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Accessibility to targeted oncology drugs in Slovenia and selected European countries

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ABSTRACT

Aim: The aim of the study is to compare the accessibility to targeted oncology drugs in Slovenia and selected European countries.
Methods: Accessibility of targeted oncology drugs was assessed by using their sales data, expressed in mg per individual dying of the cancer for which the drug was indicated.
Results: The time of introduction of targeted oncology drugs in Slovenia was in most cases similar to the comparison countries, except for alemtuzumab and rituximab. The utilisation of targeted oncology drugs in Slovenia was in most cases lower than in other comparison countries. Ibritumomab had not been used in Slovenia until 2005, similar to France, Switzerland and UK. After 2003 the utilisation of trastuzumab in Slovenia started to rise substantially, approaching the average uptake in comparison countries.
Conclusion: The utilisation of targeted oncology drugs in Slovenia was in most cases lower than in comparison countries.

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1. Introduction

From the introduction of anticancer drug therapy in the 1950s, drugs that specifically target tumour cells have been sought. However, for many antineoplastic agents their targets are not specific to neoplastic cells. As a consequence, patients on chemotherapy can experience systemic adverse effects. On the other hand, a major shift is expected in the treatment of malignancies because of the recent introduction of mechanism-based systemic therapies. These so-called targeted drugs act on targets that are differentially expressed (quantitatively or qualitatively) in neoplastic cells compared with normal host cells.[1] In this manner, targeted oncology drugs have potentially higher effectiveness compared to 'classical' oncology drugs, and cause significantly less systemic adverse effects.

Accessibility of patients and healthcare systems to new oncology drugs can be determined by the time of drug launch and the amount of drug uptake. The relatively short survival and low quality of life of cancer patients generate a high demand for rapid and sufficient uptake of new effective and safe therapeutic approaches. However, drugs used in cancer treatment are among the costliest in medical care, especially newer drugs, which have substantially higher cost compared to older agents. [2] Jönsson and Wilking found that funds expenditure on oncology drugs in 25 selected countries has risen from 5 billion EUR to more than 23 billion EUR in the period from 1995 to 2005.[3] Consequently, increased financial burden to the healthcare systems may lead to limited patients' accessibility to new targeted oncology drugs.

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The aim of this study is to compare the accessibility to targeted oncology drugs in Slovenia and selected European countries.

2. Methods

2.1. Targeted drugs in oncology

Targeted oncology drugs that had their first use before the end of 2005 were eligible for inclusion in the analysis. The selected drugs and their corresponding indications registered before the end of 2005 are presented in Table 1.[4]

2.2. Selected European countries

The following countries were included in the analysis: Austria, France, Germany, Italy, Slovenia, Sweden, Switzerland and the United Kingdom (the abbreviation 'E-8' is used hereafter).

2.3. Assessment of accessibility

The analysis was performed for the period from the first uptake of the drug to any comparison country to the end of 2005. Accessibility of targeted oncology drugs for selected countries was assessed by using sales data as a marker of actual utilisation. Slovenian sales data were obtained from PharMIS, MIS Consulting Ltd., which provides IMS data for Slovenia, whereas sales data for the other countries were obtained from IMS Health, IMS MIDAS.[5,6] Sales data of a specific drug, expressed in mg for each quarter of the year, were divided by the mortality of the cancer for which the drug was indicated in the period of the analysis (up to 2005 inclusive). For this purpose the Globocan mortality data for selected European countries for the year 2002 was used.[7] As specific mortality data for each registered indication of the selected drugs was not available, mortality data for the cancer type based on categories in the Globocan database was used. Namely, breast

Table 1 – Targeted oncology drugs and their corresponding indications registered before the end of 2005

Drug	Brand name	Indications registered before the end of 2005
Alemtuzumab	MabCampath®	– Treatment of patients with chronic lymphocytic leukaemia who have been treated with alkylating agents and who have failed to achieve a complete or partial response or achieved only a short remission (less than 6 months) following fludarabine phosphate therapy.
Bevacizumab	Avastin®	– First-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil/folinic acid or intravenous 5-fluorouracil/folinic acid/irinotecan.
Bortezomib	Velcade®	– Monotherapy treatment of progressive multiple myeloma in patients who have received at least one prior therapy and who have already undergone or are unsuitable for bone marrow transplantation.
Cetuximab	Erbitux®	– In combination with irinotecan for the treatment of metastatic colorectal cancer patients who express epidermal growth factor receptor, after failure of irinotecan-including cytotoxic therapy.
Erlotinib	Tarceva®	– Treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen.
Ibritumomab tiuxetan	Zevalin®	– Treatment of adult patients with rituximab relapsed or refractory CD20+ follicular B-cell non-Hodgkin's lymphoma.
Imatinib mesylate	Glivec®	– Treatment of adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive chronic myeloid leukaemia for whom bone marrow transplantation is not considered as the first line of treatment. – Treatment of adult and paediatric patients with Philadelphia chromosome (bcr-abl) positive chronic myeloid leukaemia in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis. – Treatment of adult patients with Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours.
Rituximab	Mabthera®	– Treatment of patients with stage III–IV follicular lymphoma who are chemoresistant or are in their second or subsequent relapse after chemotherapy. – Treatment of previously untreated patients with stage III–IV follicular lymphoma in combination with CVP chemotherapy. – Maintenance therapy for patients with relapsed/refractory follicular lymphoma responding to induction therapy with chemotherapy with or without rituximab. – Treatment of patients with CD20 positive diffuse large B cell non-Hodgkin's Lymphoma in combination with CHOP chemotherapy.
Trastuzumab	Herceptin®	– As monotherapy for the treatment of those patients who have received at least two chemotherapy regimens for their metastatic disease. Prior chemotherapy must have included at least an anthracycline and a taxane unless patients are unsuitable for these treatments. Hormone receptor positive patients must also have failed hormonal therapy, unless patients are unsuitable for these treatments. – In combination with paclitaxel for the treatment of those patients who have not received chemotherapy for their metastatic disease and for whom an anthracycline is not suitable. – In combination with docetaxel for the treatment of those patients who have not received chemotherapy for their metastatic disease.

Table 2 – Mortality rates (per 100,000 inhabitants) of different types of cancer in selected European countries obtained from the Globocan 2002 database

Country	Breast cancer	Colorectal cancer	Cancer of bronchus, trachea and lungs	Non- Hodgkin lymphoma	Multiple myeloma	Leukaemia
Austria	20	33	42	6	4	8
France	19	29	44	8	4	8
Italy	20	30	57	9	4	9
Germany	22	37	48	7	5	9
Slovenia	20	32	49	6	4	7
Sweden	17	28	35	9	6	8
Switzerland	19	25	41	8	5	7
United Kingdom	22	29	60	8	4	7

Table 3 – Incidence rates (per 100,000 inhabitants) of different types of cancer in selected European countries obtained from the Globocan 2002 database

Country	Breast cancer	Colorectal cancer	Cancer of bronchus, trachea and lungs	Non- Hodgkin lymphoma	Multiple myeloma	Leukaemia
Austria	57	64	46	14	6	11
France	70	58	46	15	6	13
Italy	64	66	65	18	8	14
Germany	68	77	52	14	6	13
Slovenia	48	57	54	12	4	9
Sweden	74	60	33	16	6	12
Switzerland	68	63	51	17	6	11
United Kingdom	69	61	67	16	7	12

cancer for trastuzumab, colorectal cancer for bevacizumab and cetuximab, cancer of bronchus, trachea and lungs for erlotinib, non- Hodgkin lymphoma for ibritumomab tiuxetan and rituximab, multiple myeloma for bortezomib, and leukaemia for alemtuzumab and imatinib mesylate. In order to compare burden of cancer between countries, mortality rate, as well as incidence rate, for selected European countries for the year 2002 are also presented in this report (see Tables 2 and 3).

Accessibility to the targeted oncology drugs was assessed by comparing the differences in time of the first entry to the healthcare system, the increase of utilisation after the first entry (date of first entry was used as the index date from which the growth was compared) and the utilisation at the end of year 2005. Furthermore, accessibility was valued in relation to affordability of different healthcare systems to uptake a new drug. For this purpose the utilisation, expressed in mg of a drug per mortality of cancer for which the drug was indicated, was divided by the gross domestic product per capita expressed in purchasing power standard for each country included in the analysis.[8]

3. Results

Among selected targeted oncology drugs, rituximab was introduced first (fourth quarter of 1997) and erlotinib was introduced last (first quarter of 2005), both of them being launched first in Switzerland. Six of nine targeted oncology drugs were first introduced in Switzerland alone or concomitantly with other countries. Slovenia was among first introducers only in the case of imatinib mesylate. Dates of targeted oncology drugs first entry to healthcare system in E-8 are presented in Table 4.

3.1. *Alemtuzumab*

Among E-8 the first recorded usage of alemtuzumab was in Germany and UK (third quarter of 2001). Utilisation of alemtuzumab in Slovenia commenced 3.25 years after the first usage in E-8 and approximately 3 years after the rest of E-8 countries.

The biggest rise in the utilisation of alemtuzumab after entering the system, expressed per individual dying of leukaemia, was in Austria, Slovenia, Sweden and the UK. Due to the relatively late introduction of alemtuzumab in Slovenia, the comparison of utilisation rise in regard to other countries is possible only in the first year after the drug uptake.

In 2005, the highest utilisation of alemtuzumab per individual dying of leukaemia was in the UK, Austria and Sweden. In Slovenia, there was no record of alemtuzumab utilisation until 2005. However, in 2005 the utilisation of alemtuzumab in Slovenia rapidly grew to a level comparable to France and Italy who had introduced alemtuzumab 3 years before. When affordability of the country to uptake the drug was taken into account, the utilisation of alemtuzumab in Slovenia was slightly above the average of E-8 utilisation. The relative positions of alemtuzumab utilisation in other E-8 countries did not change noticeably.

The utilisation of alemtuzumab is presented in Fig. 1.

3.2. *Bevacizumab*

Among E-8 the first recorded usage of bevacizumab was in Switzerland (fourth quarter of 2004). Utilisation of bevacizumab in Slovenia commenced 0.5 years after the first usage in E-8, which is similar to other E-8 countries.

Table 4 – Date of the first entry of targeted oncology drugs to the healthcare system in selected European countries

Country	Alemtuzumab	Bevacizumab	Bortezomib	Cetuximab	Erlotinib	Ibritumomab	Imatinib mesylate	Rituximab	Trastuzumab
Austria	4Q 2001	3Q 2005	2Q 2004	3Q 2004	4Q 2005	2Q 2004	4Q 2001	3Q 1998	4Q 2000
France	1Q 2002	2Q 2005	3Q 2004	3Q 2004	2Q 2005	NA	3Q 2001	1Q 1998	3Q 1999
Germany	3Q 2001	1Q 2005	2Q 2004	2Q 2004	4Q 2005	3Q 2004	4Q 2001	3Q 1998	4Q 2000
Italy	2Q 2002	4Q 2005	2Q 2005	3Q 2005	NA	3Q 2005	1Q 2002	1Q 1999	1Q 2001
Slovenia	1Q 2005	2Q 2005	4Q 2004	4Q 2004	4Q 2005	NA	3Q 2001	1Q 2001	1Q 2001
Sweden	4Q 2001	1Q 2005	2Q 2004	3Q 2004	4Q 2005	1Q 2004	4Q 2001	2Q 1998	4Q 2000
Switzerland	2Q 2002	4Q 2004	1Q 2005	1Q 2004	1Q 2005	NA	3Q 2001	4Q 1997	3Q 1999
United Kingdom	3Q 2001	1Q 2005	2Q 2004	2Q 2004	3Q 2005	NA	4Q 2001	2Q 1998	3Q 2000

1Q - 1st quarter, 2Q - 2nd quarter, 3Q - 3rd quarter, 4Q - 4th quarter.
NA - not applicable.

The biggest rise in the utilisation of bevacizumab after entering the system, expressed per individual dying of colorectal cancer, was in Austria, followed by Switzerland. Slovenia was, together with the UK, the slowest in introducing bevacizumab to the healthcare system.

At the end of 2005 the highest utilisation of alemtuzumab per individual dying of colorectal cancer was in Switzerland, followed by Austria and then France. Slovenia had the lowest utilisation of bevacizumab among E-8. When affordability of the country to uptake the drug was taken into account, the relative positions of bevacizumab utilisation among E-8 countries did not change noticeably.

The utilisation of bevacizumab is presented in Fig. 2.

3.3. *Bortezomib*

Among E-8 the first recorded usage of bortezomib was in Austria, Germany, Sweden and the UK (second quarter of 2004). Utilisation of bortezomib in Slovenia commenced 0.5 years after the first usage in E-8, which is similar to other E-8 countries following the countries with the first entry.

The biggest rise in the utilisation of bortezomib after entering the system, expressed per individual dying of multiple myeloma, was in Switzerland, followed by France and Austria. Slovenia started with relatively high utilisation of bortezomib soon after introduction, although the trend of growth could not be seen in the following quarters of the year.

At the end of 2005, the highest utilisation of bortezomib per individual dying of multiple myeloma was in Austria, France and Switzerland. Slovenia had a substantially lower utilisation of bortezomib compared to the E-8 average (after the UK, the second lowest).

When affordability of the country to uptake the drug was taken into account, the utilisation of bortezomib in Slovenia became similar to the utilisation in Sweden and significantly higher than in the UK, although still being below the E-8 average. The relative positions of bortezomib utilization in other E-8 countries did not change noticeably except in France where it became similar to that in Austria.

The utilisation of bortezomib is presented in Fig. 3.

3.4. *Cetuximab*

Among E-8 the first recorded usage of cetuximab was in Switzerland (first quarter of 2004). Utilisation of cetuximab in Slovenia commenced 0.75 years after the first usage in E-8, which is similar to other E-8 countries.

The biggest rise in the utilisation of cetuximab after entering the system, expressed per individual dying of colorectal cancer, was in France, Switzerland and Italy. Slovenia was, comparable to Sweden, relatively slow in introducing cetuximab into the healthcare system.

At the end of 2005 the highest utilisation of cetuximab per individual dying of colorectal cancer was in France and Switzerland. Slovenia had a substantially lower utilisation of cetuximab compared to the E-8 average (after the UK, the second lowest). When affordability of the country to uptake the drug was taken into account, the relative positions of cetuximab utilisation among E-8 countries did not change noticeably.

The utilization of cetuximab is presented in Fig. 4.

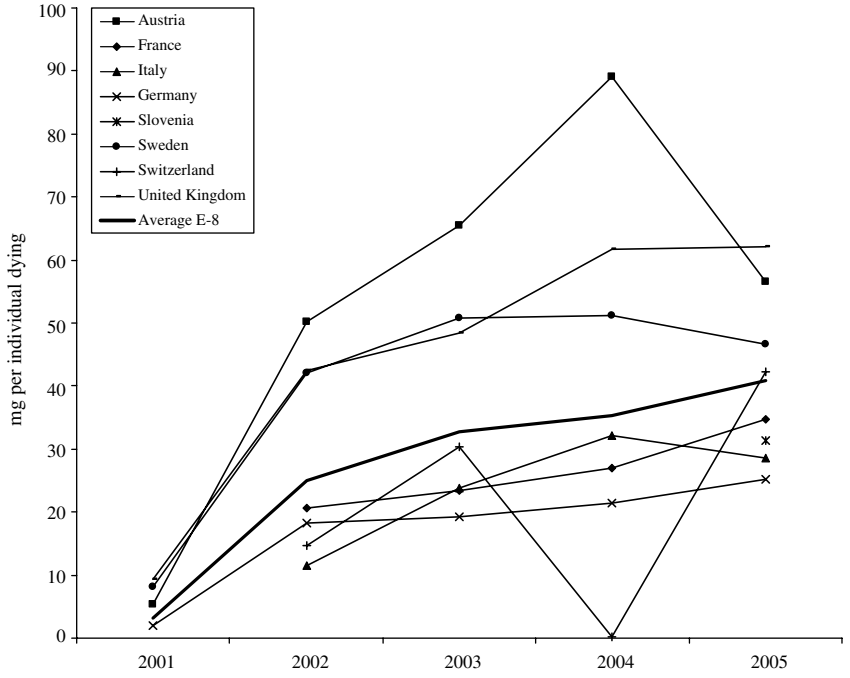

Fig. 1 – Utilisation of alemtuzumab in E-8 in mg per individual dying of leukaemia (yearly data).

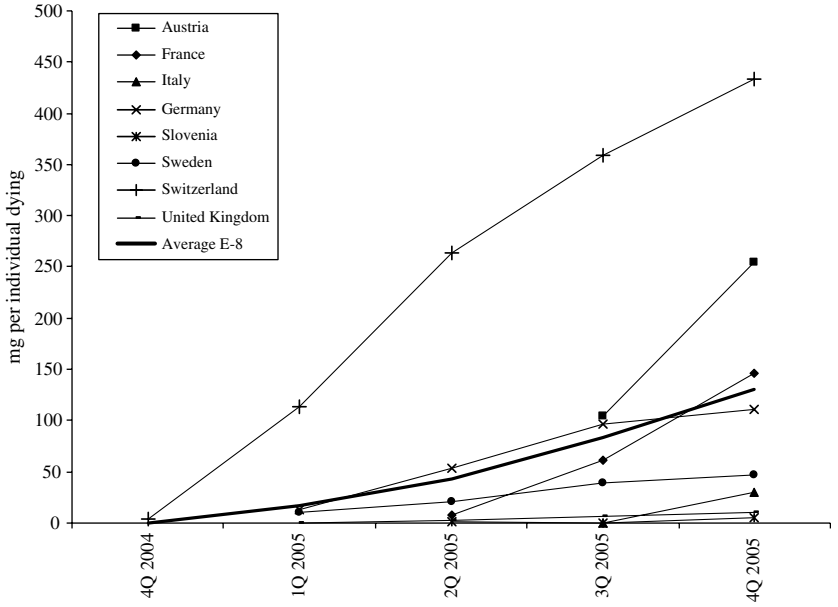

Fig. 2 – Utilisation of bevacizumab in E-8 in mg per individual dying of colorectal cancer (quarter of the year data).

3.5. *Erlotinib*

Among E-8 the first recorded usage of erlotinib was in Switzerland (first quarter of 2005). Utilisation of erlotinib in Slovenia commenced 0.5 years after the first usage in E-8, which is similar to other E-8 countries (with the exception of Italy, where the utilisation of erlotinib was not recorded until the end of 2005).

The biggest rise in the utilisation of erlotinib after entering the system, expressed per individual dying of tracheal, bronchial and pulmonary cancer, was in Austria and Germany. The utilisation in Austria became similar to the utilisation in Switzerland soon after the uptake, despite the fact that erlotinib was first available in Switzerland. At the entry of erlotinib into the Slovenian healthcare system, its utilisation was placed at a relatively low level, comparable to the UK. As the entry of erlotinib in any of the E-8 countries began in 2005, the analysis of utilisation trends is limited.

At the end of 2005 the highest utilisation of erlotinib per individual dying of tracheal, bronchial and pulmonary cancer

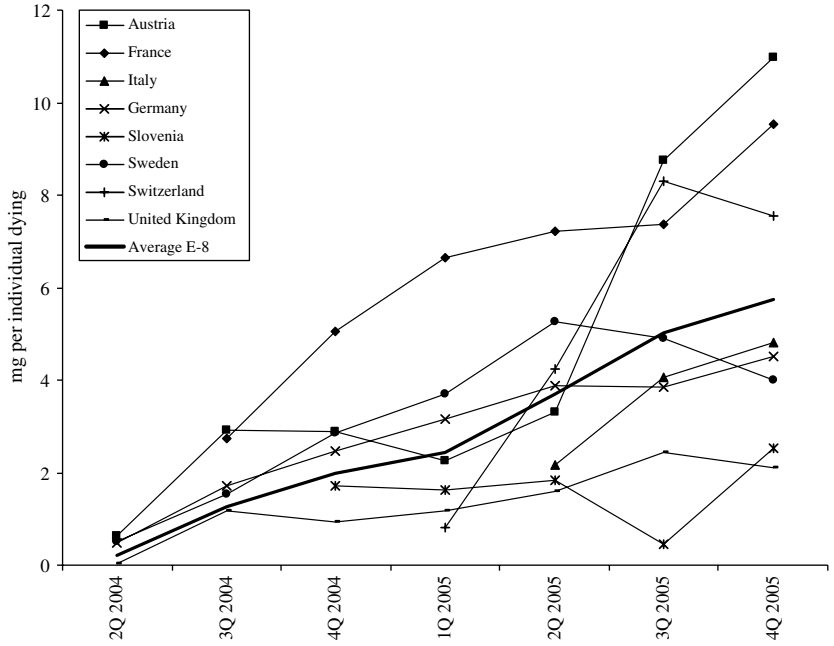

Fig. 3 – Utilisation of bortezomib in E-8 in mg per individual dying of multiple myeloma (quarter of the year data).

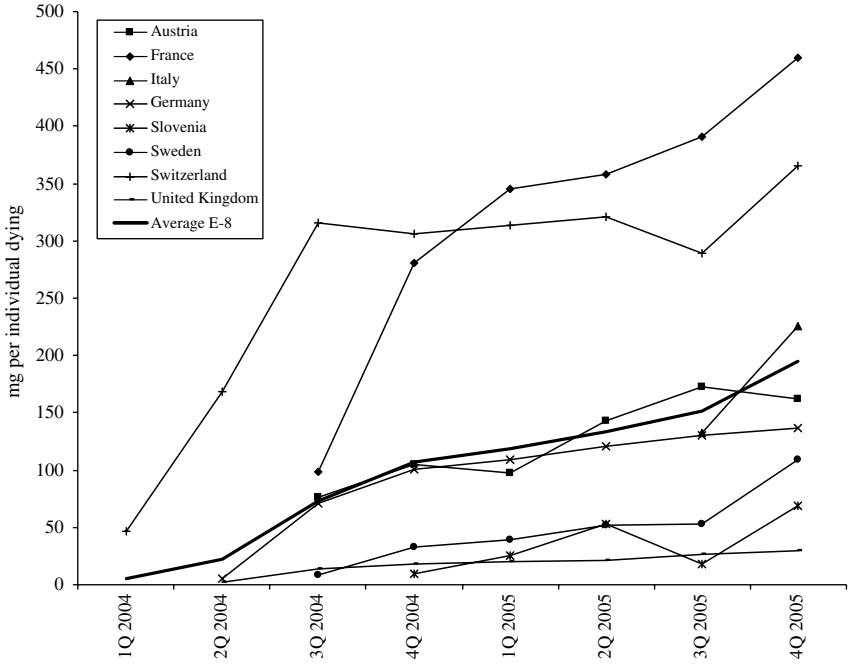

Fig. 4 – Utilisation of cetuximab in E-8 in mg per individual dying of colorectal cancer (quarter of the year data).

was in Switzerland and France. Slovenia had a substantially lower utilisation of erlotinib compared to the average E-8 utilisation. When affordability of the country to uptake the drug was taken into account, the relative positions of erlotinib utilisation among E-8 countries did not change noticeably.

The utilisation of erlotinib is presented in Fig. 5.

3.6. *Ibritumomab*

Among E-8 the first recorded usage of ibritumomab was in Sweden (first quarter of 2004). Utilisation of ibritumomab in France, Slovenia, Switzerland and the UK was not recorded until the end of 2005.

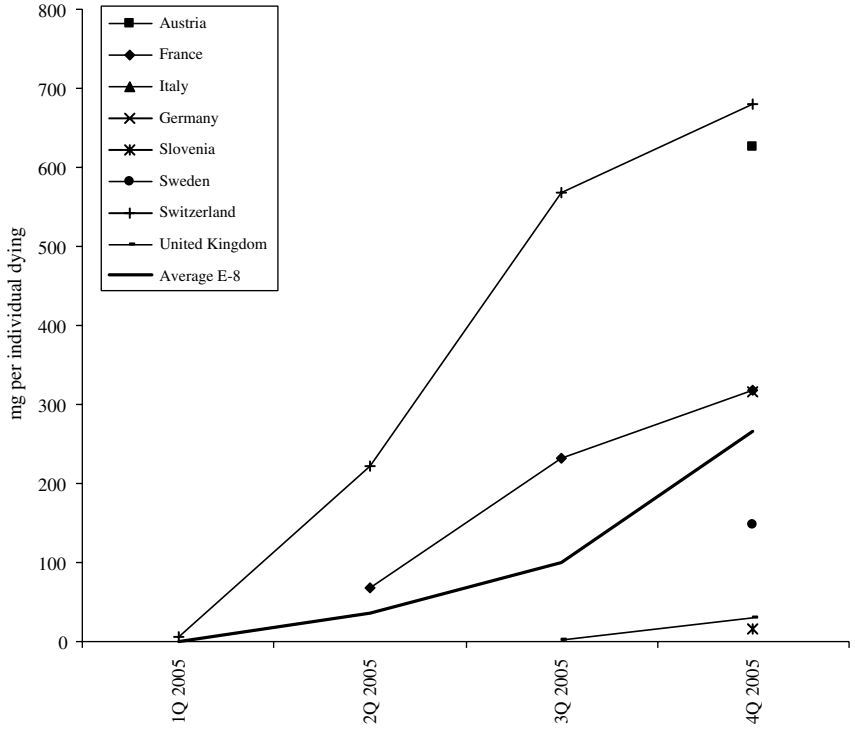

Fig. 5 – Utilisation of erlotinib in E-8 in mg per individual dying of trachea, bronchus or lung cancer (quarter of the year data).

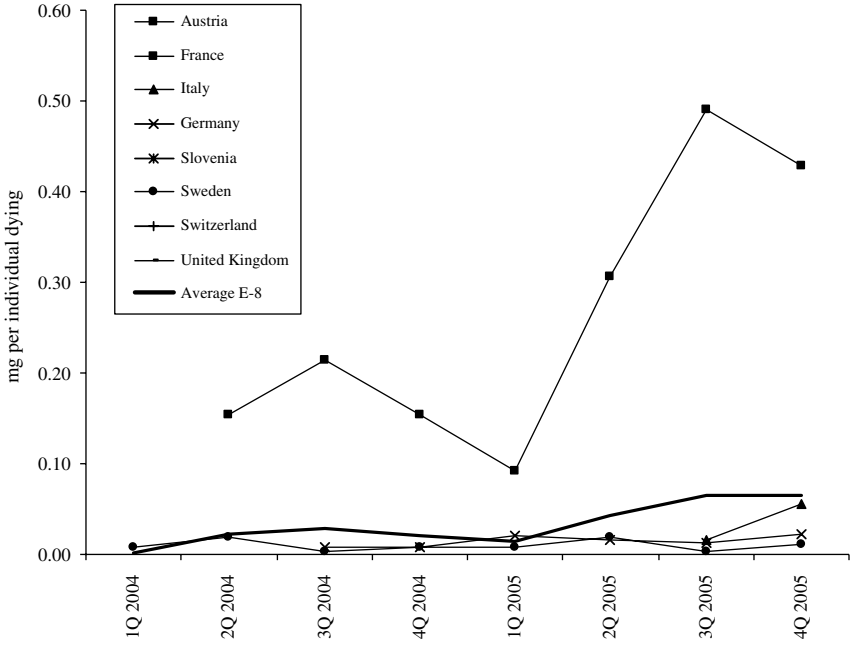

Fig. 6 – Utilisation of ibritumomab in E-8 in mg per individual dying of Non-Hodgkin lymphoma (quarter of the year data).

The biggest rise in the utilisation of ibritumomab after entering the system, expressed per individual dying of Non-Hodgkin lymphoma, was in Austria. All other countries had a substantially lower rise in the utilisation or no utilisation at all.

At the end of 2005 the highest utilisation of ibritumomab per individual dying of Non-Hodgkin lymphoma was in Austria. When affordability of the country to uptake the drug was taken into account, the relative positions of ibritumomab utilisation among E-8 countries did not change noticeably.

The utilisation of ibritumomab is presented in Fig. 6.

3.7. *Imatinib mesylate*

Among E-8 the first recorded usage of imatinib mesylate was in France, Slovenia and Switzerland (third quarter of 2001). In

the rest of the E-8 countries the first usage of imatinib mesylate was recorded mostly one quarter of the year later.

The biggest rise in the utilisation of imatinib mesylate after entering the system, expressed per individual dying of leukaemia, was in France, Austria and Switzerland. Slovenia had the lowest rise in utilisation of imatinib mesylate among the E-8 countries.

In 2005 the highest utilisation of imatinib mesylate per individual dying of leukaemia was in France, Austria and Switzerland. Slovenia had the lowest utilisation of imatinib mesylate among the comparison countries. When affordability of the country to uptake the drug was taken into account, the utilisation of imatinib mesylate in Slovenia joined the utilisation in most of the other E-8 countries, and became similar to that in the UK. In France the utilisation became outstanding compared to the rest of the E-8 countries.

The utilisation of imatinib mesylate is presented in Fig. 7.

3.8. *Rituximab*

Among E-8 the first recorded usage of rituximab was in Switzerland (fourth quarter of 1997). Utilisation of rituximab in Slovenia was first recorded 3.25 years later, which is the latest among E-8 countries.

The biggest rise in the utilisation of rituximab after entering the system, expressed per individual dying of Non-Hodgkin lymphoma, was in Austria, Slovenia and Switzerland.

In 2005 the highest utilisation of rituximab per individual dying of Non-Hodgkin lymphoma was in Austria, Switzerland and France. Slovenia had the lowest utilisation of rituximab among the comparison E-8 countries. When affordability of the country to uptake the drug was taken into account, the utilisation of rituximab in Slovenia became similar to that in Germany. The relative positions of rituximab utilisation in other E-8 countries did not change noticeably except in France where the utilisation became higher than in Switzerland.

The utilisation of rituximab is presented in Fig. 8.

3.9. *Trastuzumab*

Among E-8 the first recorded usage of trastuzumab was in France and Switzerland (third quarter of 1999). Utilisation of trastuzumab in Slovenia was first recorded 1.5 years after the first usage in E-8, which is similar to other E-8 countries.

The biggest rise in the utilisation of trastuzumab after entering the system, expressed per individual dying of breast cancer, was in Austria, Italy and Switzerland. Since the third quarter of 2003 the utilisation of trastuzumab in Slovenia has risen extraordinarily.

In 2005 the highest utilisation of trastuzumab per individual dying of breast cancer was in Austria and Switzerland. At the end of 2005 the utilisation of trastuzumab in Slovenia was almost identical to the utilisation in Germany. When affordability of the country to uptake the drug was taken into account, the utilisation of trastuzumab in Slovenia rose above the average utilisation of E-8 countries and became similar to that in Italy. The relative positions of trastuzumab utilisation in other E-8 countries changed noticeably with France, where it became slightly higher than in Austria, and Italy, where it rose above the utilisation in Sweden.

The utilisation of trastuzumab is presented in Fig. 9.

4. Discussion

The time of introduction of targeted oncology drugs in Slovenia was in most cases similar to the selected European countries, except for alemtuzumab and rituximab, where Slovenia

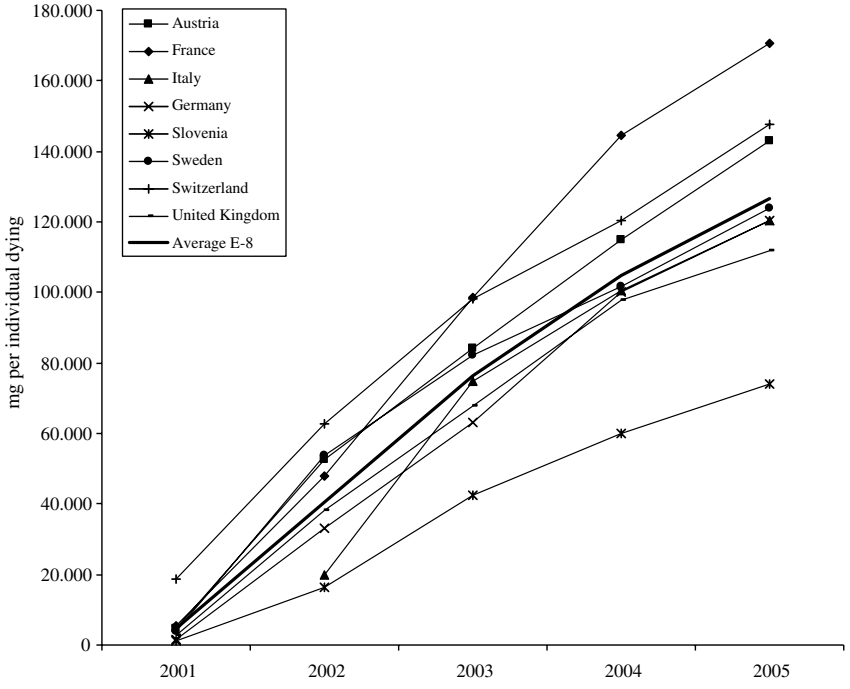

Fig. 7 – Utilisation of imatinib mesylate in E-8 in mg per individual dying of leukaemia (yearly data).

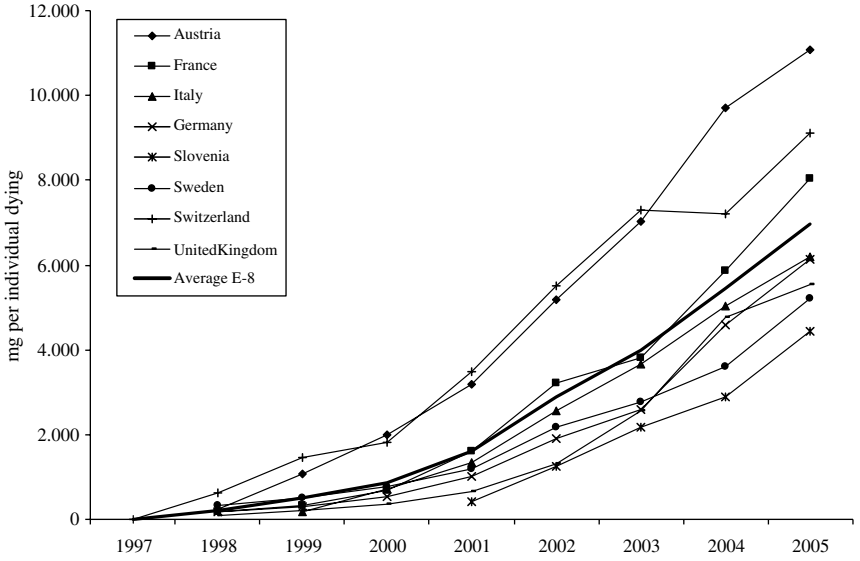

Fig. 8 – Utilisation of rituximab in E-8 in mg per individual dying of Non-Hodgkin lymphoma (yearly data).

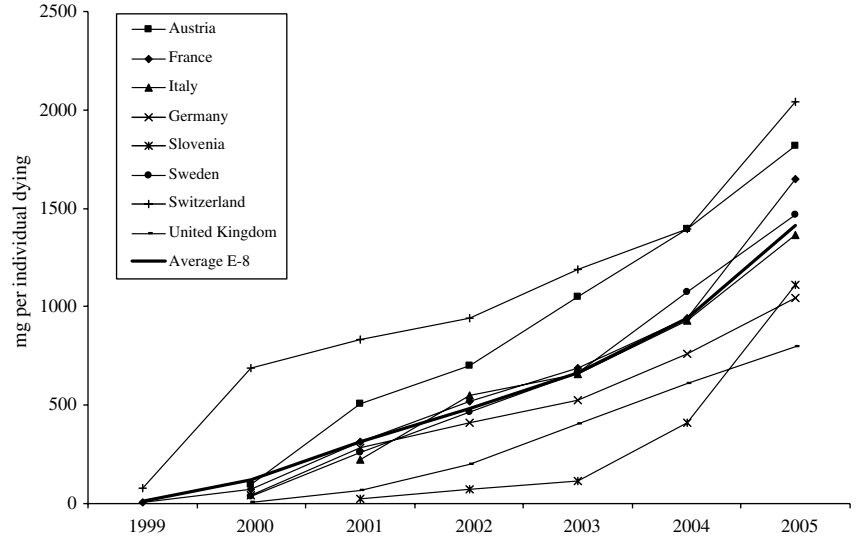

Fig. 9 – Utilisation of trastuzumab in E-8 in mg per individual dying of breast cancer (yearly data).

was lagging behind. On the contrary, the utilisation of targeted oncology drugs in Slovenia was in most cases lower than in other comparison countries. Namely, the utilisation of bevacizumab, bortezomib, cetuximab, erlotinib, imatinib mesylate and rituximab was much below the E-8 average. Ibritumomab had not been used in Slovenia until the end of 2005, similar to France, Switzerland and the UK. In contrast to the above findings was the utilisation pattern of trastuzumab in Slovenia, where the uptake in the first years after introduction was significantly lower compared to the other countries. However, after 2003, the utilisation of trastuzumab in Slovenia started to rise substantially, approaching the average use in E-8 in 2005.

Burden of disease, which is typically represented by incidence and mortality, is one of the strongest drivers for uptake of new drugs for a certain disease. Hence, the differences in the burden of cancer between comparison countries can result in the different impetus to implement new treatment strategies. Furthermore, even within a country, the differences in the burden of specific cancer type can lead to the differential allocation of resources within oncology area.

In Slovenia the incidence rate of the majority of cancer types considered in the analysis was the lowest among E-8 countries (see Table 3). On the contrary, the mortality rate was at the average of E-8 (see Table 2). Therefore, Slovenia had a relatively high mortality rate in relation to the incidence rate. This is particularly evident in the case of breast cancer, for which trastuzumab was indicated. The substantial rise in the utilisation of trastuzumab in 2003, compared to other targeted drugs available at that time, could be seen as a potential response to the needs in practice. However, in the case of trastuzumab, two other potential driving forces should be mentioned. Namely, the excellent organisation of breast cancer patients in Slovenia together with the high empathy

towards female specific cancer represented an important influence on public opinion as well as on healthcare policy makers. Furthermore, trastuzumab treatment strategy was the only treatment among targeted oncology drugs that included routine diagnostic testing in order to maximise treatment effectiveness (HER2 over-expression in the case of trastuzumab).

Other possible explanations for the differences in utilisation of targeted oncology drugs in Slovenia compared to the selected European countries are differences in the purchasing power, allocation of resources for health, prioritisation of oncology area compared to other disease areas, and the position of pharmacotherapy in clinical practice compared to surgery and radiotherapy.

Affordability of a specific country was evaluated by its gross domestic product per capita expressed in purchasing power standards, which are reflecting pricing relations among countries. In 2005, Slovenia had the GDP per capita according to purchasing power less than 20,000 standard units. All other countries except Italy had the GDP per capita according to purchasing power above 25,000; Switzerland was even above 30,000 standard units. Italy had the GDP per capita according to purchasing power of approximately 23,000 standard units. Taking into account the affordability of a specific country to uptake the new drug, the relative position of utilisation for all targeted oncology drugs in Slovenia moved slightly to a higher level compared to other E-8 countries. However, the shift was only significant in the case of alemtuzumab, rituximab and trastuzumab where the extent of utilisation was at the E-8 average level or higher.

The selected countries varied in the percentage of GDP allocated for health from 8.0% in the UK to 11.4% in Switzerland, for the period 2001–2005.[9] The Slovenian health expenditure did not differ from the above range and amounted to 8.8% of GDP. Therefore, the allocation of resources for health compared to other areas was not the key factor that could explain the low utilisation of targeted oncology drugs in Slovenia. Furthermore, the significantly higher growth of expenditure for oncology drugs compared to overall growth of drug expenditure in the time horizon of the study does not indicate that oncology was an under-resourced pharmacotherapy area in Slovenia.[10] However, a comparison of finances available for the oncology area and specifically for cancer pharmacotherapy, surgery and radiotherapy would be necessary to get an additional insight into the reasons for the differences in the utilisation of targeted oncology drugs between selected countries.

In the present study, the utilisation of targeted oncology drugs was expressed in mass unit per individual dying in order to circumvent the problem of differential drug pricing between selected countries and to make the comparison possible. Such differences were reported, for example, by Jönsson and Wilking, where prices of oncology drugs in France and Switzerland were in general higher than in the UK.[3] In order to compute the above utilisation index, mortality data from the Globocan 2002 database was used for the whole period of the analysis. Namely, specific mortality data for each year of the time horizon in the analysis was not available for all the countries. However, cancer mortality is not expected to change significantly over the relatively short time horizon that was used in the analysis.

Ideally, the utilisation of specific drugs should be weighted against the number of patients that obtained it. The present analysis weighted the utilisation of targeted oncology drugs against the mortality of cancer type for which the drug was registered. Another possible approach would be to weight the utilisation by the incidence or the number of inhabitants. As all the drugs in the analysis had been used for advanced, metastatic stages of disease in the selected time horizon, mortality weight is more appropriate than incidence. Furthermore, the results of an alternative analysis that weighted the utilisation of targeted oncology drugs against the incidence of cancer type did not change the study conclusions. In most cases the utilisation patterns were similar to those used in the analysis based on the mortality data. An exception was trastuzumab where the utilisation in Slovenia was positioned at a higher level due to higher mortality in relation to the incidence in Slovenia compared to other countries. Nonetheless, the number of inhabitants in selected countries would not take into account the variability of cancer burden among selected countries and therefore does not seem to be an optimal possible choice.

Cancer type categories used in the analysis were based on the categories used in the Globocan 2002 database. Therefore, cancer type categories covered a wider range of cancer subtypes than the range covered by the registered indications of selected drugs. Such an assumption was necessary in order to make the comparison between countries possible based on the availability of reliable mortality data. Furthermore, the assumption is not expected to have a significant influence on study findings. A specific assumption was also made in the case of imatinib mesylate which was indicated for the treatment of different types of leukaemia as well as for the treatment of gastrointestinal stromal tumours. As gastrointestinal stromal tumours are rare types of gastrointestinal cancer, mortality data for leukaemia only were considered.

The current study only took into account the indications that were relevant before the end of year 2005, which is concordant with the time horizon of the analysis. After the year 2005 new indications were registered by the European Agency for the Evaluation of Medicinal Products for most of the targeted oncology drugs included in the analysis. Furthermore, additional targeted oncology drugs were launched to the market.

In conclusion, a low utilisation of most of the targeted oncology drugs in Slovenia compared to selected European countries limits the possibility for the state-of-the-art care of cancer patients. Patients, however, wish the best possible care available at a particular time regardless of the country or healthcare system. On the contrary, all the healthcare systems operate with limited budgets. An optimal standard of care in a particular system with scarce resources can be achieved by adequate and systematic health technology assessments in order to establish the benefits as well as costs in comparison to the existing standard of care. Currently, health economics is not part of formal decision processes in the Slovenian healthcare system. Moreover, how the society and individual patient groups perceive the benefits of new treatment strategies has not been adequately studied. In this regard reference values such as additional cost per Quality Adjusted Life Years Gained do not exist in general nor in oncology.

Nonetheless, advanced pharmacotherapy is relevant but not the only way to respond to the cancer burden in Slovenia that is particularly evident in the discrepancy between mortality and incidence. Besides pharmacotherapy, early cancer diagnosis as well as advanced surgery, radiotherapy and supportive care should be taken into account and evaluated as an alternative as well as combination treatment options.

Conflict of Interest Statement

Sales data obtained from PharMIS, MIS Consulting d.o.o. and IMS Health, IMS MIDAS were provided by Roche pharmaceutical company Ltd., Slovenia.

The authors do not declare other possible conflicts of interest.

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