Clinical trials and drugs cost saving for Italian Health Service

Francesca D’Ambrosio
Fondazione IRCCS Istituto Nazionale dei Tumori

Gianfranco De Feo
Fondazione IRCCS Istituto Nazionale dei Tumori

Gerardo Botti
Fondazione IRCCS Istituto Nazionale dei Tumori

Arturo Capasso
Università degli Studi del Sannio Dipartimento di Diritto Economia Management e Metodi Quantitativi

Sandro Pignata
Fondazione IRCCS Istituto Nazionale dei Tumori

Piera Maiolino
Fondazione IRCCS Istituto Nazionale dei Tumori

Maria Triassi
Università degli Studi di Napoli Federico II Dipartimento di Sanità Pubblica

Antonio Nardone
Università degli Studi di Napoli Federico II Dipartimento di Sanità Pubblica

Franco Perrone
Fondazione IRCCS Istituto Nazionale dei Tumori

Michela Piezzo
Fondazione IRCCS Istituto Nazionale dei Tumori

Antonio Maria Grimaldi
Fondazione IRCCS Istituto Nazionale dei Tumori

Ida Palazzo
Fondazione IRCCS Istituto Nazionale dei Tumori

Immacolata De Stasio
Fondazione IRCCS Istituto Nazionale dei Tumori

Roberta D’Aniello
Fondazione IRCCS Istituto Nazionale dei Tumori

Alessandro Morabito (✉️ alessandromorabito1@virgilio.it)
Istituto Nazionale Tumori IRCCS Fondazione Pascale  https://orcid.org/0000-0002-1319-9608

Giacomo Pascarella
Fondazione IRCCS Istituto Nazionale dei Tumori
Abstract

**Background:** The cost of anticancer drugs is constantly growing. The aim of this study was determine the impact in terms of anticancer drug cost reduction for Italian Health Service due to patient participation in clinical trials.

**Methods:** We evaluated the cost of drugs administered to patients treated in clinical trials at National Cancer Institute of Naples in a four-week period. Patients with diagnosis of different cancers were considered, including adjuvant therapy and treatment for advanced disease, pharma sponsored and investigator initiated phase I, II and III clinical studies. We defined for each patient the expected standard treatment and we calculated the cost of the standard antineoplastic drugs that should be administered in clinical practice outside clinical trials. We used drug's market price to determine cost saving value. Costs other than drugs were not included in the cost saving calculation.

**Results:** From 23.10.2017 to 17.11.2017, 126 patients were treated in 34 pharma sponsored and investigator initiated clinical trials, by using experimental drugs provided free of charge by the sponsors, for an overall number of 152 cycles of therapy. We calculated that the cost of antineoplastic drugs if these patients would been treated with conventional therapies in clinical practice would account for 517,658 Euros, with an average of 5,487 Euros saved per patients for a period of four weeks.

**Conclusions:** Participating in clinical trials in which investigational antineoplastic drugs are provided free of charge by the Sponsor translates in considerable cost savings, with a tangible benefit in clinical and administrative strategies to reduce drug expenditures.

Background

The cost of anticancer drugs is constantly growing. The pharmaceutical expense for anticancer drugs has increased in Italy from 3.6 to 5 billion Euros since 2013 to 2017, leaping to +659 million Euros only in 2018. This grow ensures that all patients in Italy are able to access the best anticancer therapies. In five years (2013-2017) 54 new anti-cancer treatments were marketed worldwide and Italy has guaranteed (by 2018) the availability of 35 of these innovative molecules, ranking fifth internationally after the United States (52), Germany (43), United Kingdom (41), France (37), and ahead of Canada (33), Spain (30) and Japan (29) [1]. At a global level, this increase reached 133 billion dollars in the world in 2017 (versus 96 billion dollars in 2013). The conventional explanation among health economists is that the relentless rise in health care spending is driven by the development and diffusion of new drugs, devices, procedures, and ways of caring for patients [2]. So, many hospitals are looking at ways to reduce costs and to avoid their expenses spiral and survive by eliminating unnecessary discretionary and non-value adding costs [3]. For this purpose, health organizations can use two efficient tools, namely cost control and cost reduction. Cost control can be defined as the process of controlling how much a company or organization spends, so that costs are not greater than an agreed budget. It is a process of avoiding wasteful use of valuable resources and encouraging efficiency and cost consciousness, providing the necessary
information to the management concerned with keeping expenditure within acceptable limits [3]. Cost reduction, instead, is the process of reducing the amount of money that a company spends on wages, production, services, etc. in order to make it more profitable or a planned positive approach to reducing expenditure without compromising its quality [4]. The aim of this study was determine the impact in terms of drug cost reduction determined by patient participation in clinical trials, with investigational drugs provided free of charge by the Sponsors at an Italian Cancer Institute.

**Methods**

We evaluated patients treated with anti-neoplastic drugs within clinical trials at the National Cancer Institute of Naples, in a period of four weeks. Clinical trials included patients with different cancers, treated in adjuvant and metastatic setting, in different phases of clinical research (phase I, II and III clinical trials). Both pharma sponsored and investigator initiated clinical studies were considered for this analysis: for pharma sponsored clinical trials, all drugs were provided at no cost by the Sponsors, while investigator initiated clinical trials, the experimental drug was provided free of charge by the Pharmaceutical Company producing the drug. Drug dosage (in milligrams), number of effective administrations in the four-week period for each patient (cycles number) and market price of drugs were provided by the Hospital Pharmacy, including value added tax (VAT), as cost per milligram in the year of analysis. The frequency of drug administration was given by the protocol or standard treatment guidelines. By using the market price, we calculated the “per patient experimental drug cost” by summing the cost of each experimental drug administered to patient (Additional file 1). Each experimental drug cost was obtained multiplying the numbers cycle * experimental drug patient dosage (mg) received * market price experimental drug per mg. Adding up all “per patient experimental drug cost”, experimental drugs total cost was determined for all patients included in clinical trials. Then for each patient, we defined the expected standard treatment and we calculated the cost of the standard antineoplastic drugs that should be administered in clinical practice outside clinical trials. The “per patient standard treatment cost” was determined, multiplying the number of administration of each standard drug treatment (by protocol) in absolute value * standard drug patient dosage per mg * market price standard drug per mg (Additional file 2). For some patients, there was not a standard treatment and, therefore, the cost of conventional antineoplastic drugs was zero. The net cost saving over the duration of study period was calculated adding the “per patient standard treatment cost” of both pharma sponsored and investigator initiated studies for all patients. Costs other than drugs were (such as diagnostic tests, medical supplies, equipment and staff) not included in the cost saving calculation.

**Results**

From 23.10.2017 to 17.11.2017, 126 patients were treated within 34 clinical trials for an overall number of 152 cycles of therapy at National Cancer Institute of Naples (Additional file 3). Phase III, II and I/II clinical trials were 47%, 29% and 12%, respectively (Fig. 1a), while IIIB/IV and IV each only 3%. About 65% of patients are enrolled in Phase III and II clinical trials (Fig. 1b). Investigator initiated clinical trials were
15%, with 15 patients (12% of the total). Most of patients (53%) were enrolled by Melanoma cancer immunotherapy and innovative therapy unit (Fig. 2). Nivolumab was the experimental “drug” administered more frequently to patient (about 48%) and used in 10 clinical trials (29%), followed by Pembrolizumab and Atezolizumab used in 7 (administered to 12,7% of patients) and 5 clinical trials (administered to 9,5% of patients), respectively. Seven experimental drugs used in clinical trials were not commercialized. They were administered to 24 patients (19% of the total), mainly with lung (25%) and urogynecological (25%) cancers. All investigator initiated clinical studies, instead, used commercialized drugs. Finally, 23 patients did not presented conventional alternative anticancer treatments. They were enrolled in 11 clinical studies, 3 of which were investigator initiated studies. Among these patients, 8 were treated with experimental drugs not yet commercialized within pharma sponsored clinical studies. The cost of experimental drugs administered to all patients included in clinical trials was 431,025 Euros (Additional file 2), 344,990 Euros (80%) for patients enrolled in profit clinical trials and 86,035 Euros (20%) for patients enrolled in investigator initiated clinical trials. The treatment of the same patients in a same 4-week period with conventional therapies outside clinical trials would determine a cost of 517,658 Euros (Additional file 4), 515,804 Euros (99,64%) for patients enrolled in pharma sponsored clinical trials and 1,855 Euros (0,36%) for those enrolled in non-profit clinical trials (Table 1).

On average, the hospital saved 5,487 Euros per patient treated in pharma sponsored studies and 206 Euros for those treated within investigator initiated studies (Fig. 3). Moreover, 23 patients (22% of total) did not have standard alternative treatment: among these patients, 17 were enrolled in pharma sponsored studies (8 of which are treated with experimental drugs not on the market) and 6 in investigator initiated studies (Fig. 4).

**Discussion**

This study evaluated the effect of pharma sponsored and investigator initiated clinical trials on hospitals’ pharmaceutical expenditure. In a four-week period 126 patients treated in clinical trials were analyzed in order to quantify drugs cost reduction related to the participation in clinical trials at National Cancer Institute of Naples. Our analysis demonstrated that the hospital has saved in a month about 517,658 Euros for drugs that, otherwise, would have been loaded on the Italian National Healthcare Service. If calculated on the same number of patients and one-year period, this saving could potentially translate into a significant drug costs reduction that exceed 6 million of Euros. Some studies have already evaluated the potential economic impact of patient participation in clinical trials in terms of drugs cost saving. McDonagh et al. (2000) examined the costs and savings resulting from two pharmacy-based investigational drug services for fiscal years 1996-97. They showed that there was a cost avoidance of 2.9 million Dollars in drug costs, which was equivalent to 8% of the institutions’ annual drug budget for 1996-1997. LeFlue et al (2004), through a review of the study protocols and dispensing data for the investigational drug studies over two years, have demonstrated that trials participation achieves considerable drug cost avoidance, according to the type of study and the disease category involved. Uecke et al. (2008) quantified drug cost savings in hospitals related to clinical trials and analyzed 88 clinical trials in oncology including 29 researchers in 11 hospitals in Germany from 2002 through 2005.
with the aim to examine the relationship between researchers and hospital administrators with respect to clinical trials. The results showed a drug cost saving potential of 5.1 million Euros and an actual cost saving of 1.5 million Euros. In a retrospective cost attribution analysis to quantitate the treatment costs associated with cancer clinical trial protocols conducted in a single UK institution during 2009 and 2010 period, Liniker et al. (2013) determined an overall treatment cost saving of 388,719 Pounds in 2009 and 496,556 Pounds in 2010, largely attributable to pharmaceutical company provision of free drug supplies. Grossi et al. (2013), evaluated the cost of drugs administered in clinical practice and in clinical trials for a single Italian Lung Cancer Unit and they demonstrated that participation in clinical trials offers substantial cost savings for the Italian NHS related to drug provided free of charge by sponsors. They quantified this saving in 243,154 Euros (about 30% of the overall cost of those antineoplastic drugs charged to hospital during 2010). Calvin-Lamas et al. (2015), carried out an observational of prevalence study with retrospective collected data related to prostate cancer clinical trials during the study period (1996-2013), demonstrating a total cost avoidance of 696,002 Euros and an average cost avoidance per patient was Euros 5,118. Finally, Manes-Sevilla et al. (2018), in a retrospective observational study of the drug cost avoidance during the study period (2014-2016), calculated a total cost avoidance of 957,246 Euros and an average cost avoidance per patient of 10,756 Euros related to the supply drugs free by the sponsors. They included in this study thirty-seven clinical trials with a total of 89 breast cancer patients. Our study confirmed these findings showing a significant cost savings related to investigational drugs that are provided to the hospital free of charge by sponsor also in the era of immunotherapy. However, clinical trials conducting determines additional costs that inevitably loads on the hospital, which could affect the real economic benefit of drug cost saving. This represents a limit at also of the analyses conducted in our study, because we calculated the drugs cost saving without taking into account the costs involved in the conduction of clinical trials. In our previous research [11], we estimated that for patients included in clinical trials, the average “per patient” total costs accounted for 11.379 Euro, including overhead costs of clinical trials. Nonetheless, it should be also considered that profit clinical studies itself-repay entirely through sponsors’ grant (generally related to performing the activities envisaged by the protocol).

**Conclusion**

Cancer clinical trials may provide a range of benefits for pharmaceutical companies, researchers and patients, but also for health care organization and health systems. Our research demonstrated that treating patients within clinical trials lead to significant financial gains also in the hospital administrators perspective, leading to save the cost of conventional standard treatments and reducing drug expenditures.

**Table**

**Table 1** Cost of drugs for experimental and standard treatments
Declarations

Ethics approval and consent to participate

Ethical approval was not required for this study as it was a program of cost determination. Names and surnames of patients were not collected with the data and all identifiers were removed by Hospital Pharmacy before data analysis. The lead authors did not have access to personal data.

Consent for publication

Not applicable.

Availability of data and materials

Data and materials analyzed are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors’ contributions

Francesca D’Ambrosio, Giacomo Pascarella, Alessandro Morabito, Gianfranco De Feo, Gerardo Botti, Arturo Capasso, Antonio Nardone and Maria Triassi developed the conceptualization, data collection and interpretation, wrote the first version of the paper, revised draft versions, and prepared and submitted the final manuscript. Sandro Pignata and Piera Maiolino developed the conceptualization, data collection and interpretation. Michela Piezzo and Antonio Maria Grimaldi and Roberta D’Aniello contributed to data
collection and interpretation. Ida Palazzo and Immacolata Di Stasio contributed to data collection. Franco Perrore provided to scientific advice. All author(s) read and approved the final manuscript.

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**Figures**

**Figure 1**

Distribution of trials (1a) and patients (1b) for study phases.

**Figure 2**

Clinical trials patients distribution for organizational units.
Figure 3
Per-patient average cost saving.

Figure 4
Patients with no standard therapy treated with experimental drugs.

Supplementary Files
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