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# Pharmaceutical cost savings from the treatment of oncology patients in clinical trials

**Borja Gómez Mediavilla[1], Paloma Lanza León[2,3*], Virginia Martínez Callejo[4], David Cantarero Prieto[2,3], María Lanza Postigo[1], Matilde Salcedo Lambea[1], Yolanda Blanco Mesonero[1], María Ochagavia Sufrategui[4], Ignacio Durán[1,5] and Carmen María Sarabia Cobo[6]**

[1]Medical Oncology and Nanovaccines Research Gruop, Instituto de Investigación Valdecilla-IDIVAL, Santander, Spain

[2]Departamento de Economía, Universidad de Cantabria, Santander, Spain

[3]Health Economics Research Group, Valdecilla Biomedical Institute Research - IDIVAL, Santander, Spain

[4] Department of Hospitalary Phramacy, Hospital universitario Marqués de Valdecilla, Santander, Spain

[5] Department of Medical Oncology, Hospital Universitario Marqués de Valdecilla, Santander, Spain

[6] Department of Nursing, Universisty of Cantabria, Santander, Spain. Instituto de Investigación Valdecilla-IDIVAL, Santander, Spain

*Corresponding author: Paloma Lanza-León. Department of Economics, University of Cantabria. Av. De los Castros s/n., 39005, Santander (Cantabria), Spain. Email: paloma.lanza@unican.es

**Abstract**

**Objective:** The aim of this study was twofold: to assess the annual pharmaceutical savings associated with the treatment of cancer patients at Marqués de Valdecilla University Hospital and to estimate the cost of innovative antineoplastic therapies that patients receive as experimental treatment, both during clinical trials throughout 2020.

**Material and methods:** An observational and financial analysis of the drug cost ~~savings~~ related to clinical trials was applied. ~~Each clinical trial and the characteristics of the pathology were analyzed and matched with a therapeutic alternative.~~ Direct cost savings to the Regional Health System of Cantabria ~~were measured, related to clinical trials~~ and the cost of innovative therapies used as an experimental treatment in clinical trials were ~~was also~~ quantified. ~~as an investment.~~

**Results:** This study includes 38 clinical trials with a sample of 101 patients. ~~The findings indicate that overall, all.~~ The clinical trials analyzed provide a total cost savings of €603,350.21 and an average cost saving of €6,630.22 per patient. Furthermore, the ~~final~~ total investment amounts to €789,892.67, with an average investment of €15,488.09 per patient.

**Conclusions:** ~~This study demonstrates that~~ Clinical trials are essential for the advancement of science. Furthermore, clinical trials can be a significant source of income for both hospitals and Regional Health Systems, contributing to their financial sustainability.

**Keywords:** Avoided cost, cost saving, clinical trials, cancer, investigational medicinal product, drugs.

## 1. Background

Clinical trials are a fundamental and crucial pillar of clinical research, constituting the critical phase in which the efficacy and safety of drugs designed in basic research are analyzed in humans [1–3] Thus, pharmacological advances have significantly improved the health of patients in general and cancer patients in particular. In addition, according to the available literature, approximately 50-60% of the increased survival rates of this population is due to improvements in antineoplastic treatments. New therapeutic treatments are under continuous development. As such, between 2011 and 2016, 68 new molecules have been approved for 22 different oncological indications [4,5].

However, this success has been accompanied by a substantial increase in cost, currently causing a challenge for the different public administrations [5–7]. To mitigate the incipient increase in expenditure, arising both from the rise in pharmaceutical costs and from the emergence of new diagnostic and therapeutic technologies, certain sustainability measures have been established: price-volume agreements, maximum expenditure ceilings, maximum cost per patient and/or period or risk-sharing agreements, in which the price and financing of certain healthcare innovations are linked to both the quantity of use and the effectiveness of the products [6,8–10].

Thus, clinical trials, in addition to contributing to scientific progress, offer patients access to innovative therapies that are not yet available [11]. Although their main objective is far from the sustainability of any healthcare system, these trials can be yet another tool to help maintain controlled healthcare expenditure [12,13]. The support and promotion of research groups by Public Administrations can provide an attractive return on investments, not only at the scientific level or in terms of prestige for hospitals, professionals, and the Autonomous Community itself, but also at the purely financial level.

A review of the recent literature shows that ten studies have analyzed the potential savings in medication costs resulting from the treatment of patients in clinical trials, of which one of the studies was discarded because it included trials of non-oncological pathologies. These studies show cost savings ranging from an estimated €200,000 to over €24,000,000, with this variability depending on the number of patients and clinical trials as well as the period analyzed in each study [11–20].

Savings are defined as the avoided cost of antineoplastic treatments that patients would have received if they were not treated in a clinical trial. To calculate this cost, the standard treatment that, according to the available evidence, each patient should receive in relation to the specific characteristics of his or her pathology has been used as a reference.

According to Chapter BII, Article 32 of Royal Decree 1090/2015, of December 4, 2015, which regulates clinical trials involving drugs, the Ethics Committees for Research with Drugs and the Spanish Registry of Clinical Studies, it is mandatory for the costs of the research drugs to be covered at very least, although the studies proposed by pharmaceutical companies frequently also cover the auxiliary drugs.

## 2. Material and methods

This is a descriptive, observational or prevalence study of a financial nature, based on retrospective data collection of the clinical trials conducted at the Medical Oncology and Nanovaccines Clinical Trials Unit of the Valdecilla Research Institute (IDIVAL) during 2020.

An analysis was made of the direct savings in drugs when treating oncology patients in a clinical trial, as well as an estimate of the cost of treating patients with innovative antineoplastic therapies that are still at an early stage in the process of regulation and funding by the Ministry of Health. In this study, each clinical trial has been matched with a specific pathology that has a unique standard therapy.

The selection criteria considered are as follows. The inclusion criteria were: (1) clinical trials conducted by the Medical Oncology and Nanovaccines Clinical Trials Unit of IDIVAL at the Marqués de Valdecilla University Hospital, (2) with patients included and/or treated during the period between 01/01/2020 and 31/12/2020.

Conversely, the exclusion criteria consisted of: (1) clinical trials conducted by the Medical Oncology and Nanovaccines Clinical Trials Unit of IDIVAL at the Marqués de Valdecilla University Hospital, (2) that have had neither recruitment nor patients with active treatment during the period between 01/01/2020 and 31/12/2020.

The data analysis was divided into two main concepts: savings and investment. Savings is defined as the avoided cost of antineoplastic treatments that patients would have received if they were not treated in a clinical trial. To calculate this cost, standard treatment was used as a reference. This is defined according to the guidelines of the National Comprehensive Cancer Network (NCCN) version 2020 and the information contained in the Investigator's Brochure (IB), considering the specific characteristics of each pathology. In particular, the standard therapy has a specific periodicity, and each patient would have received a series of doses while being treated in a clinical trial. Knowing the quantity of drug per dose (mg), the number of doses the patient would have received, and the price of the standard drug (€/mg), it is possible to access the final figure of pharmaceutical savings.

Investment is understood as the cost of innovative antineoplastic therapies that are in the early stages of the process of regulation and funding by the Ministry of Health, and consequently not funded by the Cantabrian Health Service, which patients receive as part of the experimental treatment of a clinical trial. We have considered two scenarios: (1) the standard of care is not based on an antineoplastic drug and the efficacy of a new molecule is being investigated, and (2) the standard therapy is part of the medication in the clinical trial and is also combined with a new investigational therapy. In both cases, the investment figures are obtained by multiplying the dose of that received innovative therapy (mg), the number of medication infusions, and the price of the new therapy (€/mg).

To calculate the savings and investments, two essential data are considered. Firstly, the total milligrams (mg) were calculated, taking into account the dosage of medication received in the period analyzed, i.e. between January 1, 2020, and December 31, 2020. These data were consulted in the Assisted Electronic Prescription software (PEA®), an information system for the prescription of pharmacological treatments implemented at the Marqués de Valdecilla University Hospital.

To calculate the doses of the reference treatment, in the case of not having received it within the clinical trial, the average height and weight data of the Spanish population were considered, according to the 2017 National Health Survey of the Spanish National Institute of Statistics [21]. Furthermore, in these cases, full dosages have been assumed throughout the cycles without potential adjustments for toxicity or tolerance.

The sources consulted to determine the costs were:

- The BotPlus® database to determine the recommended retail price (RRP) of each medicine
- The computerized management application of the Pharmacy Service of the Hospital Universitario Marqués de Valdecilla to determine the price of medicines (laboratory sales price).

Finally, if a study had a treatment versus placebo arm, the final investment figure was reduced to 50%, assuming that the odds of receiving treatment and placebo were the same.

### 3.1. Results

In total, 38 studies were included in the overall analysis, of which 30 studies (79%) were sponsored by a pharmaceutical company and the remaining eight studies (21%) were proposed by corporate scientific groups, who only funded the experimental treatment.

The clinical trials included in this work were in different phases of research, with 3% of the clinical trials in Phase I, 34% in Phase II and the remaining 63% constituting Phase III clinical trials.

The analysis by tumor group was performed by dividing the clinical trials into genitourinary, digestive, skin, respiratory and thorax, head and neck, and breast tumors.

The genitourinary and digestive tumor groups were those with the most clinical trials, with 16 and 13 studies, respectively. In turn, the skin and respiratory and thoracic tumors groups had three studies each. Finally, two clinical trials were analyzed in the head and neck tumor group and one clinical trial in the breast tumor group.

The total number of patients included in the studies analyzed was 101 participants, of which 40 were in the genitourinary tumor group, 39 were treated in the digestive tumor group, seven were in the skin cancer group, eight in the respiratory system and thorax group, five in the head and neck tumor group and two in the breast cancer group.

**3.2. Savings**

For the purpose of analyzing savings, 32 studies were included. The remaining six studies were excluded because the standard therapeutic approach to these pathologies was not based on pharmacological treatment.

The analysis of financial savings concluded with a figure of €603,350.21 in avoided costs during the year 2020. The estimate of total expenditure on antineoplastic drugs was €18,004,880.00 in that year (2020) in the Cantabrian Health Service, so the resulting savings amount to 3.4% of the total expenditure.

When dividing the total figure by groups, the findings remained consistent with the number of studies and patients included, i.e., with the research activity of each group, although with some peculiarities. The genitourinary tumors group contributed €255,156.08 (42%), in the digestive tumors group, the savings equaled €195,185.42 (32%), in the skin tumors group it was €116,969.40 (20%), the respiratory system and thorax tumors group saved €32,338.75 (5%), the head and neck tumors group saved €3,468.93 (1%) and for the breast tumors group this amount was € 231.63 (<1%) (see Figure 1).

The average avoided cost per patient was €6,630.22 during 2020. The estimate of average expenditure per cancer patient on drugs was €7,225.27 in that year (2020) in the Cantabrian Health Service.

The average savings per patient for each of the groups was €7,290.17€ in the genitourinary tumor group, €5,136.45 in the digestive tumor group, €16,709.91 in the skin tumor group, €8,084.68 in the respiratory system and thorax tumor group, €693.78 in the head and neck tumor group and €115.81 in the breast tumor group (see Figure 2).

An analysis of the data shows that the largest net savings are generated by the digestive and genitourinary tumor groups. This fact is directly related to the fruitful research activity of both groups, which have a high number of clinical trials and high patient recruitment (see Table 1).

Additionally, the skin tumor group generated the greatest savings per patient (and savings per study) of all the groups. This is because pembrolizumab, encorafenib and binimetinib, the standard treatments for the pathologies treated in the clinical trials in this group, have a very high cost and thus generate large savings with a limited number of patients (see Tables 1 and 3).

In contrast, the breast and head and neck tumor groups are emerging groups with a low number of trials and lower recruitment to date. This explains why their net and per-patient savings figures are the lowest.

**3.3. Investment**

For the specific analysis of the investment, 16 studies were included, which met the following characteristics:

- Studies providing medication when the standard therapeutic approach does not contemplate that possibility.
- Studies that add medication to standard therapy of choice, without substituting it.
- Innovative therapy which has an established price.

The other 22 studies were excluded as they failed to meet any of these three characteristics.

The analysis of the investment yielded a total figure of €789,892.67 for the costs of using innovative therapies in the process of regulation. The contribution by tumor group in this case was €312,757.62 (40%) for the genitourinary tumor group, €244,948.40 (31%) in the case of the digestive tumor group, €31,128.65 (4%) for the skin tumor group and €201,058.00 (25%) for the respiratory system tumor group. In the case of the breast and head and neck tumor groups, the clinical trials did not meet the aforementioned characteristics required to be analyzed in this investment chapter (see Figure 3).

The average investment figure was €15,488.09/patient. An analysis of the average investment data by tumor group reveals that in the clinical trials of the genitourinary tumor group €12,029.14/patient were invested; in the digestive tumor group this sum was €13,608.24/patient; in the respiratory system and thorax tumor group the investment €50,264.50/patient; whereas in the skin tumor group the investment was €10,376.22/patient (see Figure 4).

The overall figures for both the net investment and investment per patient were higher than the savings figures. This is because, in general terms, treatments that are more novel are more expensive, and the investment quantifies the value of innovative treatments that do not have an indication approved by the State Agency for Medicines and Health Products (AEMPS) and are received as an experimental part of a clinical trial (see Table 2 and 4).

The groups that generate the greatest investment are those corresponding to digestive tumors and genitourinary tumors, due to the extensive research activity.

In this case, it should be noted that the group with the highest investment per patient is the group of respiratory and thoracic tumors (€50,264.50/patient). This figure is directly related to the cost of canakinumab, which had the highest price of all the drugs analyzed (see Table 4).

Finally, the groups of breast tumors and head and neck tumors do not have investment figures, since none of the clinical trials considered in this study met the necessary characteristics to carry out this type of analysis.

**4. Discussion**

Oncological clinical trials generate significant economic savings in antineoplastic medication, derived from the funding provided by the promoters of the treatments involved in this research. Therefore, the development of clinical trials not only collaborates towards the achievement of better results in the efficacy of therapies but can also contributes to the sustainability of Public Health Systems.

Several studies have been carried out in recent decades to quantify the savings associated with the use of research products [11-20]. Calvin-Lamas et al. [11] carried out an analysis of prostate cancer that resulted in a saving of €696,002, which translates into an average saving of €5,118 per patient, derived from five trials with 136 patients enrolled in a tertiary level university complex in the period between 1996 and 2003. Mañes-Sevilla et al. [20] quantified the savings produced by 37 breast cancer clinical trials, with 89 patients included in a large public hospital in the Autonomous Community of Madrid, in the period from 2014 to 2016, which obtained savings of €957,246, which represents an average saving of €10,756 per patient. In turn, Capdevilla et al. [12] published an analysis not only focused on savings related to drugs, but also evaluating other procedures associated with the care of patients included in clinical trials (clinical visits, imaging tests, etc.). This study reported €751,777 of savings in medication (which increased to €981,086 including other

interventions) evaluating 20 clinical trials of different oncological pathologies and with a recruitment of 68 patients in the period between 2014 and 2016.

Firstly, studies conducted in Spain are considered due to the similarity in the Healthcare System. The observed data align with those obtained in our research, although there are certain differences. Regarding the overall savings figures, differences occur with ranges ranging from €92,653 to €353,896. This is mainly due to the cost that the standard therapy of the clinical trials included in the analysis may have. Slight variations in drug prices cause the final savings figures to be significantly increased due to the amount of medication and successive infusions received. Additionally, the number of patients analyzed directly influences the final pharmaceutical savings result. Thus, the greater the number of patients, the greater the overall savings.

Nevertheless, when we analyze the savings per patient, the data normalize and the differences with the analyzed studies fall within a range between €-1,512 to €4,425. This would be the optimal way to compare the savings produced at each center considered, although differences still exist due to the previously mentioned price variations.

D' Ambrosio et al. [18] conducted a study developed at the National Cancer Institute of Naples analyzing 34 clinical trials, with 126 patients included in the period from October 23 to November 17, 2017, accounting for savings of €517,658 with an average saving of €5487 per patient. Other similar studies, such as that of Grossi et al. [16] focused on lung cancer patients, estimated a saving of 799,803 euros (5526 euros per patient) produced by the treatment of 196 patients during 2010. The results obtained by Tang et al. [17] showed significantly higher savings in their study, yielding a figure of €24,673,682.3 in savings produced by 3195 patients included in 17 clinical trials, during the period from 1999 to 2011, but which are normalized by calculating the average savings of €7,722.59 per patient. The study by Bredin et al. [15] obtained results that are consistent with those described above, indicating an estimated range of 1,275 to 21,993 euros saved per patient, during the period from January 1992 to May 2007, with 37 clinical trials analyzed and a total of 250 patients included.

When we analyze the available data in Europe, the results are in line with our findings. The evidence indicates a range of difference in savings per patient, ranging from €-1,143 to €1092, excluding the study by Bredin et al. [15] due to the lack of uniformity in the patients considered in that study.

In addition, despite focusing on hematologic pathologies, the data reported by the study by Herlendan et al. [19] are similar to the previously discussed studies, with an analysis of 43 clinical trials and 345 patients included in a university hospital in Lyon, in the period from 2011 to 2016 credited with savings of

€5,217,691.20 (€869,615.20 per year) with an average saving of €29,478.48 per patient (€5,895.69 per patient per year). Nonetheless, the results obtained by Truong et al. [13] are quantitatively superior, with savings averaging €1,447,114.92 saved per year and €70,879.09 per patient, having analyzed 36 clinical trials with 245 patients included in the period from January 1, 2006, to December 31, 2017.

Comparing our findings with those addressing hematological pathologies, we cannot draw conclusions due to the disparity of results. We have found savings per patient figures similar to the study conducted by Herlendan et al. [19], with a difference of €-734.31. However, the savings per patient figures from the study carried out by Truong et al. [13] widen this difference to €64,249.

A review of all the data obtained in the studies analyzed above allows us to support the drug-saving capacity of clinical trials.

One of the limitations of this study is that it has only considered savings focused on medication, without an in-depth analysis of other possible costs that can be avoided or generated in relation to clinical trials (human resources, complementary tests associated with the treatment or the oncological process, or the structural cost of providing a physical hospital space, among others).

In addition, the estimation of both savings and investment may have been underestimated or overestimated. This is due to the use of the average height and weight of the Spanish population according to the 2017 National Health Survey of the Spanish National Institute of Statistics, as well the estimation of full doses, without potential adjustments considering toxicities or intolerances, during the entire treatment carried out throughout the analysis period.

Finally, this may not be the most accurate scenario for the analysis of these data, given that, during the months of March to May 2020, the recruitments of most studies internationally were temporarily inactive due to the pandemic caused by the SARS-CoV2 virus.

## 5. Conclusions

Oncological clinical trials produce numerous benefits for patients, healthcare institutions and professionals. Focusing on the financial aspect, most clinical trials provide treatment free of charge for public health systems, and this is a source of extra funding in pharmaceutical expenditure. According to the results obtained, the savings produced are around 3-5% of the annual expenditure in oncological therapies, data which are in agreement with the existing literature.

In view of these findings, it is essential to continue to promote and encourage the performance of clinical trials in public hospitals. Although this is not an easy task, it has a positive impact on many aspects of healthcare systems.

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**Conflicts of interest:** The authors declare that they have no conflict of interest.

**Data availability:** All data can be obtained by contacting the corresponding author.

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**ANNEXES**

Table 1: Data collection table of net savings, savings per patient and savings per study for each group of tumors.

| GROUPS | SAVINGS | PATIENTS | €/ PATIENT | STUDIES | €/ STUDY |
|---|---|---|---|---|---|
| TUMORS OF THE GENITOURINARY SYSTEM | 255,156.08 € | 35 | 7,290.17 € | 12 | 21,263.01 € |
| TUMORS OF THE DIGESTIVE TRACT | 195,185.42 € | 38 | 5,136.46 € | 12 | 16,265.45 € |
| SKIN TUMORS | 116,969.40 € | 7 | 16,709.91 € | 3 | 38,989.80 € |
| TUMORS OF THE RESPIRATORY TRACT AND THORAX | 32,338.75 € | 4 | 8,084.69 € | 2 | 16,169.38 € |
| HEAD AND NECK TUMORS | 3.468.93 € | 5 | 693.79 € | 2 | 1,734.46 € |
| BREAST TUMORS | 231.63 € | 2 | 115.82 € | 1 | 231.63 € |
| TOTAL | 603,350.21 € | 91 | 6,630.22 € | 32 | 18,854.69 € |

Table 2: Data collection table of net investment, investment per patient and investment per study, for each tumor group.

| GROUPS | INVESTMENT | PATIENTS | €/ PATIENT | STUDIES | €/ STUDY |
|---|---|---|---|---|---|
| TUMORS OF THE GENITOURINARY SYSTEM | 312,757.62 € | 26 | 12,029.14 € | 7 | 44,679.66 € |
| TUMORS OF THE DIGESTIVE TRACT | 244,948.40 € | 18 | 13,608.24 € | 4 | 61,237.10 € |
| SKIN TUMORS | 31,128.65 € | 3 | 10,376.22 € | 1 | 31,128.65 € |
| TUMORS OF THE RESPIRATORY TRACT AND THORAX | 201,058.00 € | 4 | 50,264.50 € | 1 | 201,058.00€ |
| HEAD AND NECK TUMORS | 0.00 € | 0 | N/A | 0 | N/A |
| BREAST TUMORS | 0.00 € | 0 | N/A | 0 | N/A |
| TOTAL | 789,892.67 € | 51 | 15,488.09 € | 13 | 60,760.97 € |

Table 3. Table of savings generated by active ingredient

| | ACTIVE INGREDIENT | TOTAL DOSAGE (mg) | PRICE (euros/mg) | TOTAL SAVINGS |
|---|---|---|---|---|
| SAVINGS BY ACTIVE INGREDIENT | Aflibercept | 3352 | 3.295 | 11,044.84 € |
| | Trifluridine/Tipiracil | 840 | 1.507 | 1,265.88 € |
| | Capecitabine | 3839400 | 0.000396 | 1,520.40 € |
| | Bevacizumab | 13360 | 1.756 | 23,460.16 € |
| | Paclitaxel | 8607,9 | 0.104 | 895.22 € |
| | Gemcitabine | 191420 | 0.036 | 6,891.12 € |
| | Oxaliplatin | 11211 | 0.093 | 1,042.62 € |
| | Cisplatin | 5583 | 0.099 | 552.72 € |
| | Fluorouracil | 7200 | 0.002 | 14.40 € |
| | Trastuzumab | 3648 | 0.776 | 2,830.85 € |
| | Sorafenib | 869000 | 0.143 | 124,267.00 € |
| | Everolimus | 2590 | 6.007 | 15,558.13 € |
| | Lutetium oxodotreotide | 1 | 16000 | 16,000.00 € |
| | Vinflunine | 6734 | 3.27 | 22,020.18 € |
| | Docetaxel | 3942 | 0.142 | 559.76 € |
| | Prednisone | 1890 | 0.004 | 7.56 € |
| | Abiraterona | 82000 | 0.085 | 6,970.00 € |
| | Nivolumab | 9600 | 7.549 | 72,470.40 € |
| | Ipilimumab | 780 | 48.646 | 37,943.88 € |
| | Sunitinib | 28162,5 | 3.258 | 91,753.43 € |
| | Cabozantinib | 4260 | 3.235 | 13,781.10 € |
| | Crizotinib | 121500 | 0.263 | 31,954.50 € |
| | Doxorubicin | 816 | 0.124 | 101.18 € |
| | Cyclophosphamide | 8208 | 0.009 | 73.87 € |
| | Pembrolizumab | 7200 | 13.521 | 97,351.20 € |
| | Encorafenib | 37800 | 0.288 | 10,886.40 € |
| | Binimetinib | 7560 | 1.155 | 8,731.80 € |
| | Cetuximab | 2126 | 1.6 | 3,401.60 € |
| | | | TOTAL | 603,350.21 € |

Table 4. Table of investment generated by active ingredient

| | ACTIVE INGREDIENT | TOTAL DOSAGE (mg) | PRICE (euros/mg) | TOTAL INVESTMENT |
|---|---|---|---|---|
| TOTAL INVESTMENT BY ACTIVE INGREDIENT | Bevacizumab | 365 | 1.756 | 640.94 € |
| | Sintilimab | | Not available | - € |
| | Pembrolizumab | 11900 | 13.521 | 160,899.90 € |
| | Avelumab | 33060 | 2.891 | 95,576.46 € |
| | Pemigatinib | | Not available | - € |
| | Ibrutinib | 65520 | 0.324 | 21,228.48 € |
| | Nivolumab | 9960 | 7.549 | 75,188.04 € |
| | Durvalumab | 67500 | 2.3 | 155,250.00 € |
| | BMS986205 | | Not available | - € |
| | Atezolizumab | 22800 | 1.734 | 39,535.20 € |
| | Capivasertib | | Not available | - € |
| | Cabozantinib | 4200 | 2.235 | 9,387.00 € |
| | Canakinumab | 3800 | 52.91 | 201,058.00 € |
| | Lenvatinib | 5890 | 5.285 | 31,128.65 € |
| | | | TOTAL | 789,892.67 € |

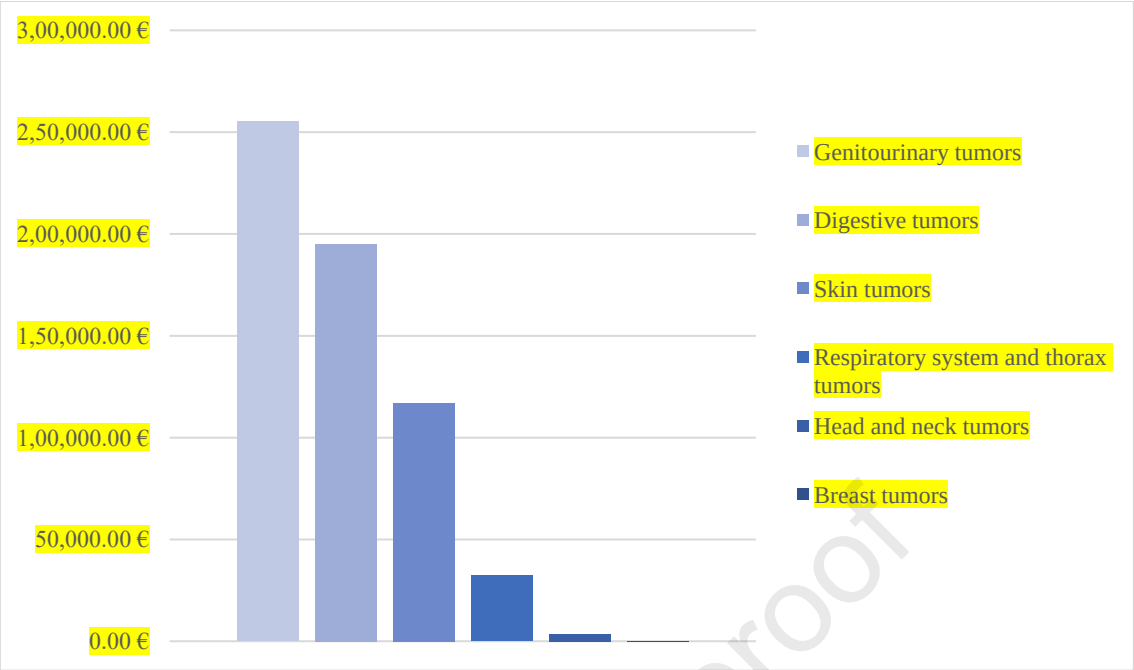


**Figure 1.** Total savings by tumor group. Source: Authors' elaboration.

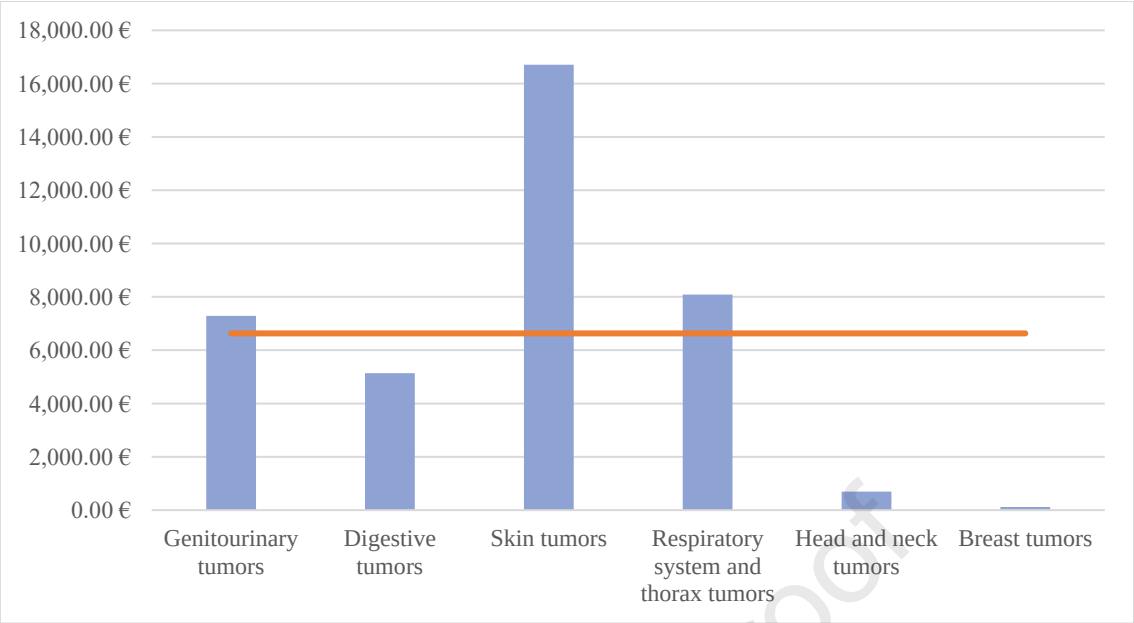


**Figure 2.** Average savings (in euros) per patient for each group of tumors. Note: average savings is represented by orange line. Source: Authors' elaboration.

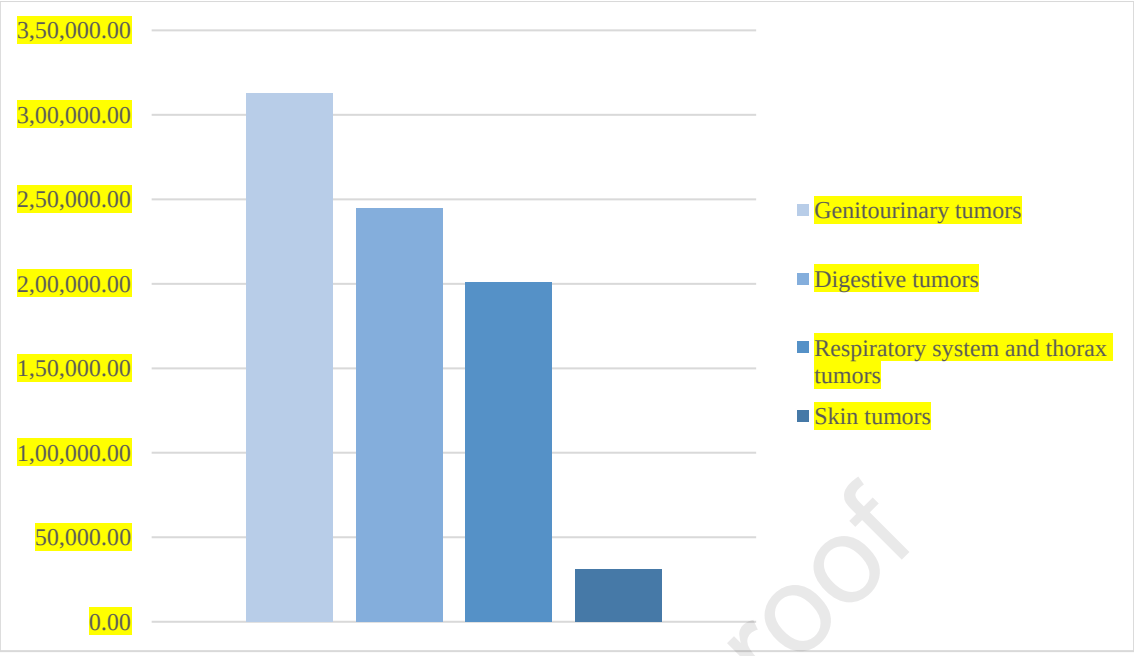


**Figure 3.** Total investment by tumor group. Source: Authors' elaboration.

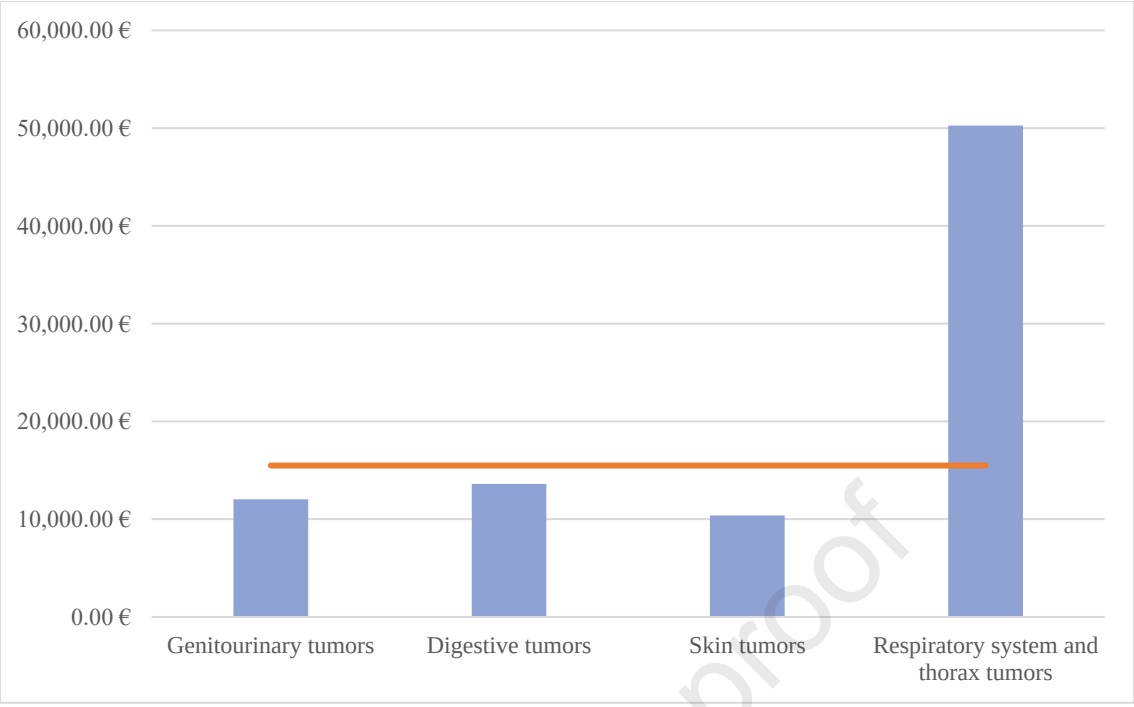


**Figure 4.** Average investment per patient (€/patient) for each group of tumors. Note: average investment is represented by orange line. Source: Authors' elaboration.

**Highlights:**

- This study calculates the pharmaceutical savings and investment associated with the treatment of cancer patients during clinical trials at a referral hospital in northern Spain.
- The findings reveal an average cost saving per patient of over €6,000, with total savings in excess of €600,000.
- With the emergence of the COVID-19 pandemic, certain pathologies, such as cancer, may have been neglected. However, in the year 2020 in Spain, 112,741 people died of cancer.
- Clinical trials may contribute to existing financial policies to cope with the budget challenge related to the high prices of oncological drugs.