Costs of Treating Lymphoproliferative Disorders in Ukraine: a Pilot Evaluation

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Chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) are two of the most widespread lymphoproliferative disorders among the adult population of Ukraine and other Central and Western European countries. Considering that pharmaceutical treatment accounts for the major part of medical expenses in the management of these conditions, the aim of this study was to assess the costs of pharmacotherapy of CLL and MM. The analysis was performed retrospectively using the results of our own pilot study, in which we examined medical histories of the patients treated at a specialized medical center in Kiev. The average annual cost of pharmacotherapy of all Ukrainian patients was 340 750 162 RUB for CLL and 89 184 759 RUB for MM. We found a negative correlation between the patient's age and the cost of pharmacotherapy.

KEYWORDS: cost of treatment, lymphoproliferative disorders.

Malignant tumors remain one of the leading causes of death in the world among chronic non-infectious diseases, with over 7.6 million deaths registered every year (13% of all deaths). The number of deaths from cancer is predicted to reach 11 million per year by 2030 [1, 2]. The high prevalence of cancer in Ukraine (348 per 100 thousand population) determines its social and economic significance and makes cancer a prioritized area for the allocation of healthcare resources [3]. Survival of cancer patients one year after diagnosis is 65.9% in Ukraine, which is not significantly different from the European average (67.3%) but considerably lower than in such countries as Island, Finland, Switzerland and Sweden [4].

Malignant tumors of lymphoid and hematopoietic tissues (ICD-10 C81-C96) are fairly common among adults in economically developed European countries [2,4]. According to the 11th issue of the National Cancer Registry (2010), morbidity and mortality due to lymphoproliferative disorders are also rather high in Ukraine (Fig. 1). For instance, mortality within one year of diagnosis is 39.3% for leukemia, 36.1% for multiple myeloma (MM), 36.5% for non-Hodgkin's lymphomas (NHL), and 12% for Hodgkin's lymphoma (HL). Five-year survival rate of Ukrainian patients with leukemia is 26.3%, NHL 28.5%, and HL 48.7%. The social significance of lymphomas and leukemias is further amplified due to their high prevalence among people of working age: HL, leukemias and NHL are among the five top malignancies affecting men between 18 and 29 years of age (16%, 10.5% and 6.5%, respectively). HL is the most common type of cancer among women of this age group (15.1%) [3]. Even though mortality due to these conditions is high, it is possible to achieve a cure or improve the patient's quality of life if the disease is diagnosed at an early stage and the patient is given timely treatment. In order to improve the supply of drugs for pharmacotherapy and promote the spread of evidence-based therapy in clinical practice, it is important to analyze the pharmaceutical market as well as the currently used and recommended methods of treating malignant tumors of lymphoid and hematopoietic tissues.

Even though tumors of lymphoid and hematopoietic tissues are not among the five most common cancers in

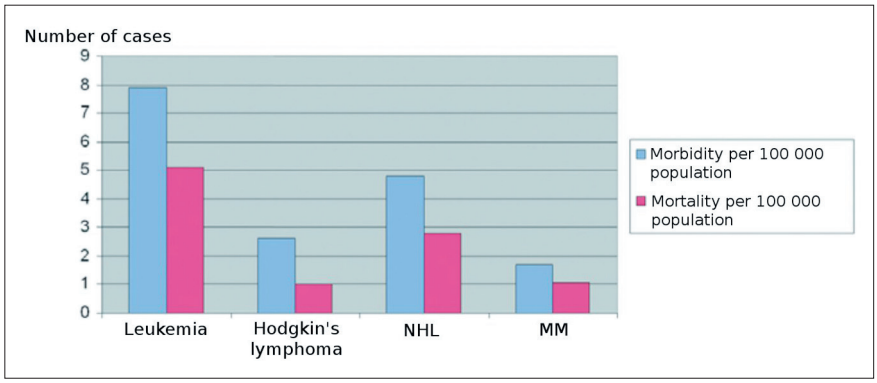

Fig. 1. **Lymphoproliferative disorders in Ukraine: morbidity and mortality.**

Ukraine, potentially they could have a major economic impact compared to other malignancies. A systematic review of studies that included patients with different types of cancer demonstrated that non-localized tumors, such as lymphoproliferative disorders, are associated with higher treatment costs [5]. Considering that CLL and MM are among the most common lymphoproliferative disorders [3], the objective of this study was to perform a pilot analysis of the cost of treating these cancers in Ukraine. According to the available publications, pharmacotherapy is the single largest component of total medical costs associated with the treatment of patients with lymphoproliferative disorders [6-10]. Because of this, only the costs of pharmacotherapy were included in the analysis.

MATERIALS AND METHODS

Our pilot evaluation of the cost of treating CLL and MM was performed using case report forms of the National Institute of Hematology (Kiev). The electronic database of this organization (Access software) contained data taken from medical histories of patients with CLL and MM, which we used for our retrospective analysis. The data were transferred from the case report forms to the database by a qualified member of the hospital staff (an assistant). Newly diagnosed patients and those who relapsed and were hospitalized at least once between 2006 and 2010 for CLL or MM were included in the analysis. Overall, the sample of MM patients consisted of 98 individuals aged between 29 and 81 (mean age 62.5), 35.6% of whom were males. The sample of CLL patients consisted of 113 individuals aged between 39 and 85 (mean age 61.3), with 61.9% males. The following characteristics were derived from the medical histories: age and gender, the stage of cancer progression, treatment administered, and disease duration.

We analyzed the cost of pharmacotherapy for the main diagnosis and comorbidities, such as anemia and bone diseases accounting for the possibility that the medications may be acquired by the patients themselves as well as by the state. To estimate the costs, we analyzed the structure of state purchases in 2010 based on eight Orders of the Ministry of Health of Ukraine (No. 360, 365, 526, 608, 686, 687, 980, 987). The spending on pharmaceutical drugs purchased under the governmental scheme in 2010 was assumed to be equal to these tariffs. The cost of medications purchased by the patients was estimated based on the prices quoted by distributors, assuming a 35% pharmacy surcharge. The currency was converted according to the rate of the Central Bank of Russia on 24.03.12 (1 hryvnia = 3.66 rubles). The statistical analysis of the correlation between the costs and the patient's age at diagnosis was performed in SPSS 12.0.

RESULTS

The analysis of medical histories revealed that CLL patients were usually prescribed cyclophosphamide, fludarabine, and vincristine. Patients diagnosed with MM usually received a combination of melphalan, prednisolone or dexamethasone and/or talidomide. Among the drugs prescribed to these patients, corticosteroids had the lowest cost of the median daily dose, while bortezomib (MM) and rituximab (CLL) had the highest (Table 1).

The average annual cost of pharmacotherapy of one MM patient was 20 114 RUB (range: from o to

Table 1. The cost of medications commonly administered to patients with MM and CLL

Drug	Cost of median daily dose, RUB	Range, RUB
Alemtuzumab	1571.81	–
Bortezomib	66 049.57	–
Vincristine	130.79	130.79 – 261.19
Dexamethasone	4.66	1.55 – 6.98
Zoledronic acid	11 069.39	–
Ibandronic acid	9677.66	–
Interferon alpha–2b	7606.37	–
Clodronic acid	44.24	–
Lomustine	10.48	5.05 – 15.52
Melphalan	123.03	123.03 – 368.67
Methylprednisolone	0.78	0.39 – 1.55
Pamidronic acid	3620.59	–
Prednisolone	0.39	0.16 – 1.64
Rituximab	55 149.01	36 675.45 – 80 414.32
Talidomide	11.25	5.43 – 22.13
Fludarabine	21 772.41	18 745.23 – 21 772.41
Chlorambucil	1.86	1.96 – 51.32
Cyclophosphamide	31.44	15.52 – 62.10

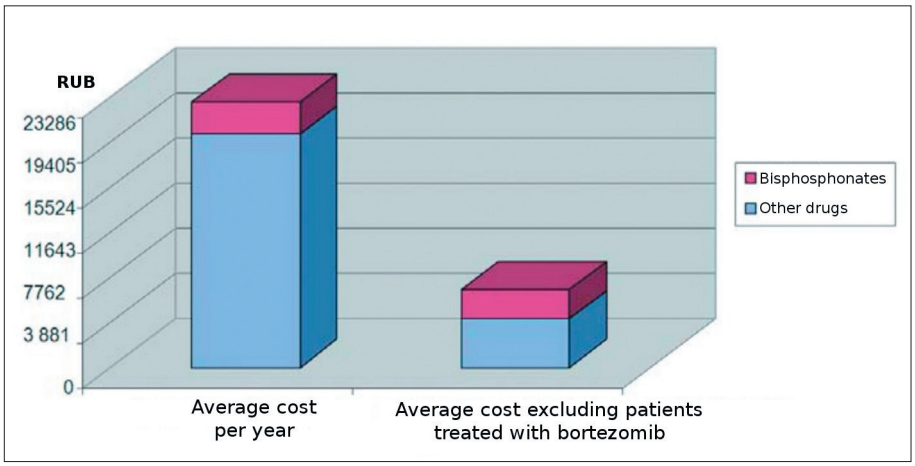

Fig. 2. **The average annual cost of pharmacotherapy of 1 patient with MM.**

62 527 RUB). Considering the prevalence of MM in Ukraine (4 434 cases), the total cost of pharmacotherapy of MM in Ukraine may be estimated at 89 184 759 RUB/year. The treatment of bone diseases associated with MM constitutes a considerable part of total expenses. On average, this treatment costs 2746 RUB per year per patient (from 0 to 5208 RUB). The most economically significant type of primary treatment is bortezomib therapy. If we exclude patients receiving bortezomib from the analysis, the total cost of pharmacotherapy drops to 4179 RUB (from 0 to 6819 RUB). Of this sum, 2487 RUB was spent on the treatment of bone diseases with bisphosphonates (ibandronic, pamidronic, clodronic, and zoledronic acids) (Fig. 2).

The average annual cost of treating one CLL patient was 39 892 RUB (from 0 to 771 272 RUB). Considering the prevalence of CLL in Ukraine (8542 cases), the total annual cost of CLL pharmacotherapy amounts to 340 750 162 RUB. Prescription of therapeutic combinations including fludarabine and rituximab had the greatest impact on the cost of CLL treatment. The average cost of a course of monotherapy with injectable fludarabine (50 mL for 3 days) is 21 080 RUB. The cost of one course of therapy with the median dose of rituximab (400 mg/day) is 36 505 RUB.

Statistical analysis of the collected data revealed that there was a negative correlation between the age of the patient at the time of diagnosis and the cost of treatment, both for CLL ($t = -2.108$, $p < 0.05$) and for MM ($t = -2.118$, $p < 0.05$). This contradicts the results of similar studies performed in other countries, in which the cost of treating elderly patients with these conditions was higher [6,7,10,11]. The limitations of the registry that we used provide one possible explanation of this result, since it did not allow us to take into account fully all the additional costs associated with treating the complications of the main disease and comorbidities. Among such medical conditions that are commonly found in patients suffering from lymphoproliferative disorders are infectious diseases, renal failure, and anemia. It is likely that the registry did not fully document the therapy administered for these conditions. Another possible reason why the treatment of elderly patients with lymphoproliferative disorders did not cost more is the low income of this age group, limiting their ability to pay for the treatment and encouraging the physicians to prescribe cheaper drugs.

From 01.04.2012 the lowest living cost in Ukraine for incapacitated people is set at 3067 RUB. The treatment of CLL and MM is a considerable economic burden for patients, especially for exposed groups such as impecunious elderly patients. This highlights the need to provide elderly patients with additional financial support, since for them malignant tumors are associated with greater financial and emotional difficulties than for younger people [12].

LIMITATIONS OF THIS STUDY AND RECOMMENDATIONS

Retrospective analysis of medical histories in a single medical center only amounts to a pilot study that may offer an approximate estimate of the cost of treating lymphoproliferative disorders in Ukraine. This analysis does not allow us to assess indirect costs of treatment. In order to generalize from the results obtained in the study sample to the general population of patients, we have to compare our results with the data from other medical centers, thus arriving at a representative sample of patients.

CONCLUSIONS

1. Our pilot analysis of the costs of pharmacotherapy demonstrated that the average annual cost of medications was 39 892 RUB for CLL patients and 20 114 RUB for MM patients. Even though less than 10% of all patients with lymphoproliferative disorders were receiving the most expensive drugs, such as rituximab (CLL therapy) and bortezomib (MM therapy), the use of these drugs had a major impact on the total spending. The expediency of

their use in clinical practice needs to be justified with the help of pharmacoeconomic analysis.

2. According to the results of this study, elderly patients are likely to be given less expensive treatment, which may be related to the high cost of therapy if these conditions are treated in accordance with the protocols developed upon the principles of evidence-based medicine. This hypothesis needs to be tested by means of a more detailed analysis.

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