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**Evolution of costs with cancer drugs in a Portuguese Hospital**

Peixoto V *et al*. Costs with cancer drugs

Vânia Peixoto, Ana Luísa Faria, Márcia Gonçalves, Joana Macedo, Sónia Rego, Emilio Macías, Aldiro Magano, Márcia Loureiro, António Araújo

**Vânia Peixoto, Ana Luísa Faria, Joana Macedo, Sónia Rego, Emilio Macías, Aldiro Magano, António Araújo**, Department of Medical Oncology, Centro Hospitalar de Entre Douro e Vouga, 4520-211 Santa Maria da Feira, Portugal

**Márcia Gonçalves, Márcia Loureiro**, Pharmacy Department, Centro Hospitalar de Entre Douro e Vouga, 4520-211 Santa Maria da Feira, Portugal

**Author contributions:** Peixoto V, Araújo A contributed to the conception and study design, acquisition of data, analysis and interpretation of data, drafting the article; Faria AL, Macedo J, Rego S, Macías E contributed to conception study, revising article critically for important intellectual content; Gonçalves M, Magano A, Loureiro M contributed to acquisition of data, analysis and interpretation of data, revising article critically for important intellectual content.

**Correspondence to: António Araújo, MD, PhD,** Department of Medical Oncology, Centro Hospitalar de Entre Douro e Vouga, Rua Doutor Cândido Pinho, 4520-211 Santa Maria da Feira, Portugal. amfaraujo@netcabo.pt

**Telephone:** +351-256-379700 **Fax**: +351-256-373867

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**Abstract**

**AIM:** To analyze the costs with cancer drugs collected in a Portuguese Hospital, and comparison with Karolinska Institutet study.

**METHODS:** For evaluation of spending on cancer drugs, were retrospectively analyzed data on overall costs with cancer drugs, obtained at the Department of Medical Oncology of the Centro Hospitalar de Entre Douro e Vouga, between 2004 and 2010. For comparative study were selected only drugs belonging to the following groups: chemotherapy, targeted therapy, immunotherapy and endocrine therapy. The selected drugs were further grouped according to its market placement year: ≤ 1998, 1999 to 2002, 2003 to 2005, 2006 to 2010. Drugs used as supportive therapy as well as bisphosphonates were excluded.

**RESULTS:** The overall costs with cancer drugs increased gradually between 2004 and 2008 (from 1911947 € to 3666284 €), with an increase in the number of patients treated during this period. The expenditure decreased in 2009 (3438155 €) and increased again in 2010 (3673116 €), but the costs increment wasn’t the same as in previous years. Chemotherapy and targeted therapy were responsible for most expenditure obtained. Drugs placed on national market before 1999 accounted for more than 50% of the expenditure up to 2007. From 2008, these drugs represented less than 50% of total expenditure. Cancer drugs placed between 1999 and 2002 accounted for 25%-35% of costs in all years studied, while drugs placed between 2003 and 2005 for less than 30%. Drugs placed between 2006 and 2010 were responsible for less than 10% of expenditure.

**CONCLUSION:** In this study, more ancient drugs were responsible for most of the expenditure until 2007, which is in agreement with the Karolinska study.

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**Key words**: Cancer; Costs; Drugs; Economy; Treatment

**Core tip:** In the last decade costs related to cancer drugs have increased significantly. This growth seems to be explained by the increase in cancer incidence, new indications for treatment for previously approved cancer drugs and to placement of new drugs on the market, frequently more expensive than the ones already for sale. The results of Karolinska Institutet demonstrated a substantially increase of available cancer drugs and costs between 1998 and 2007. The cost increment wasn’t only related to the introduction of new drugs, but actually 68% of the costs in 2007 came from drugs approved before 1999.

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**INTRODUCTION**

In Portugal, the number of inhabitants and the average life expectancy at birth increased in the last century[1,2]. The most recent data revealed that the average life expectancy in Portugal is 80.8 years, similar to the European average[3]. This increase reflects the improvement in the population's socioeconomic conditions and in the resources dedicated to health care[1,4,5].

The population aging results, among other aspects, in a growth of the incidence in chronic and incurable diseases[4,6,7]. Among them, cancer disease stands out[4,6,7]. Cancer incidence increased over the last decades and in 2008 was estimated 12.7 million new cancer cases worldwide[4,6,7]. In Portugal, the cancer incidence rate standardized by age is 428:100000 in men and 289:100000 in women[1]. Globally, the cancer disease is the second cause of death after cardiovascular diseases[1,8]. In recent years, there was a slight decrease in the mortality rate related to cancer[1,4,6-8]. However, this rate is still high[1,3-5]. In 2008, 7.6 million cancer deaths occurred worldwide[7].

The burden of cancer to society can be measured by direct and indirect costs[4,6,9,10]. Direct costs are related to expenses with prevention and treatment while indirect costs include losses of production due to inability to work caused by disease, disabilities and deaths[4,6,9,10]. Drugs are one of the most investigated components of Oncology, consuming most of its economic resources[4,8,11]. For the past years, direct costs related to cancer treatment have increased significantly[4,12-15]. This increment in costs can be explained by the increase in cancer incidence, new indications for treatment for previously approved cancer drugs and to placement of new drugs on the market, frequently more expensive than the ones already for sale[4,12,16-19]. Despite the continuous growth of expenditure with cancer drugs, it is not expected to be the same as in the last decade[4].

According to the Karolinska Institutet study, in 2007 and in Europe the cost increment wasn’t only related to the introduction of new drugs, but actually 68% of the costs came from drugs approved before 1999[4]. The increase of these drugs, from €4.3 to €26.3 per capita, was the major part of the raise in costs related to drugs for cancer[4]. In this study cancer drugs (chemotherapy, targeted therapy, endocrine therapy and immunotherapy) were grouped according to its market placement year: ≤ 1998; 1999 to 2002; 2003 to 2005; 2006 to 2007. The supportive drugs treatments were excluded[4].

In Portugal, the growth on public spending with cancer drugs has been subject of great debate[1,9]. However, data related to cancer treatment namely direct costs with drug treatments are scarce[9]. For this reason, and with the current study, it is our intention to better understand the Portuguese reality on this subject.

The aims of the current study were the analysis of costs evolution with cancer drugs, collected during the period from 2004 to 2010 at the Department of Medical Oncology of the Centro Hospitalar de Entre Douro e Vouga, the analysis of costs according to the type of drug and the date of its placement on national market, and the comparison with the results obtained in the Karolinska Institutet study.

**MATERIALS AND METHODS**

## *Study design*

After obtaining the necessary authorization by our Administration Board, we conducted a retrospective observational study analyzing the evolution of costs with cancer drugs, during the period from 2004 to 2010, in the Department of Medical Oncology of the Centro Hospitalar de Entre o Douro e Vouga. The first year being studied was 2004 because there was difficulty in obtaining data relating to previous years, and the last year being studied was 2010 since the data collection was conducted in 2011.

The Centro Hospitalar de Entre Douro e Vouga is a Portuguese medium size hospital, functioning since 1999, with 409 beds and responsible for health care to 350000 inhabitants. Until 2010, in the Department of Medical Oncology were treated solid (unless sarcomas, melanomas and tumors of the central nervous system) and hematologic malignancies, mostly in outpatient settings. After 2010, in this Department were treated only solid malignancies exclusively in outpatient.

## *Patient and drug selection*

The patients selected were those treated in the mentioned Department during the period from 2004 to 2010. Because of the incomplete records on the number of patients treated by type of treatment in the first four years under analysis, it wasn’t possible to calculate the average cost per patient and per type of treatment.

According to data provided by Pharmacy Department, were selected all the cancer drugs used during the period under analysis, in inpatient and outpatient, and divided by type of drug: chemotherapy (cytostatics), targeted therapy (monoclonal antibodies, tyrosine kinases inhibitors, mammalian target of rapamycininhibitors), immunotherapy and endocrine therapy. For analyzing the costs, were considered the absolute global cost (purchasing cost to the hospital) with each drug, provided by Pharmacy Department.

To compare our results with the Karolinska Institutet study, drugs used in the Department of Medical Oncology were grouped according to its market placement year: ≤ 1998; 1999 to 2002; 2003 to 2005; 2006 to 2010. To access dates of placement on national market, we performed an Portuguese National Authority for Medication and Healtcare Products database consultation. Because in Karolinska study the supportive drugs weren’t analyzed, in our work these drugs were excluded. Another costs with drugs not used for cancer treatment were also excluded.

# RESULTS

During 2004 and 2010 there was a gradual increase in the number of patients treated in the Department of Medical Oncology (924 patients in year 2004, 1111 in year 2005, 1222 in 2006, 1376 in 2007, 1550 in 2008, 1589 in 2009 and 1560 patients in year 2010). According to data provided by the Pharmacy Department and specifically for the period under analysis, this increase was followed by an increment on the overall costs with cancer drugs until 2008 (Figure 1A). In 2009 the global expenditure decreased, and in 2010 there was an increase in expense to values similar to 2008 (Figure 1A).

The evolution of costs, according to type of drug, obtained in this study is presented in Figure 1B. The chemotherapy and targeted therapy accounted for the most part of expenses, followed by endocrine therapy. In Table 1 are describe the drugs studied according to the year placement on national market.

The global distribution of drugs studied and used by the respective Department, according to the placement on national market, is represented by Figure 1C.

Drugs placed on the national market before 1999 accounted for more than 50% of the expenditure with drugs until 2007 (in 2004 these accounted for 83%; in 2005 for 55%; in 2006 and 2007 for 52% of the expenditure, respectively). After 2008, these drugs represented less than 50% of the total expenditure, and in the last two years of the study expenditure overlapped drugs placed between 2003 and 2005 (in 2008 these represented 40%; in 2009 34% and in 2010 31% of the costs). Drugs placed between 1999 and 2002 accounted for 25%-35% of the expenditure with drugs in every year analyzed. Analyzing the drugs placed between 2003 and 2005, there was a progressive increase in the costs (in 2004 these accounted for 0.3% of the expenditure; in 2005 for 26%; in 2006 for 13%; in 2007 for 15%; in 2008 for 20%; in 2009 for 24% and in 2010 for 34%). The most recently drugs (from 2006 to 2010) accounted for less than 10% of the expenditure, with higher spending in 2006 but with increase expenditure again after 2008.

Expenditure with chemotherapy, targeted therapy and endocrine therapy according to the date of its placement on national market are represented in Figure 2, respectively. The expenses with immunotherapy aren’t represented here because it was the least cause-related spending.

Regarding the expenditure with chemotherapy (Figures 1B and 2A), the expenses with cytostatics have decrease after 2006 and these drugs were no longer the main responsible for the costs with cancer treatment after 2007. The drugs placed on the market before 1999 accounted for the bigger share of the expenditure in all years analyzed, while drugs placed between 1999 and 2002 accounted for less than 25% of expenditure. The drugs placed between 2003 and 2005 accounted for about 20% of costs, showing a progressive decrease. More recent cytostatics accounted for less than 10% of the expenditure.

The expenses with targeted therapy have increased over the years, been the most responsible for costs after 2007 (Figures 1B and 2B). Drugs placed on the market between 1999 and 2002 were the bigger share of the expenditure in each year studied, unless in 2010 where most of the spending was with more recently drugs (placed between 2003 and 2005). Analyzing drugs placed before 1999, there was an increase in expenditure with these drugs until 2006, after which was observed a decrease in costs but with a new increment in the last year studied. The expense with drugs placed between 2003 and 2005 increased gradually during the period under analysis. The most recently drugs (placed between 2006 and 2010) used in this treatment were the least cause-related spending and this cost remained stable.

When analyzing the expenditure with drugs for endocrine therapy (Figure 2C), it was observed that drugs placed before 1999 represented the bigger share of expenses with this treatment. Drugs placed between 1999 and 2002 accounted for 25% to 33% of expenditure with this therapy in every year and drugs placed between 2003 and 2005 suffered a progressive increase on costs, more visible in 2010.

# DISCUSSION

Oncology is registering important progress in available treatments, namely in cancer drugs, therefore granting a significant improvement in healthcare along the years, both in terms of overall survival and quality of care[20-24].

In Europe, between 1998 and 2007, there was an important increment in direct costs related to cancer drugs[4,16,25]. The primary reasons for this were the new indications for already approved drugs and the introduction of new drugs costing significantly more than most of the older cancer drugs[4,6,7]. According to Karolinska study, the increment of costs was due mainly to the growth in sales of drugs already on the market[4]. In 2007, the drugs placed on the market before 1999 accounted for 68% of the total costs with drugs for cancer; drugs placed between 1999 and 2002 accounted for 17%; drugs placed between 2003 and 2005 accounted for 11%; and drugs placed between 2006 and 2007 accounted for 3%[4].

In our study the chemotherapy was the main responsible for the costs with cancer drugs until 2007, after which targeted therapy was the most responsible for expenses. In this work we observed an increase on global costs between 2004 and 2008. Some explains for this increment may be related to the increase on the number of patients treated, to more drug administration sessions per patient (data not presented) in part due to a better overall survival, and to placement of new drugs on the market, frequently more expensive than the ones already for sale. The expenditure decreased in 2009 and increased again in 2010, but the costs increment wasn’t the same as in previous years. Some of the possible reasons for the cost stability for the last 3 years are at local level. This Department of Medical Oncology has adopted some strategies such as acquisition of drugs in smaller doses, study of the cytostatics stability to determine the time allowed to administer a drug after its reconstitution, implementation of treatment guidelines at the Department for the most frequent cancer pathologies, and specific scheduling during weekdays to administer certain drugs such as monoclonal antibodies, reducing the wastes. Other reasons for this observed stability in expenses may be more general, but also with a great importance, and related to the patent expirations, bigger use of generics, increased competition and optimization on the negotiation of prices between the Healthcare Centers Board and Pharmaceutical Industries.

The global results of our study were in accordance to those published by Karolinska Institutet[4]. Up to 2007, drugs placed on national market before 1999 were the main responsible for expenses. Some reasons for this may be the new treatment indications for these drugs and the loss of some of these drugs patents leading to a reduction of its price. Drugs available between 1999 and 2002 came in second place regarding expenditure, whereas drugs placed on the market between 2003 and 2005 came in third place. Recently placed drugs (from 2006) accounted for a smaller percentage of costs. However, after 2008 there was a reduction in costs for previously available drugs followed by a gradual increase in the expenditure with new drugs.

Nevertheless, these results may be affected by several confounding factors that influence the price of pharmaceuticals, such reimbursement and pricing policy, and the Portuguese financial system. Other limitations in our study are related to the retrospective analysis and the period studied that make a selection bias with many confounding factors.

In summary, in this study more ancient drugs were responsible for most of the expenditure in cancer treatments until 2007, after which we observed an increase in expenditure on new drugs. Despite this increase in expenses on new drugs in the last 3 years analyzed, the increment of costs with cancer drugs wasn’t the same as in the previously years. However, more studies must take place to understand the Portuguese reality.

**COMMENTS**

***Background***

Drugs are one of the most investigated components of Oncology, consuming most of its economic resources. For the past years, direct costs related to cancer treatment have increased significantly. This growth seems to be explained by the increase in cancer incidence, new indications for treatment for previously approved cancer drugs and to placement of new drugs on the market, frequently more expensive than the ones already for sale. However, in Portugal data related to cancer treatment cost is scarce.

***Research frontiers***

The results of Karolinska Institutet demonstrated a substantially increase of available cancer drugs and costs between 1998 and 2007. The cost increment wasn’t only related to the introduction of new drugs, but actually 68% of the costs in 2007 came from drugs approved before 1999. In 2007, drugs placed between 1999 and 2002 accounted for 17% of the total costs; drugs placed between 2003 and 2005 accounted for 11%; and drugs placed between 2006 and 2007 accounted for 3%.

***Innovations and breakthroughs***

In this work we observed an increase on global costs with cancer drugs that may be explained by the increase on the number of patients treated, new indications for treatment for previously approved drugs, and the placement of new drugs on the market. These results were in accordance to those published by Karolinska Institutet. Up to 2007, drugs placed on national market before 1999 were the main responsible for expenses. Some reasons for this may be the new treatment indications for these drugs and the loss of some of these drugs patents leading to a reduction of its price. Drugs available between 1999 and 2002 came in second place regarding expenditure, whereas drugs placed on the market between 2003 and 2005 came in third place. Recently placed drugs (from 2006) accounted for a smaller percentage of costs. However, after 2008 there was a reduction in costs for previously available drugs followed by a gradual increase in the expenditure with new drugs.

***Applications***

The study results suggest that more ancient drugs were responsible for most of the expenditure in cancer treatments, but costs with new cancer drugs are increasing.

 ***Terminology***

The burden of cancer to society can be measured by direct and indirect costs. Direct costs are related to expenses with prevention and treatment while indirect costs include losses of production due to inability to work caused by disease, disabilities and deaths. Costs with chemotherapy drugs are related to expenditure with cytostatics, and costs with targeted therapy to monoclonal antibodies, tyrosine kinase inhibitors and mammalian target of rapamycin inhibitors.

***Peer review***

The paper is interesting. It will benefit readers in the field of hospital economic.

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A



B



C

Figure 1 Evolution of global costs with cancer drugs. A: Evolution of global costs with cancer drugs used at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga; B: Evolution of costs by type of drug obtained at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga; C: Evolution of costs with cancer drugs, used at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga, according to its market placement year.



A



B



C

Figure 2 Evolution of costs associated to therapy. A: Evolution of costs associated to chemotherapy treatment, at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga, according to its market placement year; B: Evolution of costs associated to targeted therapy, at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga, according to its market placement year; C: Evolution of costs associated to endocrine therapy, at the Department of Medical Oncology of Centro Hospitalar de Entre Douro e Vouga, according to its market placement year.

Table 1 Drugs selected in the study and its date of introduction on Portuguese market

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Drugs on national market before 1999** | **Market placement year** | **Drugs on national market before 1999** | **Market placement year** | **Drugs on national market between 1999 and 2010** | **Market placement year** |
| Aldesleukin | 1992 | Epirubicin | 1992 | Bleomycin | 2001 |
| Amifostine | 1995 | Estramustine | 1982 | Capecitabine | 2001 |
| Anastrozole | 1996 | Etoposide | 1998 | Exemestane | 1999 |
| Bicalutamide | 1998 | Fludarabine | 1995 | Hydroxyurea | 2001 |
| Bleomycin | 1998 | Fluorouracil | 1997 | Imatinib | 2001 |
| Carboplatin | 1989 | Flutamide | 1998 | Ketoconazole | 2002 |
| Carmustine | 1983 | Gemcitabine | 1996 | Leuprorelin | 1999 |
| Chlorambucil | 1966 | Goserelin | 1998 | Liposomal Doxorubicin | 2000 |
| Cisplatin | 1980 | Idarubicin | 1995 | Oral vinorelbine | 2001 |
| Cyclophosphamide | 1960 | Ifosfamide | 1979 | Raltitrexed | 2001 |
| Cyclosporine | 1990 | Interferon Alfa-2A | 1998 | Temozolomide | 1999 |
| Cyproterone | 1994 | Intravenous vinorelbine | 1993 | Trastuzumab | 2000 |
| Cytarabine | 1996 | Irinotecan | 1997 | Anagrelide | 2004 |
| Dacarbazine | 2000 | Letrozole | 1997 | Bevacizumab | 2005 |
| Dactinomycin | 1980 | Megestrol | 1987 | Bortezomib | 2004 |
| Docetaxel | 1995 | Melphalan | 1966 | Cetuximab | 2004 |
| Doxorubicin | 1998 | Mercaptopurine | 1997 | Erlotinib | 2005 |
| Methotrexate | 1993 | Rituximab | 1998 | Fulvestrant | 2004 |
| Mitomycin | 1984 | Tamoxifen | 1984 | Interleukin 2 | 2005 |
| Mitoxantrone | 1998 | Tegafur | 1985 | Pemetrexed | 2004 |
| Octreotide | 1989 | Thalidomide | 1961 | Azacitidine | 2008 |
| Oxaliplatin | 1993 | Topotecan | 1996 | Lapatinib | 2008 |
| Paclitaxel | 1997 | Vaccine, Bacillus Calmette-Guerin | 1992 | Sorafenib | 2006 |
| Pegylated Liposomal Doxorubicin | 1996 | Vinblastine | 1991 | Sunitinib | 2006 |
| Procarbazine | 1998 | Vincristine | 1993 | Temsirolimus | 2007 |
|  |  |  |  | Trabectedin | 2008 |