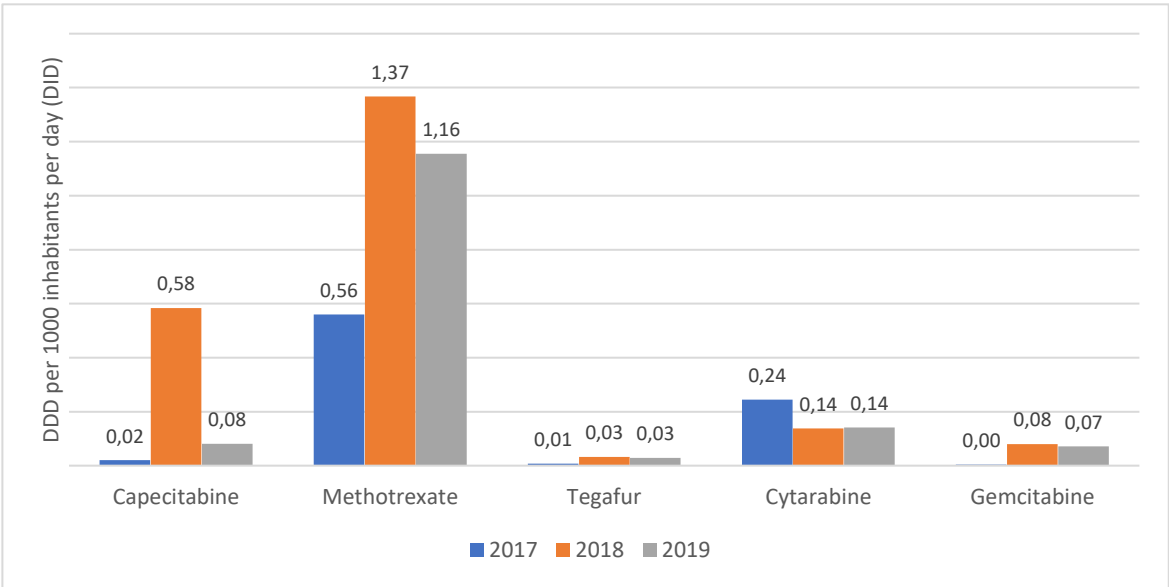


Figure 3 – Consumption of "L01B Antimetabolites" from 2017 to 2019 (DDD per 1000 inhabitants per day (DID)

In the consumption structure of the 'L02 Antineoplastic hormonal agents' in 2019, the leading pharmacological groups were "L02BA Anti-Estrogens," "L02BG Enzyme inhibitors," and "L02AE Gonadotropin-releasing hormone analogues," with consumption rates of 0.23, 0.19, and 0.15 DID,

respectively. The least consumed drugs from 2017 to 2019 were from the "L02BB Anti-Androgens" and "L02BX Other hormone antagonists and related agents" groups, with consumption rates of 0.02 and 0.01 DID, respectively (Figure 4).

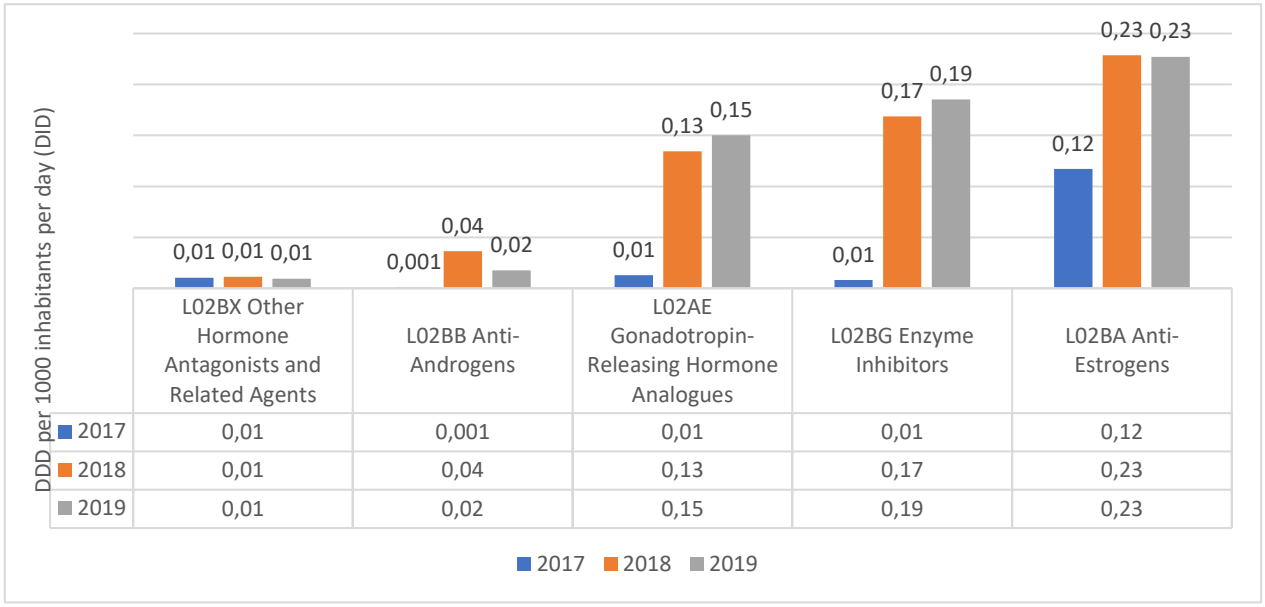


Figure 4 – Consumption of 'L02 Antineoplastic hormonal agents' purchased under the GVFMC from 2017 to 2019, by pharmacological groups

In terms of consumption share in 2019, the leading antineoplastic medicines were from the groups "L02BA Anti-Estrogens," "L02BG Enzyme inhibitors," and "L02AE Gonadotropin-releasing hormone analogues," with shares of 39%, 31%, and 25%, respectively. These were followed by the "L02BB Anti-Androgens" and "L02BX Other hormone antagonists and related agents" groups, with shares of 3% and 2%, respectively, of the total consumption.

Among the "L02BA Anti-Estrogens" group, there was a notable increase in the consumption of Toremifene in 2019, with an 86% rise since 2017, reaching 0.127 DID compared to 0.016 in 2017. Fulvestrant also showed a slight increase in consumption in 2019 compared to 2017, reaching 0,019 DID. Conversely, the consumption of Tamoxifen decreased in 2019 compared to 2017, with consumption rates of 0.088 and 0.099 DID, respectively. It is important to note that these hormonal antineoplastic medicines are used for long-term treatment.

The consumption of drugs in the "L02BG Enzyme inhibitors" group also showed a leading position in the consumption dynamics from 2017 to 2019. Letrozole and Anastrozole in this group demonstrated a stable increase in consumption over the three years. In 2019, the consumption rates of these drugs were 0.102 and 0.082 DID, respectively.

The analysis of the "L02AE Gonadotropin-releasing hormone analogues" group showed an 86% increase in the consumption of Triptorelin in 2019 (0.106 DID) compared to 2017 (0.009 DID) and a stable increase in the consumption of Leuprorelin. However, Leuprorelin was the least consumed drug in this group in 2019. Goserelin had the highest consumption in 2018, with a consumption rate of 0.041 DID. In 2019, the consumption of Goserelin decreased to 0.035 DID.

4. Discussion

This study has shown that it is possible to carry out a comparative analysis of the consumption of cancer drugs, both in terms of pharmacological groups and individual drugs, in order to assess the rationality of their use.

In 2019, the top two "L01" categories were "L01E Protein kinase inhibitors" and "L01B Antimetabolites", with consumption rates of 0.213 and 0.212 DID. The least consumed categories were "L01D Cytotoxic antibiotics and related compounds" (0.006 DID) and "L01F Monoclonal antibodies and drug conjugates"(0,004 DID).

The most consumed antineoplastic medicines by INN in 2019 was Imatinib from the group 'L01E Protein kinase inhibitors'. Consumption of this drug increased by 25.5%, reaching 0.094 DID in 2019 compared to 0.071

DID in 2017. After Imatinib, Sorafenib, Lapatinib, Nilotinib and Sutinib were the most consumed drugs in 2019. In 2019, Imatinib was included in the clinical guidelines for Kazakhstan for the treatment of breast cancer, lung cancer, gastric cancer, cervical cancer, colorectal cancer, rectal cancer, oesophageal cancer, prostate cancer, hepatocellular carcinoma and pancreatic cancer, despite being recommended for the treatment of 'chronic myeloid leukaemia', acute lymphoblastic leukaemia' and as an option as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettine 2006 criteria (based on tumour size, location and mitotic rate). Thus, comparison of domestic clinical recommendations with the indications of international clinical guidelines first of all revealed discrepancies in the main indications [23-25]. Meanwhile, according to some authors, despite the efficacy of Imatinib as an antitumor drug, its use is sometimes associated with severe cardiovascular side effects - from induced arrhythmias to heart failure [26-28]. Given the lack of data on the use of Imatinib in specific nosologies, we recommended an evaluation of Imatinib use to justify prescribing in healthcare organizations. Our data support the opinion of N.J. Latino et al. that 'the expert review of the Kazakhstan treatment protocols for solid tumors identified instances where the protocols were not consistent with acknowledged standards of care regarding indications, medicine combinations and lines of treatment. In the haematological formulary, a small subset of medicines was used for indications outside of ESMO CPG recommendations [29].

Regarding the "L01B Antimetabolites" group, the most consumed drugs in 2018-2019 were Methotrexate, Cytarabine, Capecitabine, Gemcitabine, and Tegafur. Notably, there was a significant increase in the consumption of Methotrexate and Capecitabine in 2018. However, Methotrexate consumption decreased to 1.16 DID in 2019 compared to 1.37 DID in 2018. Considering the increase in Imatinib consumption in 2019, it is possible that cancer treatment regimens involving Methotrexate were partially replaced by targeted therapy with Imatinib. Due to the lack of data on the use of drugs for specific conditions, there is no solid basis for this assertion. Despite the decrease in consumption, Methotrexate remained the leading drug in the "L01B Antimetabolites" group in 2019 with a consumption rate of 1.16 DID. In contrast, Tegafur was the least consumed, with a rate of 0.03 DID. It should be noted that Methotrexate is one of the most widely consumed antineoplastic medicines worldwide and is used not only for cancer but also for autoimmune diseases [30].

The most consumed drug in terms of INN in 2019 from the L02 group "Antineoplastic hormonal agents" was Toremifene from the "L02BA Anti-Estrogens" subgroup. Compared to 2017 (0.017 DID), consumption of Toremifene increased more than tenfold in 2019, while the consumption of Tamoxifen remained the same (0.099, 0.090, 0.088 DID). It is worth noting that the main indication for Toremifene according to the clinical guidelines of Kazakhstan is breast cancer, which holds leading positions in morbidity and mortality statistics among the population of Kazakhstan. According to the BNF, Toremifene is used for hormone-dependent metastatic breast cancer in postmenopausal women. In the BMJ Best Practice, Toremifene is not mentioned in the recommendations for "Breast Cancer" and "Metastatic Breast Cancer" [24,23]. Thus, given that Toremifene's prescription according to international experience has a narrow range of indications, its leading consumption also suggests irrational use. During the revision of this clinical guidelines in 2022, Toremifene, along with its use for hormone-dependent metastatic breast cancer in postmenopausal women, was designated as the main drug with a 100% probability of use.

Overall, the analysis results do not show significant changes in the consumption of antineoplastic medicines purchased under the GVFMC, including the structure and volume of the top 10 most consumed drugs in terms of INN. The most commonly used antineoplastic medicines under the GVFMC were purchased in accordance with the list and clinical guidelines.

It is also noteworthy that off-label drug use is widely practiced worldwide in cancer treatment, especially among patients with metastatic cancer and palliative care patients. According to a systematic review (23 studies), off-label drug use in hospitalized patients ranged from 18% to 41%, and among adult cancer patients, 13-71% received at least one chemotherapy drug prescribed off-label. However, more thorough studies and reliable clinical recommendations are needed to establish a favorable benefit-risk ratio for patients when prescribing therapy at each level of cancer care to facilitate the rational use of off-label drugs [31].

According to WHO data, in 2019, comprehensive cancer treatment services were provided in more than 90% of high-income countries and less than 15% of low-income countries [32]. A retrospective cohort study assessing the use of antineoplastic therapy in adult cancer patients at Vall d'Hebron University Hospital, the largest hospital complex in Catalonia, Spain (2010-2019), showed that of the 112 antineoplastic medicines,

50% were for targeted therapy drugs, 41,07% for cytostatics, 7.14% for immunotherapeutic drugs, and 1.79% for radiopharmaceuticals [33]. Similarly, the current analysis of drug consumption in oncology in Kazakhstan for 2017-2019 also demonstrated increased consumption of targeted drugs like Imatinib, Lapatinib, Nilotinib, Sorafenib, and Sunitinib from the "L01X Other antineoplastic agents" group, along with the use of cytostatics and hormonal antineoplastic medicines.

Some limitations of this work should be acknowledged. Firstly, the lack of prescription information specifying the indication for which the antineoplastic medicines was prescribed, including the absence of data on cancer stage, surgical history, and cancer morphology, meant that the full rationality of antineoplastic medicines treatment could not be assessed. Secondly, the absence of a national cancer registry detailing topography, morphology, behavior of neoplasms, and their biological properties complicates the assessment of patient provision with antineoplastic medicines compared to other countries based on the DDD per 1000 population per day indicator.

5. Conclusions

The results of the study showed that there are two key problems in the clinical practice of oncologists. Firstly, there is inadequate assessment of adherence to the indications for use of drugs for a particular type of cancer pathology in the development of clinical guidelines. Secondly, it is necessary to improve the assessment of the availability of antineoplastic medicines in comparison with other countries in terms of DDD per 1000 people per day. It is recommended that the electronic register of cancer patients at national level be improved to include information on cancer stage, surgical history and cancer morphology, topography, neoplasm behavior and biological characteristics, as well as information on prescriptions, and to introduce into the routine practice of oncological dispensaries at the local level regular analysis of drug consumption using the ATC/DDD methodology. This analysis revealed trends and dynamics in the consumption of these drugs, which provides an opportunity to improve the efficiency of optimizing the supply of drugs in oncology, including compliance with evidence-based recommendations such as ESMO/NCCN/NICE, thereby improving patient access to medicines.

Data Availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest. The authors declare that there are no conflicts of interest.

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Author Contributions: Conceptualization, methodology, project administration, supervision, funding acquisition, writing original draft, writing—review and editing—G.Zh.; data curation, formal analysis, software, investigation, validation—D.B.; investigation, visualization, writing—review and editing—B.E. All authors have read and agreed to the published version of the manuscript.

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Қазақстандағы ісікке қарсы жүйелі терапия (SACT) кезінде ісікке қарсы дәрілік заттарды тұтынуды бағалау үшін ATC/DDD әдісін қолдану

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Түйіндеме

Қатерлі ісіктің ғаламдық жүктемесінің жедел өсуі аурушаңдықтың артуы және өлім-жітімнің төмендеуімен сипатталады. Сонымен қатар, жаңа инновациялық емдеу әдістерінің дамуы пациенттердің өмір сүру ұзақтығын айтарлықтай арттырды. Нәтижесінде ісікке қарсы дәрілік заттарды тұтыну көлемі өсуде. Қазақстан Республикасының бюджеті есебінен сатып алынатын ісікке қарсы дәрілік заттардың тұтынылуын бақылау және зерттеу арқылы олардың тиімді пайдаланылу сапасын арттыру. Зерттеу екі кезеңде жүргізілді. Бірінші кезеңде ісікке қарсы дәрілік заттардың тұтынылуы Дүниежүзілік денсаулық сақтау ұйымы (ДДСҰ) ұсынған ATC/DDD әдістемесі негізінде талданды. Есептеу және талдау үшін 2017–2019 жылдардағы дәрілік заттарды сатып алу деректері пайдаланылды. Екінші кезеңде алынған нәтижелер 2019–2024 жылдарға арналған Қазақстан Республикасында қолданылатын клиникалық хаттамалармен салыстырылып, әртүрлі онкологиялық аурулар кезінде олардың қолданылу негізділігі бағаланды. Қазақстанда сатып алынатын онкологиялық препараттардың кең ассортиментіне қарамастан, ATC «L01» коды бар препараттардың тек 54%-ы және ATC «L02» коды бар препараттардың 31%-ы ДДСҰ тізіміне сәйкес келеді. ATC «L01» кодындағы онкологиялық препараттар құрылымында жетекші фармакологиялық топтар «L01E Протеинкиназа ингибиторлары» және «L01B Антиметаболиттер» болды, олардың тұтынылу көрсеткіштері сәйкесінше 0,213 және 0,212 DID құрады. «L01D Цитотоксикалық антибиотиктер және сабақтас заттар» тобы ең аз тұтынылған (1,15%). ATC «L02» кодындағы препараттар құрылымында жетекші топтар — «L02BA Антиэстрогендер», «L02BG Фермент ингибиторлары» және «L02AE Гонадотропин-рилизинг-гормон аналогтары» болды, олардың

үлесі тиісінше 39%, 31% және 25% құрады. Ұлттық клиникалық ұсынымдарды халықаралық нұсқаулықтармен салыстыру сәйкессіздіктерді анықтады. Ісікке қарсы дәрілік заттарды тұтынуды ATC/DDD халықаралық әдістемесі арқылы талдау олардың тұтыну үрдістері мен динамикасын анықтауға мүмкіндік берді. Бұл онкология саласындағы фармацевтикалық қамтамасыз етуді оңтайландыру тиімділігін арттыруға, сондай-ақ ESMO/NCCN/NICE сияқты дәлелді нұсқаулықтарды сақтау арқылы пациенттердің дәрілік заттарға қолжетімділігін жақсартуға мүмкіндік береді.

Түйін сөздер: ATC/DDD, Қазақстан, ісікке қарсы дәрілік заттар, ісікке қарсы жүйелі терапия, дәрілік заттарды басқару.

Применение метода ATC/DDD для оценки потребления противоопухолевых препаратов при системной противораковой терапии (SACT) в Казахстане

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Резюме

Быстро растущая глобальная нагрузка по онкологическим заболеваниям характеризуется увеличением заболеваемости и снижением смертности. Кроме того, разработка новых инновационных методов лечения значительно увеличила продолжительность жизни пациентов. В результате растет потребление противоопухолевых препаратов. Мониторинг и исследование потребления противоопухолевых препаратов, закупаемых за счет бюджета Республики Казахстан, направлены на повышение качества их использования. Исследование проводилось в два этапа. На первом этапе потребление противоопухолевых препаратов анализировалось с использованием методологии Всемирной организации здравоохранения по классификации анатомо-терапевтическо-химическая классификация лекарственных средств и определенной суточной дозе. Для расчета и анализа потребления использовались данные о закупках лекарственных средств за 2017–2019 годы. На втором этапе результаты оценивались и сравнивались с клиническими протоколами, применяемыми в Республике Казахстан за период 2019–2024 годов, для оценки обоснованности применения при различных онкологических заболеваниях. Несмотря на более широкий ассортимент закупаемых в Казахстане онкологических препаратов, только 54% препаратов с кодом анатомо-терапевтическо-химической классификации лекарственных средств «L01» и 31% с кодом анатомо-терапевтическо-химической классификации лекарственных средств «L02» соответствуют списку Всемирной организации здравоохранения. В структуре потребления онкологических препаратов с кодом ATC «L01» ведущими фармакологическими группами были «L01E Ингибиторы протеиновых киназ» и «L01B Антиметаболиты» с уровнями потребления 0,213 и 0,212 DID соответственно. Наименее потребляемой группой были «L01D Цитотоксические антибиотики и родственные вещества» — 1,15%. В структуре кодов ATC «L02» ведущими препаратами были группы «L02BA Антиэстрогены», «L02BG Ингибиторы ферментов» и «L02AE Аналоги гонадотропин-рилизинг гормона» с долями 39%, 31% и 25% соответственно. Сравнение национальных клинических рекомендаций с международными руководствами выявило расхождения. Анализ потребления противоопухолевых препаратов с использованием международной анатомо-терапевтическо-химическая классификации лекарственных средств и методологии определенной суточной дозы выявил тенденции и динамику потребления этих лекарственных средств, что позволяет повысить эффективность оптимизации фармацевтического обеспечения в онкологии, включая соблюдение доказательной базы, такой как рекомендации Европейского общества медицинской онкологии, Национальной комплексной сети по борьбе с раком и Национального института здравоохранения и совершенствования медицинской помощи, улучшая доступ пациентов к лекарствам.

Ключевые слова: ATC/DDD, Казахстан, противоопухолевые препараты, системная противораковая терапия, управление лекарственными средствами.