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Evolution of Pharmaceutical Expenditure and Cost Avoidance in Cancer Clinical Trials: A 10-Year Retrospective Study of Adult Solid Tumor Patients (Highlights longitudinal "evolution" in drug patterns alongside DCA.)

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ABSTRACT

This retrospective review from a single institution aimed to outline the clinical profile of adult individuals with solid malignancies who entered oncology trials across a decade (2010–2019) and to quantify drug cost avoidance (DCA) attributable to sponsor-funded treatments. Sponsor-supported pharmaceutical costs were estimated using the annual market price of each antineoplastic product that Vall d'Hebron University Hospital (HUVH) would otherwise have paid. Across the study window, 2930 trials were run, enrolling 10, 488 subjects. The number of studies rose from 140 in 2010 to 459 in 2019 (a 228% rise). Early-phase, high-complexity designs—such as phase I and basket studies—represented 34.3% of all trials. Marked shifts in research trends were observed: in 2010, targeted agents represented 79.4% of drug spending and cytotoxics 20.6%, whereas by 2019, immunotherapies made up 68.4%, targeted agents 24.4%, and cytotoxic drugs only 7.1%. Altogether, 421 distinct anticancer medicines were employed; diversity expanded from 47 agents used in 2010 (with 7 of them responsible for 92.8% of expenses) to 317 agents in 2019 (with 33 accounting for 90.6% of spending). Total antineoplastic expenditure for patients treated outside trial settings was EUR 120, 396, 096. The value of investigational medications supplied by sponsors reached EUR 107, 306, 084, generating a potential DCA of EUR 92, 662, 609. Overall, clinical trials not only advance medical innovation and patient care but also offer substantial opportunities to mitigate oncology-related costs.

Keywords: Clinical trial, Solid tumors, Drug cost avoidance, Pharmaceutical spending, Sponsor, Academic research

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Introduction

Integrating scientific developments promptly into oncology practice is increasingly complex due to the rapid expansion of approved therapies and evolving drug indications. Every antineoplastic agent in use today emerges from clinical research led by both industry and academic groups [1]. Industry-sponsored studies deliver new anticancer products, yet commercial priorities may diverge from real clinical gaps. Academic programs refine therapeutic strategies, design novel combinations, and center research on patient-focused needs. According to registrations at ClinicalTrials.gov, approximately 65% of studies are financed by public health entities, government bodies, universities, or research networks [2]. Data from EudraCT (2005–2013) indicate that 39% of trials were initiated by non-commercial sponsors [2], although more recent statistics (2005–2022) reveal a decline to 20% [3], a trend that poses future challenges for oncology progress. Areas such as radiotherapy and surgical innovation rely predominantly on academic research, amplifying the essential role of non-commercial institutions. Patients enrolled in trials gain access to experimental therapeutics unavailable elsewhere and contribute to scientific advancement. Despite growing concern about rising cancer-care costs, information on cost reductions associated with academic trials is still scarce. Matched analyses have shown that participation in oncology studies

does not significantly raise direct healthcare expenditures [4-9], while investigational drug programs at academic centers have yielded considerable DCA across multiple specialties, including oncology [10-12].

Previous reports illustrate this economic value: an assessment of 88 cancer trials across 11 German hospitals (2002–2005) documented EUR 1.5 million in savings [13]; at the Italian National Institute for Cancer Research, inclusion of 44 individuals in 12 sponsored studies reduced 2010 drug spending by 30% and provided additional grant income [14]; analysis of 17 phase III studies with 3195 patients by the NCIC Clinical Trials Group (1999–2011) estimated DCA of CAD 27, 952, 512, with targeted agents accounting for 43% [15]. In the UK, management of 357 patients across 53 protocols (2009–2010) resulted in GBP 885, 275 in avoided drug costs [16]. A review of five international phase III prostate cancer trials involving 136 participants showed total savings of EUR 696, 002 (EUR 5118 per patient) between 1996 and 2013 [17]. Among 89 breast cancer patients treated within 37 trials (2014–2016), the difference between investigational drugs and standard regimens corresponded to EUR 957, 246 in avoided cost (EUR 10, 756 per patient) [18]. In another Spanish National Health System site, treatment spending for 68 cancer patients in 20 trials was 79% lower than standard care, with protocol-level differences ranging from an extra EUR 8193 to a saving of EUR 59, 770 [19].

However, there remains a lack of large-scale, real-world assessments of DCA across extensive portfolios of sponsored oncology trials. Therefore, this investigation aimed to assess antineoplastic drug expenditures and estimate cost savings in a large cohort of adults with solid tumors participating in sponsored trials at a single center across ten years. The stratification by trial phase, drug class, tumor type, and active agents represents a unique aspect of this analysis. Quantifying drug-related economic benefits in such a broad population may help dispel concerns about added costs associated with running clinical trials.

Materials and Methods

Study design and patient population

This investigation was a retrospective review carried out at a single institution and involved adults with solid malignancies who participated in any active clinical study between 2010 and 2019 in the Medical Oncology Department of Vall d'Hebron University Hospital (HUVH), Barcelona, Spain. Information on drug-related expenditures for adults with solid tumors treated at HUVH during the same decade—but outside clinical research programs—had been previously documented [20].

HUVH serves as the principal tertiary referral center in Catalonia and ranks among the country's largest hospitals. It operates within the national public health network, which ensures universal, no-cost medical coverage for all Spanish residents regardless of personal or socioeconomic characteristics. For oncology patients, antineoplastic therapies are reimbursed by the regional health authority. The institution provides care to a reference population of 430, 000 and functions with an annual budget of EUR 630 million [21]. The Medical Oncology Department collaborates closely with the Vall d'Hebron Institute of Oncology (VHIO), while the Pharmacy Department supports general medicine, trauma, pediatrics, and maternal care and manages both the Outpatient Prescriptions Unit and the Oncology Pharmacy Unit distributed across multiple day-hospital areas.

Eligibility criteria included adults aged 18 years or older, of either sex, diagnosed with malignant solid tumors, enrolled in a clinical trial, and receiving any antineoplastic therapy administered orally or via parenteral routes. Parenteral administration encompassed intravenous, intramuscular, and subcutaneous delivery. Individuals with solid tumors not participating in a clinical trial were excluded. Ethical approval was deemed unnecessary due to the study's quality-of-care focus.

Study variables

For each participant, several variables were collected: the clinical trial phase (including phase 0; phase I and basket designs; phase II specific to tumor type; phase III; and post-authorization or rollover studies); the cancer category, classified by anatomic site or system using National Cancer Institute criteria [22]; and the pharmacologic classification of antineoplastic agents based on International Common Denomination (ICD), International Non-Proprietary Names (INN), or the Spanish Agency of Medicines and Medical Devices [23]. Drugs were grouped into cytotoxic agents, immunotherapies, targeted treatments, and other active compounds. For each subgroup, both the number of treated patients and corresponding drug expenditures were recorded annually whenever data were available.

Pharmaceutical spending, sponsor support, and drug cost avoidance

Information for patients taking part in clinical trials from 2010 to 2019 was extracted from the VHIO Clinical Trials Management System, Fundanet (Cantabria, Spain), version 2020-13 (https://vhio.fundanetsuite.com/EstudiosClinicos/, accessed 20 June 2020). Data were transferred into Microsoft Excel to compile yearly metrics: total number of trials open to recruitment; number of studies with ongoing enrolment classified by phase and cancer type; number of participants by trial phase; and number of individuals actively receiving treatment within each phase.

All sponsor-supplied pharmaceutical products were included in the financial assessment whenever these medications were commercially available at the time of use. In double-blind randomized designs, where the Pharmacy Department was blinded to treatment identity until code unblinding, drug costs were estimated by applying the allocation ratio across the study arms. Two economic analyses were performed:

1. Sponsor-related drug contribution:
   The value of antineoplastic drugs provided by sponsors was calculated using the actual yearly market prices of the same pharmaceutical products that HUVH would have needed to purchase in the absence of sponsor support. The methodology used to determine drug acquisition costs was previously described [20].
2. Estimation of annual drug cost avoidance (DCA):
   The average per-patient yearly cost of antineoplastic therapy for each tumor group—based on patients receiving standard care at HUVH during 2010–2019 and not enrolled in research—had been established in earlier work [20]. This annual average cost, specific to tumor location, was then applied to the number of trial participants to approximate the expenditure the hospital would have incurred if these individuals had been treated outside clinical research programs during the same period. DCA by tumor site was computed only for patients receiving intravenous antineoplastic agents, as anonymized records lacked cancer-site details for participants treated exclusively with oral medications.

Statistical analysis

The dataset was summarized using descriptive methods. Categorical variables are presented as counts and percentages, while continuous variables are shown as means with standard deviations (SD), or as medians with interquartile ranges (IQR; 25th–75th percentile) when distributions were non-normal. All analyses were carried out using the Pharmacy Analytics Manager, version 2022.1.0 (https://www.asserta.net, accessed 20 July 2020).

Results and Discussion

Clinical trials and study population

Across the years 2010–2019, a total of 2930 actively recruiting studies were implemented in the Medical Oncology Department for solid tumor management. Of these, 140 trials occurred in 2010 and 459 in 2019, reflecting a 228% rise. As displayed in **Table 1**, phase I and basket designs—considered high-complexity trials—represented 34.3% of all studies. Trials concentrating on a single tumor category accounted for 76.5%, although non–tumor-specific studies increased substantially from 36 in 2010 to 103 in 2019, marking a 186% expansion.

Table 1. Number of clinical trials conducted with active recruitment at any time across the study interval.

Year	Total Clinical Trials	Phase 0 *n (%)*	Phase I & Basket *n (%)*	Phase II *n (%)*	Phase III *n (%)*	Post-Authorization & Rollovers *n (%)*
2010	140	0	37 (26.4)	54 (38.6)	49 (35.0)	0
2011	161	0	48 (29.8)	57 (35.4)	56 (34.8)	0
2012	219	0	66 (30.1)	85 (38.8)	68 (31.0)	0
2013	232	0	75 (32.3)	96 (41.4)	61 (26.3)	0
2014	251	0	83 (33.1)	99 (39.4)	64 (25.5)	5 (2.0)
2015	303	0	106 (35.0)	94 (31.0)	89 (29.4)	14 (4.6)
2016	370	0	129 (34.9)	117 (31.6)	108 (29.2)	16 (4.3)
2017	374	0	137 (36.6)	107 (28.6)	111 (29.7)	19 (5.1)
2018	421	0	161 (38.2)	131 (31.1)	107 (25.4)	22 (5.2)

2019	459	1 (0.2)	162 (35.3)	141 (30.7)	121 (26.4)	34 (7.4)
2010–2019	**2930**	**1 (0.03)**	**1004 (34.3)**	**981 (33.5)**	**834 (28.5)**	**110 (3.7)**

Between 2010 and 2019, 10, 488 individuals received antineoplastic therapy in the context of clinical trials; 4964 (47.3%) were treated with intravenous agents, and 5524 (52.7%) with oral medications. The distribution of 7488 patients receiving active therapy across different trial phases from 2016 to 2019 is shown in **Figure 1**.

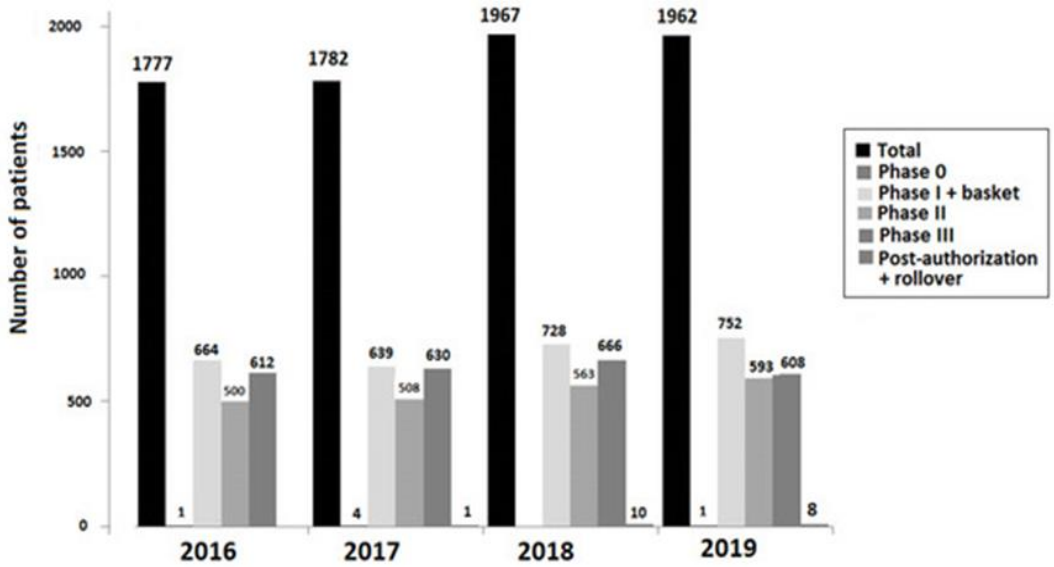

Figure 1. Distribution of 7488 patients receiving active treatment across trial phases (2016–2019).

Pharmaceutical costs in clinical trials (sponsor financial input)

Over the decade examined, total sponsor-funded spending on study medications reached EUR 107, 306, 084. Of this amount, EUR 72, 266, 379 corresponded to intravenous antineoplastics, and EUR 35, 039, 705 to oral therapies **(Table 2)**.

Table 2. Pharmaceutical expenditure by type of antineoplastic therapy in clinical trials, 2010–2019. NR: not registered.

Year	Sponsor-Supplied Antineoplastic Drug Costs	Intravenous	Oral
2010		EUR 2, 457, 850	NR
2011		EUR 1, 700, 250	NR
2012		EUR 2, 203, 633	NR
2013		EUR 3, 331, 912	EUR 1, 845, 309
2014		EUR 4, 636, 490	EUR 2, 022, 064
2015		EUR 4, 120, 596	EUR 2, 876, 494
2016		EUR 6, 220, 320	EUR 3, 545, 183
2017		EUR 12, 675, 915	EUR 6, 086, 139
2018		EUR 17, 844, 749	EUR 8, 166, 853
2019		EUR 17, 074, 664	EUR 10, 497, 663
Total		**EUR 72, 266, 379**	**EUR 35, 039, 705**
Overall (2010–2019)	**EUR 107, 306, 084**		

Expenditure by drug class

Data on drug-class expenditures were available for 2013–2019. Collectively, intravenous and oral antineoplastic drugs accounted for 94% of total spending (EUR 100, 944, 351). As indicated in **Table 3**, targeted therapies represented the largest share (58%), followed by immunotherapies (35.3%) and cytotoxic agents (6.7%). Costs

increased markedly from EUR 5, 177, 221 in 2013 to EUR 27, 572, 327 in 2019. Annual growth varied widely—from 5.1% (2014–2015) to 92.1% (2016–2017) and 6% (2018–2019).

Table 3. Expenditure by pharmacological category and study year, 2013–2019.

Category	Cytotoxic Drugs	Immunotherapy	Targeted Therapy	Other Drugs	Total
Intravenous	EUR 6, 322, 282	EUR 35, 623, 961	EUR 23, 958, 403	–	**EUR 65, 904, 646**
Oral	EUR 424, 306	–	EUR 34, 609, 333	EUR 6, 066	**EUR 35, 039, 705**
Total (All Routes)	**EUR 6, 746, 588**	**EUR 35, 623, 961**	**EUR 58, 567, 736**	**EUR 6, 066**	**EUR 100, 944, 351**
Breakdown by Study Year (All Routes Combined)					
Year	**Cytotoxic Drugs**	**Immunotherapy**	**Targeted Therapy**	**Other Drugs**	**Total**
2013	EUR 957, 915	EUR 590, 250	EUR 3, 629, 056	–	**EUR 5, 177, 221**
2014	EUR 613, 360	EUR 1, 517, 637	EUR 4, 527, 558	–	**EUR 6, 658, 554**
2015	EUR 796, 317	EUR 222, 342	EUR 5, 978, 431	–	**EUR 6, 997, 090**
2016	EUR 891, 738	EUR 2, 536, 316	EUR 6, 337, 449	–	**EUR 9, 765, 502**
2017	EUR 1, 175, 345	EUR 6, 900, 964	EUR 10, 685, 745	–	**EUR 18, 762, 054**
2018	EUR 1, 001, 328	EUR 12, 169, 256	EUR 12, 841, 019	–	**EUR 26, 011, 603**
2019	EUR 1, 310, 587	EUR 11, 687, 195	EUR 14, 568, 479	EUR 6, 066	**EUR 27, 572, 327**

For the complete 10-year period, expenditure data by class were available for intravenous antineoplastic drugs **(Table 4)**. Significant shifts in treatment patterns occurred:

- In 2010, targeted agents accounted for 79.4% of spending, with cytotoxic drugs at 20.6%.
- By 2019, immunotherapy represented 68.4%, targeted therapy 24.4%, and cytotoxic agents just 7.1%.

Corresponding patient distribution also changed between 2010 and 2019:

- Cytotoxic therapy: 75.2% → 33.8%
- Immunotherapy: 0.8% → 67.2%
- Targeted therapy: 54.2% → 28%

Table 4. Pharmaceutical expenditure by intravenous antineoplastic drug class, 2010–2019.

Year	Cytotoxic Drugs	Immunotherapy	Targeted Therapy	Total Sponsor-Supplied Expenditure	% Change vs. Previous Year
2010	EUR 506, 138	–	EUR 1, 951, 712	EUR 2, 457, 850	–
2011	EUR 599, 725	–	EUR 1, 100, 526	EUR 1, 700, 250	−30.8%
2012	EUR 860, 070	–	EUR 1, 343, 563	EUR 2, 203, 633	29.6%
2013	EUR 863, 237	EUR 590, 250	EUR 1, 848, 425	EUR 3, 331, 912	51.2%
2014	EUR 568, 777	EUR 1, 517, 637	EUR 2, 550, 076	EUR 4, 636, 490	39.1%
2015	EUR 787, 984	EUR 222, 342	EUR 3, 110, 270	EUR 4, 120, 596	−11.1%

2016	EUR 866, 817	EUR 2, 536, 316	EUR 2, 817, 187	EUR 6, 220, 320	51.0%
2017	EUR 1, 047, 329	EUR 6, 900, 964	EUR 4, 727, 621	EUR 12, 675, 915	103.8%
2018	EUR 940, 547	EUR 12, 169, 256	EUR 4, 734, 946	EUR 17, 844, 749	40.8%
2019	EUR 1, 217, 591	EUR 11, 687, 195	EUR 4, 169, 878	EUR 17, 074, 664	−4.3%

Expenditure by individual antineoplastic agent

Altogether, 421 different anticancer drugs were utilized. Diversity expanded markedly:

- 47 agents in 2010, with 7 accounting for 92.8% of total spending.
- 317 agents in 2019, with 33 responsible for 90.6% of expenditures **(Table 5)**.

Table 5. Antineoplastic drugs administered in clinical trials in 2010 and 2019.

2010			**2019**		
Antineoplastic Agent	**Expenditure**	**% of Total**	**Antineoplastic Agent**	**Expenditure**	**% of Total**
Trastuzumab	EUR 919, 484	37.4	Pembrolizumab	EUR 3, 590, 128.10	13.0
Bevacizumab	EUR 449, 063	18.3	Nivolumab	EUR 2, 489, 205.42	9.0
Aflibercept/placebo	EUR 301, 600	12.3	Cabozantinib	EUR 2, 392, 934.10	8.7
Docetaxel	EUR 191, 287	7.8	Atezolizumab	EUR 1, 983, 242.04	7.2
Pemetrexed	EUR 145, 919	5.9	Bevacizumab	EUR 1, 696, 849.55	6.1
Cetuximab	EUR 145, 079	5.9	Palbociclib	EUR 1, 449, 416.28	5.3
Panitumumab	EUR 129, 287	5.3	Olaparib	EUR 1, 338, 767.04	4.9
Subtotal (Top 7)		**92.8**	Lorlatinib	EUR 1, 094, 262.59	4.0
			Ipilimumab	EUR 786, 563.46	2.8
			Pembrolizumab	EUR 670, 891.67	2.4
			Pemetrexed	EUR 615, 425.91	2.2
			Pertuzumab	EUR 581, 406.00	2.1
			Avelumab	EUR 568, 416.00	2.1
			Abiraterone	EUR 500, 524.62	1.8
			Pembrolizumab/placebo	EUR 405, 841.74	1.5
			Cetuximab	EUR 393, 887.10	1.4
			Lenvatinib	EUR 386, 416.81	1.4
			Dinutuximab	EUR 348, 727.07	1.3
			Atezolizumab/placebo	EUR 326, 070.63	1.2
			Osimertinib	EUR 300, 501.60	1.1
			Sunitinib	EUR 299, 647.57	1.1
			BMS-986213/Nivolumab	EUR 289, 906.56	1.0
			Axitinib	EUR 280, 783.80	1.0
			Enzalutamide	EUR 274, 394.96	1.0
			Trastuzumab s.c.	EUR 271, 830.00	1.0
			Apalutamide	EUR 259, 110.00	0.9
			Ipilimumab/placebo	EUR 222, 314.53	0.8
			Trastuzumab	EUR 217, 028.66	0.8
			Alectinib	EUR 204, 001.91	0.7
			Panitumumab	EUR 183, 674.66	0.7
			Nivolumab/placebo	EUR 183, 520.80	0.7
			Niraparib	EUR 181, 838.25	0.7
			Olaratumab/placebo	EUR 181, 812.21	0.7
			Subtotal (Top 33)		**90.6**

Expenditure by tumor site

In 2010, intravenous anticancer therapy was administered across 17 tumor types, with 5 sites (breast, colon, ovary, non–small cell lung cancer, and prostate) contributing 90% of total treatment costs. By 2019, this increased to 30 tumor categories, with 15—including non–small cell lung cancer, advanced solid tumors, breast, colon, and ovary—making up 90% of expenditures **(Table 6)**. In 2019, the largest proportions of treated patients were those with advanced solid tumors (20.2%) and non–small cell lung cancer (17.5%).

Table 6. Percentages of pharmaceutical expenditures and treated patients by tumor site in trials using intravenous antineoplastic drugs, 2010 and 2019.

2010			**2019**		
Tumor Location	**% of Total Expenditure**	**% of Total Patients**	**Tumor Location**	**% of Total Expenditure**	**% of Total Patients**
Breast	46.4	34.8	Lung, non-small cell	27.0	17.5
Colon	18.0	19.1	Advanced solid tumor	10.1	20.2
Ovary	14.3	8.7	Breast	9.5	9.9
Lung, non-small cell	9.6	13.5	Colon	8.0	7.6
Prostate	5.8	3.0	Ovary	7.0	5.2
Pancreas endocrine	1.9	0.8	Melanoma	6.2	5.4
Rectum	1.5	3.2	Kidney	5.2	3.7
Advanced solid tumors	1.3	8.4	Pancreas exocrine	2.9	4.3
Oral cavity and oropharynx	0.4	1.6	Uterine cervix	2.7	3.4
Stomach	0.3	1.6	Lung, small cell	2.6	2.7
Pancreas exocrine	0.2	2.4	Endometrium	2.3	3.2
Lung, small cell	0.2	0.5	Urinary bladder	2.2	2.7
Urinary bladder	0.04	2.2	Stomach	2.2	3.1
Kidney	0.02	0.5	Oral cavity and oropharynx	2.1	2.2
Soft tissue sarcoma	0.01	0.3	Mesothelioma	1.7	1.5
Endometrium	0.01	0.8	Esophagus	1.5	1.1
Extrahepatic bile duct	0.0	0.3	Soft tissue sarcoma	1.4	1.0
			Rhinopharynx/cavum	1.2	0.4
			Neuroendocrine	0.7	1.4
			Hepatic carcinoma	0.7	0.5
			Thymoma	0.7	0.5
			Brain	0.5	0.7
			Prostate	0.5	1.0
			Squamous cell skin cancer	0.4	0.3
			Larynx/hypopharynx	0.3	0.09
			Rectum	0.2	0.6
			Basal cell carcinoma	0.2	0.2
			Merkel carcinoma	0.07	0.2
			Extrahepatic bile duct	0.02	1.1
			Urothelial cancer	0.0	0.09
			Adrenal		0.09
			Anus		0.4
			Pancreas endocrine		0.5
			Thyroid		0.3
			Gallbladder		0.09

Estimation of potential drug cost avoidance

Table 7 summarizes the projected savings in antineoplastic medication expenses avoided for patients enrolled in clinical trials during the study period. The overall pharmaceutical cost offset reached EUR 92, 662, 609, consisting of EUR 34, 463, 891 for intravenously administered antineoplastic agents and EUR 58, 198, 718 for oral therapies.

Table 7. Estimated antineoplastic drug cost avoidance for patients in clinical trials from 2010 to 2019.

Year	Antineoplastic Drug Costs Avoided (DCA)	Intravenous	Oral	Total
2010		EUR 1, 650, 750	EUR 4, 541, 111	**EUR 6, 191, 865**
2011		EUR 1, 205, 680	EUR 6, 829, 844	**EUR 8, 035, 524**
2012		EUR 1, 322, 395	EUR 4, 141, 530	**EUR 5, 463, 925**
2013		EUR 2, 349, 744	EUR 3, 994, 676	**EUR 6, 344, 420**
2014		EUR 2, 157, 533	EUR 4, 933, 760	**EUR 7, 091, 293**
2015		EUR 3, 034, 919	EUR 6, 474, 355	**EUR 9, 509, 274**
2016		EUR 4, 087, 619	EUR 6, 370, 112	**EUR 10, 457, 731**
2017		EUR 4, 722, 001	EUR 5, 911, 956	**EUR 10, 633, 957**
2018		EUR 7, 266, 822	EUR 7, 196, 238	**EUR 14, 463, 060**
2019		EUR 6, 666, 428	EUR 7, 805, 132	**EUR 14, 471, 560**
Total (2010–2019)		**EUR 34, 463, 891**	**EUR 58, 198, 718**	**EUR 92, 662, 609**

Tumor types with the highest DCA included breast cancer, rectal cancer, non-small cell lung cancer, and melanoma.

To contextualize these findings for the institution, prior data showed that pharmaceutical spending on antineoplastic agents for solid-tumor patients treated outside clinical trials totaled EUR 120, 396, 096 over 2010–2019 [20]. During that same interval, sponsors supplied trial medications worth EUR 107, 306, 084, resulting in a potential DCA of EUR 92, 662, 609 **(Table 8)**.

Table 8. Pharmaceutical spending for solid-tumor treatment during 2010–2019.
NR: not registered.

Year	Standard-Care Pharmaceutical Expenditure		Sponsor-Supplied in Clinical Trials		Drug Cost Avoidance (DCA)	
	Intravenous	Oral	Intravenous	Oral	Intravenous	Oral
2010	EUR 6, 565, 263	EUR 2, 579, 163	EUR 2, 457, 850	NR	EUR 1, 650, 750	EUR 4, 541, 115
2011	EUR 4, 464, 740	EUR 3, 271, 684	EUR 1, 700, 250	NR	EUR 1, 205, 680	EUR 6, 829, 844
2012	EUR 4, 695, 722	EUR 2, 853, 205	EUR 2, 203, 633	NR	EUR 1, 322, 395	EUR 4, 141, 530
2013	EUR 4, 436, 132	EUR 2, 437, 685	EUR 3, 331, 912	EUR 1, 845, 309	EUR 2, 349, 744	EUR 3, 994, 676
2014	EUR 5, 770, 959	EUR 3, 302, 873	EUR 4, 636, 490	EUR 2, 022, 064	EUR 2, 157, 533	EUR 4, 933, 760
2015	EUR 7, 596, 964	EUR 4, 346, 928	EUR 4, 120, 596	EUR 2, 876, 494	EUR 3, 034, 919	EUR 6, 474, 355

2016	EUR 9, 769, 375	EUR 4, 581, 945	EUR 6, 220, 320	EUR 3, 545, 183	EUR 4, 087, 619	EUR 6, 370, 112
2017	EUR 9, 475, 022	EUR 4, 990, 955	EUR 12, 675, 915	EUR 6, 086, 139	EUR 4, 722, 001	EUR 5, 911, 956
2018	EUR 11, 252, 776	EUR 6, 723, 301	EUR 17, 844, 749	EUR 8, 166, 853	EUR 7, 266, 822	EUR 7, 196, 238
2019	EUR 12, 666, 317	EUR 8, 615, 087	EUR 17, 074, 664	EUR 10, 497, 663	EUR 6, 666, 428	EUR 7, 805, 132
Total (2010–2019)	**EUR 76, 693, 270**	**EUR 43, 702, 826**	**EUR 72, 266, 379**	**EUR 35, 039, 705**	**EUR 34, 463, 891**	**EUR 58, 198, 718**
Grand Total	**EUR 120, 396, 096**		**EUR 107, 306, 084**		**EUR 92, 662, 609**	

Figure 2 illustrates the share of antineoplastic drug costs attributed to routine healthcare (mean 66%, range 41%–82%) versus sponsor-funded trial treatments (mean 44%, range 18%–59%). Sponsor contributions represented 89% of the medication expenditure incurred by HUVH for treating cancer patients receiving antineoplastic drugs in standard care.

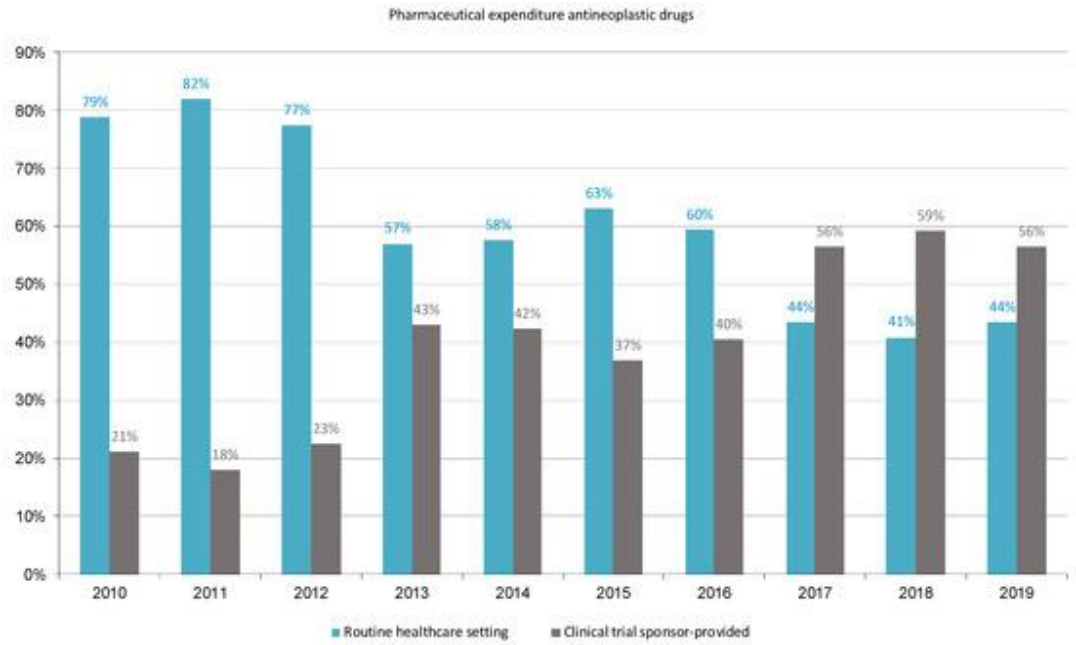

Figure 2. Proportion of antineoplastic drug expenditures in routine care compared with sponsor-supported clinical trial treatment.

Figure 3 displays the percentages of antineoplastic spending for solid tumors in routine care (mean 62%, range 49%–60%) and the portion potentially avoided through trial-related savings (mean 48%, range 40%–51%). The DCA accounted for 77% of HUVH's total antineoplastic drug costs for solid-tumor patients in routine practice.

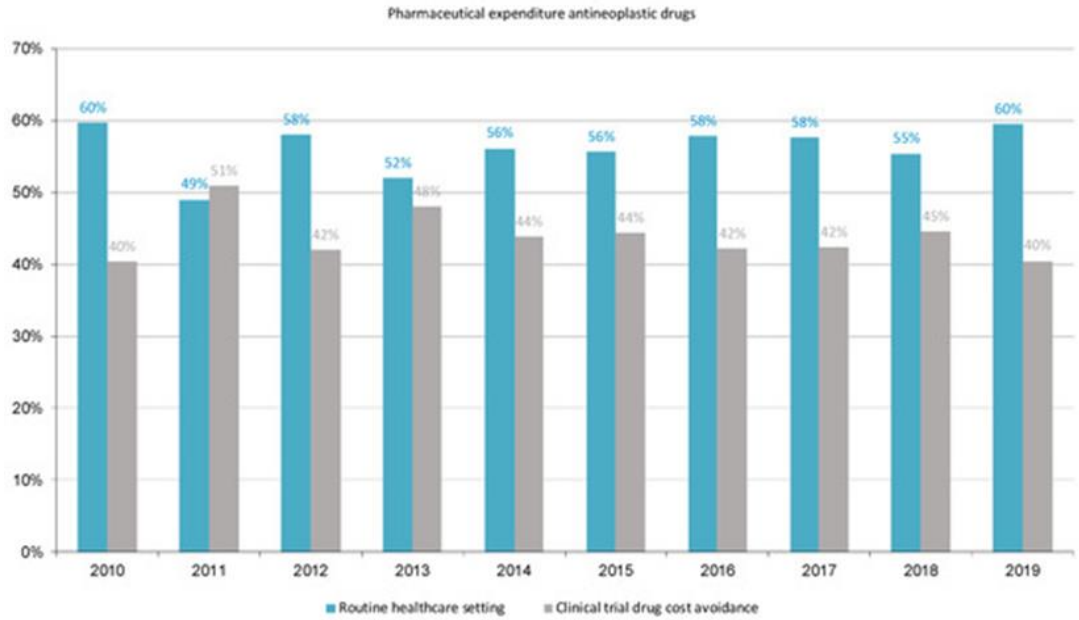

Figure 3. Proportion of antineoplastic drug expenditures in routine care and costs avoided through sponsor funding.

The Vall d'Hebron Institute of Oncology (VHIO) is a leading cancer research center that adopts a translational model, integrating multidisciplinary teams to promote personalized and precision-based cancer treatment. VHIO's scientific structure includes three major programs—preclinical, translational, and clinical research—supported by advanced technologies. Each unit is dedicated to converting research output into concrete patient benefits (see https://vhio.net).

Across 2010–2019, a substantial number of clinical studies targeting solid tumors were active at the center. In 2019, 459 cancer clinical trials were open to recruitment, with 162 (35.3%) corresponding to phase I and basket designs. In the same year, 1962 patients were treated within clinical trials, representing 41.4% of all solid-tumor patients managed in the Medical Oncology Department; 38.4% of them participated in the 162 early-phase and basket studies. According to the Spanish Registry of Clinical Studies (REEC), as of August 2020, there were 597 ongoing adult cancer trials in Spain, including 188 (31.5%) phase I studies [24], highlighting the prominence of VHIO and HUVH within the national oncology research ecosystem.

During the 10-year period, 10, 488 individuals were enrolled in clinical trials, generating sponsor-provided antineoplastic drugs valued at EUR 107, 306, 084. The projected DCA, using our methodology, amounted to EUR 92, 662, 609. All calculations employed the same purchase prices applicable to HUVH at the time each drug was prescribed. The lower DCA relative to sponsor-supplied drug value stems from the lower costs of antineoplastic therapies used in routine care (the basis for DCA estimation) compared with the novel, high-priced treatments administered in trials.

The spending patterns between trial participants and standard-care patients reflect the heavier reliance on innovative, high-cost treatments in clinical research: targeted and immunotherapy agents represented 93.31% of expenditures in the trial cohort versus 81.37% in routine practice, while cytotoxic/other drugs accounted for 6.69% and 18.63%, respectively [20]. Overall, sponsor contributions and DCA corresponded to 89% and 77%, respectively, of HUVH's total antineoplastic spending for solid-tumor care across the decade studied.

Academic research has long been viewed as a contributor to the sustainability of public healthcare systems [25, 26], with clinical trial sponsors offering measurable advantages to institutions [27, 28]. Still, estimating DCA in oncology patients enrolled in trials has been inconsistently reported, largely because hospital information systems are often inadequate and because sponsor-provided study drugs are typically excluded from pharmacoeconomic evaluations of cancer treatments [29]. Earlier investigations examining the costs of treating clinical trial participants have been performed in healthcare settings in the USA, Canada, Germany, the UK, Italy, Taiwan, and Spain [10-18, 30]. While all reported financial gains for institutions when externally financed study medications are used, comparisons are hindered by methodological variability—whether studies analyzed only marketed or

investigational drugs, differences in control-arm regimens, variations in standard-of-care therapies, and discrepancies in drug cost sources.

Our analysis incorporated two separate estimates: (1) the expenditure that HUVH would have incurred if it had financed the drugs supplied by trial sponsors (similar to the approach taken by Calvin-Lamas *et al*. [17]), interpreted as an avoided institutional cost; and (2) the DCA representing the cost that would have been generated if trial participants had instead received routine healthcare treatment. This approach is more aligned with real-world practice than relying solely on theoretical standard-of-care or control-arm estimates used in past studies [10, 11, 13, 14, 17, 18]. Additional distinguishing aspects of our work include a 10-year observation period, a large patient cohort, inclusion of multiple trial phases, and detailed stratification by drug class, administration route, tumor site, and individual antineoplastic agents.

Across the decade examined, the distribution of clinical trial activity by drug class shifted markedly: cytotoxic therapies decreased from 20.6% in 2010 to 7.1% in 2019, targeted therapies declined from 79.4% to 24.4%, and immunotherapy reached 68.4% in 2019. Shen *et al.* [12] reported that targeted drugs accounted for 84.1% of total cost avoidance in a 2008 analysis in Taiwan, with lapatinib showing the greatest impact. In phase III trials assessed by Tang *et al.* [15] from 1999 to 2011, targeted agents represented 43% of overall DCA.

Among patients treated with intravenous therapies, 40 tumor sites were represented, involving 421 different agents, underscoring the extensive penetration of trial activity into clinical practice. Fifteen tumor types were responsible for 90% of sponsor financial contributions, most notably non-small cell lung cancer, advanced solid tumors, and breast, colon, and ovarian cancers.

Historically, many studies have focused on single tumor groups—such as lung cancer and mesothelioma [14], prostate cancer [17], breast cancer [18], or broad "all-cancer" analyses without organ specificity. Bredin *et al.* [30] evaluated 37 trials grouped into five categories (lung, gynecologic, neurologic, hematologic, and genitourinary) and demonstrated wide cost-avoidance variability influenced by factors such as trial duration, number of treatment days per cycle, and drug prices. In Tang *et al.* [15], most of the 17 trials included breast, lung, and ovarian tumors. In our dataset for 2019, trials involving intravenous and oral antineoplastic drugs included 1122 patients, comprising 25.8% gastrointestinal tumors, 23.3% lung cancer, 13% breast tumors, 11.8% gynecologic cancers, and 9.5% genitourinary tumors. Half of the sponsor-provided drug value originated from the following agents: pembrolizumab (13%), nivolumab (9%), cabozantinib (8.7%), atezolizumab (7.2%), bevacizumab (6.2%), and palbociclib (5.3%).

A limitation of our work is that supportive care medications were not incorporated into the analysis. According to Bredin *et al.* [30], antiemetics and colony-stimulating factors represent 2.9% of expenses associated with cytotoxic agents, while antidiarrheal and antihistamine treatments account for 0.28% of the costs of targeted therapy. In our earlier investigation [20], supportive treatments (antiemetics, erythropoietins, colony-stimulating growth factors, and hypocalcemia treatments) represented 4.6% of total drug spending for solid-tumor management in routine care, with a decline to 1.4% by 2019. Other trial-related cost factors, such as administrative or infrastructure expenses, were outside the scope of this study.

With respect to commercial versus non-commercial trials, applying findings across healthcare systems with differing funding structures is inherently challenging. A Canadian review of oncology trial unit finances from 2007–2011 reported losses in cooperative-group studies due to unfunded or underfunded follow-up activities; increasing enrollment in industry-funded trials was used to compensate, yet growing follow-up requirements amplified the deficit each year [31]. Although clinical trial participants undergo more frequent assessments—resulting in additional tests and procedures—patients receiving routine standard-of-care (SOC) therapies are also treated with expensive drugs [8]. The dominant factor equalizing costs between groups is the free provision of antineoplastic agents in trials, which accounts for the most substantial difference in overall medication expenditures [9]. In a retrospective analysis of 68 adult oncology patients across 20 clinical trials at a Spanish institution, despite a 32% higher procedural burden, drug-related costs were 79% lower among trial participants, leading the authors to conclude that maintaining a balanced portfolio of commercial and non-commercial trials is the most financially sustainable model [19].

A key limitation of this study is that it does not quantify the overall administrative infrastructure costs required to conduct clinical trials, nor the expenses associated with all clinical procedures (such as follow-up visits, management of toxicities, or treatment failures). Likewise, variables that could further clarify the significance of cost reductions linked to obtaining trial medications at no charge—such as demographic or socio-economic characteristics of participating patients—were not examined. These aspects were intentionally excluded because

the goal of this work was not to assess the financial viability of the clinical trials unit itself (which is largely supported by industry-generated income), but rather to document both the sponsor-provided drug expenditure and the potential pharmaceutical costs avoided specifically within the framework of national-system reimbursement of antineoplastic therapy.

The evaluation of the economic impact was carried out from the perspective of the public payer—the national healthcare administration—since all individuals in our country are entitled to universal, free access to funded oncologic treatments, irrespective of their demographic or socio-economic profile. Importantly, clinical trials not only contribute to scientific and clinical advancement but also help reduce the fiscal burden of cancer care on public health systems [32].

In summary, the distinct value of this analysis lies in several major differences from earlier publications [4-19, 30]: it encompasses all consecutive oncology patients participating in industry-supported trials, includes every tumor type, and focuses on the Medical Oncology Department of the largest hospital in Spain, which also conducts the greatest volume of oncology trials nationally. Examination of 2930 clinical studies involving 10, 488 individuals with solid tumors across 30 anatomical sites revealed a substantial DCA amounting to EUR 92, 662, 609. The detailed dataset provided here may serve as a useful benchmark for future comparative investigations.

Conclusion

The research activity carried out through oncology clinical trials at HUVH has facilitated the rapid introduction of innovative therapies and has contributed substantially to knowledge that informs routine clinical practice. Simultaneously, these trials reduce financial pressure on the public healthcare system through the provision of study drugs at no cost and through the pharmaceutical expenses potentially avoided when comparing trial-based treatment with real-world standard-care costs reimbursed by the national health system.

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