Access to innovative cancer drugs in Poland in comparison with selected European Union countries and Switzerland

Report ordered by
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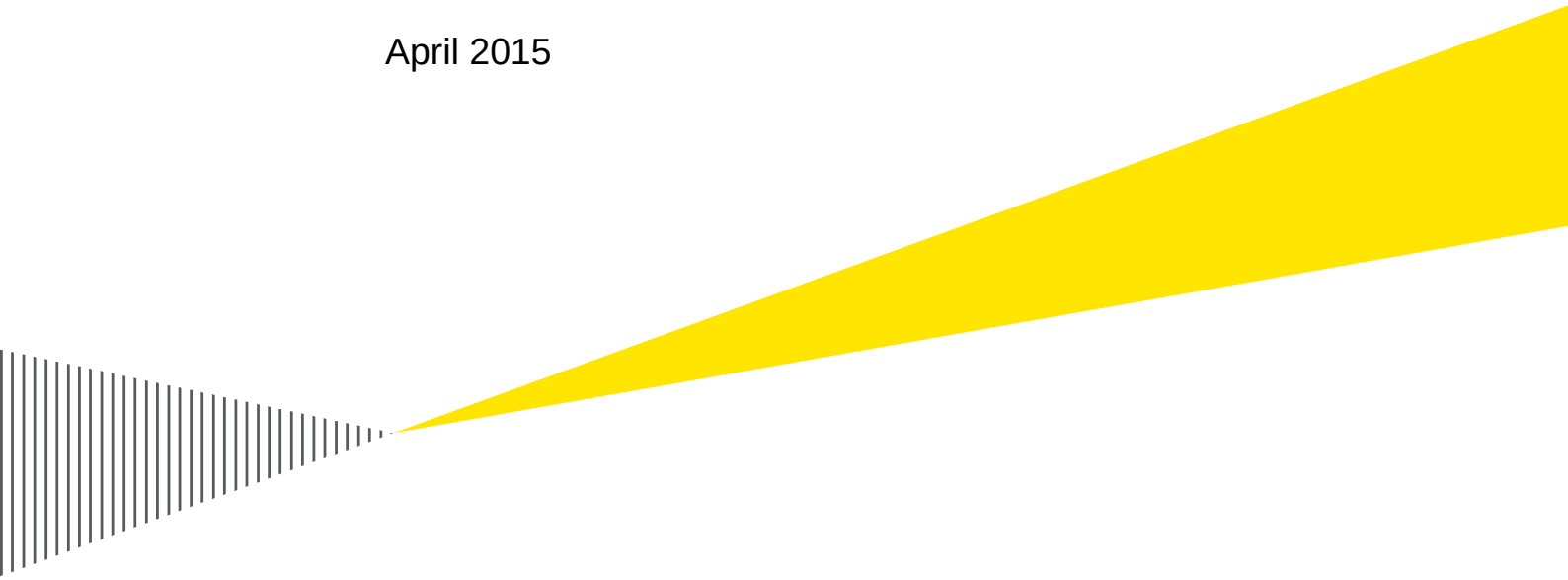

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Contents

1. Summary of analyses

Malignancies for years have been one of the most serious challenges for the health care systems. In the European Union countries, there are over 2.6 million new cases of cancer every year. Cancer is the second most common cause of death, accounting for over 1.2 million deaths. In Poland, more than 150,000 people are diagnosed with cancer every year. The Polish Cancer Society (PTO), in its report titled "Current Cancer Control in Poland", points to some alarming developments and anticipates a significant (over 25%) increase in the incidence of cancer in our country by 2025, as compared with 2011.

An analysis of 5-year survival rates in patients diagnosed with cancer puts Poland in the group of countries whose health care systems are least efficient in cancer patient care. The situation may further deteriorate with the anticipated increase in the incidence of cancer unless preventive measures are taken early enough.

Taking into account dramatically changing social conditions in Poland, cancer will pose a challenge to the social and economic stability of our country. Cancer is the main cause of death in individuals aged 20-64 years and the second leading cause of death in the entire population.
In this context, the problem of effectiveness of the current model of cancer care in Poland becomes a key one. The model includes:

- prevention (primary and secondary),
- early diagnostics,
- therapy,
- drugs used,
- rehabilitation, and
- palliative care.

In this report, the extent of drug use and access to modern cancer pharmacotherapy was analysed. Below, the results of the analyses concerning the availability of innovative cancer drugs are presented from two perspectives:

- the extent of reimbursement and
- the actual drug utilisation.

For this analysis, countries with developed health care systems as well as countries of our region have been selected. The analyses were conducted for Poland and 12 selected European countries, i.e. Austria, the Czech Republic, France, Germany, Hungary, Italy, the Netherlands, Romania, Slovakia, Spain, Switzerland and the United Kingdom (in this report referred to as “the 13 countries”).
In the analysis, 30 cancer drugs have been included which have been authorised for marketing by the European Medicines Agency (EMA) since 2004 and meet the following criteria:

a) high utilisation level as measured by sales in kilograms,

b) high sales value in the period of 12 months, i.e. 2013Q4–2014Q3.

These include: Abraxane, Adcetris, Afinitor, Alimta, Avastin, Dacogen, Erbitux, Halaven, Inlyta, Iressa, Jakavi, Jevtana, Kadcyla, Nexavar, Perjeta, Sprycel, Stivarga, Sutent, Tafinlar, Tarceva, Tasigna, Tyverb (Tykerb), Vectibix, Vidaza, Votrient, Xalkori, Yervoy, Yondelis, Zaltrap and Zelboraf, offered by 16 different global pharmaceutical companies. The selected drugs are used in treatment of the most common cancers, i.e. lung, colorectal, breast, and prostate cancer, and, among others,

in treatment of pancreatic, renal and hepatic tumours, as well as in treatment of leukaemia and Hodgkin lymphoma.
All the drugs reviewed in the report have been licensed for sale in the European Union by the European Medicines Agency (EMA) and have been authorised locally by the HTA authority[1] (Switzerland).

The analyses included the following main issues:

(1) the actual utilisation level of innovative drugs in individual countries, based on relative sales volumes (chapter 5);

(2) availability of the innovative drugs through reimbursement systems, with determination if the range of therapeutic indications approved in a specific country in which a specific drug is reimbursed does not significantly limit drug availability for patients (chapter 6);

(3) the time after which patients gain access to innovative drugs. For that purpose, the time that elapsed between the EMA's decision on granting marketing authorisation and the achievement of an adequate sales level was specified for all the investigated drugs and countries (chapter 7).

1 Swiss Health Technology Assessment

Basic information on methodology and definitions

1. **Available reimbursed drug** means that:
    a. a specific drug is reimbursed;
    b. reimbursement conditions do not limit the group of patients in whom a specific drug may be used in relation to the indications approved by the EMA;
    c. the patient does not incur significant financial costs related to the access to a specific drug through the reimbursement system.

    In addition, **drug available with restricted access** means that:
    a) a specific drug is reimbursed;
    b) reimbursement conditions limit the group of patients in whom a specific drug may be used in relation to the indications approved by the EMA;
    c) access to a specific drug through the reimbursement system is associated with significant costs incurred by the patient because the payer would reimburse only a small portion of the purchase.

    Unavailable drug means that a specific drug is not reimbursed.

2. The comparison of utilisation of a specific drug between individual countries required the adoption of an appropriate comparative method (normalisation). For this purpose, the term **relative sales volume** was introduced, representing the number of standard packs sold per the number of deaths (in a specific country in 2011) caused by diseases in which a specific drug is indicated. Normalisation makes it possible to compare countries of different population size and epidemiology.

3. For every analysed drug, three countries (**TOP3 countries**) with the highest relative sales volume were identified. Mean relative sales volume in these countries was a reference point for the assessment of drug utilisation in other countries.

4. To define the extent of drug utilisation in a given country, the following levels were assumed:
    - **noticeable level:** 3% of the relative sales volume[2] in TOP3 countries
    - **considerable level:** 10% of the relative sales volume in TOP3 countries
    - **significant level**: 25% of the relative sales volume in TOP3 countries.

Basic data sources

The analyses presented in this report were performed using mainly the following data sources:

1. Epidemiology data
    - Incidence and 5-year survival: WHO – GLOBOCAN 2012 base
    - Mortality – EUROSTAT
2. Information on marketing authorisation in Europe and Switzerland:
    - European Medicines Agency (EMA)
    - Swiss Federal Office of Public Health (FOPH)
3. Data concerning drug sales:
    - PADDS IMS MIDAS Q3/2014, for 2004Q1–2014Q3

Other data sources are specified in the text, in places in which they are referred to.

[2] Sales in the period of 12 months, i.e. 2013Q4–2014Q3

Main observations and conclusions

The analyses presented in this report show that cancer patients in Poland have more restricted access to innovative cancer drugs than patients in other countries.

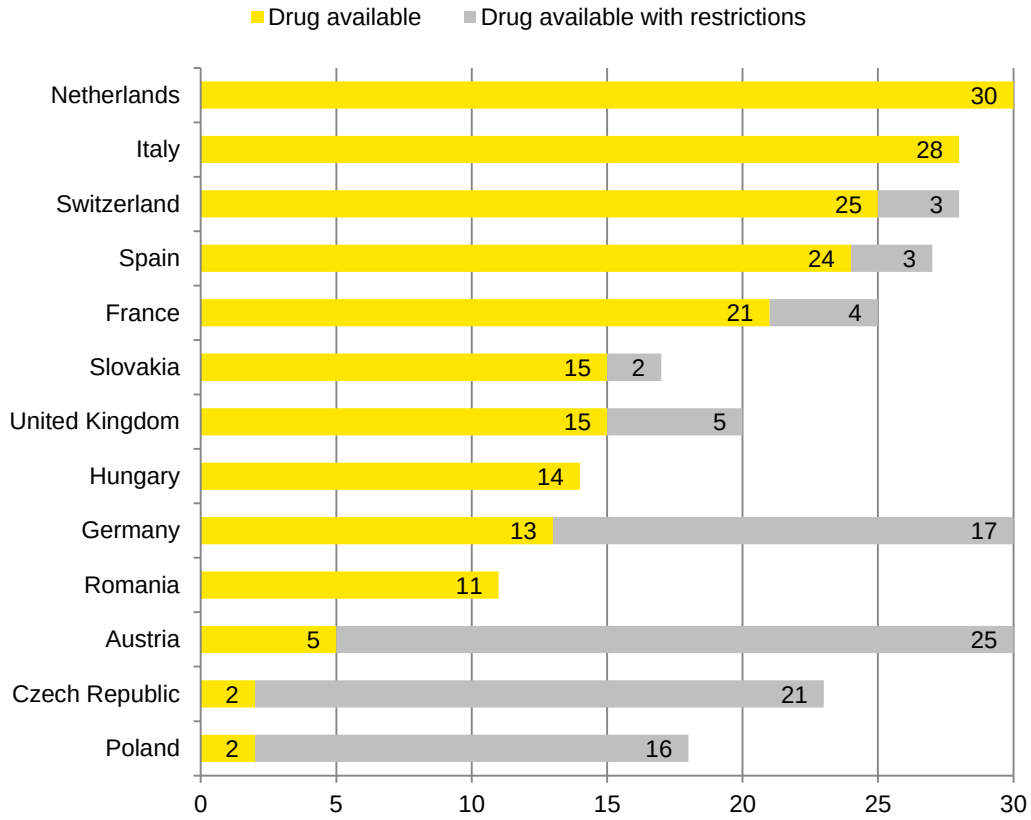
1. **In Poland, only two innovative cancer drugs are reimbursed without any restrictions in relation to the indications approved by the EMA, and this is the lowest number of all the countries included in the analysis.**
2. **In Poland, drug utilisation – even that of reimbursed drugs – is very low in comparison with the other investigated countries.**
3. **The drugs are placed on the reimbursement list late, which is reflected by the period of time that elapses between the EMA's authorisation and the achievement of a noticeable level of drug utilisation. This period is one of the longest in all the investigated countries.**

In Poland, access to cancer drugs is provided in therapeutic programmes and chemotherapy programmes introduced by the Ministry of Health. In therapeutic programmes, additional criteria for drug application are defined. Those criteria are more stringent than the indications approved by the EMA. This makes access to innovative therapies difficult for Polish patients.

In our country (in January 2015), only 2 of the 30 analysed drugs were available without restrictions regarding therapeutic indications. This is the lowest number of innovative drugs available without restrictions in all the 13 investigated countries. Another 16 innovative drugs were available in therapeutic programmes, with restrictions concerning therapeutic indications.

The total number of 18 reimbursed drugs is one of the lowest numbers in the investigated countries.

Graph 1. Access to 30 innovative cancer drugs through reimbursement systems, status as of January 2015.



Source: own material; 1) Poland: http://www.mz.gov.pl/leki/refundacja/programy-lekowe, 2) The Netherlands: http://www.medicijnkosten.nl; 3) Germany: http://www.akdae.de/Stellungnahmen/AMNOG/A-Z/index.html; 4) Austria: EKO: http://www.erstattungskodex.at/portal27/portal/hvbportal/content/contentWindow?contentid=10007.693707&action=2&viewmode=content; 5) Italy: AIFA: http://www.agenziafarmaco.gov.it/it/content/liste-di-trasparenza-e-rimborsabilit%C3%A0; 6) Switzerland: FOPH: http://www.bag.admin.ch/themen/krankenversicherung/00263/00264/00265/index.html?lang=en; 7) Spain: http://Vademecum.es;8) France: http://base-donnees-publique.medicaments.gouv.fr/index.php#result; 9) Czech Republic: SUKL: http://www.sukl.eu/; 10) United Kingdom: CDF: http://www.ppa.org.uk/edt/February_2015/mindex.htm, 11) Slovakia: SUKL: http://www.sukl.sk/; 12) Hungary: OEP:http://www.oep.hu/iframes/gyogyszerkereso,http://www.oep.hu/felso_menu/lakossagnak/ellatas_magyarorszagon/egeszsegugyi_ellatasok/Spec_ellatas/teteles_gyogyo.html; 13) Romania: CNAS: http://www.cnas.ro/page/lista-medicamentelor-2015.html. Accessed on: 30 January 2015

A detailed list of drugs and their availability or restricted access in individual countries are presented in table 1.

Table 1. Availability of drugs through reimbursement systems, status as of January 2015.

Drug	Poland	Netherlands	Germany	Austria	Italy	Switzerland	Spain	France	Czech Republic	United Kingdom	Slovakia	Hungary	Romania
ABRAXANE													
ADCETRIS													
AFINITOR													
ALIMTA													
AVASTIN													
DACOGEN													
ERBITUX													
HALAVEN													
INLYTA													
IRESSA													
JAKAVI													
JEVTANA													
KADCYLA													
NEXAVAR													
PERJETA													
SPRYCEL													
STIVARGA													
SUTENT													
TAFINLAR													
TARCEVA													
TASIGNA													
TYVERB													
VECTIBIX													
VIDAZA													
VOTRIENT													
XALKORI													
YERVOY													
YONDELIS													
ZALTRAP													
ZELBORAF													
No. of drugs available	2	30	13	5	28	25	24	21	2	15	15	14	11
No. of drugs available with restrictions	16	0	17	25	0	3	3	4	21	5	2	0	0
Total	18	30	30	30	28	28	27	25	23	20	17	14	11

– available (reimbursed)
– available (reimbursed) with restrictions
– unavailable (not reimbursed)

Source: Authorised websites of the entities involved in reimbursement, detailed information: see source information to graph 1.

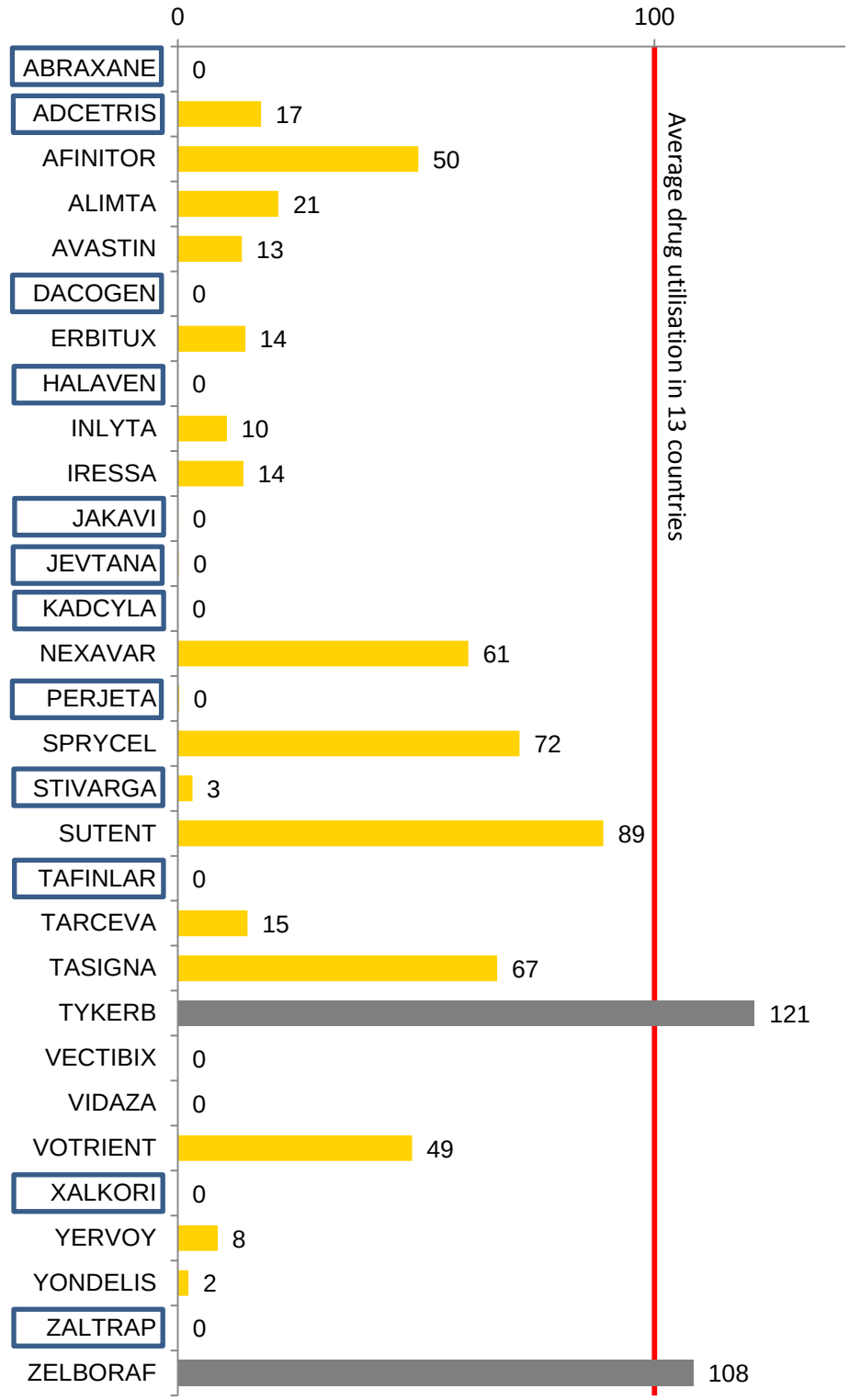
The utilisation level of innovative drugs in Poland – in comparison with the mean utilisation level in the 13 investigated countries – is one of the lowest. Only in two cases, the utilisation level exceeded the mean value for the analysed 13 European countries. This applies to Tyverb (Tykerb; used in treatment of breast cancer) and Zelboraf (used in patients with skin cancer). The utilisation level of 10 reimbursed drugs does not exceed 25% of the mean level in 13 countries.

Based on these analyses, it may be observed that in Poland exceptionally stringent criteria for placing innovative drugs on the reimbursement list have been adopted, which significantly limits their use.

Low utilisation level of innovative drugs, as measured by their sales volume, is caused by numerous restrictions with respect to the EMA-approved indications assumed in therapeutic programmes. This means reduction of the public payer's expenses but also reduction of the population of patients who might benefit from innovative therapies.

In addition, it should be noticed that Poland fails to benefit from favourable prices which provide an opportunity to offer access to innovative therapies to a larger group of patients at a relatively lower cost. As shown in chapter 5, in Poland prices of innovative cancer drugs are usually lower than mean prices in the 13 investigated countries.

Graph 2. Comparison of drug utilisation level in Poland and in the 13 analysed countries (100 = mean utilisation level in the 13 countries*) between 2013Q4 and 2014Q3



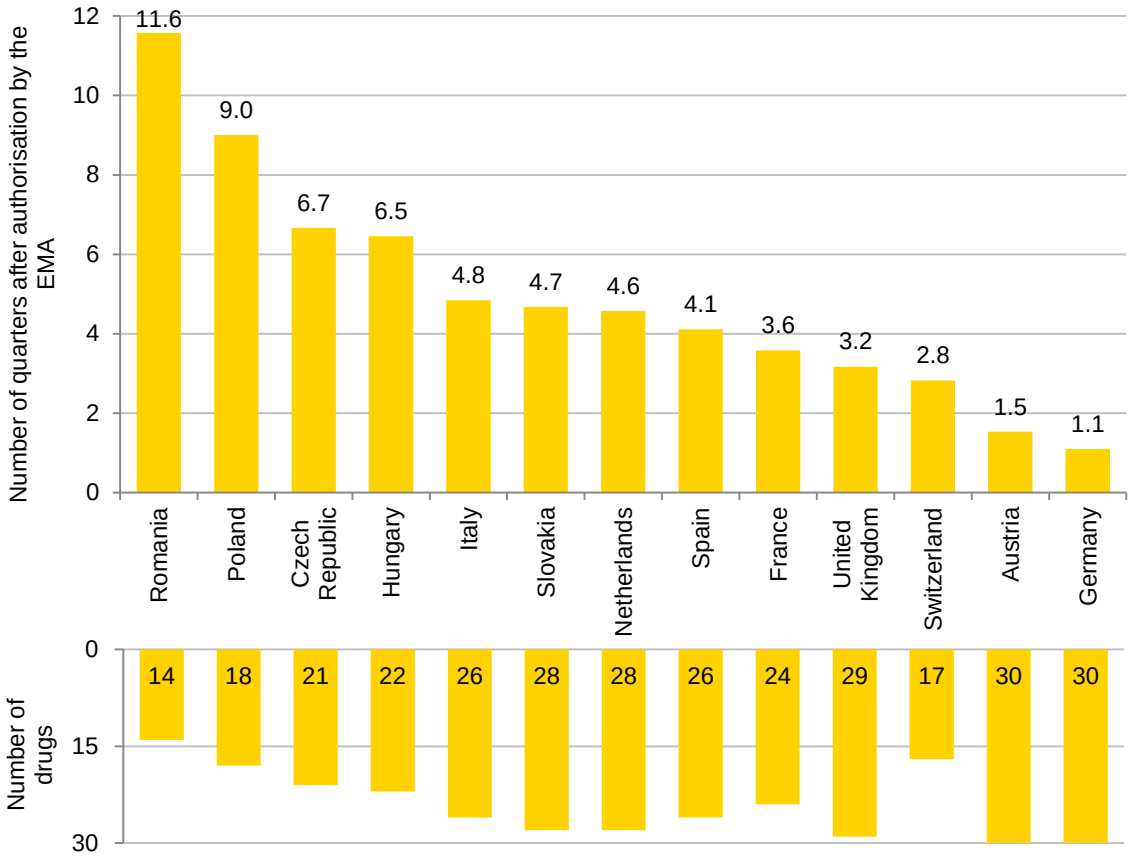
*) *The 13 countries are: Austria, the Czech Republic, France, Germany, Hungary, Italy, the Netherlands, Poland, Romania, Slovakia, Spain, Switzerland, and the United Kingdom.*

☐ *A drug not reimbursed in Poland.*

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

In cancer, time factor is one of the key elements affecting treatment efficacy. In order to see how quickly patients gain actual access to the drugs, we analysed the time (in quarters) between authorisation by the EMA and the achievement of a noticeable utilisation level in a specific country.
In Poland, a noticeable utilisation level is on average achieved as late as after nine quarters (i.e. over two years) following authorisation by the EMA. It is the second longest waiting time period in all countries included in the analysis (the longest waiting time of 12 quarters was observed in Romania).

Graph 3. Mean time (in quarters) between authorisation by EMA and the achievement of a noticeable utilisation level for innovative drugs.



The number of quarters was determined for the drugs for which a significant level was achieved
Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

In table 2 the period (in quarters) in which a noticeable utilisation level was achieved for individual drugs is presented.

Table 2. Mean time (in quarters) between authorisation by EMA and the achievement of a noticeable utilisation level for innovative drugs.

Drug	Poland	13 countries
ABRAXANE	N/A	11
ADCETRIS	4	0
AFINITOR	2	1
ALIMTA	17	2
AVASTIN	32	3
DACOGEN	N/A	2
ERBITUX	14	1
HALAVEN	level not achieved	2
INLYTA	7	1
IRESSA	14	3
JAKAVI	level not achieved	1
JEVTANA	2	1
KADCYLA	N/A	0
NEXAVAR	5	0
PERJETA	level not achieved	1
SPRYCEL	3	1
STIVARGA	level not achieved	1
SUTENT	3	0
TAFINLAR	level not achieved	1
TARCEVA	7	1
TASIGNA	6	2
TYKERB	0	0
VECTIBIX	15	2
VIDAZA	N/A	2
VOTRIENT	2	2
XALKORI	N/A	0
YERVOY	12	0
YONDELIS	13	2
ZALTRAP	level not achieved	1
ZELBORAF	4	0

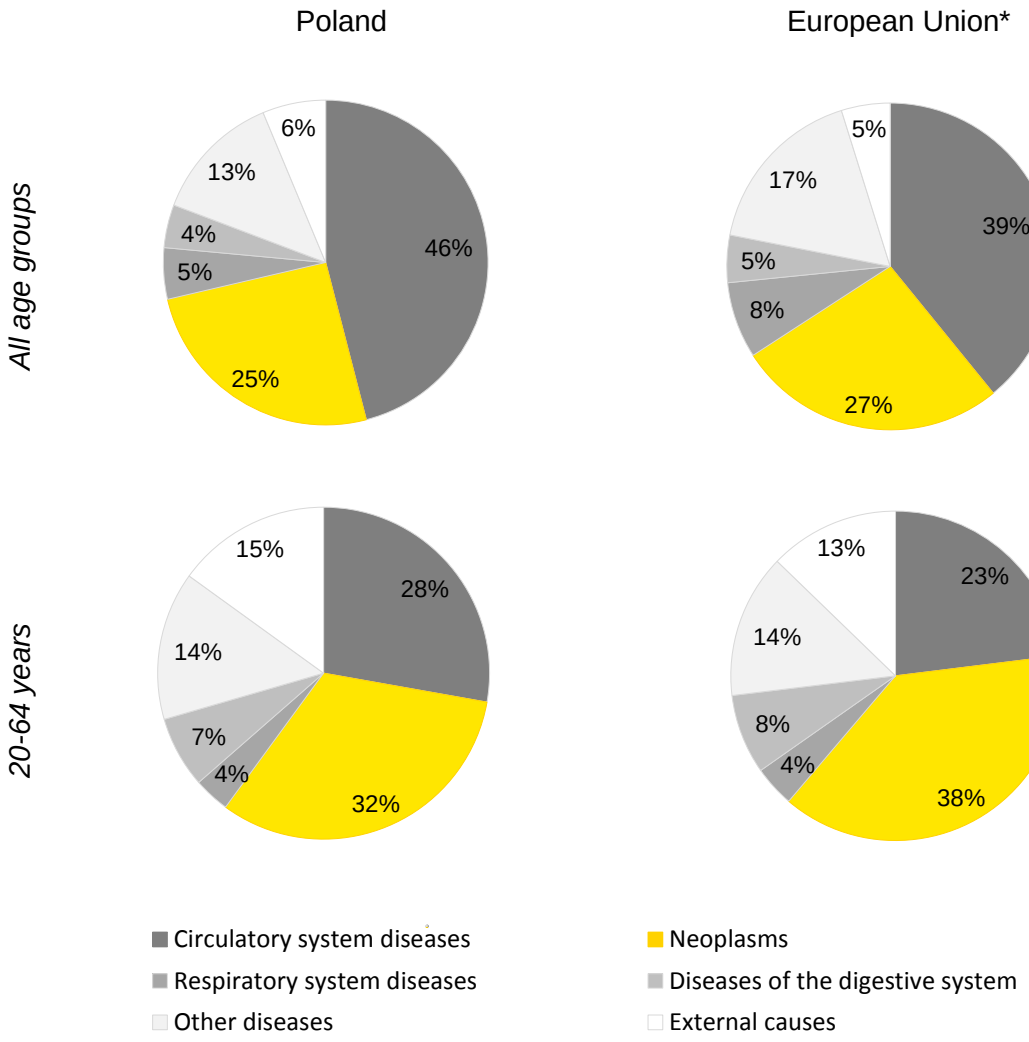
"0" means that the sale of a specific drug achieved a noticeable level in the same quarter in which the marketing authorisation was granted by the EMA.
Level not achieved – the sale of a specific drug did not achieve a noticeable level in the period between authorisation by the EMA and 2014Q3.
N/A – data concerning the sale of a specific drug in Poland were not available in the PADDS IMS MIDAS Q3/2014 database.
Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

2. The problem of cancer

Cancer poses a very serious and growing social problem in Europe and in Poland. For the last decades, the incidence of cancer has been increasing. The problem affects not only patients, but also their families and friends.

Malignancies are the second most common cause of death both in the EU (27%) and in Poland (25%). Moreover, they are the leading cause of death in individuals aged 20-64 years, accounting for 38% of deaths in the EU and 32% in Poland.

Graph 4. Death causes in Poland and in the European Union in all age groups and in individuals aged 20-64 years



*Source: WHO data for 2010; *without Greece due to lack of ICD-10 codes*

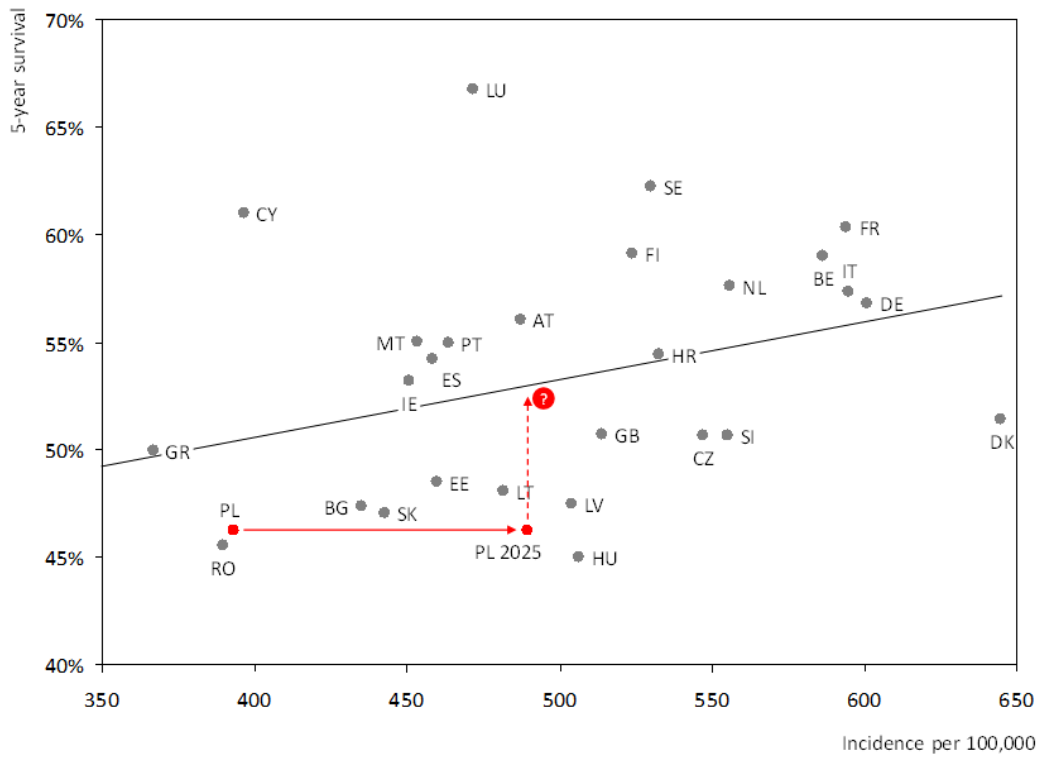
Despite huge efforts made by institutions responsible for shaping and implementing health care policies as well as the medical communities and patient organisations, malignancies for years have been one of the most serious challenges for the health care systems.

In the European Union countries, there are over 2.6 million new cases of cancer every year[3]. Cancer is the second leading cause of death, accounting for over 1.2 million deaths[4].

In 2012, over 150,000 individuals were diagnosed with cancer in Poland,[5] and the Polish Cancer Society (PTO), in its report titled 'Current Cancer Control in Poland', points to some alarming developments and anticipates a significant (over 25%) increase in the incidence of cancer in our country by 2025, as compared with 2011.

An analysis of 5-year survival rates in patients diagnosed with cancer puts Poland in the group of countries which are least successful in coping with cancer-related problems (see graph 2). The situation may further deteriorate with the anticipated increase in the incidence of cancer.

Graph 5. Cancer incidence and 5-year survival rates in European countries



Data sources: 5-year survival and incidence: Globocan, 2012; anticipated incidence in Poland in 2025: PTO (2014), Current Cancer Control in Poland

In many circles and communities, the opinion is voiced that cancer care effectiveness should radically improve and the standards and health technologies available in other European countries should be introduced.

[3] Overall cancer incidence (excluding non-melanoma skin cancer); source: GLOBOCAN 2012

[4] Mortality from all types of cancers (excluding non-melanoma skin cancers); source: GLOBOCAN 2012

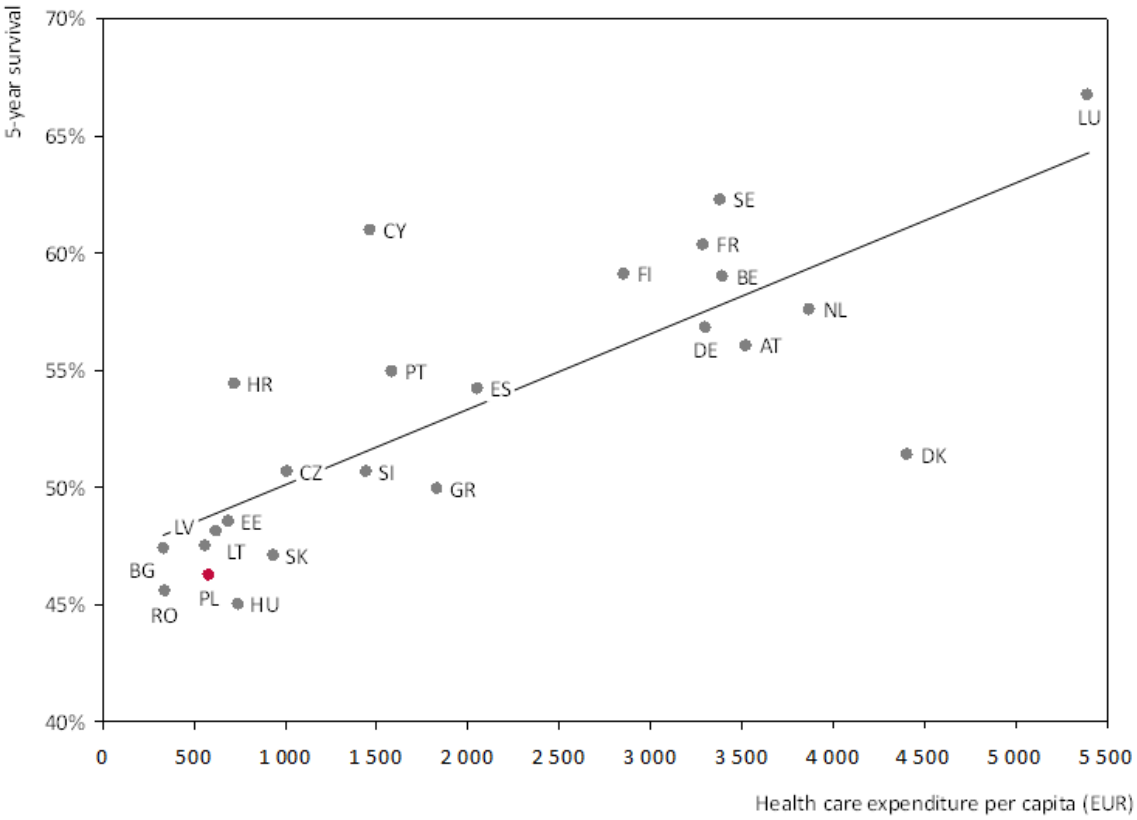
[5] GLOBOCAN 2012

To meet these expectations, cancer care must be adequately organised and resources necessary for effective prevention and treatment available.

Means applied to address the problem of adequate cancer care include the adoption of national cancer control strategies or programmes in individual countries. Coordinated, complex activities and the amount of financial resources allocated for health care have a significant impact on 5-year survival rates in cancer patients.

Indeed, as a rule, in higher-income countries with higher health care expenditure per capita, higher 5-year survival rates are observed (graph 6). It is also notable that even in high-income countries with annual expenditure of about EUR 3,500 per capita, the rates range considerably from 50% to 65%.

Graph 6. Health care expenditure per capita and 5-year survival rates in European countries

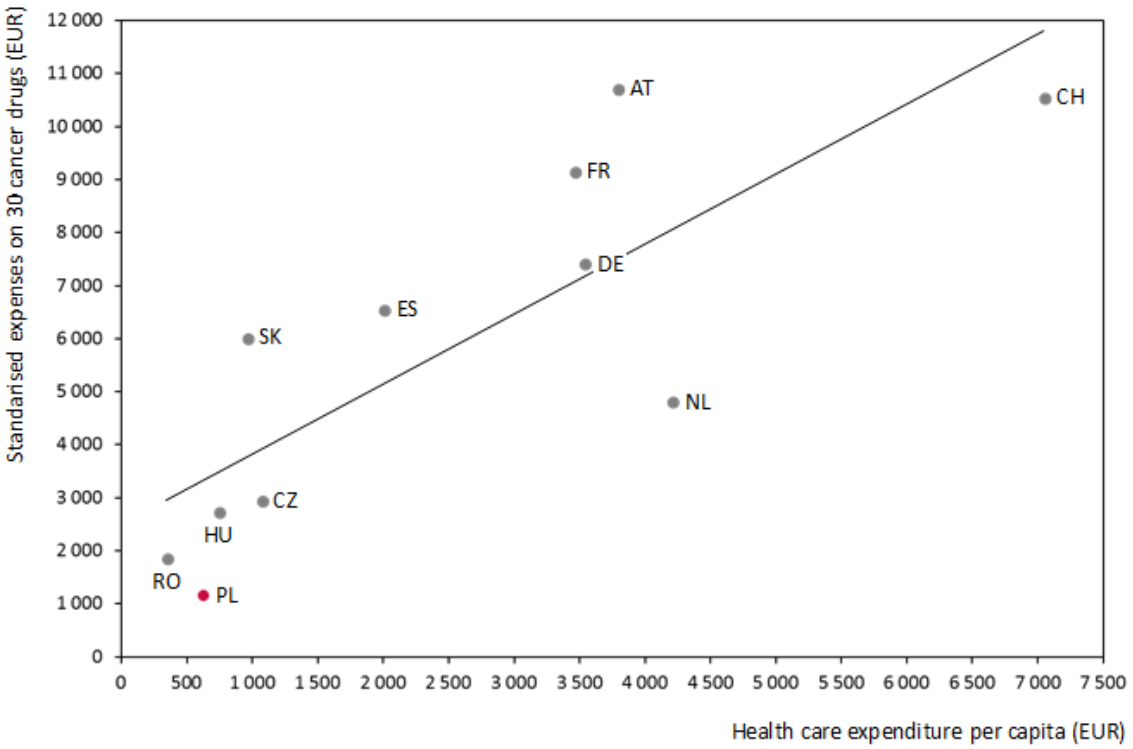


Source: EUROSTAT: health care expenditure per capita in the years 2007–2012; GLOBOCAN2012: 5-year survival rates in 2012

With respect to the expenses on the 30 analysed innovative drugs, one may see (graph 7) that the expenses are significantly higher in high-income Western European countries than in our region.

However, it is notable that even in high-income countries with annual health care expenditure of about EUR 3,500 per capita, a significant difference in expenses on innovative cancer drugs may be seen (cf. The Netherlands vs. France and Austria). Also in our region, significant differences in expenses on innovative drugs may be seen in countries in which annual health care expenditure is about EUR 1,000 per capita (cf. Poland vs. the Czech Republic and Slovakia), with the lowest expenses being incurred in Poland.

Graph 7. Health care expenditure per capita (2012) and standardised* expenses on 30 innovative cancer drugs (2013Q4 – 2014Q3).



**Expenses on the 30 cancer drugs were normalised using the number of deaths caused by malignancies for which the 30 drugs are indicated.*

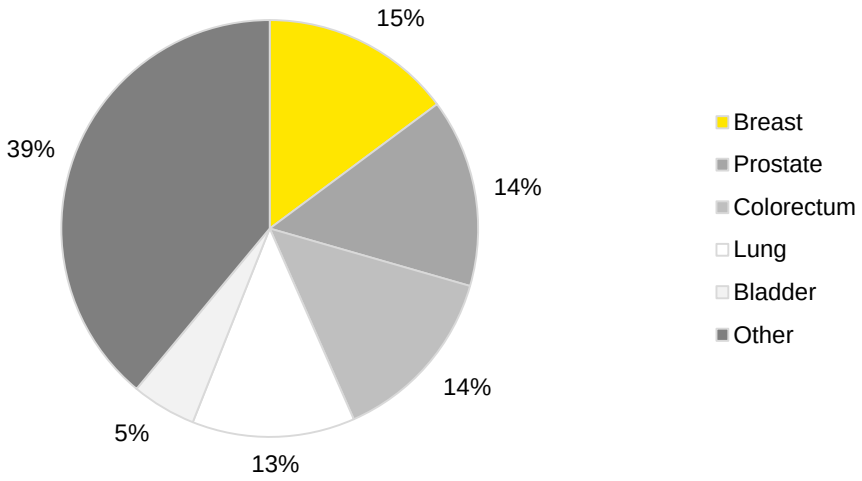
Source: EUROSTAT: health care expenditure per capita in 2012; PADDS IMS MIDAS Q3/2014: expenses on innovative cancer drugs.

2.1 Epidemiological data – Poland and other European countries

In this chapter, basic information concerning the scale of the cancer problem and the efficacy of therapeutic options used in Poland and in other European countries is presented. Data regarding the incidence and 5-year survival rates make it possible to consider and assess the scale of the cancer problem in Poland in the context of other countries.

Population health is measured by the incidence rate, i.e. the number of new cases or affected individuals in a specified period of time in the investigated population. Below, the overall cancer incidence rate (graph 8) and the rates for the most common cancers in the European Union (i.e. lung, colorectal, prostate, and breast cancer) are presented (graphs 9-12).

Graph 8. Incidence of individual types of cancer in 2012 in the EU countries.



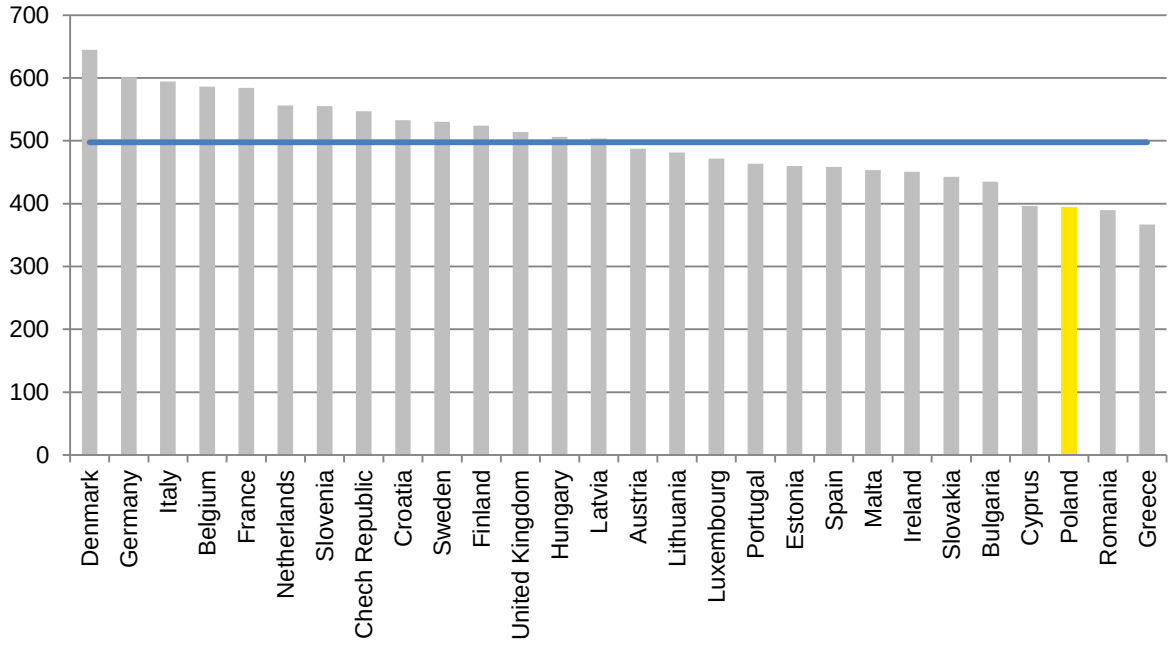
Source: GLOBOCAN 2012 data

In Poland, overall cancer incidence is lower than mean incidence in the EU, and amounts to 393 new cases per 100,000. Similar relationships were demonstrated for breast, prostate and colorectal cancer. Lung cancer is an exception – its incidence rate in Poland is one of the highest in the European Union. However, low incidence does not mean that cancer is not a significant problem in Poland. Actually, not all cases of cancer are detected, and some of them are identified only as the cause of death.

In 2010, cancer was the second leading cause of death in all age groups in Poland, and the leading cause of death in individuals aged 20-64 years. It is anticipated that in 10 years cancer will become the most common cause of death[6]. The number of new cases will increase by 30,000 in one decade, and will reach 185,000 new cases per year in 2025[7].

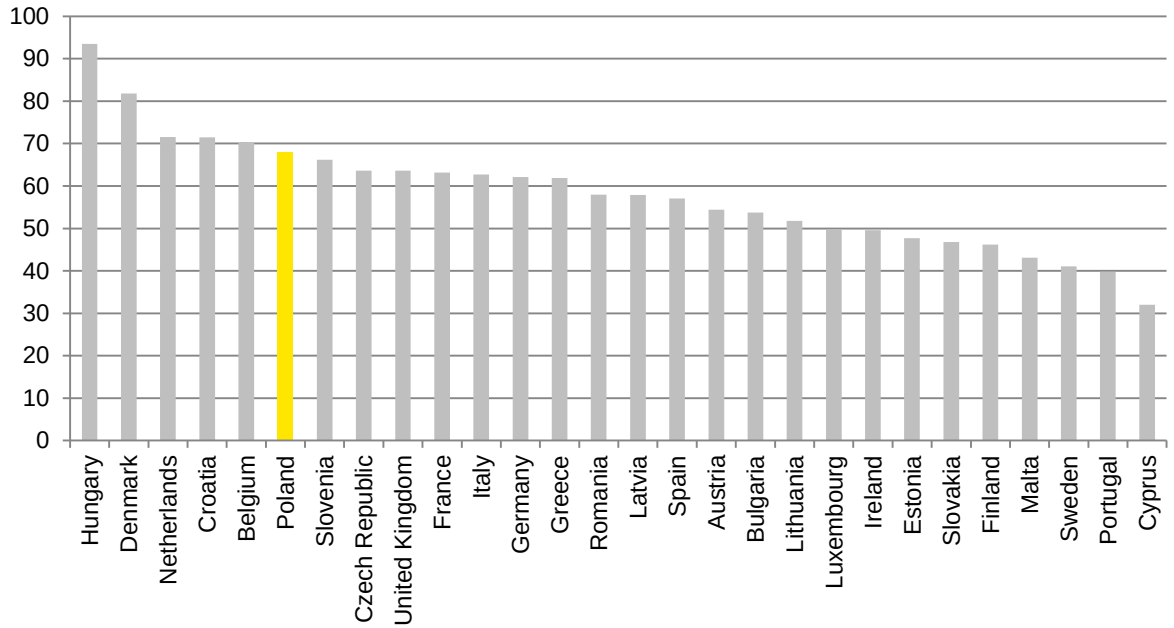
[6]PTO (2014), "Current Cancer Control in Poland", prepared by PWC for the Polish Cancer Society, May 2014.
[7] Ibid.

Graph 9. Incidence of cancer (excluding non-melanoma skin cancer) per 100,000 in 2012.



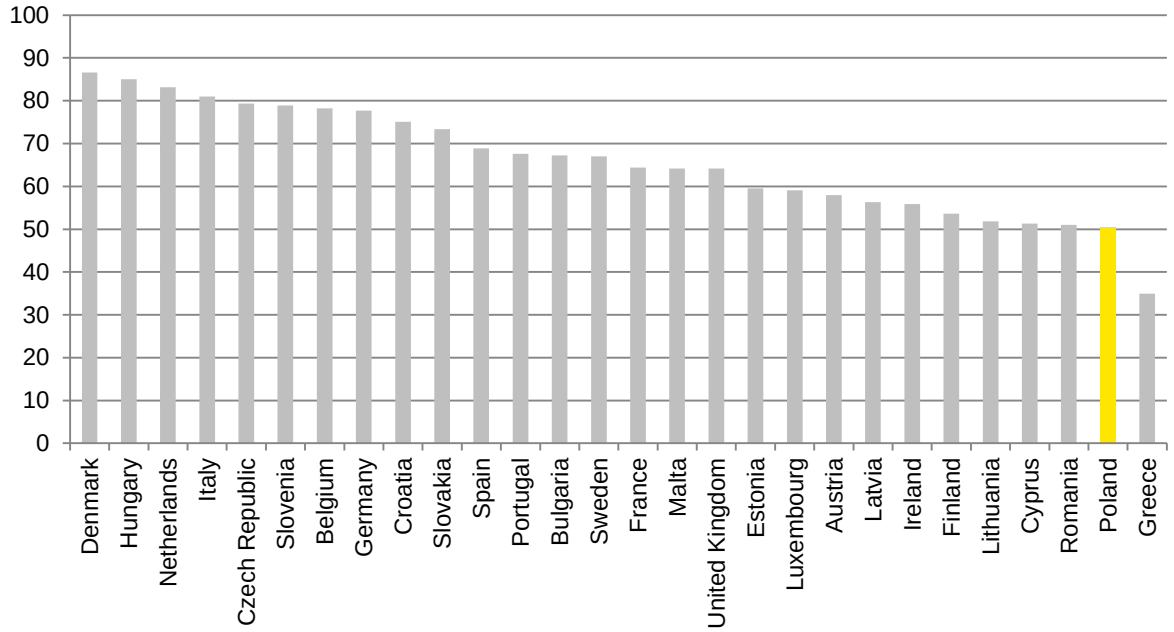
Source: WHO, GLOBOCAN2012; population data: EUROSTAT

Graph 10. Incidence of lung cancer per 100,000 in 2012 in the EU countries.



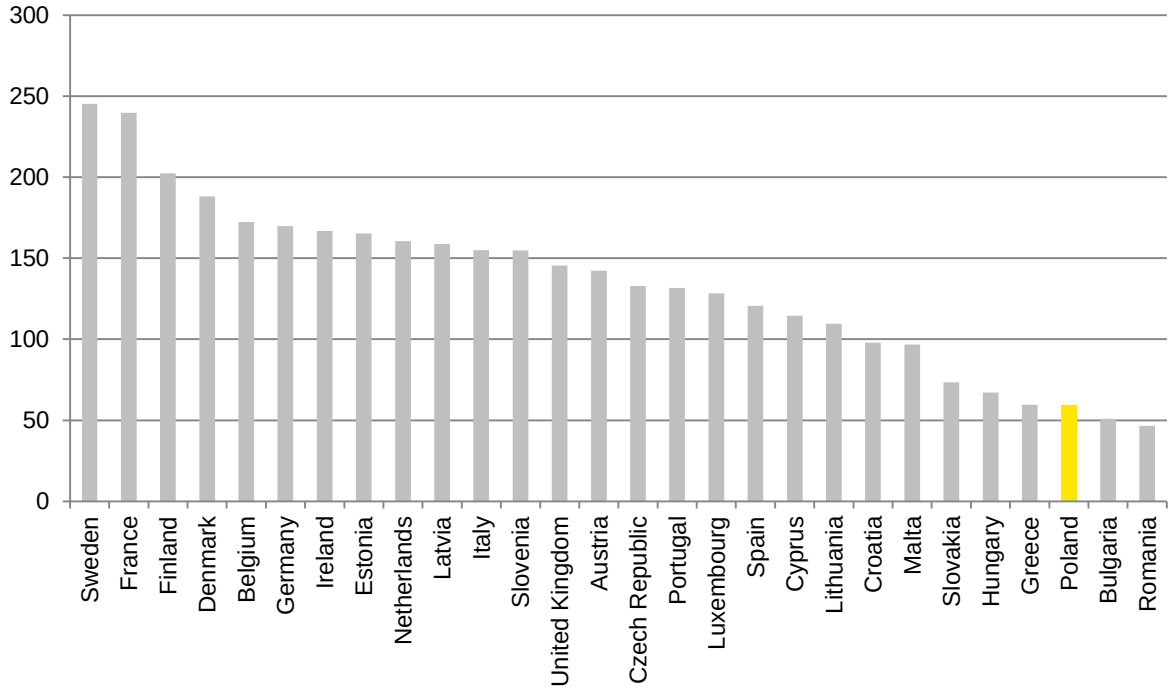
Source: WHO, GLOBOCAN2012; population data: EUROSTAT

Graph 11. Incidence of colorectal cancer per 100,000 in 2012 in the EU countries.



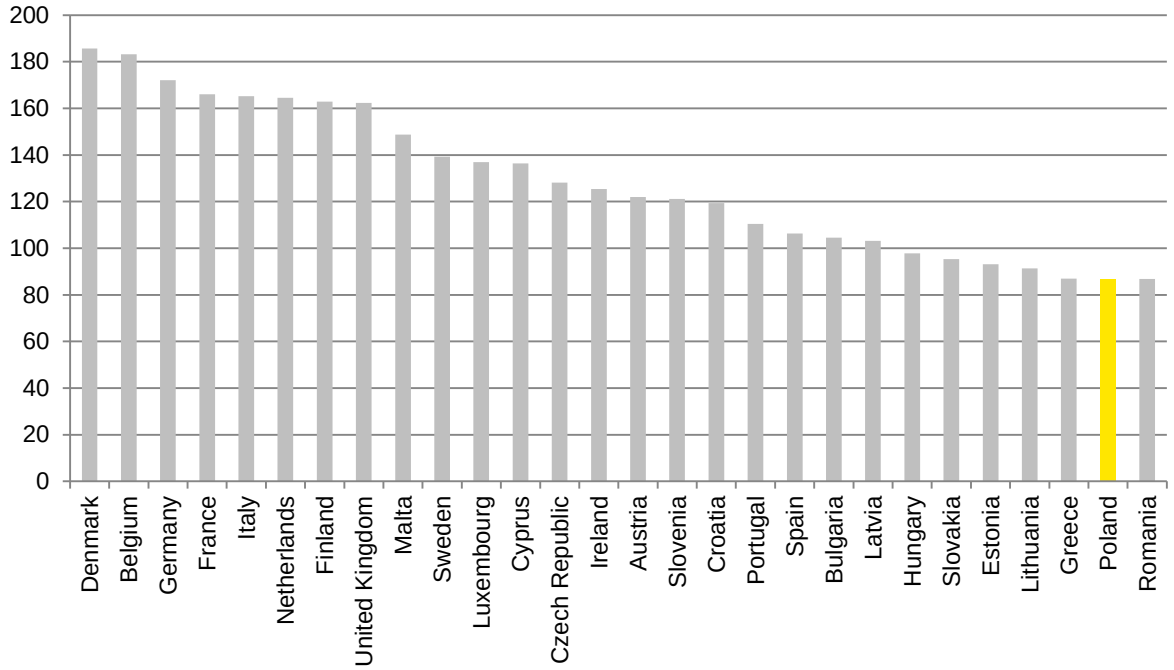
Source: WHO, GLOBOCAN2012; population data: EUROSTAT

Graph 12. Incidence of prostate cancer per 100,000 in 2012 in the EU countries.



Source: WHO, GLOBOCAN2012; population data: EUROSTAT

Graph 13. Incidence of breast cancer per 100,000 in 2012 in the EU countries.



Source: WHO, GLOBOCAN2012; population data: EUROSTAT

Survival rate is considered one of the best measures of cancer care effectiveness in a specific country. It indicates the proportion of individuals at a given age and suffering from cancer who will survive a given period of time (usually 5 years) in relation to individuals at the same age and not suffering from cancer who will survive the same period of time. It is usually expressed as percentage or a number per 100,000 individuals. Two basic elements are taken into account:

- the stage at which the disease was diagnosed – early diagnosis improves the patient's chances of survival,
- efficacy of cancer therapy – higher efficacy improves the patient's chances of survival.

Higher survival rates indicate more effective cancer care in a specific country. On the following graphs, 5-year survival rates (percentages) in 2012 for selected European countries are presented, overall and for the most common types of cancer, i.e. breast, colorectal, prostate, and lung cancer.

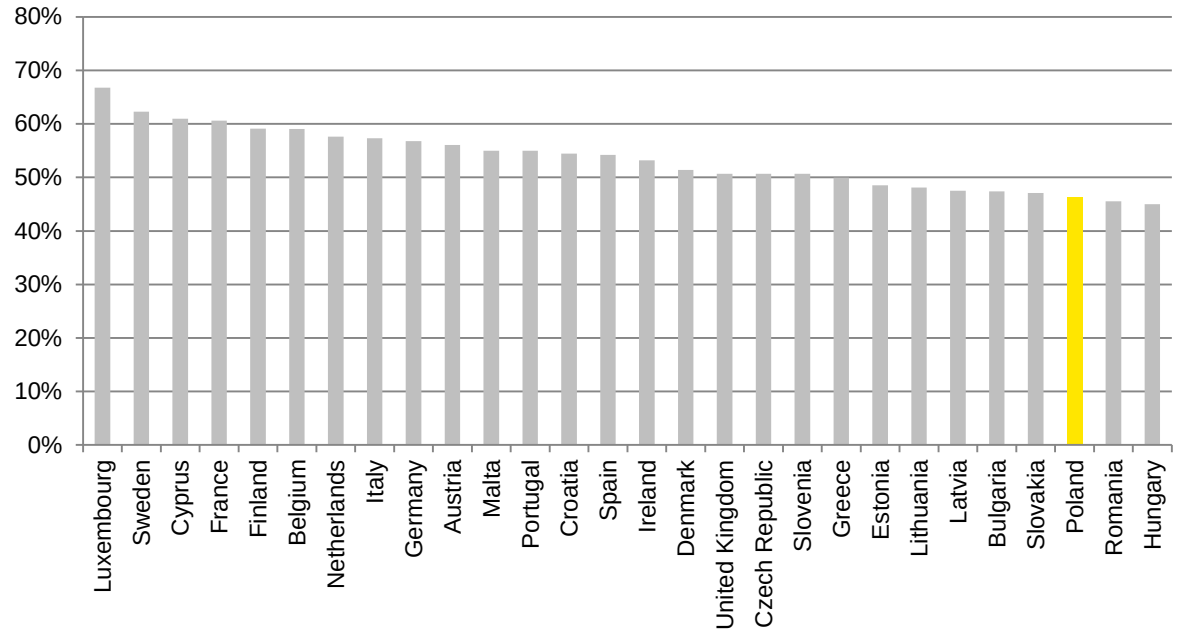
Only in patients with lung cancer and breast cancer, the 5-year survival rates in Poland are close to the mean European values.

In Poland, 5-year survival rate in patients with lung cancer is 20% and is the lowest in comparison with the survival rates in patients with other cancers (colorectal: 46%, breast: 79%, prostate: 65%). In the case of lung cancer, the results are to the least degree related to the quality of treatment – in most cases patients are diagnosed at too late a stage of the disease. In a significant number of countries, 5-year survival rates for lung cancer patients are low, regardless of the treatment method or the level of cancer care.

In Poland, survival rates in patients with colorectal, prostate, or breast cancer are among the lowest in comparison with other European Union countries, indicating relatively low effectiveness of cancer care. In the group of countries analysed in this report, low overall survival rates in cancer patients were also observed in Romania, Slovakia, Hungary, and Bulgaria.

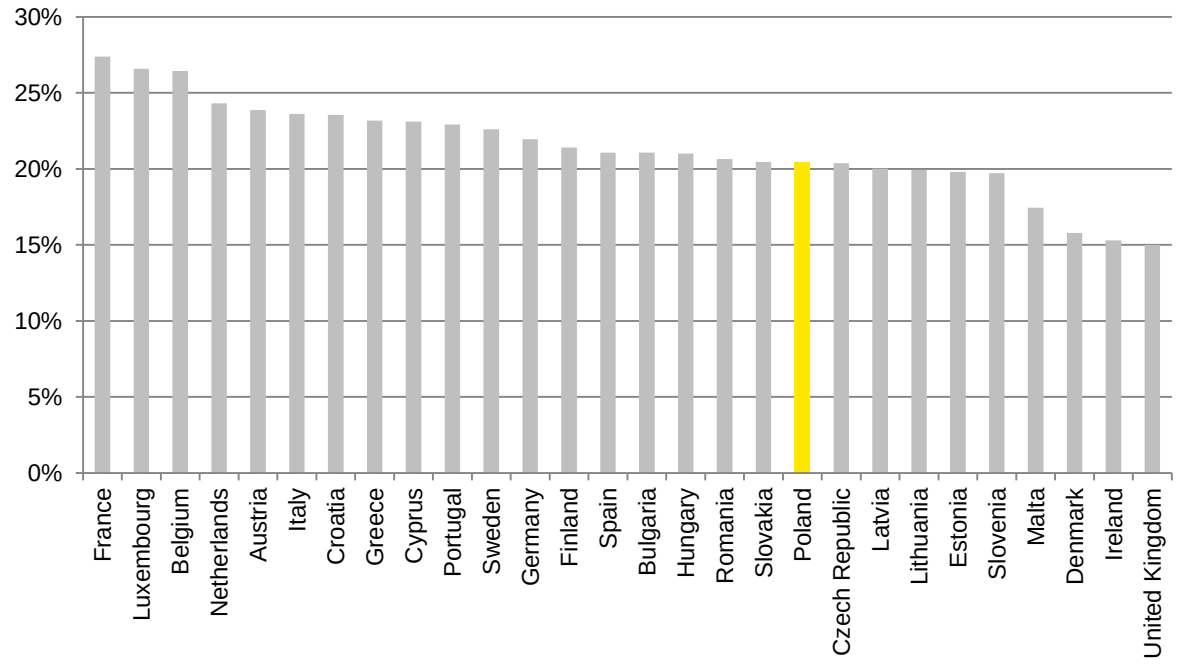
As presented below, among the investigated countries, the best results were obtained in France, the Netherlands, Germany, and Austria.

Graph 14. 5-year survival rates in patients with cancer (excluding non-melanoma skin cancer) in the EU countries



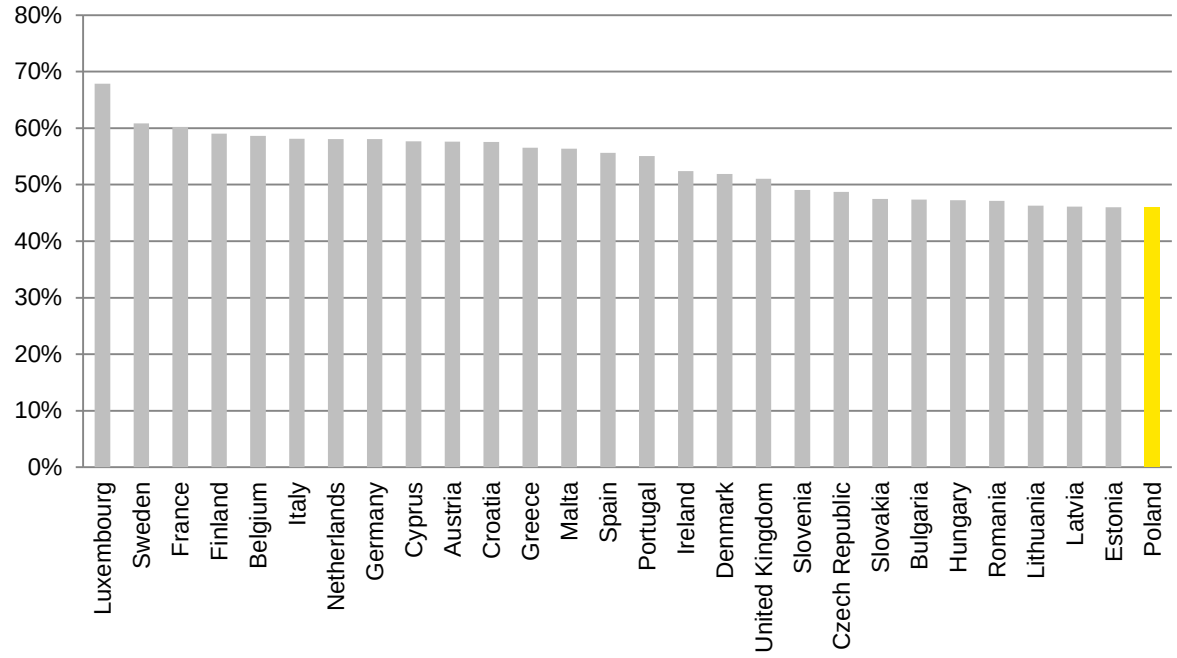
Source: WHO, GLOBOCAN2012, data for the year 2012

Graph 15. 5-year survival rates in patients with lung cancer in the EU countries



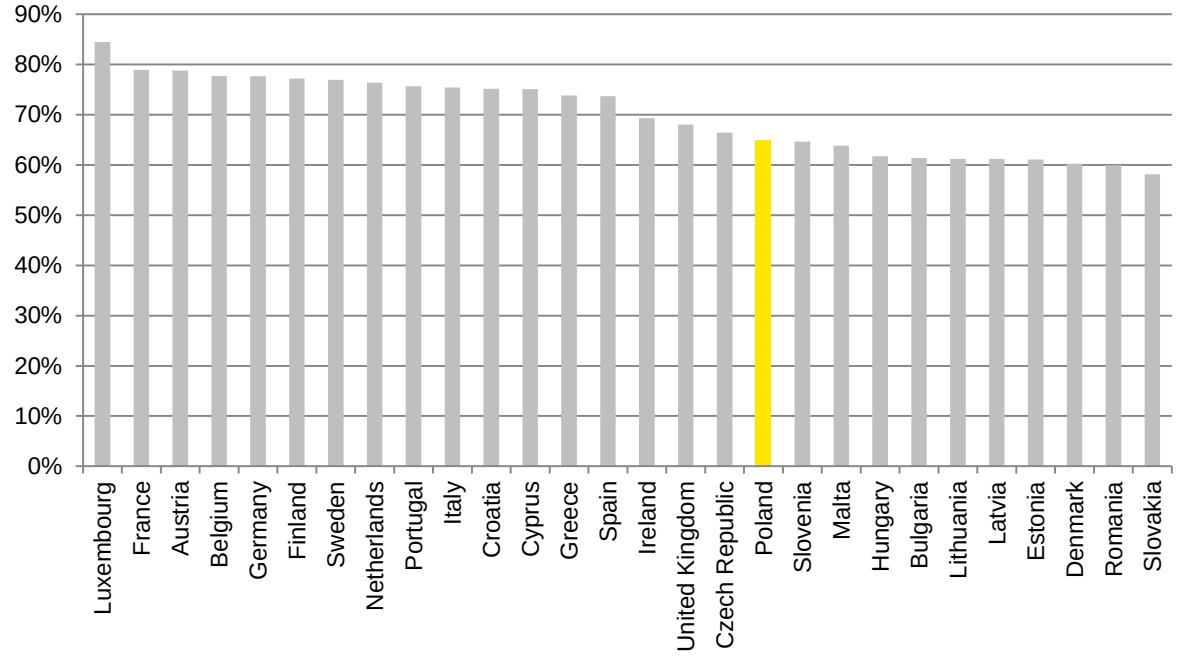
Source: WHO, GLOBOCAN2012, data for the year 2012

Graph 16. 5-year survival rates in patients with colorectal cancer in the EU countries



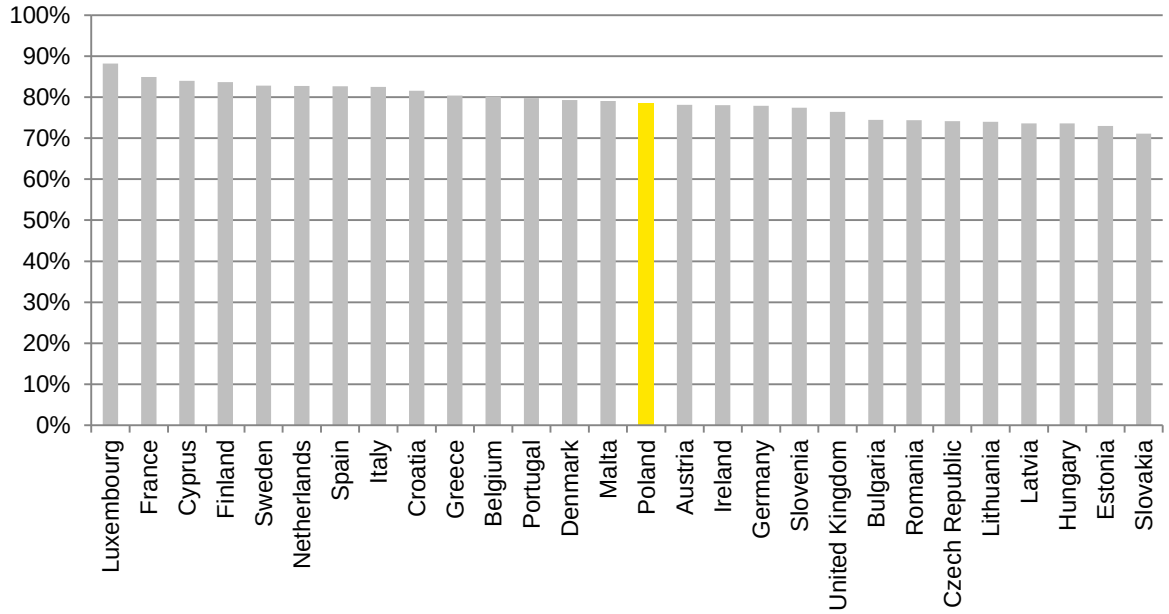
Source: WHO, GLOBOCAN2012, data for the year 2012

Graph 17. 5-year survival rates in patients with prostate cancer in the EU countries



Source: WHO, GLOBOCAN2012, data for the year 2012

Graph 18. 5-year survival rates in patients with breast cancer in the EU countries



Source: WHO, GLOBOCAN2012, data for the year 2012

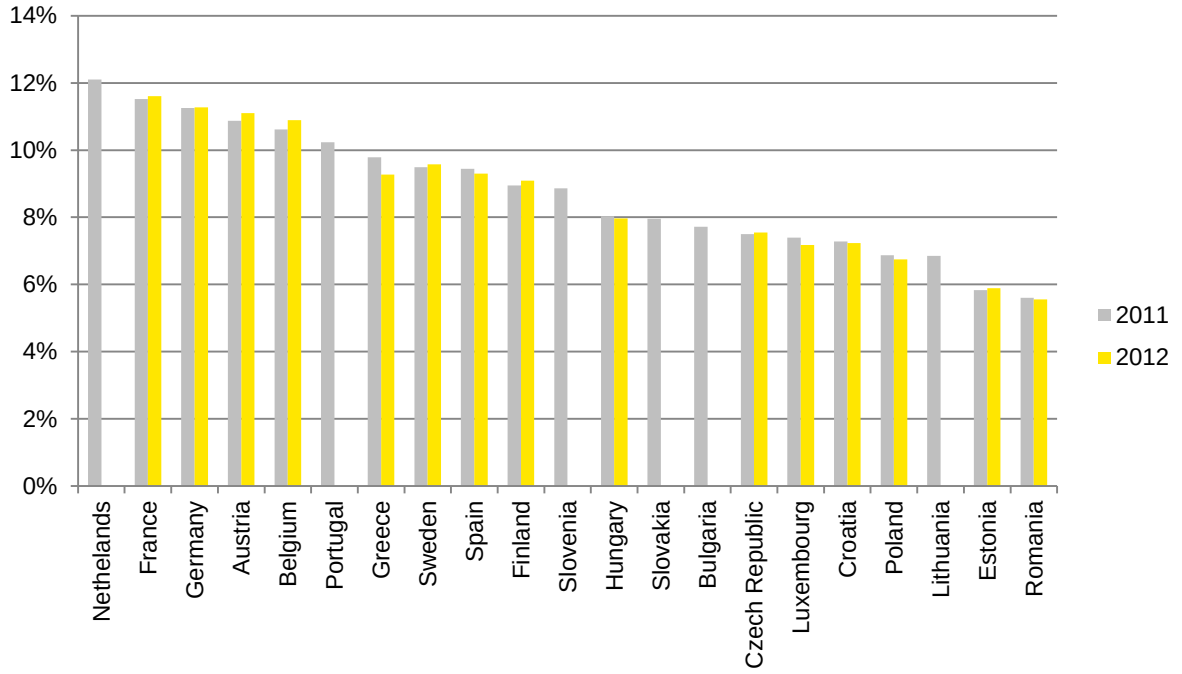
3. Cancer care resources

3.1 Health care expenditure in Europe and cancer care expenditure in selected countries

Access to health care services, including cancer care services, depends, among others, on the amount of resources allocated for the health care system and the effectiveness of their utilisation. On the graph below, health care expenditure expressed as percentage (%) of the GDP in European Union countries in 2011–2012 is presented.

The percentage of GDP spent on health care in Poland was relatively low in comparison with other European countries at about 7% (both in 2011 and 2012), while the mean value for the EU countries was 10% (years 2011 and 2012).

Graph 19. Percentage of GDP spent on health care in the EU countries in the years 2011–2012.



Source: EUROSTAT

The structure of health care and cancer care expenditure per capita in individual countries is summarised in the table below.

In comparison with other analysed countries, both health care and cancer care expenditure in Poland – expressed as GDP percentage and per capita – is the lowest:

- cancer care expenditure per capita in Poland is EUR 42,
- while, for comparison, cancer care expenditure per capita in the Czech Republic is EUR 85, i.e. twice as much.

Table 3. Health care and cancer care expenditure in selected countries – a comparison.

Country/type of services	GDP per capita EUR (a)	Health care expenditure as % of GDP (b)	Health care expenditure percapita (EUR)	Cancer care expenditure as % of health care expenditure (c)	Cancer care expenditure per capita (EUR)
Poland	10,100	6.9%	697	6.0%	42
United Kingdom	29,800	9.4%	2,801	6.1%	171
Norway	75,700	9.4%	7,116	2.5%	178
France	31,300	11.6%	3,631	4.3%	156
Czech Republic	14,200	7.5%	1,065	8.0%	85
USA	40,000	17.7%	7,080	4.7%	333

Source: EY, "Cancer care systems in selected countries", April 2014

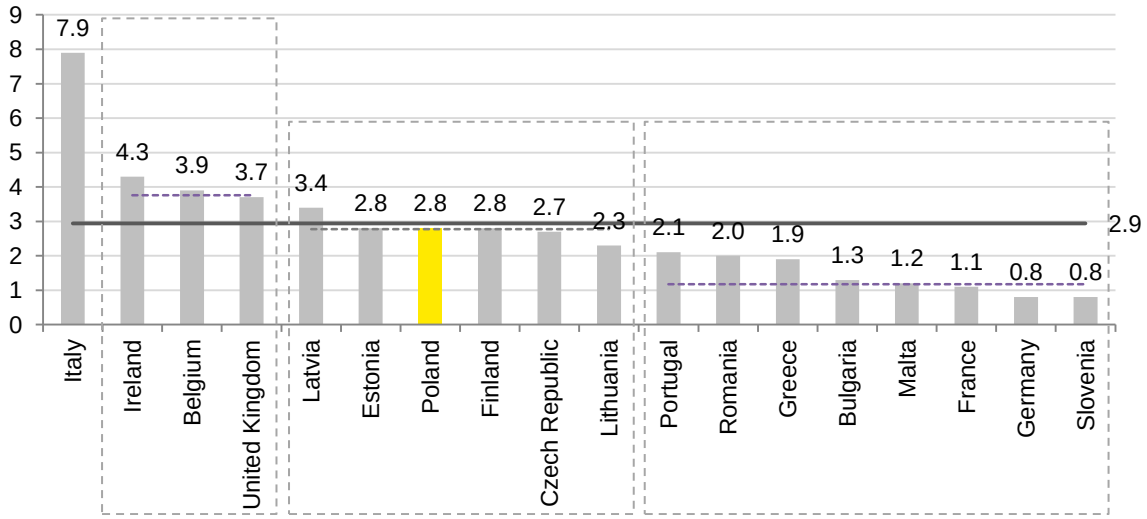
a) Eurostat data for 2013 or 2012 (in the case of data accounting for the purchasing power), b) OECD data for 2011 (2012 for France and Norway), c) Data for Poland and the Czech Republic for 2011, for the USA and the UK for 2010, for Norway for 2007, and for France – mean value from various sources for the years 2009–2013. Compiled on the basis of: Cancer Research UK, Cancer Service: Reverse, Pause or Progress, December 2012, Institute for Fiscal Studies, Public Payment and Private Provision, Nuffield Trust, May 2013, R. Luengo-Fernandez et al., Economic burden of cancer across the European Union: a population-based cost analysis, University of Oxford, October 2013, The National Cancer Institute, Cancer Trends Progress Report – 2011/2012 Update, NIH, DHHS, Bethesda, MD, August 2012, http://progressreport.cancer.gov, SINTEF, Costs of cancer in the Nordic countries – a comparative study of health care costs and public income loss compensation payments related to cancer in the Nordic countries in 2007; Société Française de Radiothérapie Oncologique: Livre blanc de la radiothérapie en France, 2013; INCa (ed.), Les cancers en France en 2013. Collection état des lieux et des connaissances, Boulogne-Billancourt Cedex, January 2014 and CNAMTS, Améliorer la qualité du système de santé et maîtriser les dépenses: propositions de l'Assurance Maladie Rapport au ministre chargé de la sécurité Sociale et au parlement sur l'évolution des charges et produits de l'assurance maladie au titre de 2014 (loi du 13 août 2004) pour 2014 and Economic information on health care, Zdravotnická Statistika ČR 2012, www.uzis.cz.

3.2 Resources of cancer care systems in selected European countries

The quality of cancer care and the extent to which patients' health needs are satisfied are directly related to the resources available in the cancer care system. Apart from financial means, these resources include specialist equipment and qualified medical staff.

As to the number of oncologists[8] per 100,000 inhabitants, Poland does not differ from other European countries. In 2011, there were on average 2.8 oncologists per 100,000 individuals, while the mean value in the selected European countries was 2.9. However, these values do not directly reflect the number of patients provided with care per physician. With the anticipated increase of the cancer incidence rate to 185,000 per year in the coming decade, one may expect an increased demand for oncologists.

Graph 20. Number of oncologists per 100,000 inhabitants in 2011.



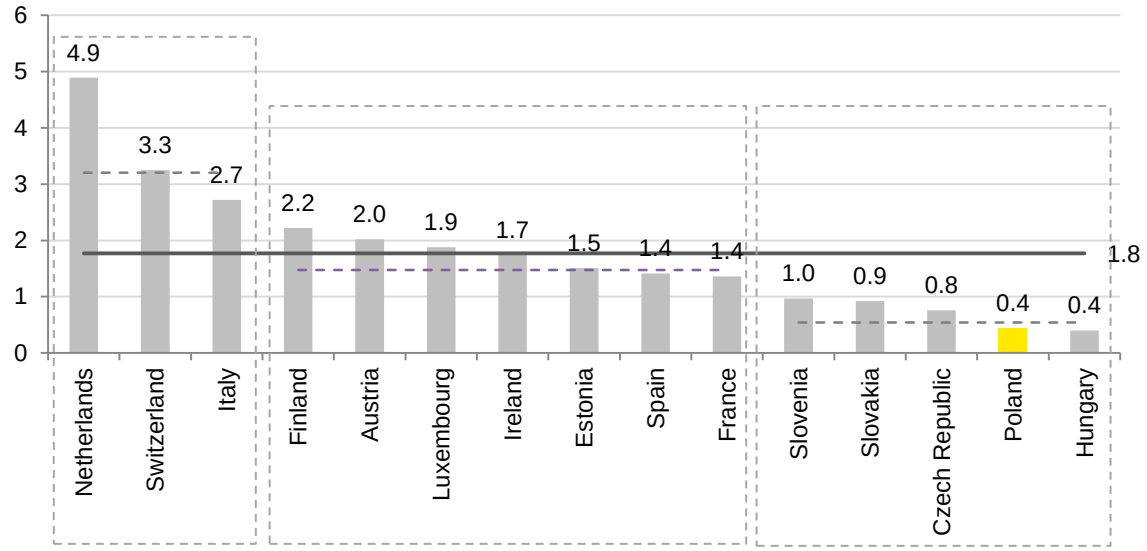
Source: EUROSTAT

The number of medical devices used in diagnostics and treatment of cancer is a measure of availability of both cancer care resources in general and modern health technologies. On the graphs below, the number of PET scanners, CT scanners, mammography units and radiotherapy equipment units in selected European countries in 2012 are presented.

In Poland, equipment resources are relatively more constrained than in the other analysed European countries. PET (positron emission tomography) scanners, which play a vital role in effective diagnostics of cancer, are the least accessible. In Poland, there is less than 0.44 scanner per one million, while the mean for the analysed countries is 1.8. The highest number of scanners is available in highly developed countries, i.e. the Netherlands (4.9) and Switzerland (3.3). Less than one scanner per one million is available in Central European countries, i.e. Slovakia (0.9), the Czech Republic (0.8), Poland (0.44) and Hungary (0.4). It is worth noting that in this group the number of scanners in Poland and Hungary is significantly lower than that in the Czech Republic which ranks right above them.

[8] Specialists in oncology (including clinical oncology, chemotherapy, paediatric oncology and haematology), excluding surgery.

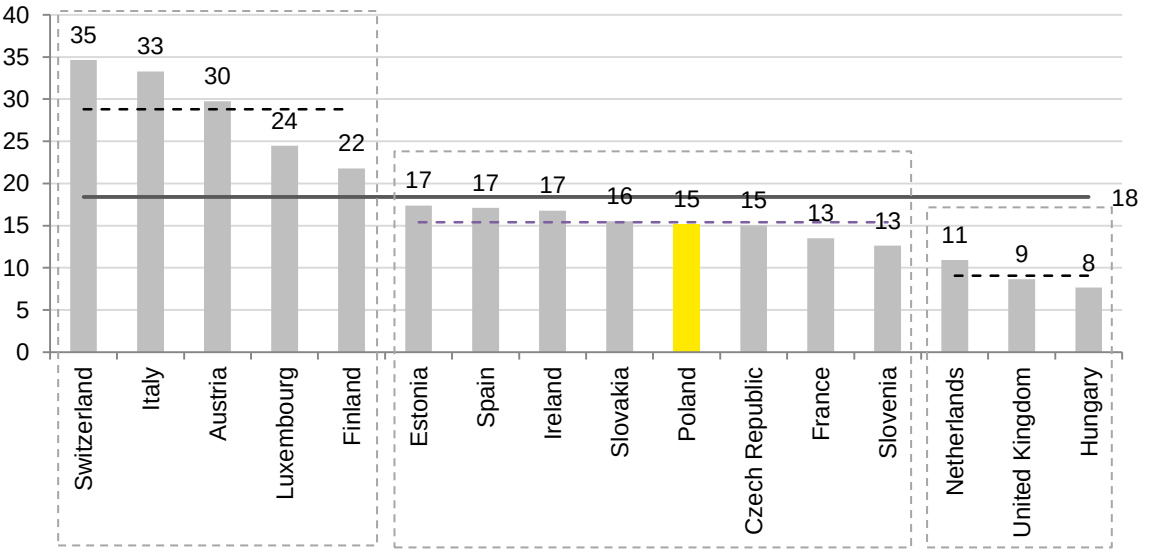
Graph 21. PET scanners per one million inhabitants in a specific country in 2012.



Source: OECD

With respect to access to CT scanners, in Poland – with 15.2 scanners per one million – the situation is a little better than in the other selected European countries. Although the number of CT scanners in Poland is higher than, among others, in France (13.5), the Netherlands (10.9) and the United Kingdom, the number is still lower than the mean value of 19.7. It is also worth noting that CT scanners in Poland are most easily accessible in comparison with other medical equipment included in this analysis.

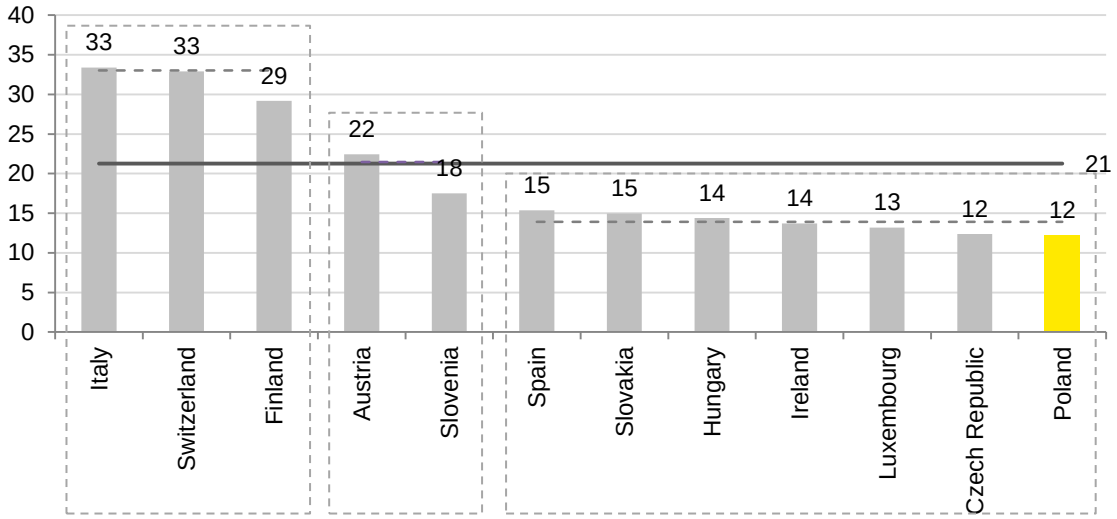
Graph 22. CT scanners per one million inhabitants in a specific country in 2012.



Source: OECD

With respect to access to mammography units, in Poland the number (12.3) is also relatively lower in comparison with the other selected European countries (mean: 21 per one million inhabitants). The highest number of mammography units is available in Italy (33.4), Switzerland (32.9), Finland (29.2), and Austria (22.4). These countries also have the largest health care budgets and better access to other medical equipment discussed in this chapter. In Poland, the number of mammography units in comparison with other medical equipment listed in this chapter is relatively high (only the access to CT scanners is better).

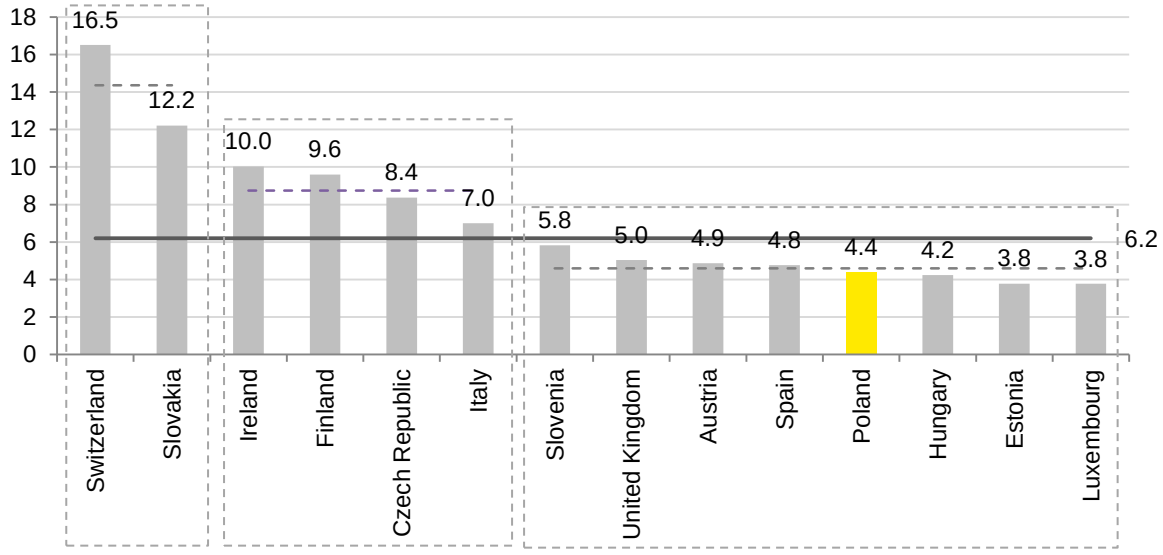
Graph 23. Mammography units per one million inhabitants in a specific country in 2012.



Source: OECD

In Poland, the number of radiotherapy equipment units was also relatively low, and in 2012 amounted to 4.4 per one million inhabitants. The mean number of units in all the analysed countries was 6.2. The highest number of available radiotherapy equipment units was reported in Switzerland (16.5) and Slovakia (12.2). The lowest number of such units was noted in Estonia and Luxembourg (3.8).

Graph 24. Radiotherapy equipment units per one million inhabitants in a specific country[9].



Source: OECD

[9] Data for the United Kingdom for 2011, data for other countries concern the year 2012.

4. The approach of regulatory authorities to innovation

4.1 European and local authorisation – the EMA/HTA process

Before a medicine may be launched on the European market, relevant authorisation must be obtained. No medicinal product may be marketed in a European Union member state without:

- authorisation granted by the appropriate authority of a member state (HTA process) – so-called "local authorisation" or the "national procedure"; such authorisation is valid only on the territory of the state in which it was granted;
- authorisation granted through the mutual recognition procedure – an applicant submits a request for evaluation of a medicinal product in one of the member states. The procedure involves registration and granting of marketing authorisation for a medicinal product on the basis of an evaluation report prepared by the appropriate authority of a member state (a reference state) in which the product has already been registered. Within ninety days of receiving the documents, every member state decides whether it will recognise the decision of the reference state;
- authorisation granted by the European Medicines Agency (EMA) – so-called "centralised authorisation", valid in all European Union states.

The European Medicines Agency (EMA) is responsible for the evaluation and supervision of medicinal products in the European Union. Pharmaceutical companies submit marketing authorisation applications for their products to EMA. Depending on the product type, either the Committee for Medicinal Products for Human Use or the Committee for Veterinary Medicinal Products evaluates the application. If the safety and efficacy of a specific pharmaceutical is proven, the Committee issues a positive opinion, which is passed on to the Commission so that marketing authorisation may be granted. The marketing authorisation is binding in all European Union member states.

In 2001, the Committee for Orphan Medicinal Products (COMP) was established at EMA. It reviews applications from individuals or companies developing medicinal products intended for the treatment of rare diseases ("orphan drugs"[10]). In 2004, the Committee for Herbal Medicinal Products (HMPC) was established to prepare opinions on traditional herbal medicines[11]. In 2007, the Paediatric Committee (PC) was established. It issues opinions on the development of medicinal products for children up to 17 years of age.

Marketing authorisation may be obtained only by companies with their seats on the territory of the European Union. Every marketing authorisation application must include:

- name and composition of the medicinal product,
- description of the manufacturing method,
- therapeutic indications,
- contraindications and undesirable effects,
- posology,
- method of administration and use,
- expected shelf life,
- warnings and precautions for storage and use of the medicinal product,
- waste disposal method,

[10] **Orphan drugs** – medications used in treatment of rare diseases.
Rare diseases include genetic diseases of chronic, severe course, which affect mostly children and frequently lead to physical and mental retardation; their prevalence in a specific population does not exceed 5 in 10,000. These include: cystic fibrosis, porphyria, cystinosis, Gaucher disease, Fabry disease, tyrosinemia, homocystinuria, haemophilia, haemochromatosis, Duchenne muscular dystrophy and Becker muscular dystrophy, myotonic dystrophy, achondroplasia, spinal muscular atrophy, Rett syndrome, Cri du Chat syndrome, Down syndrome, Turner syndrome, Dravet syndrome, Huntington's disease, Friedreich disease, fragile X syndrome and Angelman syndrome.

[11] **Herbal medicine, botanical medicine, phytomedicine** – according to the European Scientific Cooperative on Phytotherapy, they are medically useful products that contain as active ingredients medicinal plants, their parts or substances derived from them, or their combination, which have been processed.

- risk to natural environment,
- description of the manufacturer's control methods,
- results of pharmaceutical, preclinical and clinical studies,
- summary of the applicant's pharmacovigilance system,
- copy of a marketing authorisation obtained in another member state or a third state,
- a statement that clinical trials conducted outside the EU were conducted in accordance with the principles of good clinical practice, observing ethical requirements specified in Directive 2001/20/EC regarding the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

The outcomes of preclinical and clinical trials do not have to be presented if the pharmaceutical company demonstrates in the application that a medicine is a biosimilar or generic product, i.e.

- the medicine is essentially similar to the original medicinal product that has been authorised for use for at least eight years in a member state or in the European Union,
- medical use of the active ingredients has been approved in the EU for at least ten years, and their safety level is acceptable.

In exceptional circumstances and after consultation with the applicant, marketing authorisation may be granted on certain conditions regarding the safety of the medicinal product and the obligation to inform about all events related to its use. This type of authorisation may be granted only on the condition that the applicant’s inability to provide full information on the medicine efficacy and safety when used under normal conditions has been proven.

The medicine will not be authorised if, in the opinion of EMA:

- the risk-benefit balance is not favourable (safety criterion),
- therapeutic efficacy has not been sufficiently proven (with the exception of homoeopathic products to which this criterion is not applied),
- qualitative and quantitative composition of the medicinal product is inconsistent with that declared (qualitative criterion),
- information and documents submitted with the application do not comply with the regulations.

The procedure of granting marketing authorisation for a medicinal product must not take longer than 210 days.

The EMA creates and maintains the EudraVigilance database for the purpose of gathering information about medicinal products authorised for marketing in the European Union and providing all the appropriate authorities with simultaneous access to such information and the possibility to exchange it. The EudraVigilance database gathers information on adverse drug reactions related to the use of a product in approved indications as well as to the off-label use, identified as a result of studies conducted after marketing authorisation was granted. On the basis of this information, an annual report is prepared and then passed on to the Commission, the European Parliament and the Council.

The Agency takes the following steps with regard to medicinal products for human use authorised via the centralised procedure:

- monitoring of the effectiveness of risk minimisation measures as part of the risk management system,
- assessment of the risk management system updates,
- monitoring of the EudraVigilance data.

5. Utilisation of cancer drugs in Europe

5.1 Expenditure on innovative cancer drugs

For the purpose of this analysis, innovative cancer drugs were selected on the basis of the following criteria:

- classified in the ATC L01 group – antineoplastic and immunomodulating agents – cytostatics,
- licensed by EMA after 2004,
- non-generics,
- non-biosimilars.

From the list thus obtained, 40 drugs with the highest utilisation level in kilograms (as measured by the sales volume) in 12 months (2013Q4–2014Q3) were selected. Then, 30 drugs with the highest sales value in 12 months (2013Q4–2014Q3) were selected. The sales value indicates the burden imposed on the payers' budgets in the investigated countries if the drug is reimbursed. In both cases, only the utilisation level and the sales value in the 13 investigated countries were taken into account, i.e. in Poland, Austria, the Czech Republic, France, Spain, the Netherlands, Germany, Romania, Slovakia, Switzerland, Hungary, Italy and the United Kingdom. The sales value of drugs qualified for the analysis is presented in table 4.

Table 4. Sales value of 30 innovative cancer drugs in 13 countries.

Item	Drug	Manufacturer	Sales value (million EUR)				
			2013Q4	2014Q1	2014Q2	2014Q3	Total 12 months
1	AVASTIN	Roche Registration Limited	348	346	348	358	1,399
2	ALIMTA	Eli Lilly Nederland B.V.	141	143	148	155	587
3	ERBITUX	Merck KGaA	103	100	99	101	403
4	SUTENT	Pfizer Limited	87	84	83	84	339
5	AFINITOR	Novartis Europharm Ltd.	77	76	81	82	316
6	YERVOY	Bristol-Myers Squibb Pharma EEIG	61	68	84	90	302
7	TASIGNA	Novartis Europharm Ltd.	70	68	72	75	286
8	SPRYCEL	Bristol-Myers Squibb Pharma EEIG	63	65	68	70	265
9	VIDAZA	Celgene Europe Ltd.	60	63	63	69	255
10	TARCEVA	Roche Registration Ltd.	58	56	55	54	223
11	NEXAVAR	Bayer Pharma AG	51	47	48	47	193
12	ZELBORAF	Roche Registration Ltd.	39	38	40	40	158
13	VOTRIENT	Glaxo Group Ltd.	34	37	40	43	153
14	JAKAVI	Novartis Europharm Ltd.	28	32	36	40	136
15	VECTIBIX	Amgen Europe B.V.	27	29	32	35	124
16	IRESSA	AstraZeneca AB	30	29	19	29	117
17	PERJETA	Roche Registration Limited	17	24	31	38	110
18	JEVTANA	Sanofi-Aventis Group	25	28	28	27	109
19	INLYTA	Pfizer Ltd.	18	18	21	24	81
20	TYKERB	Glaxo Group Limited	21	20	20	19	80
21	KADCYLA	Roche Registration Ltd	2	14	23	28	66
22	ABRAXANE	Celgene Europe Ltd	12	14	19	21	65
23	YONDELIS	Pharma Mar S.A.	15	14	14	14	57

Item	Drug	Manufacturer	Sales value (million EUR)				
			2013Q4	2014Q1	2014Q2	2014Q3	Total 12 months
24	HALAVEN	Eisai Europe Ltd.	12	14	14	15	55
25	XALKORI	Pfizer Ltd.	11	12	14	16	52
26	TAFINLAR	GlaxoSmithKline Trading Services Limited	3	9	15	18	46
27	STIVARGA	Bayer Pharma AG	10	12	12	11	44
28	ADCETRIS	Takeda Pharma A/S	9	9	10	15	43
29	ZALTRAP	Sanofi-Aventis Group	5	7	8	9	30
30	DACOGEN	Janssen-Cilag International N V	6	6	7	8	28
Total			**1,443**	**1,482**	**1,552**	**1,635**	**6,122**

Source: PADDS IMS MIDAS Q3/2014 Database

The 12-month expenditure [12] on innovative drugs is presented on graph 25 on which the investigated countries are divided into two groups according to similar economic development. The number “100” represents the average level of expenditure in the investigated countries.

Expenditure on innovative drugs is the highest in the group of highly developed countries (the United Kingdom, Italy, the Netherlands, Spain, France, Germany, Switzerland, and Austria). Mean expenditure in this group is 15% higher than mean expenditure in all the 13 investigated countries.

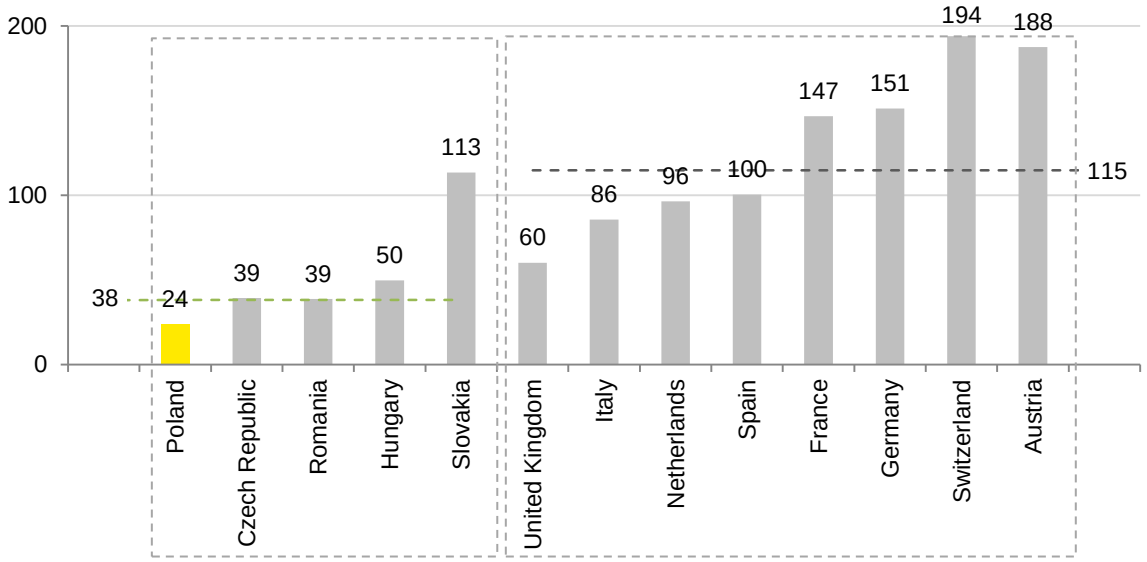
In the other group of countries (Poland, the Czech Republic, Romania, Hungary, and Slovakia), mean expenditure on innovative cancer drugs amounted to 38% of the mean value for the 13 investigated countries.

The highest expenditure on innovative cancer drugs is incurred in Switzerland – 94% higher than the mean value for the 13 countries. It is also worth noting that of the 30 analysed drugs, 28 are reimbursed in this country. Moreover, in the case of 25 reimbursed drugs, access is not restricted by additional criteria with respect to the indications approved by EMA. Availability of drugs through reimbursement systems is presented in detail in chapter 6. In Austria, expenses on innovative drugs are 88% higher than the mean value for the 13 countries. Access to hospital drugs is not subject to major restrictions in this country. The health budget is at the disposal of hospitals and is allocated per diagnosis related groups, making it possible to reimburse drugs authorised for marketing in this country (i.e. approved by EMA or locally in Austria). A similar solution has been adopted in Germany, where drug expenses are 51% higher than the mean for the 13 countries (the third highest amount). The reimbursement system in Germany is described in chapter 8.

The lowest expenses on innovative cancer drugs are incurred in Poland – 24% of the mean value for the 13 countries. However, it is worth noting that in Poland the prices of most of the analysed drugs are lower than mean prices in the 13 investigated countries (see chapter 5).

[12] Expenditure on the 30 selected drugs in the 13 analysed European countries.

Graph 25. Relative expenses on innovative cancer drugs in 13 countries, in the period 2013Q4–2014Q3.



Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

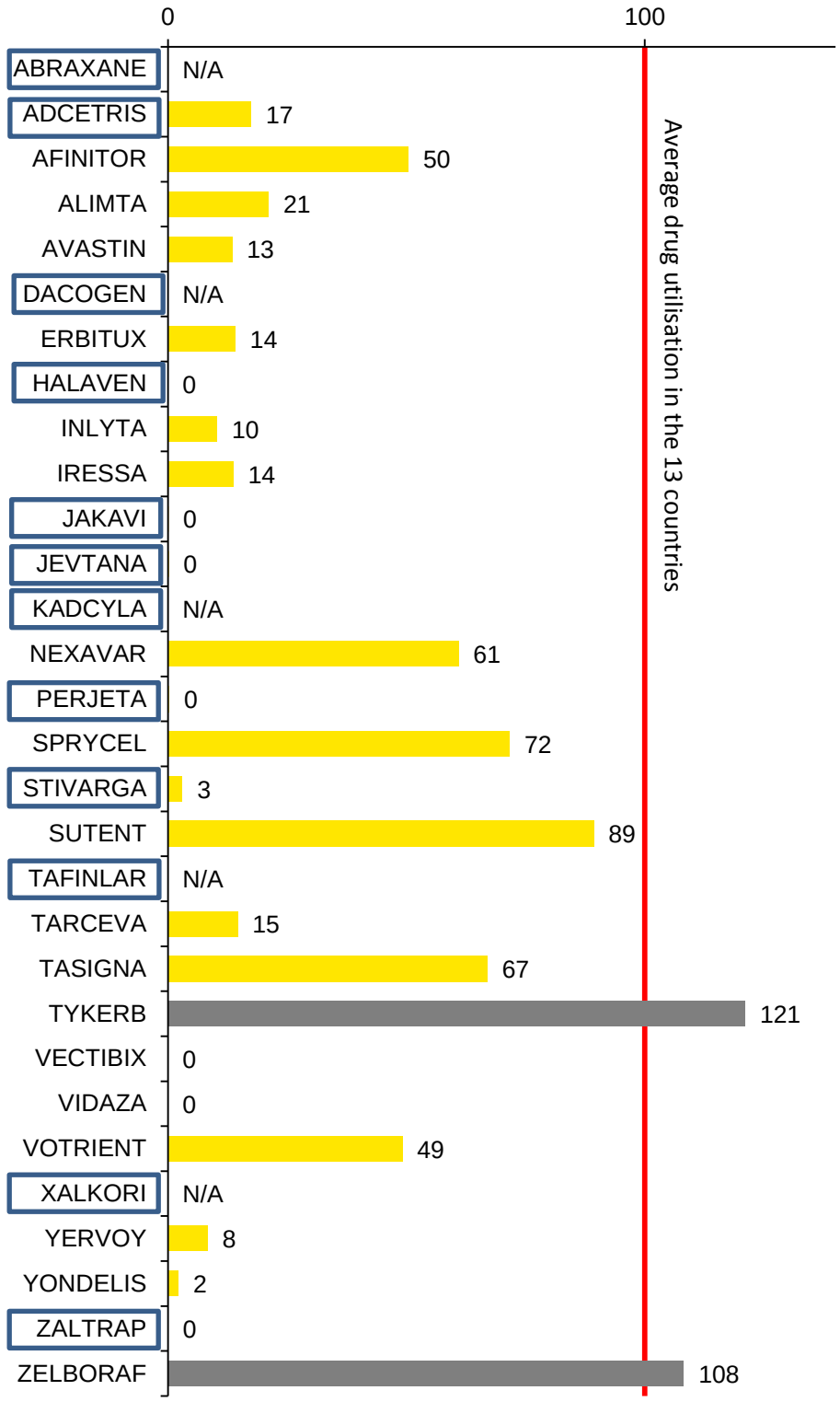
5.2 Comparison of sales of the 30 selected cancer drugs in 13 countries

In this chapter, the sales (in packs) of the selected 30 drugs in the period 2013Q4–2014Q3 in Poland is compared with the values in the other analysed countries. The number of packs represents the relative sales level and was normalised according to the definition provided in Chapter 1.

Only in the case of 2 drugs (Zelboraf and Tyverb) used in treatment of melanoma and breast cancer, respectively, the utilisation level (the sales volume) in Poland exceeds the mean sales in 13 countries.

Graphs representing the sales of all 30 drugs in 13 European countries can be found in Appendix 1 to this report.

Graph 26. Comparison of the drug utilisation level in Poland and in the 13 countries (100 = mean utilisation level in the 13 countries*) in the period 2013Q4–2014Q3.

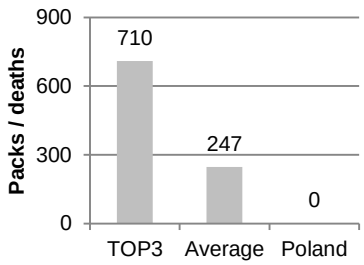


*) *The 13 countries are: Austria, the Czech Republic, France, Germany, Hungary, Italy, the Netherlands, Poland, Romania, Slovakia, Spain, Switzerland, and the United Kingdom.*

A drug not reimbursed in Poland.

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

ABRAXANE



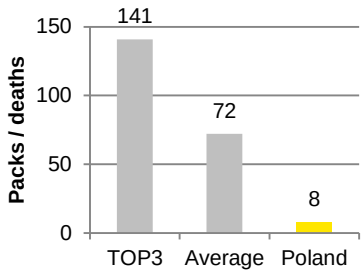
TOP3: Austria, Spain, Germany

In Poland, the drug is unavailable (not reimbursed).

Abraxane (paclitaxel) is used in treatment of metastatic breast cancer and metastatic pancreatic adenocarcinoma (in combination with gemcitabine).

The drug is available as vials containing powder for suspension for infusion. Each vial contains 100 mg or 250 mg of paclitaxel. On the graph, sales data for 100 mg vials are presented.

ADCETRIS



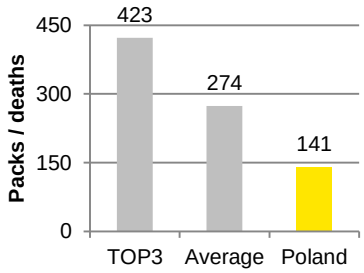
TOP3: Switzerland, Slovakia, Hungary

In Poland, the drug is unavailable (not reimbursed).

Adcetris (brentuximab vedotin) is used in treatment of adult patients with relapsed or refractory Hodgkin lymphoma and systemic anaplastic large-cell lymphoma (sALCL).

The drug is available as vials containing powder for suspension for infusion. Each vial contains 50 mg of brentuximab vedotin. On the graph, sales data for 50 mg vials are presented.

AFINITOR



TOP3: France, the Netherlands, Spain

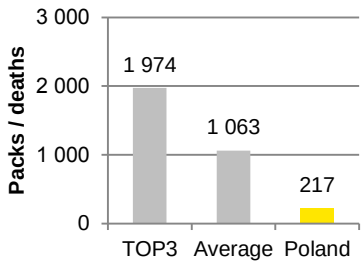
In Poland, the drug is available (reimbursed) with restrictions.

Afinitor (everolimus) is used in treatment of:

- advanced hormone receptor-positive breast cancer without HER2/neu overexpression;
- in treatment of unresectable or metastatic well- or moderately-differentiated pancreatic neuroendocrine tumors;
- in treatment of patients with advanced renal cell carcinoma and disease progression during or after anti-VEGF (vascular endothelial growth factor) therapy.

The drug is available as tablets containing 2.5 mg, 5 mg or 10 mg of everolimus. For the purpose of this analysis, the amount of drug was calculated as packs of 10 (5 mg) tablets.

ALIMTA



TOP3: Switzerland, France, Austria

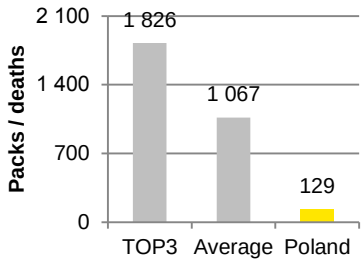
In Poland, the drug is available (reimbursed).

Alimta (pemetrexed):

- in combination with cisplatin is indicated in treatment of chemotherapy-naïve patients with unresectable malignant pleural mesothelioma;
- in combination with cisplatin in first-line treatment of patients with locally advanced or metastatic non-small-cell lung cancer of other than predominantly squamous cell histology.

The drug is available as vials containing powder for concentration for solution for infusion. Each vial contains 100 mg or 500 mg of pemetrexed. On the graph, sales data for 100 mg vials are presented.

AVASTIN



TOP3: Austria, France, Slovakia

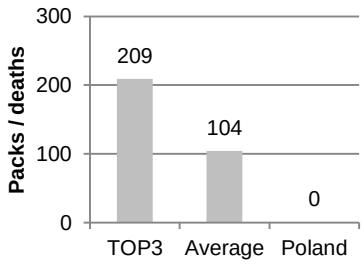
In Poland, the drug is available (reimbursed) with restrictions.

Avastin (bevacizumab) is an innovative cancer drug used in treatment of:

- metastatic colon or rectal cancer (in combination with fluoropyrimidine-based chemotherapy);
- disseminated breast cancer (in combination with paclitaxel);
- non-small-cell, non-squamous lung cancer (in combination with platinum-based chemotherapy);
- advanced ovarian, fallopian tube, or primary peritoneal cancer (in combination with carboplatin and paclitaxel);
- advanced or metastatic renal cell carcinoma (mRCC).

The drug is available as vials containing liquid for concentration for solution for infusion. Each 4 ml or 16 ml vial contains 100 mg or 400 mg of bevacizumab, respectively. On the graph, sales data for 4 ml vials are presented.

DACOGEN



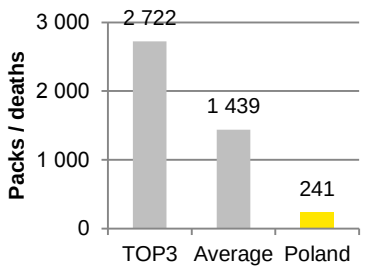
TOP3: Switzerland, Germany, Austria

In Poland, the drug is unavailable (not reimbursed).

Dacogen (decitabine) is an innovative cancer drug used in treatment of patients aged 65 years or older, with newly diagnosed (for the first or a subsequent time) acute myeloid leukaemia (AML) who are not eligible for standard chemotherapy.

The drug is available as vials containing powder for concentration for solution for infusion. Each vial contains 50 mg of decitabine.

ERBITUX



TOP3: France, Switzerland, Austria

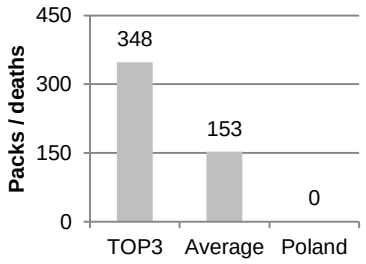
In Poland, the drug is available (reimbursed) with restrictions.

Erbitux (cetuximab) is used in treatment of:

- patients with epidermal growth factor receptor (EGFR)-expressing, RAS wild-type metastatic colorectal cancer;
- patients with squamous cell cancer of the head and neck;

The drug is available as vials containing solution for infusion. Each 20 ml or 100 ml vial contains 5 mg of cetuximab per 1 ml. On the graph, sales data for 50 ml (2 mg/1 ml) vials are presented.

HALAVEN



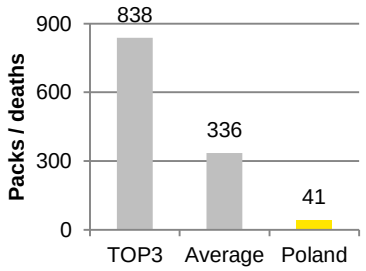
TOP3: France, Austria, Switzerland

In Poland, the drug is unavailable (not reimbursed).

Halaven (eribulin) is an innovative cancer drug used in treatment of patients with locally advanced or metastatic breast cancer and progression after at least one chemotherapeutic regimen used in advanced disease.

The drug is available as vials containing solution for injection. Each 2 ml or 100 ml vial contains 440 units of eribulin per 1 ml of the solution. On the graph, sales data for 2 ml (440 U/ml) vials are presented.

INLYTA



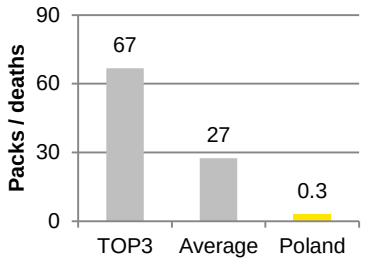
TOP3: France, Switzerland, Austria

In Poland, the drug is available (reimbursed) with restrictions.

Inlyta (axitinib) is used in treatment of adult patients with advanced renal cell carcinoma (RCC), after failure of previous sunitinib or cytokine treatment.

The drug is available as film-coated tablets containing 1 mg, 3 mg, 5 mg, or 7 mg of axitinib. On the graph, sales data for Inlyta packs of 56 tablets containing 1 mg of the active ingredient are presented.

IRESSA



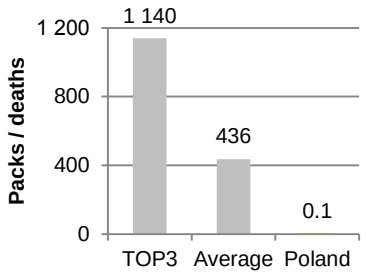
TOP3: Slovakia, Austria, France

In Poland, the drug is available (reimbursed) with restrictions.

Iressa (gefitinib) is an innovative cancer drug used in treatment of adult patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) with an activating EGFR-TK mutation.

The drug is available as film-coated tablets containing 250 mg of gefitinib. On the graph, sales data for Iressa packs of 30 tablets containing 250 mg of the active ingredient are presented.

JAKAVI



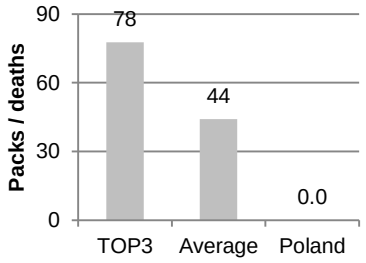
TOP3: Switzerland, Germany, France

In Poland, the drug is unavailable (not reimbursed).

Jakavi (ruxolitinib) is an innovative cancer drug used in treatment of disease-related enlarged spleen or other symptoms in adults with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis.

The drug is available as film-coated tablets containing 5 mg, 10 mg, 15 mg, or 20 mg of ruxolitinib. On the graph, sales data for Jakavi packs of 56 tablets containing 5 mg of the active ingredient are presented.

JEVTANA



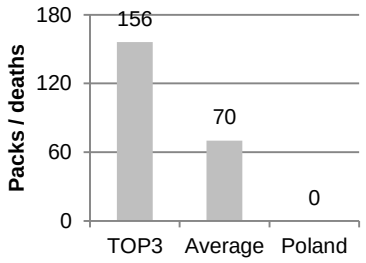
TOP3: Switzerland, France, the Netherlands

In Poland, the drug is unavailable (not reimbursed).

Jevtana (cabazitaxel) is an innovative cancer drug used in combination with prednisone or prednisolone in treatment of patients with hormone-refractory metastatic prostate cancer, after previous docetaxel-based chemotherapy.

The drug is available as concentrate for solution for infusion. Each 1 ml of concentrate contains 40 mg of cabazitaxel. On the graph, sales data for 1,5 ml vials are presented.

KADCYLA



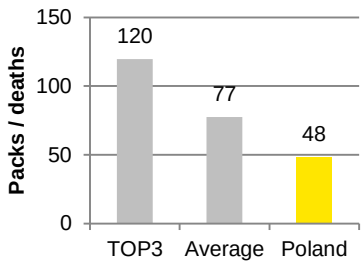
TOP3: Switzerland, Germany, Austria

In Poland, the drug is unavailable (not reimbursed).

Kadcyla (trastuzumab emtansine) is used in treatment of adult patients with HER2-positive, unresectable, locally advanced or metastatic breast cancer after previous therapy with trastuzumab and a taxane, administered separately or in combination.

The drug is available as vials containing powder for solution for injection (20 mg/ml). Each vial contains 100 mg or 160 mg of trastuzumab with emtansine. On the graph, sales data for single vials containing 100 mg of trastuzumab with emtansine are presented.

NEXAVAR



TOP3: Romania, France, Austria

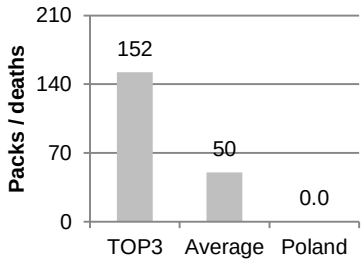
In Poland, the drug is available (reimbursed) with restrictions.

Nexavar (sorafenib) is used in treatment of patients with:

- hepatocellular carcinoma;
- advanced renal cell carcinoma after failure of previous therapy with interferon-alpha or interleukin-2, or if patients are ineligible for such a therapy;
- progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma refractory to radioactive iodine.

The drug is available as film-coated tablets containing 200 mg of sorafenib. On the graph, sales data for packs containing 112 tablets are presented.

PERJETA



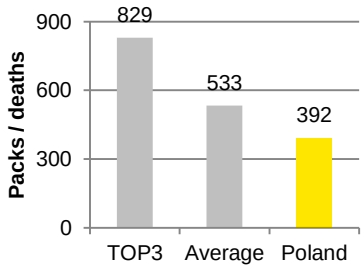
TOP3: Switzerland, Austria, Germany

In Poland, the drug is unavailable (not reimbursed).

Perjeta (pertuzumab) is used in combination with trastuzumab and docetaxel in adult patients with metastatic or unresectable locally recurrent HER2-positive breast cancer who have not received anti-HER2 therapy or chemotherapy for metastatic disease.

The drug is available as concentrate for solution for infusion. One 14 ml vial contains 420 mg of pertuzumab (30 mg/ml). On the graph, sales data for single 14 ml vials are presented.

SPRYCEL



TOP3: Romania, France, the Netherlands

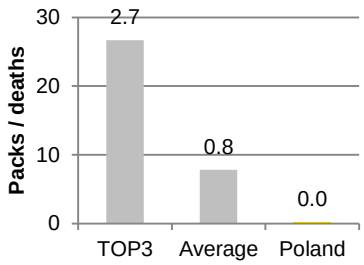
In Poland, the drug is available (reimbursed) with restrictions.

Sprycel (dazatinib) is used in treatment of patients with:

- newly diagnosed, Philadelphia chromosome-positive (Ph+) chronic myeloid leukaemia (CML) in chronic phase;
- chronic myeloid leukaemia in chronic, accelerated or blast crisis phase, if resistant or intolerant to previous therapy, including therapy with imatinib mesylate;
- chromosome-Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL), and lymphoblastic blast crisis of CML, if resistant or intolerant to previous therapy.

The drug is available as film-coated tablets. One tablet contains 20 mg, 50 mg, 70 mg, 80 mg, 100 mg, or 140 mg of dazatinib. On the graph, sales data for single packs of 56 tablets containing 200 mg of the active ingredient are presented.

STIVARGA



TOP3: Switzerland, Austria, Germany

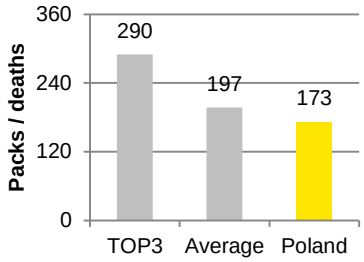
In Poland, the drug is unavailable (not reimbursed).

Stivarga (regorafenib) is used in treatment of patients with:

- metastatic colorectal cancer (CRC) who have been previously treated or are not considered candidates for other available therapies, i.e. fluoropyrimidine-based chemotherapy, or anti-VEGF or anti-EGFR therapy;
- unresectable or metastatic gastrointestinal stromal tumours (GIST) who progressed on or are intolerant to prior treatment with imatinib and sunitinib.

The drug is available as film-coated tablets. One tablet contains 40 mg of regorafenib. On the graph, sales data for packs containing 84 tablets of Sprycel (40 mg) are presented.

SUTENT



TOP3: Slovakia, France, Czech Republic

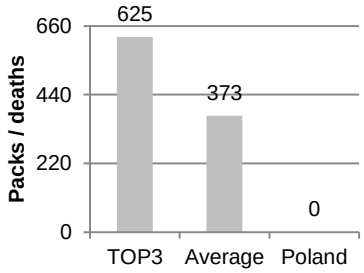
In Poland, the drug is available (reimbursed) with restrictions.

Sutent (sunitinib) is used in treatment of patients with:

- gastrointestinal stromal tumours (GIST). Sutent is used in treatment of patients with GIST, in whom the tumour is unresectable or has disseminated to other organs. The product is used after failure of treatment with imatinib;
- metastatic renal cell carcinoma – the type of renal cancer which has disseminated to other organs;
- pancreatic neuroendocrine tumours which disseminated to other organs and which cannot be resected. Sutent is used for progressive, well-differentiated tumours.

The drug is available as capsules. One capsule contains 12.5 mg, 25 mg, 37.5 mg, or 50 mg of sunitinib. On the graph, sales data for packs containing 30 capsules (12.5 mg) are presented.

TAFINLAR



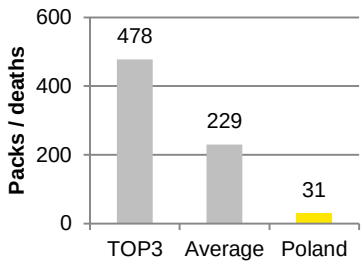
TOP3: Germany, the Netherlands, France

In Poland, the drug is unavailable (not reimbursed).

Tafinlar (dabrafenib) is an innovative cancer drug used in monotherapy in treatment of adult patients with unresectable or metastatic melanoma with BRAF-V600 mutation.

The drug is available as capsules. One capsule contains 50 mg or 75 mg of dabrafenib. On the graph, sales data for packs containing 28 capsules (50 mg) are presented.

TARCEVA



TOP3: Slovakia, France, Romania

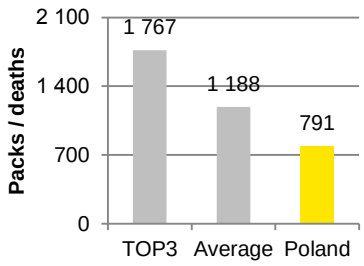
In Poland, the drug is available (reimbursed) with restrictions.

Tarceva (erlotinib) is used:

- in first-line treatment of patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) with activating EGFR mutations;
- in combination with gemcitabine in treatment of patients with metastatic pancreatic cancer.

The drug is available as film-coated tablets. One tablet contains 25 mg, 100 mg, or 150 mg of erlotinib. On the graph, sales data for packs containing 30 tablets (25 mg) are presented.

TASIGNA



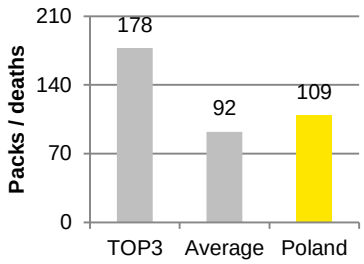
TOP3: Slovakia, Switzerland, Germany

In Poland, the drug is available (reimbursed) with restrictions.

Tasigna (nilotinib) is used in treatment of adult patients with newly diagnosed, Philadelphia chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase.

The drug is available as film-coated tablets. One tablet contains 150 mg or 200 mg of nilotinib. On the graph, sales data for packs containing 28 capsules (150 mg) are presented.

TYVERB



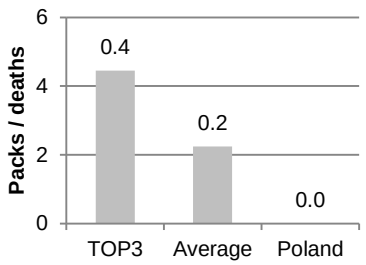
TOP3: Slovakia, Spain, Italy

In Poland, the drug is available (reimbursed) with restrictions.

Tyverb/Tykerb (lapatinib) is an innovative cancer drug used in treatment of adult patients with breast cancer whose tumours overexpress HER2 (ErbB2).

The drug is available as film-coated tablets. One tablet contains 250 mg of lapatinib. On the graph, sales data for packs containing 70 tablets (250 mg) are presented.

VECTIBIX



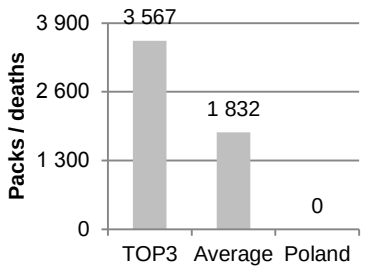
TOP3: Austria, the Netherlands, Germany

In Poland, the drug is available (reimbursed) with restrictions.

Vectibix (panitumumab) is used in treatment of adult patients with wild-type RAS metastatic colorectal cancer (mCRC).

The drug is available as vials containing concentrate for solution for infusion. Each vial contains 100 mg of panitumumab in 5 ml of concentrate, 200 mg of panitumumab in 10 ml, or 400 mg of panitumumab in 20 ml. On the graph, sales data for 5 ml vials (20 mg/ml) are presented.

VIDAZA



TOP3: Spain, Switzerland, Austria

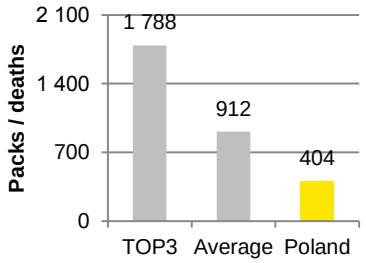
In Poland, the drug is available (reimbursed).

Vidaza (azacitidine) is used in treatment of adult patients not eligible for hematopoietic stem cell transplantation and diagnosed with:

- myelodysplastic syndromes (MDS) of intermediate and high risk, according to the International Prognostic Scoring System (IPSS);
- chronic myelomonocytic leukaemia (CMML) with 10-29% bone marrow blasts, without a myeloproliferative disorder;
- acute myeloid leukaemia (AML) with 20-30% of blasts and multilineage dysplasia, according to the WHO classification.

The drug is available as vials containing powder for suspension for injection. Each vial contains 100 mg of azacitidine. After reconstitution, each ml of suspension contains 25 mg of azacitidine. On the graph, sales data for vials containing 100 mg of powder are presented.

VOTRIENT



TOP3: Switzerland, Slovakia, Austria

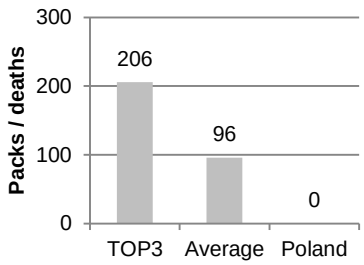
In Poland, the drug is available (reimbursed) with restrictions.

Votrient (pazopanib) is used:

- in first-line treatment of adult patients with advanced renal cell carcinoma (RCC) and in treatment of patients who had received previous cytokine therapy;
- in treatment of patients with specific subtypes of advanced soft tissue sarcoma (STS) who had received previous chemotherapy in treatment of disseminated disease or who had disease progression within 12 months after induction therapy preceding radical treatment or adjuvant treatment.

The drug is available as film-coated tablets. One tablet contains 200 mg or 400 mg of pazopanib. On the graph, sales data for packs containing 30 tablets (200 mg) are presented.

XALKORI



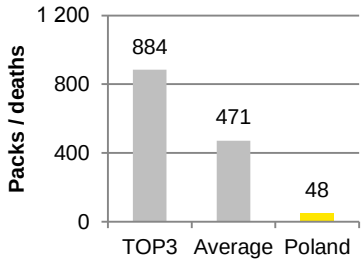
TOP3: France, Switzerland, Austria

In Poland, the drug is unavailable (not reimbursed).

Xalkori (crizotinib) is used in treatment of adult patients with previously treated ALK-positive non-small-cell lung cancer (NSCLC).

The drug is available as capsules. One capsule contains 200 mg or 250 mg of crizotinib. On the graph, sales data for packs containing 60 capsules of Xalkori (200 mg) are presented.

YERVOY



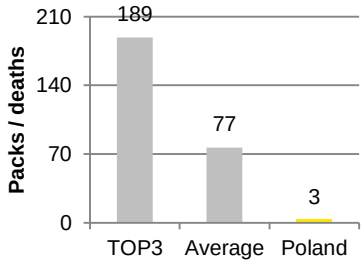
TOP3: France, Austria, Germany

In Poland, the drug is available (reimbursed) with restrictions.

Yervoy (ipilimumab) is a cancer drug used in treatment of advanced (unresectable or metastatic) melanoma in adults.

The drug is available as vials containing concentrate for solution for injection. Each vial contains 50 mg of ipilimumab in 10 ml of concentrate or 200 mg of ipilimumab in 40 ml. On the graph, sales data for 10 ml vials (5 mg/ml) are presented.

YONDELIS



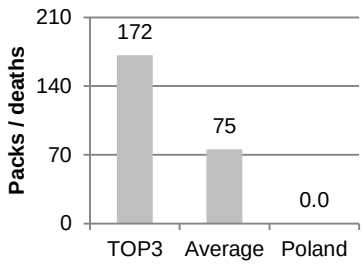
TOP3: Austria, Italy, Spain

In Poland, the drug is available (reimbursed) with restrictions.

Yondelis (trabectedin) is used in treatment of adult patients with advanced soft tissue sarcoma after failure of anthracyclines and ifosfamide or patients not eligible for treatment with those drugs.

The drug is available as vials containing powder for suspension for infusion. Each vial contains 250 units or 1 mg of trabectedin. After reconstitution, each ml of suspension contains 50 units of trabectedin. On the graph, sales data for vials containing 250 U of powder are presented.

ZALTRAP



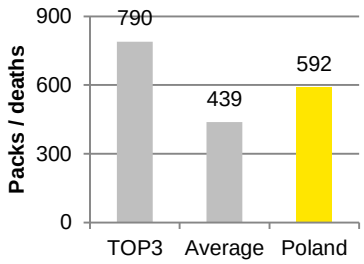
TOP3: Switzerland, Austria, Germany

In Poland, the drug is unavailable (not reimbursed).

Zaltrap (aflibercept) is used in treatment of advanced melanoma (unresectable or metastatic) in adults.

The drug is available as vials containing concentrate for solution for infusion. Each vial contains 100 mg of aflibercept in 4 ml of concentrate or 200 mg of aflibercept in 8 ml. On the graph, sales data for 4 ml vials of Zaltrap (25 mg/ml) are presented.

ZELBORAF



TOP3: France, Switzerland, Italy

In Poland the drug is available (reimbursed) with restrictions.

Zelboraf (vemurafenib) is an innovative cancer drug used in treatment of melanoma (disseminated to other organs or unresectable). The drug is applicable only in patients with BRAF-V600 mutation in melanoma cells.

The drug is available as film-coated tablets. One tablet contains 240 mg of vemurafenib. On the graph, sales data for packs containing 56 tablets (240 mg) are presented.

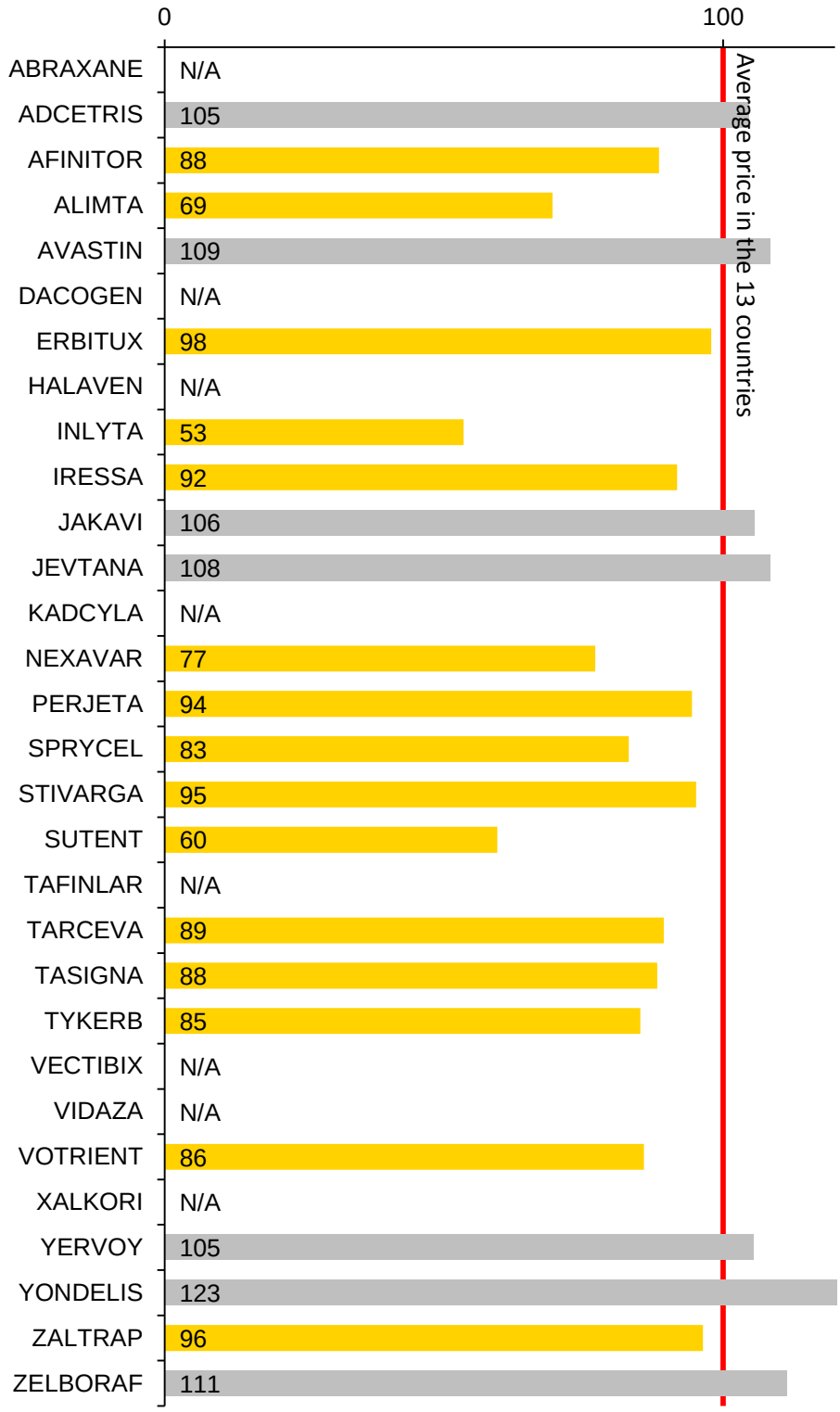
In Poland,[13] the prices of innovative drugs are (among) the lowest in Europe.

In the analysed group of 22 drugs, for which the sales in Poland (in the period 2013Q4–2014Q3) was recorded, the prices of 15 were lower than the European mean price, and in the case of two drugs, they were lower by over 25%.

Poland makes little use of the preferential prices and drug availability, imposing numerous drug use restrictions in therapeutic programmes.

13 Prices calculated on the basis of the manufacturers' sales values.

Graph 27. Comparison of mean drug prices in Poland and in the 13 countries (100 = mean price in the 13 countries*) in the period 2013Q4–2014Q3



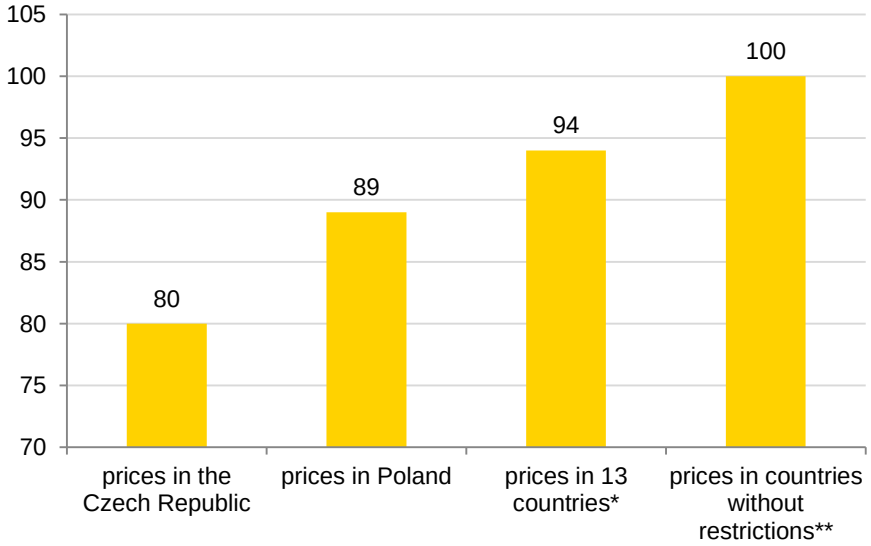
**) Prices in the period 1Q2013-3Q2014 in 13 countries: the Czech Republic, France, Germany, the Netherlands, Slovakia, Spain, the United Kingdom, Italy, Austria, Hungary, Poland, Romania, Switzerland; N/A – not available.*

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

The analysis of innovative drugs prices shows significant differences between individual countries. Below (graph 28), prices of drug packages are compared[14]. The prices of the drug package in Poland would be lower by 5 pp. than prices in the 13 analysed countries and by 11 pp. than prices in countries without drug use restrictions. At the same time, it should be noted that the prices of the drug package in the Czech Republic would be lower by 14 pp. than prices in the 13 investigated countries.

In summary, average prices of these drugs in Poland are lower than average prices in the investigated countries but higher than those in the Czech Republic, which may constitute a reference point for the prices on the Polish market.

Graph 28. Innovative drug package price index in countries without reimbursement restrictions (prices in countries without restrictions = 100)



**) Prices in the period 1Q2013-3Q2014 in 13 countries: the Czech Republic, France, Germany, the Netherlands, Slovakia, Spain, the United Kingdom, Italy, Austria, Hungary, Poland, Romania, Switzerland.*

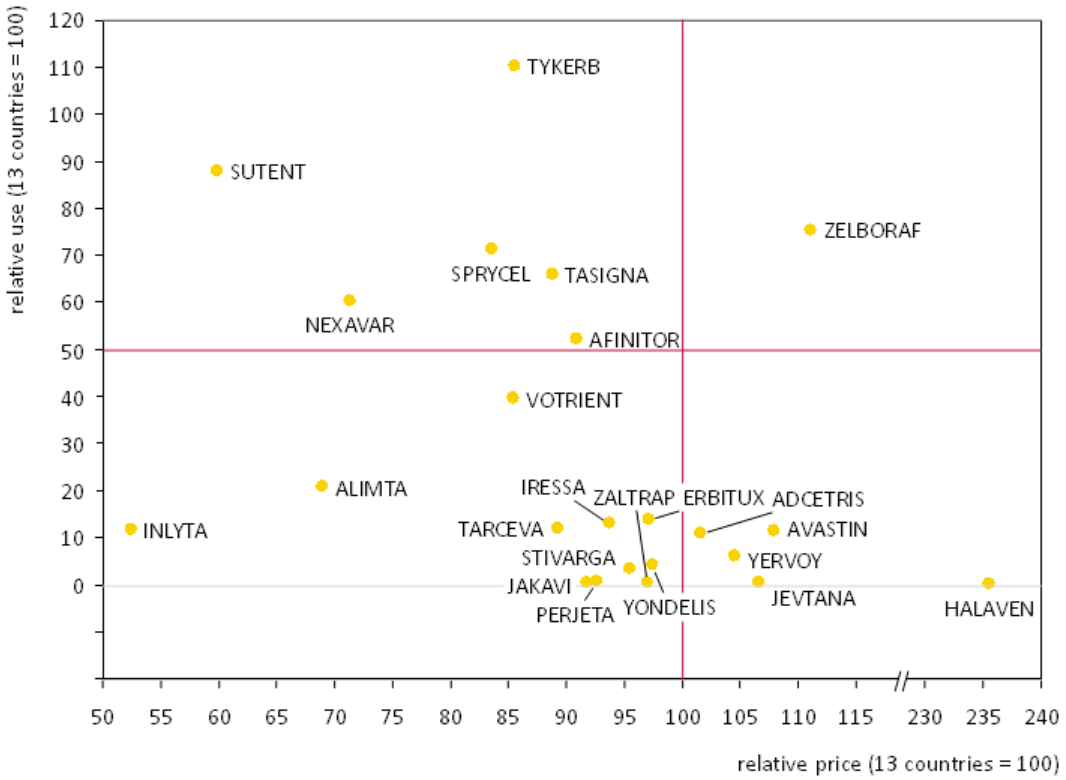
***) prices in the period 1Q2013-3Q2014 in the following countries: Germany, the Netherlands, Italy, Austria, Switzerland, Spain*

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

Attractive prices of innovative drugs in Poland make it possible to consider appropriate changes in the scope of reimbursement to provide cancer patients with increasingly wider access to innovative therapies. It would be particularly beneficial with respect to products of the highest therapeutic efficacy in comparison with currently used drugs.

[14] Mean drug utilisation in the investigated 13 countries and six countries with no drug use restrictions in the period 2013Q1–2013Q3

Graph 29. Utilisation and prices of the analysed drugs in Poland in comparison with the 13 analysed European countries in the period 2013Q4–2014Q3



**) The 13 countries are: Poland, Austria, the Czech Republic, France, Spain, the Netherlands, Germany, Romania, Slovakia, Switzerland, Hungary, Italy, and the United Kingdom.*

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

6. Analysis of drug availability

6.1 Classification of 30 drugs in 13 countries by availability (available, available with restrictions, unavailable)

Selected innovative cancer drugs were classified into three categories according to their availability through the payers' reimbursement systems in selected European countries:

- available:
  - the drug is available through the payer's reimbursement system;
  - therapeutic indications for which the drug is reimbursed are not restricted in relation to the indications listed in the EMA documentation;
  - the drug is reimbursed in 100% or through co-payment and the patient does not need to pay a significant price per pack;
- available with restrictions:
  - the drug is available through the payer's reimbursement system;
  - therapeutic indications for which the drug is reimbursed are restricted in relation to the indications listed in the EMA documentation;
  - the drug is reimbursed only through co-payment and the patient must pay a significant price per pack;
  - in the case of Austria and Germany, the drug has not been placed on the reimbursement list but can be accessed through the hospital budget (allocated for DRGs);
- unavailable:
  - the drug is unavailable through the payer's reimbursement system, and its use in therapy is not financed from other public funds (such as the Cancer Drugs Fund in the United Kingdom).

This classification takes into account drugs present on reimbursement lists and used in therapeutic programmes in selected European countries in January 2015. The classification is presented in Table 5.

Table 5. Availability of drugs through reimbursement systems. Status as of January 2015.

Drug	Poland	Netherlands	Germany	Austria	Italy	Switzerland	Spain	France	Czech Republic	United Kingdom	Slovakia	Hungary	Romania
ABRAXANE													
ADCETRIS													
AFINITOR													
ALIMTA													
AVASTIN													
DACOGEN													
ERBITUX													
HALAVEN													
INLYTA													
IRESSA													
JAKAVI													
JEVTANA													
KADCYLA													
NEXAVAR													
PERJETA													
SPRYCEL													
STIVARGA													
SUTENT													
TAFINLAR													
TARCEVA													
TASIGNA													
TYVERB													
VECTIBIX													
VIDAZA													
VOTRIENT													
XALKORI													
YERVOY													
YONDELIS													
ZALTRAP													
ZELBORAF													
No. of drugs available	2	30	13	5	28	25	24	21	2	15	15	14	11
No. of drugs available with restrictions	16	0	17	25	0	3	3	4	21	5	2	0	0
Total	18	30	30	30	28	28	27	25	23	20	17	14	11

– available (reimbursed)

– available (reimbursed) with restrictions

– unavailable (not reimbursed)

Source: 1) Poland: http://www.mz.gov.pl/leki/refundacja/programy-lekowe; 2) the Netherlands: http://www.medicijnkosten.nl; 3) Germany: http://www.akdae.de/Stellungnahmen/AMNOG/A-Z/index.html; 4) Austria: EKO: http://www.erstattungskodex.at/portal27/portal/hvbportal/content/contentWindow?contentid=10007.693707&action=2&viewmode=content; 5) Italy: AIFA: http://www.agenziafarmaco.gov.it/it/content/liste-di-trasparenza-e-rimborsabilit%C3%A0; 6) Switzerland: FOPH: http://www.bag.admin.ch/themen/krankenversicherung/00263/00264/00265/index.html?lang=en; 7) Spain: http:// Vademecum.es; 8) France: http://base-donnees-publique.medicaments.gouv.fr/index.php#result; 9) Czech Republic: SUKL: http://www.sukl.eu/; 10) United Kingdom: CDF: http://www.ppa.org.uk/edt/February_2015/mindex.htm, 11) Slovakia: SUKL: http://www.sukl.sk/,; 12) Hungary: OEP: http://www.oep.hu/iframes/gyogyszerkereso, http://www.oep.hu/felso_menu/lakossagnak/ellatas_magyarorszagon/egeszsegugyi_ellatasok/Spec_ellatas/tetelels_gyogyo.html; 13) Romania: CNAS: http://www.cnas.ro/page/lista-medicamentelor-2015.html. Accessed on: 30 January 2015

The number of drugs available through the reimbursement system without restrictions is the highest in the Netherlands (30), Italy (26), Switzerland (25), Spain (22), and France (21). To those, one may add Germany and Austria where the budget for hospital drugs is allocated for the group of patients with a given indication.

The number of drugs available through the reimbursement system without restrictions is the lowest in Poland (2) and the Czech Republic (2). However, it is worth mentioning that the overall number of drugs available through the Czech reimbursement system (i.e. classified as available and available with restrictions) is higher than in Poland (23 drugs in the Czech Republic and 18 in Poland).

The number of drugs available through the reimbursement system is the lowest in Romania (11), Hungary (14) and Slovakia (17); however, the scope of indications for use is not limited in any of those countries.

7. Analysis of the time that elapsed before drugs were available

7.1 Drug availability from authorisation by EMA/HTA through the reimbursement decision to the achievement of a considerable sales level

In this chapter, the time is analysed that must elapse between authorisation by EMA, the first sale of a drug in a given country, and the achievement of the following sales levels:

- noticeable level: 3% of relative sales volume[15] in TOP3 countries,
- considerable level: 10% of relative sales volume in TOP3 countries,
- significant level: 25% of relative sales volume in TOP3 countries.

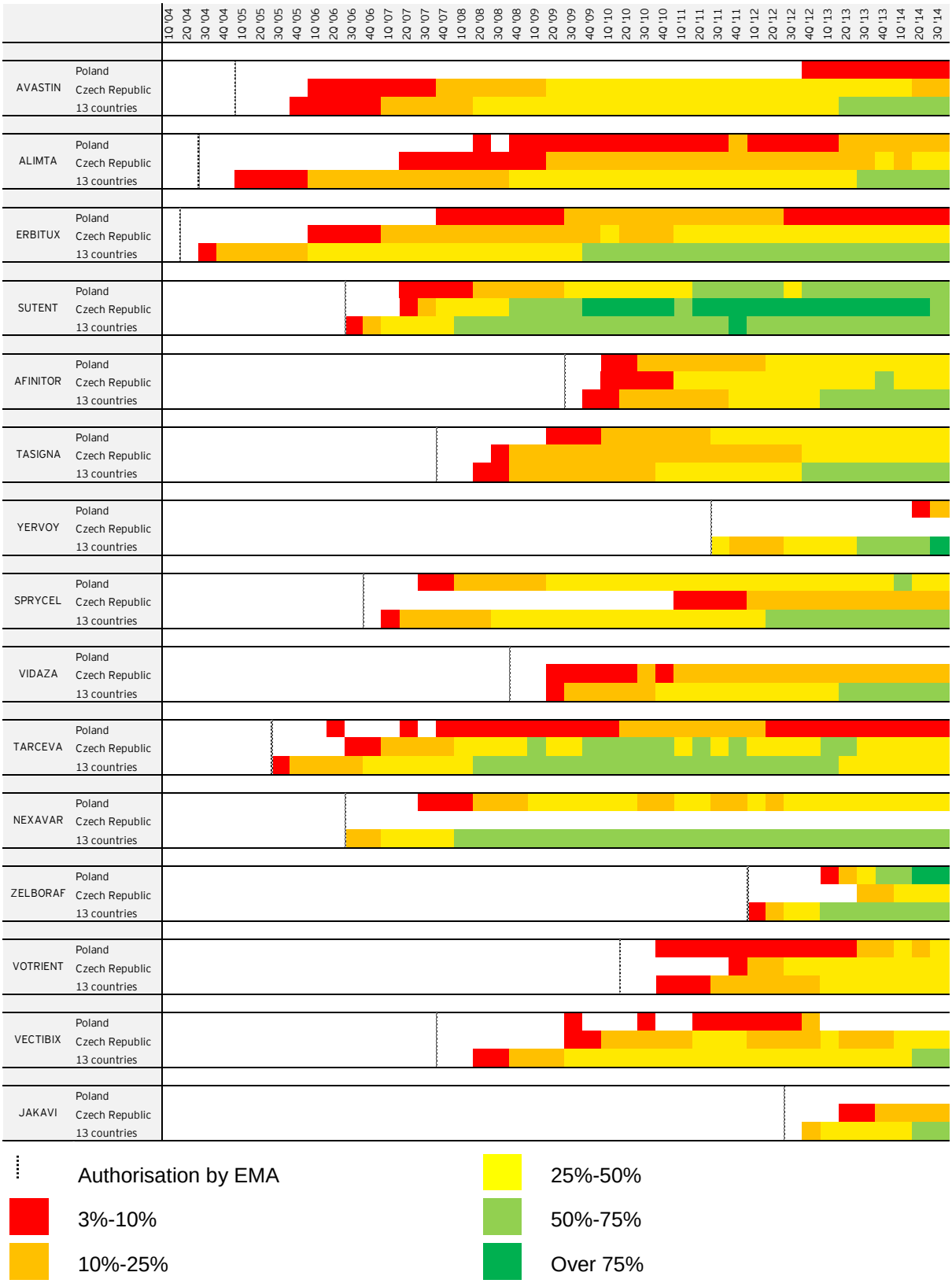
The aim of the analysis was to demonstrate when a drug was actually available for purchase after marketing authorisation was granted (organisation of a distribution network) and how restrictions concerning drug access through the reimbursement system affected the time needed to achieve an increase in drug utilisation (sales volume) to selected levels.

Although it takes a relatively short time to obtain marketing authorisation for innovative drugs in Poland (graph 30) on the basis of the EMA certification, their utilisation is significantly lower than in other European countries.

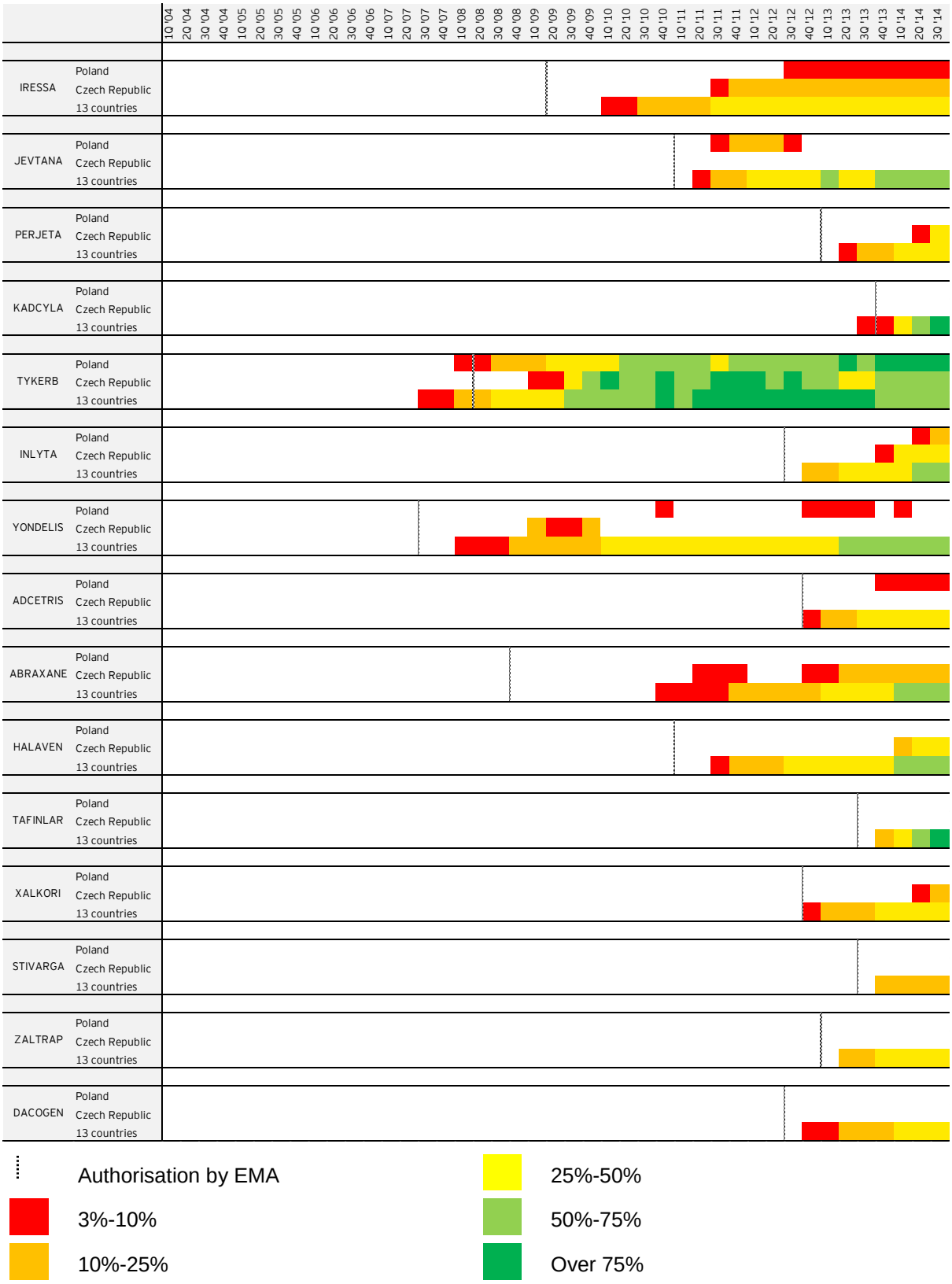
Only in the case of four innovative drugs, i.e. Tyverb, Sutent, Zelboraf and Sprycel, indicated for patients with certain cancers (breast cancer, pancreatic cancer, skin cancer, and leukaemia, respectively), utilisation exceeded 50% of the TOP3 level, while for 10 drugs used, among others, in treatment of lung and colorectal cancer, utilisation did not exceed the significant level (i.e. 25% of the TOP3 level). Many drugs are not reimbursed in Poland or their utilisation (Alimta, Avastin, Jevtana, Tarceva and Vectibix) is among the lowest in the investigated group of countries.

[15] Sales in the period of 12 months, i.e. 2013Q4–2014Q3.

Graph 30. First sales of the drugs in Poland in relation to the date of authorisation by EMA



% in relation to mean (volume of sales/number of deaths) drug utilisation in the period 2013Q4–2014Q3 in “TOP3” countries for a specific drug.



% in relation to mean (volume of sales/number of deaths) drug utilisation in the period 2013Q4–2014Q3 in “TOP3” countries for a specific drug.

Graph 31 shows how much time (expressed in quarters) elapsed from authorisation by EMA to the actual availability for purchase (beginning of distribution) in selected European countries.

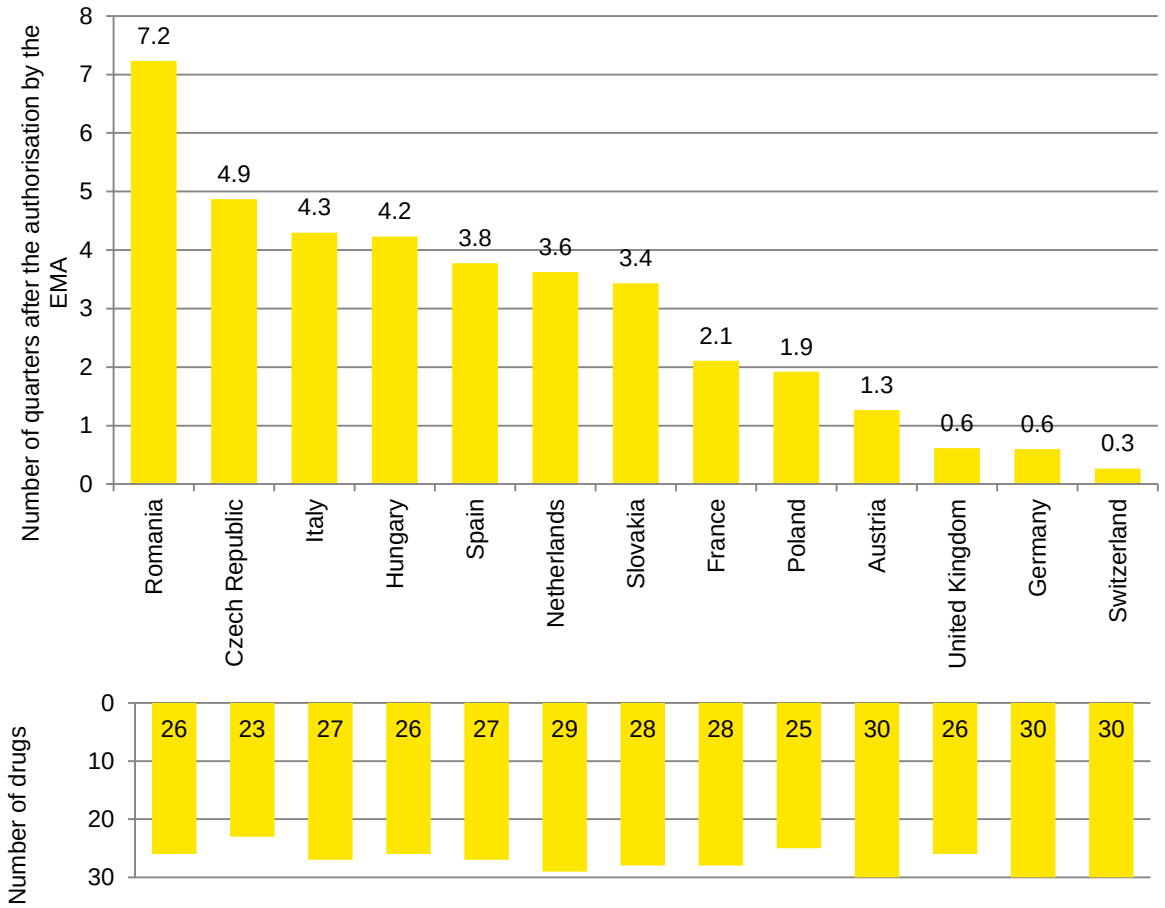
Mean time to the first sale of the drugs was the shortest in Switzerland (mean: 0.3 quarter after authorisation by EMA), Germany (0.6), the United Kingdom (0.6) and Austria (1.3).

In Switzerland, which is not a part of the European Union, drugs are authorised locally (HTA). In most cases, authorisation was granted at a time similar to that of EMA authorisation, or even several months earlier. The greatest discrepancies concern the following drugs: Iressa (EMA: 2009, HTA: 2004), Vidaza (EMA: 2008, HTA: 2006) and Yondelis (EMA: 2007, HTA: 2009).

The longest time to the first sale was observed in Romania – 7.2 quarters after authorisation by EMA.

In Poland, innovative drugs may be purchased by patients with their private means quite quickly, as soon as after 1.9 quarters following authorisation by EMA. The sales were noted for 25 of 30 drugs, 16 of which are currently reimbursed.

Graph 31. Mean time (in quarters) between authorisation by EMA and the first sale for innovative drugs.



The number of drugs represents the number of drugs (of all the 30 investigated drugs) for which sales were noted.

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

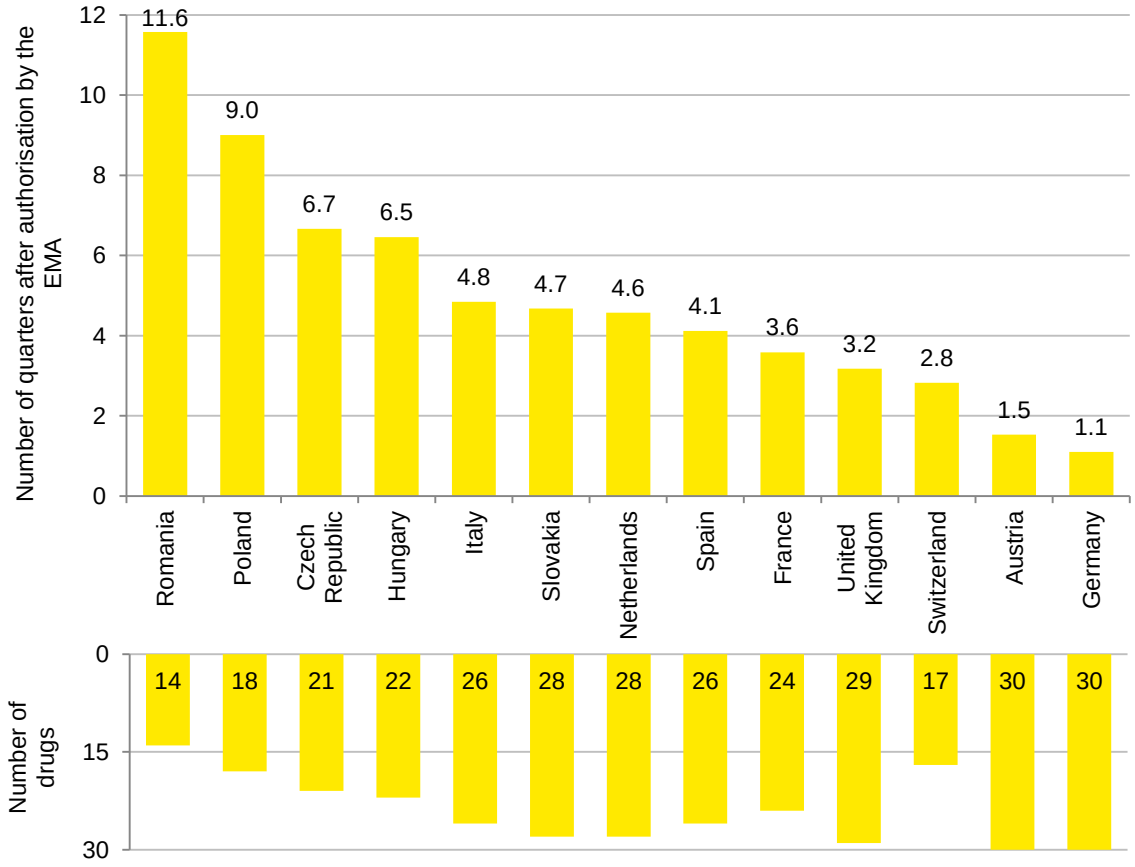
Another analysed period was that between authorisation by EMA and the achievement of a noticeable utilisation level in a specific country.

A trend is visible towards more rapid achievement of this sales level in highly developed countries where the cancer care systems are comprehensive and include investment in medical equipment and prevention programmes as well as access to innovative drugs through reimbursement systems.

A significant sales level was achieved most quickly in Germany (1.1 quarters) and Austria (1.5 quarters) which resulted from the approach to drug reimbursement discussed above.

Achievement of a noticeable sales level takes the longest time in Romania – almost 3 years (11.6 quarters), followed by Poland – over 2 years (9.0 quarters).

Graph 32. Mean time (in quarters) between authorisation by EMA and the achievement of a noticeable utilisation level for innovative drugs.



The number of drugs represents the number of drugs (of all the 30 investigated drugs) for which the level of 3% of the TOP3 sales volume was achieved.

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

On Graph 33, the time needed to achieve a considerable [16] and significant[17] utilisation level in the investigated countries is presented.

[16] considerable level: 10% of the relative sales volume in TOP3 countries

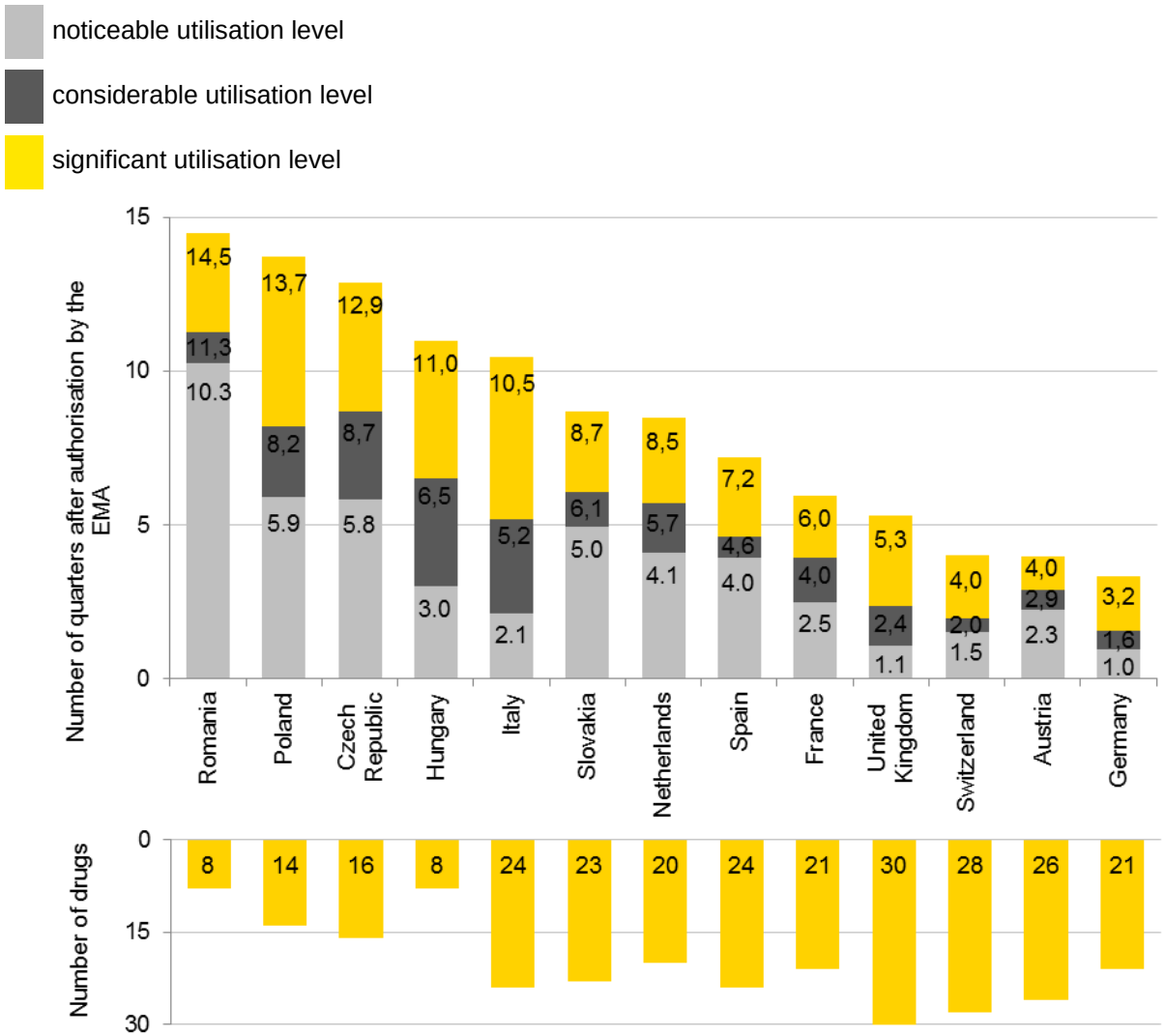
[17] significant level: 25% of the relative sales volume in TOP3 countries

The ranking looks similar to the previous one. The shortest time to achieve both utilisation levels was observed in Germany (considerable: 1.6; significant: 3.2), Austria (considerable: 2.9; significant: 4.0), and Switzerland (considerable: 2.0; significant: 4.0).

The time to achieve increased utilisation was the longest in Romania (considerable level: 11.3; significant level: 14.5), Poland (considerable level: 8.2; significant level: 13.7), and the Czech Republic (considerable level: 8.7; significant level: 12.9).

The fact that the time required for the achievement of a significant sales level is longer results from restrictions imposed by the cancer care payer on access to drugs through the reimbursement system. The scope of restrictions is different, which results in the stabilisation of drug utilisation (sales volume) at various levels in selected countries.

Graph 33. Mean time (in quarters) between authorisation by EMA and the achievement of a considerable and significant utilisation level for innovative drugs.



The number of drugs represents the number of drugs (of all the 30 investigated drugs) for which the level of 25% of the TOP3 sales volume was achieved.

Source: PADDS IMS MIDAS Q3/2014 data, own analysis.

8. Drug reimbursement models

In this chapter, drug reimbursement models in Poland, the Czech republic, Germany and the United Kingdom are presented. A summary is presented in table 6.

Table 6. Comparison of drug reimbursement models in selected countries.

	Poland	Czech Republic	Germany	United Kingdom
Financing	NHF covers the costs up to the reimbursement limit for a specific drug.	The patient incurs a part of the drug costs; the rest is funded from the Statutory Health Insurance.	SHI covers the costs of reimbursed drugs.	NHS covers the costs of reimbursed drugs.
Reimbursed drugs	Drugs of proven efficacy placed on the reimbursement list.	Drugs of proven efficacy placed on the reimbursement list.	All authorised drugs are reimbursed, Except products put on the so-called negative list.	Drugs of proven efficacy placed on the reimbursement list.
Reimbursement levels	100%, 50%, 30% or payment of a lump sum.	100% or co-payment for selected drugs.	100% for prescription drugs and some OTC drugs.	100% for prescription drugs.
Reimbursement schemes for cancer drugs	Therapeutic programmes and chemotherapy.	GHIF budget[18] for hospital drugs. No special reimbursement schemes.	SHI budget for hospital drugs allocated per diagnosis related groups. Budget is allocated by hospitals.	Some drugs are funded by NHS. Others are financed from a special Cancer Drugs Fund.

[18] GHIF, General Health Insurance Fund – organisation responsible for the management of the health care budget in the Czech Republic, a counterpart of Polish NHF.

8.1 Poland

In Poland, the National Health Fund (NHF), subordinate to the Minister of Health, is the entity that finances health care services.

The appropriate authority to issue a decision concerning placement of a product on the reimbursement list is the Minister of Health. The Agency for Health Technology Assessment in Poland (AHTAPol) and the Transparency Board are also involved in the reimbursement procedure.

Reimbursement decisions are issued for 2, 3, or 5 years.

Reimbursement applies to:

- drugs,
- foods for particular nutritional uses, and
- medical devices.

The Act provides for a total reimbursement budget not exceeding 17% of the total public funds allocated for guaranteed services in the NHF financial plan.

Reimbursed products are provided to patients:

- free of charge,
- for a lump sum,
- for 30% or 50% of the funding limit, up to the funding limit assumed for a specific limit group (determined on the basis of criteria specified in the law). Accordingly, the NHF covers the cost of drug purchase up to the assumed limit, and the patient is obliged to pay the rest.

Cancer drugs are reimbursed in 100% in therapeutic programmes and chemotherapy programmes. The therapeutic programme defines:

- eligibility criteria for treatment,
- programme exclusion criteria,
- dosing regimen,
- method of administration,
- the list of diagnostic procedures performed at screening for the programme and necessary for treatment monitoring.

The programme eligibility criteria are more stringent than the drug indications listed in the EMA decision regarding authorisation for marketing in Europe.

Access to drugs that have been placed on the list of chemotherapy agents is not limited with respect to the indications approved by EMA.

8.2 Czech Republic

In the Czech Republic, the health care system operates on the basis of Statutory Health Insurance which is provided by nine health insurance funds. The country has a population of about 10.5 million. The system is funded from two combined budgets – public and private. The health care system covers 76.6% of expenses, state and territorial budgets cover about 7.2%, and private expenditure reaches about 16.2%.

Patients incur part of the total drug costs, while health insurance funds cover the remaining costs, by means of direct payment to pharmacies.

The maximum contribution of the insured individual is about EUR 200 per year. Once that level is achieved, the health insurance funds will cover 100% of the treatment costs, minus a lump sum per prescription (EUR 1.20). The reimbursement level is the same for all residents of the Czech Republic.

All reimbursed drugs are placed on the reimbursement list.

Maximum drug prices and reimbursement levels are determined by the State Institute for Drug Control – SUKL (Státní ústav pro kontrolu léčiv). The Ministry of Health of the Czech Republic is also involved in the regulation of pharmaceutical product prices.

In case of hospitalisation, reimbursement covers pharmaceutical products, also those processed for individual needs, radiopharmaceuticals and products for transfusion, which have lower prices, depending on disease severity and extent; therefore, the patient's co-payment is eliminated.

To determine the terms and level of reimbursement, SUKL classifies a given pharmaceutical product into a reference group. A group includes pharmaceutical products which have similar or close efficacy and safety, and similar clinical use, which makes them interchangeable.

The Institute for Insurance also decides on highly innovative products for which data on efficacy or clinical therapy outcomes are not sufficient. The Institute issues reimbursement decisions only when it is in the public interest, when the available data show therapeutic benefits of a highly innovative pharmaceutical product, and the product meets all the conditions necessary to determine the terms and level of reimbursement by the payer. In addition, such a highly innovative product has to be reimbursed in at least one other state. The Institute may determine the reimbursement level and terms for 12 months and may renew the decision three times.

8.3 United Kingdom

The National Health System (NHS) covers 100% of drug costs, with the exception of non-prescription drugs. Patients pay a small fixed fee per prescription; exemptions include persons aged > 60 or < 16 years, and persons aged 16-18 years and in full-time education.

Guidance on the use of pharmaceuticals is issued by the National Institute for Health and Clinical Excellence (NICE). In drug evaluation, NICE uses mainly ratio methods, in particular those based on the quality-adjusted life year (QALY) measure[19], where one QALY is equal to one year of life in perfect health. NICE estimates that interventions costing less than GBP 20,000 per QALY are cost effective. Interventions costing between GBP 20,000 and GBP 30,000 are subject to discussion, and those costing over GBP 30,000 are rarely made accessible. Currently, NICE assesses about 40% of new drugs introduced to the British market a year.

NHS is obliged to finance the drugs recommended by NICE, but negative recommendation does not preclude funding of a drug or intervention. NICE does not negotiate drug prices. This is the task of the Department of Health.

Cancer drugs are also financed for from a special Cancer Drugs Fund (CDF), which was established and is supervised by the National Health Services (and will be supported until the end of March 2016). The aim of CDF is to provide reimbursement of cancer drugs that have not been approved by the National Institute for Health and Care Excellence (NICE).

CDF has a list of drugs which it makes accessible and defines the conditions (disease stage and interventions that must or must not be made) and method of administration. The CDF criteria are more stringent than the drug indications listed in the EMA decision regarding authorisation for marketing in Europe.

In some cases – on patients' request – other drugs, used in treatment of rare cancers, may be placed on the CDF's list.

The lists of drugs are complemented by the Chemotherapy Clinical Reference Group, within which four regional expert teams operate.

[19] See: Calculating QALYs, comparing QALY and DALY calculations
http://heapol.oxfordjournals.org/content/21/5/402.full (status as on 20/03/2015)

Financing of cancer drugs may be considered if at least one of the following conditions is met:

- the drug (in monotherapy or in combination therapy) has been assessed by NICE, the therapy has been deemed ineffective, and as a result has not been recommended for reimbursement, or NICE has decided on making a recommendation but only with respect to some of the indications listed in the EMA decision regarding marketing authorisation;
- the drug (in monotherapy or in combination therapy) has not been assessed by NICE yet;
- the drug (in monotherapy or in combination therapy) has received negative recommendation for reimbursement by NICE;
- the drug (in monotherapy or in combination therapy) has not been considered a priority drug by NHS and as a result no principles of reimbursement have been established.

Another way to increase access to innovative drugs is the process of Promising Innovative Medicine (PIM). PIM is part of the Early Access to Medicine Scheme (EAMS), whose aim is to provide patients suffering from severe, life-threatening conditions access to drugs for which marketing authorisation has not been granted yet. Under the scheme, the Medicines and Healthcare Products Regulatory Agency (MHRA) assesses drugs for their efficacy and possible risks. The MHRA opinion is valid for one year and may be renewed, but it does not replace the authorisation procedure.

8.4 Germany

In Germany, universal access to health care is guaranteed by the Statutory Health Insurance (SHI), which is compulsory for all citizens (about 80.5 million). The SHI covers about 85.5% of the population, 10% have private insurance, and 5% are covered by fixed compensation premiums. Drug costs are paid by the SHI directly to pharmacies.

All drugs which have been authorised in Germany are reimbursed by the SHI. However, the Ministry of Health, through the Quality Assurance Institute (QAI), may exclude drugs considered not cost-effective and that provide no additional benefits. The drugs are then put on a so-called negative list of not reimbursed drugs.

Patients pay 10% of the drug price, with the minimum fee of EUR 5 and the maximum rate of EUR 100 per prescription over the annual limit calculated on the basis of their income. Drugs with price 30% below the reference price are excluded.

The general reimbursement rules do not apply to children aged up to 12 years, for whom both prescription and non-prescription drugs are paid for in total (100%). For children aged up to 18 years, all prescription drugs and non-prescription drugs for specified indications are reimbursed. For adults, the total costs (100%) are refunded in the case of all prescription drugs and several non-prescription drugs for specified indications.

Drugs intended for hospital use (including cancer drugs) and funds for therapy (including reimbursement) are allocated on the basis of Diagnosis Related Groups (DRGs). The DRG system classifies patients into groups by diagnosis, age, complications etc. Additional budget resources are also allocated to special groups within DRGs, i.e. ZE, responsible, among others, for dialysis and therapy with special drugs.

For every drug that has been authorised in Germany, a decision on reimbursement or placement on the negative list is issued within 12 months of marketing authorisation. In the reimbursement process, benefits of a specific medicine are assessed. A benefit, supported by clinical trials, is presented by the manufacturer in the reimbursement application. An assessment is carried out by the Institute for Quality and Efficiency in Healthcare (IQWiG), and the decision is made by G-BA – the committee responsible for the decision on reimbursement of health care interventions.

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