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Drug Cost Avoidance Analysis of Cancer Clinical Trials in Spain: A Study on Cost Contributors and Their Impact

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Abstract

Objective: Analyze the cost contributors and their impact on the drug cost avoidance (DCA) resulting from cancer clinical trials over the period of 2015-2020 in a tertiary-level hospital in Spain (HCUVA). **Methods:** We performed a cross-sectional, observational, retrospective study of a total of 53 clinical trials with 363 patients enrolled. We calculated the DCA from the price of the best standard of care (i.e.: drugs that the institution would otherwise fund). A linear regression model was used to determine cost contributors and estimate their impact. **Results:** The total DCA was ~5.1 million euros (31 clinical trials; 177 enrollees), representing 30% and 0.05% approximately of the annual pharmaceutical expenditures at the HCUVA and for the Spanish Health System, respectively. Cancer type analysis showed that lung cancer had the highest average DCA by trial, indicating that treatments in these trials were the most expensive. Linear regression analysis showed that the number of patients in a trial did not significantly affect that trial's DCA. Instead, cancer type, phase trials, and intention of treatment were significant cost contributors to DCA. Compared to digestive cancer trials, breast and lung trials were significantly more expensive, ($p < 0.05$ and $p < 0.1$, respectively). Phase III trials were more expensive than Phase II ($p < 0.05$) and adjuvant trials were less expensive than palliative ($p < 0.001$). **Conclusion:** We identified key cancer clinical trial characteristics that significantly impacted the estimated DCA. Our work provides the groundwork to explore DCA contributors with potential to enhance public relations material and serve as a negotiating tool for budgeting, thus playing an important role to inform decisions about resource allocation.

Keywords: Hospital management, Linear regression, Healthcare costs, Sustainability, Clinical Trials, Oncology.

1. Introduction

Cancer has one of the most significant impacts on health budgets^{1,2}, and estimations predict that the number of new cases will increase over the next two decades to 29.5 million per year by 2040³. Worryingly, the lack of situation analysis and budgeting concerning this pathology has been identified as one of the main obstacles threatening the sustainability of health systems⁴. Recent studies propose clinical trials as an alternative new element to introduce sustainability into the

Health System⁵, aiming to prevent economic failure. Clinical trials investigate new diagnosing, treating, and managing cancer to improve the standard of care treatment⁶. For patients, the benefits of clinical trials include gaining access to experimental treatments when no other options exist and to new therapies not yet available⁷, while contributing to the advancement of medical research. However, the economic benefits of running oncologic clinical trials for hospital administrators are often not considered. One potential financial benefit of clinical trials is drug cost avoidance (DCA)^{8,9}, resulting when trial subjects receive industry-sponsored treatment drugs that the institution would otherwise fund¹⁰. Previous studies have quantified DCA derived from cancer clinical trials in different settings^{11,12}, proven their efficacy to alleviate the economic pressure in the Health system. However, there are no studies on cost contributors and their impact on DCA to the best of our knowledge. The purpose of this study was to analyze the cost contributors and their impact on the DCA resulting from cancer clinical trials throughout 2015-2020 in a tertiary-level hospital in Spain (HCUVA). We calculated the DCA from the price of the best standard of care. The total DCA was ~5.1 million euros, representing 30% and approximately the 0,05% of the annual pharmaceutical expenditures at the HCUVA and for the Spanish Health System, respectively. Cancer type, phase trials, and intention of treatment were significant cost contributors to DCA. Breast and lung trials were significantly more expensive than digestive cancer trials ($p < 0.05$ and $p < 0.1$, respectively). Phase III trials were more expensive than Phase II ($p < 0.05$) and adjuvant trials were less expensive than palliative ($p < 0.001$). Our work provides the groundwork to explore DCA contributors with the potential to enhance public relations material and serve as a negotiating tool for budgeting, thus playing an essential role in informing resource allocation decisions.

2. Methods

2.1 Identifying eligible trials

We reviewed clinical trials performed from 2015 to 2020 at the oncology department of HCUVA. Trials were excluded when (i) no patients were enrolled, (ii) screening failed, (iii) DCA could not be calculated due to insufficient drug information, and (iv) were observational phase 4 trials in which the experimental treatment was not industry-sponsored.

2.2 Calculating DCA

Pharmacy and patient records for eligible trials were reviewed to determine each subject's treatment duration and quantity of the drug. Because the cost of the experimental drug in the clinical trials was unavailable, we calculated the best standard of care DCA using a reference price list. When the standard of care drug dosage depends on the body surface area, we used standardized parameters for men and women (1.96 kg/m² and 1.68 kg/m², respectively). Equation [1] shows how we calculated the DCA.

$$DCA = Price\ per\ cycle \times Number\ of\ cycles\ per\ trial \quad [1]$$

2.3 Linear regression analysis

We constructed a regression model using four control variables: number of patients, cancer type, trial phases, and intention of treatment. Equation [2] shows our regression model. We set our baseline constant as digestive cancer, palliative treatment, and Phase II trials (β_0 ; namely the intercept) to establish a comparison for the indicator variables. The dependent variable was the DCA from each trial. The variable number of patient (npatients) is numeric, and the other three variables are composed of characteristic values. We then created indicator variables to translate characteristic values into numeric (e.g., indicator column for breast cancer will indicate breast cancer as 1, other cancer types as 0). Using the 'lm' function of the R statistic software, the coefficient estimates (β) of each variable represents the magnitude of its impact on trial DCA while holding other factors constant.

$$DCA = \beta_0 + \beta_1 npatients + \beta_2 CancerType + \beta_3 Intention + \beta_4 Phase + \varepsilon_i \quad [2]$$

3. Results

3.1. Study sample

We reviewed 53 industry-sponsored clinical trials with a total of 363 patients enrolled, from 2015 to 2020, at the oncology department of HUCVA. We excluded three trials that had no patient enrolled, 13 trials (65 patients) were in phase IV, for six trials (21 patients), we could not calculate the DCA and 100 patients failed the screening. The final sample studied included 31 trials, enrolling 177 patients (**Figure 1**). The number of patients per study ranged from 1 to 17. Trials were distributed among seven tumor groups; the most common was breast cancer (13 trials), followed by digestive (6), gynecology (5), lung (4), prostate (1), melanoma (1), and sarcoma (1). The final sample had phase II and III trials (7 and 24, respectively) with palliative (25), adjuvant (4) and neoadjuvant (2) intentions.

3.2. Drug cost avoidance

The DCA in all trials was calculated by the price of the standard treatment, including a total of 35 drugs. The estimated DCA during the study period was ~5.1 million euros (**Table 1**). The median estimated DCA per year was 962,272 € and 36,294 € per trial. DCA in this study represents approximately 30% and 0,05% of the annual pharmaceutical expenditures at the Medical Oncology Department at HCUVA and for the Spanish Health System (15), respectively (The hospital pharmacy service provided us with the pharmaceutical budget for the HCUVA). We found that DCA did not increase proportionally to the number of trials or number of patients (**Table 2**). For instance, in 2016, the DCA was 1,6 million euros from 4 trials and 23 patients, while in 2019, it was 0.9 million euros from 9 trials and 59 patients. Only 6.5 % of DCA came

from Phase II and 93.5% from phase III. Regarding the intention of clinical trials, palliative trials represented 89.2 % of the DCA, followed by neoadjuvant and adjuvant (9.3 % and 1.5 %, respectively). Next, we conducted a cancer type analysis of the DCA and found that breast cancer had the highest DCA (**Table 3**). However, lung cancer had the highest average DCA by trial, and it was twice as much the breast cancer's, indicating that, on average, lung cancer treatments were the most expensive (**Table 3**). Digestive cancer had the least expensive treatments on average.

3.2. Cost contributor's analysis

Next, we wished to investigate the impact magnitude of each cost contributor on the DCA. Our regression model showed that the number of patients in a trial did not significantly affect that trial's DCA (**Table 4**). However, we found a significant impact on cancer type, phase trials, and intention of treatment (**Table 4**). Specifically, compared to digestive cancer trials, breast and lung cancer trials were 587,640 € ($p < 0.05$) and 381,678 € ($p < 0.1$) more expensive, respectively. Similarly, Phase III trials were 539,305 € ($p < 0.05$) more expensive than Phase II, and regarding the intention of the trials, adjuvant trials were 751,058 € ($p < 0.001$) less expensive than palliative (**Table 4**).

4. Discussion

This paper estimated the DCA from industry-sponsored oncological clinical trials that took place in HCUVA between 2015 and 2020. To estimate the DCA, we used the price of the best standard of care, resulting in ~5.1 million euros (**Table 1**). Other DCA estimations performed in a single institution have shown similar saving percentages for the hospital or institution budget^{11,12}. Thus, supporting the idea that the DCA from oncological clinical trials provides economic savings, and may help to sustain the national health system. A limitation of our and previous studies is that other non-pharmaceutical costs were not considered, implying the savings derived from oncological clinical trials could be underestimated. Additionally, our study contained a unique sample of trials that had a diverse number of enrollees, cancer types, intentions of the treatments and phase, making our DCA estimations difficult to be directly compared with other estimated DCA. For instance, previous studies have estimated DCA by variables such as the number of patients, the length, or phases of the trials¹¹, the pharmacological categories^{13,14} or pathology type¹⁴.

Our initial data exploration showed that variations in the number of clinical trials and patients enrolled per year did not represent a proportional variation in the annual DCA (**Table 2**), incentivizing us to further investigate other potential DCA contributing factors. Our cancer type analysis of the DCA showed that lung cancer trials had the highest average DCA per trial compared with other cancer types, suggesting lung cancer treatments could be the most expensive

(**Table 3**). This agrees with the observation that the DCA per patient varies drastically among tumor groups¹⁵. We suspected that other trial characteristics, such as treatment intention and phases, could also have significant impacts on DCA. Therefore, to further investigate and isolate each individual characteristic's impact on DCA, we constructed a linear regression model as illustrated in equation [2]. The linear regression results (**Table 4**) shows that the number of patients enrolled in a trial had a trivial contribution to DCA, which agrees with our previous observation (**Table 2**). Thus, suggesting other contributors could carry more weight on influencing DCA. Indeed, our linear regression analysis confirmed that certain cancer types, trial phases, and treatment intention had a significant impact on DCA (**Table 4**). Specifically, we found that palliative trials tend to be 751,058 € ($p < 0.001$) more expensive than adjuvant trials while holding other variables constant. Similarly, breast and lung cancer trials were 587,640 € ($p < 0.05$) and 381,678 € ($p < 0.1$) more expensive than digestive cancer trials, respectively. These findings could be explained by the varying dosage requirements for differing trials, the length of time patients remain on trial drugs due to progression of disease, and the cost of the treatments. For example, in our study, each treatment cycle's price between trials ranged from 43 € to 8640 € (**Table 1**). These price differences reflect that innovative therapies, such as cyclin inhibitors and immunotherapy, are significantly more costly than other standard chemotherapies^{11,16}. The increasing number of new options for prevention, diagnosis, and treatment, makes studies of the DCA of the new therapies increasingly important to inform decisions about resource allocation. Our study might be useful for hospital management by providing a projection on future DCA derived from clinical trials based on their characteristics.

5. Conclusion

We identified key cancer clinical trial characteristics that significantly impacted the estimated DCA. Our work provides the groundwork to explore DCA contributors with the potential to enhance public relations material and serve as a negotiating tool for budgeting, thus playing an essential role in informing resource allocation decisions.

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Author contributions: PR-C, JLAR and DASM studied the databases and identified eligible trials. DASM and JLAR estimated the DCA and analyzed the trial's distribution. HJ performed

the linear regression study and prepared the figures and tables. HJ wrote the first draft of the paper. DASM and FS-L supervised the study. FS-L finalized the manuscript for review by all authors.

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Figures

Figure 1

Flow chart of the process to identify eligible trials.

Supplementary Files

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- [Table1.pdf](#)
- [Table2.pdf](#)
- [Table3.pdf](#)
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