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Budget Impact Analysis of Olaparib for the Management of Patients with Homologous Recombination Repair (HRR)-Mutated Castration-Resistant Metastatic Prostate Cancer in Argentina

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Abstract

Objectives The aim of this study was to perform a budget impact analysis (BIA) of introducing olaparib treatment for adult patients with metastatic castration-resistant prostate cancer in Argentina.

Methods A BIA model was used to estimate the cost difference between the current scenario (without olaparib) and the new scenario (incorporation of olaparib) for a third-party payer over a 5-year time horizon. The budgetary impact is estimated at the national health system level and by healthcare sectors in Argentina. Input parameters were obtained from the literature and validated by local expert opinion. Direct medical costs were obtained from both the Institute for Clinical Effectiveness and Health Policy (IECS) unit cost database and public data in Argentina. The microcosting estimation was used for key variables of the analysis. All costs are reported in US dollars (US\$) as for October 2022 (1 US\$ = 152.59 Argentine pesos). One-way sensitivity analyses and scenario analyses were conducted to evaluate the model robustness.

Results The incorporation of olaparib, with a wholesale price per pack of US\$3176, was associated with a weighted average of the budget impact per member per month (PMPM) of US\$0.0191 for the national health system, being slightly higher than the estimated budgeted high impact threshold (US\$0.0153). The PMPM budget impact for a 5-year average ranged between US\$0.007 (public sector) and US\$0.033 (private sector). The duration of treatment with olaparib was the most influential parameter in the budget impact results.

Conclusions The introduction of olaparib for the treatment of metastatic castration-resistant prostate cancer has a high budget impact for Argentina's health system. These findings are informative to support policy decisions aimed to expand the current treatment landscape for prostate cancer.

1 Introduction

Prostate cancer is the second most prevalent cancer in men after lung cancer. Annually, nearly 1.2 million new cases are diagnosed worldwide and 35,000 deaths are attributed to prostate cancer, making it one of the leading causes of cancer-related death in men. In Argentina, it is estimated there are approximately 11,686 new cases and more than 3900 deaths annually [1].

Prostate cancer is slowly progressing and most cases are diagnosed in the early and potentially curable stages. Approximately 10% of patients are in the advanced stages of disease, while a proportion of patients are diagnosed with early disease relapse despite treatment [2]. It is estimated

that approximately 20% of patients with metastatic prostate cancer have germline mutations in deoxyribonucleic acid (DNA) repair genes [3]. Tumors with mutations that alter the function of genes involved in DNA damage repair by homologous recombination repair (HRR) have been shown to be associated with the most aggressive clinical behavior of prostate cancer. The most frequent mutations are the Breast Cancer 1 gene (BRCA 1) and the Breast Cancer 2 gene (BRCA 2), which are found in approximately 11% of patients with metastatic castration-resistant prostate cancer (mCRPC) [4, 5].

Current therapeutic strategies for the treatment of patients with advanced castration-sensitive prostate cancer are based on hormone therapy-seeking androgen deprivation, either chemically or surgically. Despite prolonged periods of disease control under treatment, almost 90% of patients will progress to the mCRPC stage [2, 3, 6]. Recently,

Key Points for Decision Makers

Introducing olaparib for metastatic castration-resistant prostate cancer in Argentina will lead to an additional average monthly cost of \$0.0191 per member per month for the national health system, which exceeds the high-impact budget threshold (\$0.0153).

The increase in costs due to the introduction of olaparib is primarily driven by the drug's price; however, the analysis indicates potential savings in managing adverse effects and administering the treatment.

Decision makers should evaluate coverage and reimbursement policies carefully, considering sector-specific impacts and potential strategies such as rebates, discounts, or phased introductions.

the inclusion of new hormonal agents (NHAs), such as abiraterone and enzalutamide, and the use of chemotherapy (taxanes and platinum) and radium (radium 223) in the treatment cascade have shown benefits in the survival of patients with mCRPC [7].

Olaparib belongs to the family of enzyme poly (ADP-ribose) polymerase (PARP) inhibitors. PARP inhibitors (PARPi) prevent DNA repair in mutated cells, leading to altered cellular homeostasis and resulting in death in tumor cells with gene damage [8].

The phase III PROfound study [9] showed the efficacy of olaparib in treating men with mCRPC who had disease progression and alterations in genes involved in HRR. They experienced longer progression-free survival, with a median of 7.4 months versus 3.6 months (hazard ratio [HR] 0.34, 95% confidence interval [CI] 0.25–0.47; $p < 0.001$) and improved overall survival (18.5 months vs. 15.1 months in the control group). Specifically, those with mutations in *BRCA1*, *BRCA2*, or ataxia-telangiectasia mutated (*ATM*) genes had significantly better outcome [9, 10].

Olaparib was approved by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) [11–13]. In Argentina, the National Administration of Drugs, Food and Medical Technology (ANMAT, acronym in Spanish) also approved olaparib for the treatment of adult patients with castration-resistant metastatic prostate cancer mutated in the somatic HRR gene who have progressed after prior treatment with enzalutamide or abiraterone [14].

The cost-effectiveness evidence for the use of olaparib is mixed. Dan Su and colleagues published a cost-effectiveness study for the use of olaparib in mCRPC with multiple alterations in genes involved in DNA repair, under the perspective of the US payer, and found that it was cost

effective [15]. On the other hand, in China, the use of olaparib for the same population was shown not to be cost effective for the Chinese healthcare system [16].

In Argentina, there is a gap in economic evidence on olaparib as a treatment for mCRPC. This study aimed to estimate the budget impact of including olaparib as a treatment for metastatic prostate cancer in the healthcare system of Argentina.

2 Methods

2.1 Model Structure

The budget impact model (BIM) provided by AstraZeneca was developed in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA); the model has been reviewed, validated and adapted to the Argentinian setting. Figure 1 displays the analytical structure of the model. The BIM considers a hypothetical third-party payer with 1,000,000 male individuals who were covered to estimate two scenarios: the current scenario (without olaparib) and the projected scenario (incorporation of olaparib). A comparison of the current and projected scenarios provided an estimate of the budget impact over a 5-year time horizon for the coverage of olaparib for the management of patients with HRR-mutated castration-resistant metastatic prostate cancer previously treated with NHA. The perspective of the analysis was the third-party public payer, the third-party social security payer, and the third-party private payer in the Argentinian health system. In Argentina, the healthcare system is decentralized and fragmented into three sectors: public, social security, and private. The social security sector is the largest and provides healthcare coverage to approximately 46% of the Argentine population, 16% are covered by the private sector, and approximately 38% of the population is covered by the public sector [17].

Budget impact outcomes were presented in absolute and relative terms and per member per month (PMPM) calculations. We followed the principles of good practice in budget impact modeling to elaborate this report, published by the Professional Society for Health Economics and Outcomes Research (ISPOR) task force [18]. The epidemiological data were sourced from the literature; however, for data not available in the literature, we consulted and validated the data with a local oncology expert.

2.2 Model Assumptions

The incidence of prostate cancer was constant throughout the 5-year time horizon. For the current scenario, we assumed a constant market share for each treatment regimen. We also

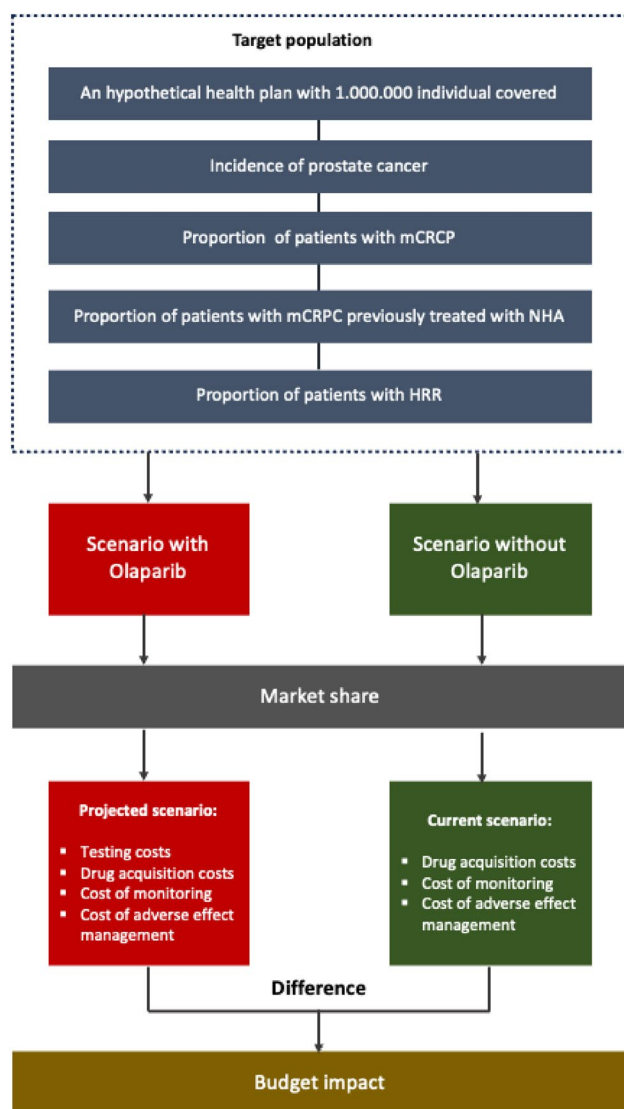


Fig. 1 Analytical structure of the model. *mCRPC* metastatic castration-resistant prostate cancer, *NHA* new hormonal agents, *HRR* homologous recombination repair gene

assumed that the access rate to olaparib for each healthcare sector was constant in the 5-year time horizon. Lastly, no discount rates or adjustment for inflation were considered.

2.3 Target Population

Male patients with mCRPC whose disease had progressed during treatment with NHAs (enzalutamide or abiraterone) were included in the model. The incidence of prostate cancer was estimated to be 0.18% [1]. Of the total number of patients with prostate cancer, approximately 15% had metastatic prostate cancer resistant to castration [7]. Based on the local clinical oncologist expert opinion,

approximately 60% of patients are treated with NHAs. Moreover, approximately 90% of prostate cancer patients progress to resistance, with the need to initiate a second line of treatment. It is estimated that 18% of patients will progress to mutated HRR (estimated based on data published by de Bono et al. [9], as mutations were detected in 778/4425 patients selected for screening), making them candidates for olaparib, and that 5.69 patients must be tested to identify one patient who tests positive for HRR [9]. Electronic supplementary material (ESM) S7 Fig. 3, presents the flowchart of prostate cancer patients eligible for olaparib treatment.

2.4 Intervention and Comparators

The intervention was olaparib monotherapy 300 mg twice daily. Comparators were chosen based on the clinical experience of the local oncologist expert. In Argentina, abiraterone, enzalutamide, cabazitaxel, and docetaxel are the currently commercialized and indicated therapies for patients with mCRPC whose disease has progressed during treatment with NHAs (enzalutamide or abiraterone). The dosages of the interventions and comparators were based on the published trial results [9, 19, 20].

2.5 Market Share

The market share for each comparator and the intervention were calculated based on the opinions and projections provided by the local oncologist expert. In the current scenario, the olaparib market share was assumed to be zero.

The estimation of olaparib's market share penetration varies across different third-party payers, each attempting to capture the unique characteristics of the Argentine healthcare system in terms of high-cost drug access and coverage within distinct healthcare sectors. Based on local clinical expert opinion, the market penetration for olaparib during the first year was 7%, 25% and 32% for the third-party public payer, third-party social security payer, and third-party private payer, respectively. Market shares are reported in ESM Table S1.

2.6 Cost Components

Direct medical costs associated with treatment were considered for analysis, and included the acquisition costs of mCRPC drug treatments, administration costs, adverse event (AE) costs, monitoring costs, and HRR test costs. All costs were estimated in Argentinian pesos (ARS) and then converted to US dollars (US\$) as at October 2022 (1 US\$ = 152.59 ARS) [21].

The drug acquisition costs were obtained from public databases that report the retail price of drugs marketed in Argentina [22]. We used the most recent retail price to perform the analysis, and converted the retail prices to wholesale prices by applying the conversion factor (laboratory output price) suggested by the Argentinian Ministry of Economy [23]. For each drug, the total drug acquisition cost was estimated from the wholesale price, the dosage of the therapy administered, and the mean duration of treatment. For the estimation of treatment durations, 7.5 months was used for olaparib [9], 3.6 months was used for enzalutamide and abiraterone [9], 7 months was used for docetaxel [20], and 5.5 months was used for cabazitaxel [19]. It should be noted that the treatment durations for enzalutamide and abiraterone from the PROfound study were taken into account in order to homogenize the populations.

For all drugs, we assumed there was no wastage. We assumed that the drug acquisition costs were the same for the three perspectives of the analysis. For drugs administered according to weight, a mean patient weight of 80 kg was used [24]. The dosage, wholesale price per pack, and annual treatment costs per patient for olaparib and comparators are presented in Table 1.

The cost of each intravenous drug administration was obtained from the Institute for Clinical Effectiveness and Health Policy (IECS) unit cost database and is estimated for the third-party public payer, third-party social security payer, and third-party private payer at \$72.54, \$115.59, and \$131.56, respectively [25]. This cost included the use of the oncologic room to administer the drugs. We assumed that oral administration has no cost.

The monitoring costs and costs of AEs were estimated using the microcosting approach. The identification, rate of use, and measurement of health resources used for disease management were estimated by the opinion of a local expert, the unit costs by health sector were obtained from the IECS unit cost database, and the drug acquisitions costs were obtained from public databases and converted to wholesale prices [22, 23, 25]. The health resources included medical consultations (oncologist), laboratory tests (blood count,

testosterone, urea, creatinine, ionogram, hepatogram, and blood glucose) and images (chest computed tomography [CT] scan with contrast, and CT pelvis and abdomen with contrast). The cost of prednisone as an add-on drug to treatment with abiraterone, docetaxel and cabazitaxel was also considered. This cost was \$5.95 per month. The unit cost per health resource and the quantities used in the monitoring costs are available in the ESM Tables S2 and S3.

On the other hand, the AEs included in the model were fatigue, hypertension, anemia, febrile neutropenia, thrombocytopenia, pneumonia, urinary tract infection, sepsis, pulmonary embolism, and vomiting. These AEs were grade 3/4 according to the Common Terminology Criteria for Adverse Events version 4 [26], and were in line with those reported in the clinical trials for each treatment [27–29]. The AEs excluded were dyspnea and asthenia, as their management does not require associated clinical practices. Prevalence rates per AEs are reported in ESM Table S4, and the monitoring costs and AE costs are presented in Table 2.

The cost of the HRR test for the private sector was obtained from a private laboratory in Argentina where the HRR test is currently performed, while the cost of the HRR test for the public and social security sectors were estimated by applying cost ratios between sectors, which were obtained from the IECS unit cost base [25]. We assumed a hypothetical scenario whereby all patients with mCRPC whose disease had progressed during treatment with NHAs are tested with HRR; there is no difference in the access rate by health sector. Finally, estimated HRR testing costs for the public, social security, and private sectors were \$350.52, \$673.27, and \$680.00, respectively.

2.7 Decision Rule—Budgetary Impact Threshold

Our study employed the methodology utilized by the National Commission for Health Technology Assessment and Clinical Excellence of the Ministry of Health (CONETEC, acronym in Spanish), the local Health Technology Assessment, in the country to estimate a threshold

Table 1 Dosage, wholesale price per pack, and annual treatment costs per patient for olaparib and comparators. Source: Public database conversion factor (laboratory output price) suggested by the Argentinian Ministry of Economy [22, 23]

Regimen	Dosage	Type of administration	Pack	Wholesale price per pack	Annual treatment costs per patient
Olaparib	600 mg daily	Oral	150 mg * 56	\$3176.32	\$83,854.80
Abiraterone	1000 mg daily	Oral	500 mg * 60	\$2924.38	\$36,392.28
Enzalutamide	160 mg daily	Oral	40 mg * 120	\$4477.81	\$55,723.80
Cabazitaxel	25 mg/m ² every 3 weeks	Intravenous	60 mg/1.5 mL * 1	\$4583.58	\$63,336.84
Docetaxel	75 mg/m ² every 3 weeks	Intravenous	80 mg/2 mL * 1	\$396.24	\$13,309.44

Costs are reported in 2022 US dollars

of high budgetary impact. This approach is reported in the study by Pichon-Riviere and colleagues, which is particularly relevant for countries lacking their own estimates [30]. The reference value of the high budgetary impact threshold is estimated at 0.00016 health spending units (0.00008–0.00024). The estimation of the threshold of high budget impact in Argentina for 2022 was made using the reference value and updating the estimate of total health expenditure. The latter is estimated using the Gross Domestic Product (GDP) data and total population of Argentina, as well as the average of the last 10 available years of healthcare expenditure as a percentage of GDP [31, 32]. The threshold estimation was carried out for each healthcare sector using the per capita healthcare expenditures estimated and reported in the study by Espinola and colleagues [33]. Accordingly, it was estimated that the PMPM threshold of high budget impact was \$0.0153 for the health system. In addition, the per capita healthcare expenditure values were used to quantify conversion factors and thus estimate the threshold of high budget impact for each healthcare sector. Therefore, the PMPM threshold of high budget impact was estimated at \$0.0110 for the public sector, \$0.0146 for social security, and \$0.0261 for the private sector.

Table 2 Monthly monitoring costs per patient and adverse event costs, by healthcare sector. Source: Estimation using the microcosting approach, with cost sources from the IECS BCU and public databases [22, 23, 25]

	Public sector	Social security	Private sector
Monthly monitoring costs per patient			
Olaparib	\$47.35	\$60.16	\$67.29
Abiraterone	\$22.43	\$27.28	\$29.74
Enzalutamide	\$16.49	\$21.33	\$23.79
Cabazitaxel	\$54.62	\$68.51	\$75.80
Docetaxel	\$54.62	\$68.51	\$75.80
Adverse event costs			
Fatigue	\$52.63	\$70.81	\$84.07
Hypertension	\$400.70	\$667.73	\$1273.42
Anemia	\$981.24	\$1489.04	\$1858.03
Febrile neutropenia	\$3989.81	\$4538.85	\$5426.60
Thrombocytopenia	\$346.71	\$377.54	\$392.06
Pneumonia	\$1983.01	\$2697.09	\$4325.86
Urinary tract infection	\$25.79	\$43.57	\$49.12
Sepsis	\$3626.48	\$4721.55	\$7240.62
Pulmonary embolism	\$1317.51	\$1904.89	\$3256.12
Vomiting	\$307.81	\$538.28	\$982.94

Costs are reported in 2022 US dollars

2.8 Sensitivity Analysis

To evaluate the effect of uncertainty associated with the parameters of the model on the budget impact results, deterministic (one-way) sensitivity analyses (DSAs) for the base case were performed. The parameters varied from their default values by $\pm 10\%$. For the cost of the intervention, a variation of $\pm 25\%$ was considered given the lack of information on its variability.

2.9 Scenario Analysis

An alternative scenario was developed under the assumption that HRR testing is not accessible in the health system in Argentina, and consequently, it is necessary to have previously performed the BRCA test in order to provide olaparib. This scenario is not too distant from the reality in Argentina, given that the HRR is nowadays only available for a few private providers.

We estimated that 11% of the prostate cancer patients who progress to resistance will be BRCA receptor-positive, making them candidates for olaparib [9]. Moreover, 9.10 patients must be tested to identify one patient who tests positive for BRCA [9]. BRCA testing costs for the public sector, social security, and private sector were \$351.24, \$639.52, and \$681.40, respectively. These costs were retrieved from the IECS unit cost database [25].

2.10 Model Validation

The model structure and calculations were reviewed and validated by academic experts from the IECS, and all input parameters were initially reviewed and validated by a local oncologist expert. Suggestions for revision and/or adaptation were addressed prior to conducting the analysis.

3 Results

3.1 Target Population

For a cohort of 1,000,000 men, the target population comprised 26 individuals each year. The target population estimate is available in ESM Table S5.

3.2 Budget Impact Analysis

Table 3 shows the budget impact detailed by health sector, year, and cost component. The net impact is positive for every year and for the health sector, and shows a growing trend. Drug acquisition and testing are the most relevant cost drivers. The estimation shows savings related to the

cost of management of adverse effects and administration of the treatment.

For the third-party public payer, the budget impact is \$56,767 in year 1 and \$112,588 in year 5; for the third-party social security payer, the incremental cost is \$205,550 in year 1 and increases up to \$417,065 in year 5; and for the third-party private payer, the budget impact is \$271,476 in year 1 and \$544,314 in year 5. For all perspectives of the analyses, drug costs were the most relevant cost drivers. The acquisition cost of the drugs in the budget impact represents approximately 97% for the third-party public payer and 92% for the remaining two perspectives of analyses.

In Fig. 2, we report the current and projected PMPM budget impact associated with the inclusion of olaparib for each healthcare sector and the total national health system. On average, the introduction of olaparib increased the cost by \$0.007 PMPM, \$0.025 PMPM, and \$0.033 PMPM for the third-party public, social security, and private payer sectors, respectively. The budgetary impact in the public sector is noted to stay below the threshold for high budgetary impact, while in the social security and private sectors, it moderately exceeds this threshold. To obtain the budgetary impact PMPM of the total health system, we performed a weighted average of the results of the three health sectors and their coverage rates (38%, 46%, and 16% for the public, social security, and private sectors, respectively). The results of the PMPM budgetary impact for the health system were approximately \$0.0191 PMPM, being slightly higher than the estimated budgetary high impact threshold of 0.0153.

If we extrapolate the results to the total population in Argentina, comprising around 16 million adult males, the expected number of patients would be around 416 and would represent a weighted average total cost to the health system of approximately \$5,959,200.

3.3 Sensitivity Analysis

The one-way sensitivity analysis results for the third-party social security payer are depicted in Fig. 3. The acquisition cost of olaparib is the parameter that has the most impact on the budget, followed by the mean duration of treatment. When the acquisition cost of olaparib was increased by 25%, the net budget impact was increased to 39.91%, and when the duration of the treatment with olaparib was increased by 10%, the net budget impact was increased to 14.65%. When mean body surface area (square meters) was reduced by 10%, the net budget impact was increased to 5.42%, and when the market rate of olaparib in the first-year increased by 25%, the net budgetary impact increased to 4.57%. The remaining parameters have a lower impact (<3%) on the net budget impact. These results are also similar across the other perspectives. ESM Fig. 1 and Fig. 2 are available with the

results of the sensitivity analysis for the public and private sectors.

3.4 Alternative Scenario

3.4.1 Target Population

For a cohort of 1,000,000 males, the target population comprised 16 individuals each year. For the alternative scenario, we assumed that all epidemiological parameters were fixed during the timeframe of the analysis, and thus the size of the target population remains unchanged.

3.4.2 Budget Impact Analysis

In Fig. 4, the results of the alternative scenario are presented, only testing the target population with BRCA. The net budgetary impact is lower compared with the base case due to the lower number of patients who are candidates for olaparib after the test.

4 Discussion

This study estimated the budget impact of the coverage of olaparib for the treatment of mCRPC in Argentina. Considering a hypothetical cohort of 1,000,000 individuals who were covered and an estimated wholesale price for olaparib of \$3176 per 150 mg box of 56 pills, the introduction of olaparib resulted in incremental costs. Our findings show that the sum of the net budget impact for the 5 years was \$412,391, \$1,515,073 and \$1,986,039 for the third-party public, social security, and private payer sectors, respectively. The drug cost accounted for 97% of the budget impact for the public sector and 92% for the social and private sectors. The estimation shows savings related to the cost of management of adverse effects and administration of the treatment. The results of the weighted average budgetary impact for the health system was approximately \$1,152,683, being slightly higher than the estimated budgeted high impact threshold.

Our findings reflect that the incremental cost estimated for the third-party public payer perspective falls below the high budgetary impact threshold, whereas for the third-party social security and private payer sectors, the estimated results surpass the threshold. One reason that explains these findings is because the public sector has the lowest market share for olaparib, meaning that the target population is smaller. In Argentina, depending on the sector, the population has access to the most advanced technologies, while others must wait hours for basic technologies (such as an appointment with the medical doctor) [34]. Our modeling strategy tries to capture those nuances,

Table 3 Absolute budget impact for the current (without olaparib) and projected scenario (with olaparib) for a third-party payer

Cost component	Current scenario (A)					Projected scenario (B)					Budget impact (C)				
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5
Third-party public payer															
Drug acquisition	\$511,474	\$511,474	\$511,474	\$511,474	\$511,474	\$566,489	\$576,945	\$589,197	\$603,558	\$620,401	\$55,014	\$65,471	\$77,722	\$ 92,084	\$108,926
Drug administration	\$9633	\$9633	\$9633	\$9633	\$9633	\$8902	\$8787	\$8652	\$8492	\$8305	– \$731	– \$846	– \$981	– \$1140	– \$1328
Monitoring	\$5662	\$5662	\$5662	\$5662	\$5662	\$5906	\$5951	\$6002	\$6062	\$6131	\$244	\$288	\$340	\$399	\$469
Adverse events	\$29,044	\$29,044	\$29,044	\$29,044	\$29,044	\$27,515	\$27,332	\$27,116	\$26,863	\$26,565	– \$1529	– \$1712	– \$1928	– \$2181	– \$2479
HRR test	–	–	–	–	–	\$3768	\$4397	\$5131	\$5991	\$6999	\$3768	\$4397	\$5131	\$5991	\$6999
Total cost	\$555,813	\$555,813	\$555,813	\$555,813	\$555,813	\$612,580	\$623,411	\$636,098	\$650,967	\$668,401	\$56,767	\$67,597	\$80,285	\$95,154	\$112,588
Third-party social security payer															
Cost component	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5
Drug acquisition	\$511,474	\$511,474	\$511,474	\$511,474	\$511,474	\$700,824	\$738,645	\$782,936	\$834,825	\$895,644	\$189,349	\$227,171	\$271,462	\$323,351	\$ 384,170
Drug administration	\$15,350	\$15,350	\$15,350	\$15,350	\$15,350	\$11,113	\$10,502	\$9780	\$8927	\$7918	– \$4237	– \$4848	– \$5569	– \$6423	– \$ 7,432
Monitoring	\$7094	\$7094	\$7094	\$7,094	\$7094	\$8160	\$8371	\$8615	\$8899	\$9228	\$1065	\$1276	\$1521	\$1804	\$ 2,134
Adverse events	\$34,118	\$34,118	\$34,118	\$34,118	\$34,118	\$28,156	\$27,605	\$26,951	\$26,178	\$25,260	– \$5962	– \$6513	– \$7167	– \$7941	– \$ 8,858
HRR test	–	–	–	–	–	\$25,335	\$29,557	\$34,497	\$40,279	\$47,051	\$25,335	\$29,557	\$34,497	\$40,279	\$ 47,051
Total cost	\$568,037	\$568,037	\$568,037	\$568,037	\$568,037	\$773,587	\$814,679	\$862,780	\$919,109	\$985,101	\$205,550	\$246,643	\$294,743	\$351,072	\$ 417,065
Third-party private payer															
Cost component	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5	Year 1	Year 2	Year 3	Year 4	Year 5
Drug acquisition	\$511,474	\$511,474	\$511,474	\$511,474	\$511,474	\$762,442	\$811,307	\$868,527	\$935,559	\$1,014,119	\$250,967	\$299,833	\$357,053	\$424,084	\$502,645
Drug administration	\$17,470	\$17,470	\$17,470	\$17,470	\$17,470	\$11,433	\$10,549	\$9504	\$8267	\$6804	– \$6037	– \$6921	– \$7966	– \$9203	– \$10,666
Monitoring	\$7843	\$7843	\$7843	\$7,843	\$7843	\$9462	\$9773	\$10,134	\$10,553	\$11,038	\$1620	\$1931	\$2292	\$2710	\$3195
Adverse events	\$41,961	\$41,961	\$41,961	\$41,961	\$41,961	\$33,988	\$33,232	\$32,334	\$31,268	\$30,001	– \$7973	– \$8729	– \$9627	– \$10,693	– \$11,959
HRR test	–	–	–	–	–	\$32,899	\$38,382	\$44,797	\$52,306	\$61,099	\$32,899	\$38,382	\$44,797	\$52,306	\$61,099
Total cost	\$578,747	\$578,747	\$578,747	\$578,747	\$578,747	\$850,224	\$903,243	\$965,296	\$1,037,952	\$1,123,061	\$271,476	\$324,496	\$386,549	\$459,205	\$544,314

Costs are expressed in 2022 US dollars

HRR homologous recombination repair

Fig. 2 Budget impact per member per month associated with the inclusion of olaparib for each health security system. Costs are expressed in 2022 US dollars

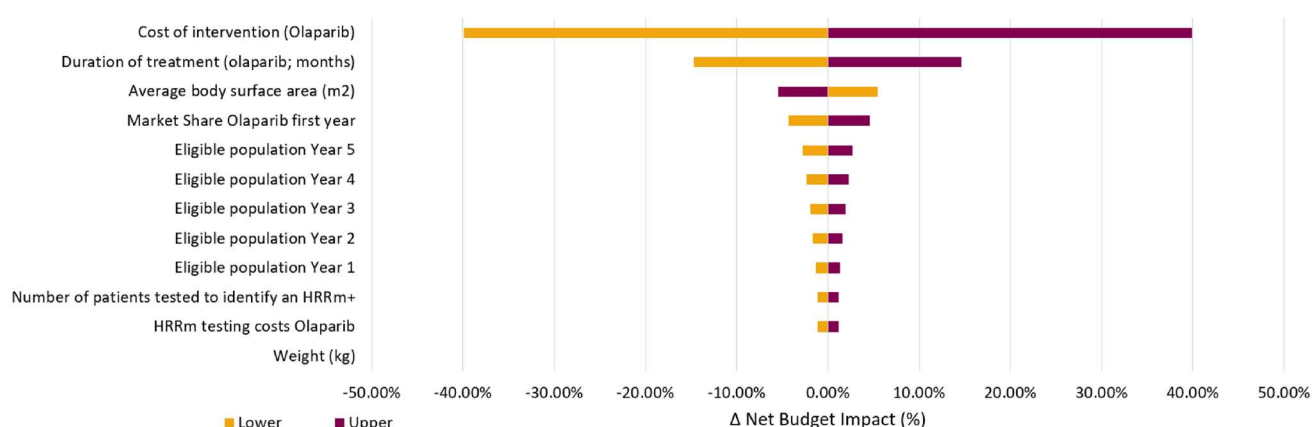
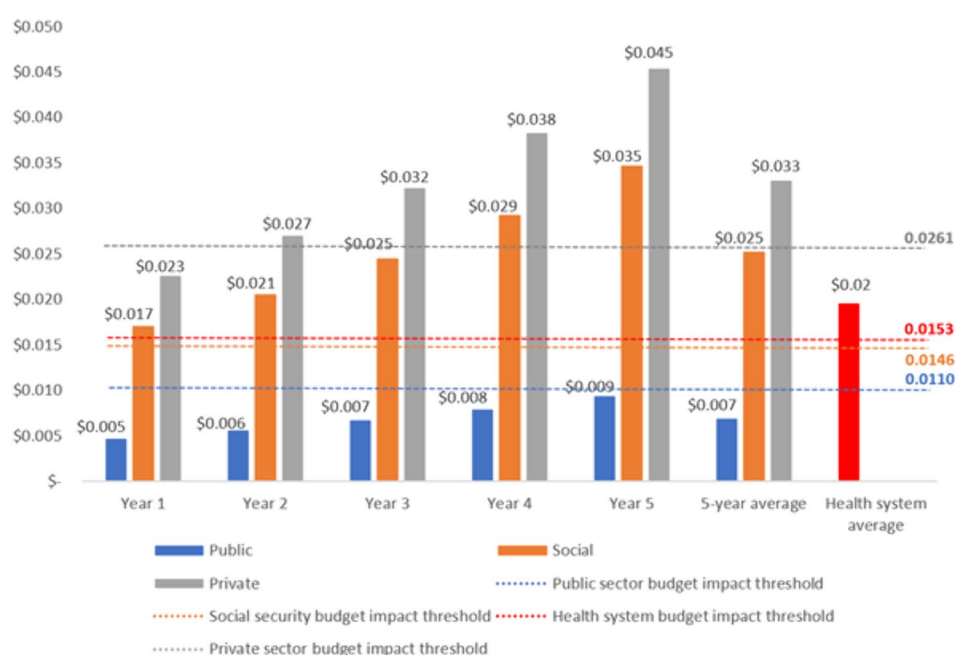


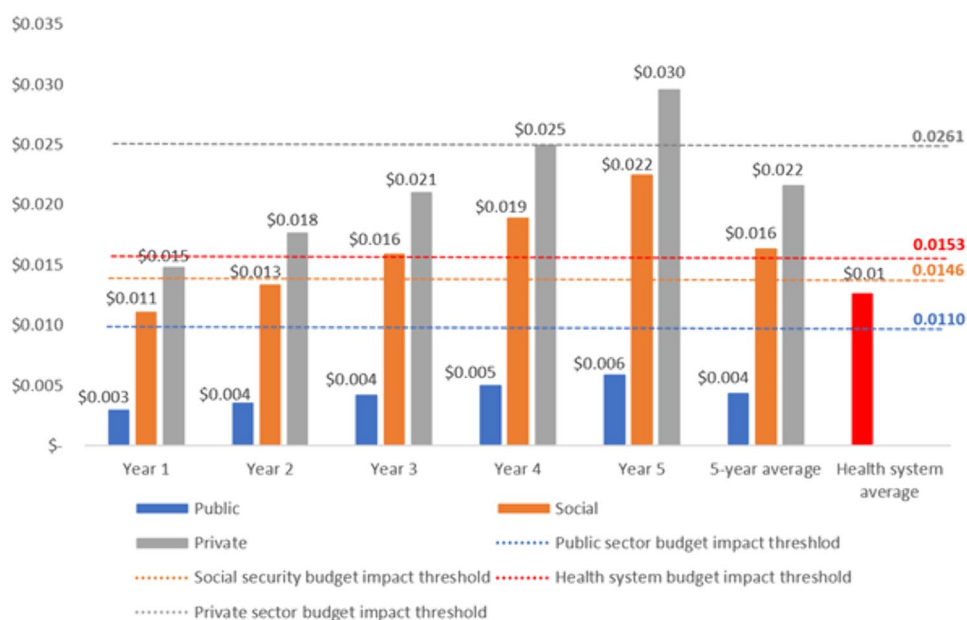
Fig. 3 Tornado diagram for the one-way sensitivity analysis on the net budget impact. Results are for the third-party social security payer. *HRRm* homologous recombination repair mutation

and together with the DSA results, our findings allow decision makers to support coverage or reimbursement policy decisions depending on the sector. For instance, the price has a relevant impact on the budget, which may reflect on rebates or discounts discriminated according to the health sector. On the other hand, it is important to highlight that an incremental cost result surpassing the predetermined threshold serves as a signal to the health system regarding its financing approach. Decision makers should thoroughly evaluate various coverage alternatives. In certain instances, these outcomes have led to the implementation of discount or phased introduction policies.

No budget impact evidence was found in other low- and middle-income countries to compare our results.

Economic evidence of olaparib for the management of mCRPC is mostly in the form of economic evaluation in the high-income settings. For instance, from the US payer perspective, Li and colleagues found that olaparib is not cost effective in comparison with control treatment in mCRPC patients [35]. On the other hand, Su et al. estimated the cost effectiveness of olaparib in mCRPC with multiple alterations in genes involved in DNA repair, using the US payer perspective [15]. Two scenarios were analyzed—one in which patients had to have at least one genetic alteration in *BRCA1*, *BRCA2* and the *ATM* gene (scenario A), and one in which the remaining patients could have alterations in any of the 15 prespecified genes (scenario B). In scenario A, the estimated incremental cost-effectiveness ratio (ICER) was

Fig. 4 Budget impact per member per month associated with the alternative scenario of the inclusion of olaparib for each health security system. Costs are expressed in 2022 US dollars



\$116,903 per quality-adjusted life-year (QALY) gained. In scenario B, olaparib yielded an additional 0.068 QALYS and saved \$1980 compared with standard care, making it a cost-saving option. From the US payer perspective, a similar cost-saving result was estimated by Xu and colleagues [16], yet they found no cost-effective results when they ran the analyses for China. Lastly, for the UK, the National Institute for Health and Care Excellence (NICE) found that the most likely cost-effectiveness estimates are within what NICE considers an acceptable use of National Health System resources [36].

The current study has some limitations to note. First, due to the absence of local epidemiological evidence, data from other countries and contexts were utilized. While we had a local oncology expert who reviewed, adapted, and validated the epidemiological evidence for the Argentine context, it is important to highlight that relying on a single expert is also a limitation. Second, our findings rely on market share projections for olaparib, which introduces an element of uncertainty. We tested this uncertainty in the DSA, but based on the analyses, the parameters seem not to drive big changes in the final outcomes of the BIM. On the other hand, we relied on indirect estimates to calculate the HRR test cost for the third-party social security and public payer perspectives. In addition, given that the HRR test is only available in Argentina through some private providers, and we did not have available information regarding future rates of test accessibility, we assumed a hypothetical scenario where there were no differences in the rate of access based on healthcare.

In addition, the study proposed a high budgetary impact threshold to guide decision makers, although we highlight that it is only a reference value that must be taken with caution. The estimates are based on preliminary empirical

estimates performed by Pichon-Riviere and colleagues [30]. In order to have more precise estimates, further research is required to estimate the threshold based on the economic productivity for each health system perspective. Furthermore, given the current macroeconomic conditions in Argentina, it is important to approach the presented results with caution and give particular attention to the fluctuation of drug prices and the clinical management of the condition.

In addition, an interesting point for discussion, based on the results, revolves around the criteria of efficiency and affordability surrounding the definitions of thresholds in economic evaluation studies to guide decision making. The cost-effectiveness threshold represents the healthcare system's marginal opportunity cost to finance one QALY. Therefore, it also reflects the affordability of that healthcare technology. However, in the case of costly innovative interventions with a significant budget impact, it is likely that the opportunity cost to cover the technology exceeds the previously defined cost-effectiveness threshold, assuming fixed budgets. Thus, a high budget impact becomes a reason to reduce the price, either directly or indirectly (e.g., by lowering the cost-effectiveness threshold).

On the other hand, if the budget impact analysis (BIA) remains separate from the cost-effectiveness analysis, the BIA informs decision makers about the size of financial adjustments needed to adopt the new technology. These adjustments could include a reduction in the price of the new technology, but could also involve disinvestments in other technologies and raising additional funds. In the context of public healthcare systems, this would imply an increase in government funding. In the social security or private sectors, this would mean higher premiums or patient co-payments.

Therefore, keeping the budget impact separate provides not only more options but also more responsibility to the decision maker.

5 Conclusion

The incorporation of olaparib, a therapy now recommended by evidence-based guidelines, for the treatment of mCRPC was associated with increased costs for all three health systems in Argentina. These findings are informative to support policy decisions aimed at expanding current prostate cancer treatment.

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Declarations

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Conflict of Interest Natalia Espinola, Constanza Silvestrini, Carla Colaci, Daniela Sugg, Carlos Rojas-Roque, Jessica Coelli, and Federico Augustovski have no conflicts of interest to declare that are relevant to the contents of this article.

Availability Of Data And Material All data involved in this study are included in the main manuscript and its supplementary information files.

Code Availability The model used during the current study is available from the corresponding author upon reasonable request.

Ethical approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Authors' Contributions Concept and design: NE. Formal analysis: CS, CC, DS. Review, interpretation and discussion of the results: NE, CS, CC, DS, JC. Writing – original draft: CS, CC. Writing – reviewing and editing, NE, FA, CRR, DS, JC. Approval of the final version of the manuscript, NE, CS, CC, DS, CRR, JC, FA.

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References

1. World Health Organization. International Agency for Research on Cancer. Globocan Argentina 2020. 2021. <https://gco.iarc.fr/today/data/factsheets/populations/32-argentina-fact-sheets.pdf>. Accessed 8 July 2024.
2. Datri L, Korbenfeld E, Naveira M, Novas C, Quero LB, Vera K, Romero M, Corsico S, Mendez L, Faura V, Silva C. Clinical characteristics of patients with castration-resistant prostate cancer and alterations in homologous recombination repair genes. *RevOnco*. 2019;24(2).
3. Parker C, Castro E, Fizazi K, Heidenreich A, Ost P, Procopio G, Tombal B, Gillessen S, ESMO Guidelines Committee. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2020;31(9):1119–34. <https://doi.org/10.1016/j.annonc.2020.06.011>.
4. Pritchard CC, Mateo J, Walsh MF, De Sarkar N, Abida W, Beltran H, Garofalo A, Gulati R, Carreira S, Eeles R, Elemento O, Rubin MA, Robinson D, Lonigro R, Hussain M, Chinnaiyan A, Vinson J, Filipenko J, Garraway L, Taplin ME, AlDubayan S, Han GC, Beightol M, Morrissey C, Nghiem B, Cheng HH, Montgomery B, Walsh T, Casadei S, Berger M, Zhang L, Zehir A, Vijai J, Scher HI, Sawyers C, Schultz N, Kantoff PW, Solit D, Robson M, Van Allen EM, Offit K, de Bono J, Nelson PS. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. *N Engl J Med*. 2016;375(5):443–53. <https://doi.org/10.1056/NEJMoa1603144>.
5. Shah S, Rachmat R, Enyima S, Ghose A, Revythis A, Boussios S. BRCA mutations in prostate cancer: assessment, implications and treatment considerations. *Int J Mol Sci*. 2021. <https://doi.org/10.3390/ijms222312628>.
6. American Cancer Society. Prostate Cancer: Types of Treatment. Cancer.net (ASCO). 2022 [cited 2023 Mar 14]. <https://www.cancer.net/cancer-types/prostate-cancer/types-treatment>. Accessed 8 July 2024.
7. Mansinho A, Macedo D, Fernandes I, Costa L. Castration-resistant prostate cancer: mechanisms, targets and treatment. *Adv Exp Med Biol*. 2018;1096:117–33. https://doi.org/10.1007/978-3-319-99286-0_7.
8. Risdon EN, Chau CH, Price DK, Sartor O, Figg WD. PARP inhibitors and prostate cancer: to infinity and beyond BRCA. *Oncologist*. 2021;26(1):e115–29. <https://doi.org/10.1634/theoncologist.2020-0697>.
9. de Bono J, Mateo J, Fizazi K, Saad F, Shore N, Sandhu S, Chi KN, Sartor O, Agarwal N, Olmos D, Thiery-Vuillemin A, Twardowski P, Mehra N, Goessl C, Kang J, Burgents J, Wu W, Kohlmann A, Adelman CA, Hussain M. Olaparib for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;382(22):2091–102. <https://doi.org/10.1056/NEJMoa1911440>.
10. Hussain M, Mateo J, Fizazi K, Saad F, Shore N, Sandhu S, Chi KN, Sartor O, Agarwal N, Olmos D, Thiery-Vuillemin A, Twardowski P, Roubaud G, Özgüroğlu M, Kang J, Burgents J, Gresty C, Corcoran C, Adelman CA, de Bono J. Survival with olaparib in metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;383(24):2345–57. <https://doi.org/10.1056/NEJMoa2022485>.
11. LYNPARZA® (olaparib). Highlights of prescribing information. US FDA; 2014 [cited 2023 May 23]. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208558s0141bl.pdf. Accessed 8 July 2024.
12. FDA approves olaparib for HRR gene-mutated metastatic castration-resistant prostate cancer. US FDA; 2020 [cited 2023 May 23]. <https://www.fda.gov/drugs/resources-information-appro>

- ved-drugs/fda-approves-olaparib-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer. Accessed 8 July 2024.
13. Lynparza. European Medicines Agency (EMA); 26 Dec 2014 [cited 2023 May 23]. <https://www.ema.europa.eu/en/medicines/human/EPAR/lynpa/lynpa.htm#authorisation-details-section>. Accessed 8 July 2024.
 14. Olaparib. Disposal/Reference: EX-2020-75421293-APN-DGA#ANMAT. ANMAT; 2021 Mar.
 15. Su D, Wu B, Shi L. Cost-effectiveness of genomic test-directed olaparib for metastatic castration-resistant prostate cancer. *Front Pharmacol*. 2020;11:610601. <https://doi.org/10.3389/fphar.2020.610601>.
 16. Xu C, Cai J, Zhuang J, Zheng B, Chen L, Sun H, Zheng G, Wei X, Liu M. Cost-effectiveness of olaparib, a PARP inhibitor, for patients with metastatic castration-resistant prostate cancer in China and United States. *Ann Transl Med*. 2022;10(15):830. <https://doi.org/10.21037/atm-22-3637>.
 17. Bonanno D, Codebó O, Di Lollo MP, Dinerstein N, Dorigo A, Gazia MV, Poyard E, Vega A, Iummato LE, Almeida V. [Health situation analysis in Argentina]. Buenos Aires: Ministry of Health; 2018. https://bancos.salud.gob.ar/sites/default/files/2019-12/0000001392cnt-analisis_de_situacion_de_salud_-_republica_argentina_-_asis_2018_compressed.pdf. Accessed 8 July 2024.
 18. Sullivan SD, Mauskopf JA, Augustovski F, Jaime Caro J, Lee KM, Minchin M, Orlewska E, Penna P, Rodriguez Barrios JM, Shau WY. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. *Value Health*. 2014;17(1):5–14. <https://doi.org/10.1016/j.jval.2013.08.2291>.
 19. de Wit R, de Bono J, Sternberg CN, Fizazi K, Tombal B, Wülfing C, Kramer G, Eymard JC, Bamias A, Carles J, Iacovelli R, Melichar B, Sverrisdóttir Á, Theodore C, Feyerabend S, Helissey C, Ozatlgan A, Geffriaud-Ricouard C, Castellano D. Cabazitaxel versus abiraterone or enzalutamide in metastatic prostate cancer. *N Engl J Med*. 2019;381(26):2506–18. <https://doi.org/10.1056/NEJMoa1911206>.
 20. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, Oudard S, Théodore C, James ND, Turesson I, Rosenthal MA, Eisenberger MA. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med*. 2004;351(15):1502–12. <https://doi.org/10.1056/NEJMoa040720>.
 21. Central Bank of Argentina. Exchange rate by date. Central Bank of Argentina [cited 2022 Oct]. https://www.bcra.gob.ar/MedioSPago/Tipos_de_Cambio_SML.asp. Accessed 8 July 2024.
 22. Alfabet. Drug prices. Alfa Beta Group. 2022 [cited 2022]. <http://www.alfabeta.net/precio/>. Accessed 8 July 2024.
 23. Garfinkel F, Méndez Y. Value Chain Reports: Health, Pharmacy and Medical Equipment. Buenos Aires: Office for Economic Policy and Development Planning; 2016 Dec. Report No.: 21.
 24. 4th National Survey Risk Factors Survey. National Directorate for Health Promotion and Control of Chronic Non-Communicable Non-Communicable Diseases. Ministry of Health and Social Development, Argentina [cited 2023 Apr 5]. https://bancos.salud.gob.ar/sites/default/files/2020-01/4ta-encuesta-nacional-factores-riesgo_2019_principales-resultados.pdf. Accessed 8 July 2024.
 25. Palacios A, Balan D, Garay OU. HT3 base de costos unitarios en salud en Argentina: una fuente de información continuamente actualizada para evaluaciones económicas y análisis de impacto presupuestario en un sistema de salud fragmentado. *Value Health Reg Issues*. 2019;19 (Suppl S8). <https://doi.org/10.1016/j.vhri.2019.08.042>.
 26. Common Terminology Criteria for Adverse Events (CTCAE). National Cancer Institute, NIH. 2010 [cited 2023 Apr 5]. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm. Accessed 8 July 2024.
 27. Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, Silverberg JI, Deleuran M, Kataoka Y, Lacour JP, Kingo K, Worm M, Poulin Y, Wollenberg A, Soo Y, Graham NMH, Pirozzi G, Akinlade B, Staudinger H, Mastey V, Eckert L, Gadkari A, Stahl N, Yancopoulos GD, Ardeleanu M, SOLO 1 and SOLO 2 Investigators. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335–48. <https://doi.org/10.1056/NEJMoa161020>.
 28. Simpson EL, Lacour JP, Spelman L, Galimberti R, Eichenfield LF, Bissonnette R, King BA, Thyssen JP, Silverberg JI, Bieber T, Kabashima K, Tsunemi Y, Costanzo A, Guttman-Yassky E, Beck LA, Jones JM, DeLozier AM, Gamalo M, Brinker DR, Cardillo T, Nunes FP, Paller AS, Wollenberg A, Reich K. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: results from two randomized monotherapy phase III trials. *Br J Dermatol*. 2020;183(2):242–55.
 29. Guttman-Yassky E, Teixeira HD, Simpson EL, Papp KA, Pangan AL, Blauvelt A, Thaçi D, Chu CY, Hong HCH, Katoh N, Paller AS, Calimlim B, Gu Y, Hu X, Liu M, Yang Y, Liu J, Tenorio AR, Chu AD, Irvine AD. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. *Lancet*. 2021;397(10290):2151–68.
 30. Pichon-Riviere A, Drummond M, García Martí S, Augustovski F. Application of economic evidence in health technology assessment and decision-making for the allocation of health resources in Latin America: Seven key topics and a preliminary proposal for implementation. Inter-American Development Bank; 2021 Jul. <https://publications.iadb.org/publications/spanish/document/Aplicacion-de-la-evidencia-economica-en-la-evaluacion-de-tecnologias-sanitarias-y-la-toma-de-decisiones-sobre-asignacion-de-recursos-sanitarios-en-America-Latina-siete-temas-clave-y-una-propuesta-preliminar-de-implementation.pdf>. Accessed 8 July 2024.
 31. The World Bank database. The World Bank [cited 2023 Jun]. <https://data.worldbank.org/>.
 32. National Institute of Statistics and Censuses (INDEC). Macroeconomics aggregates. National Accounts. Buenos Aires; 2022 [cited 2022]. <https://www.indec.gob.ar/indec/web/Nivel4-Tema-3-9-47>. Accessed 8 July 2024.
 33. Espinola, N Palacios, A Augustovski, F Pichon-Riviere, A. Estimación del gasto en salud per cápita por tipo de cobertura en Argentina: propuesta y estimaciones iniciales. Instituto de Efectividad Clínica y Sanitaria; 2019.
 34. Huñis AP. A current view of oncology in Argentina. *Ecancer-medicalscience*. 2016;10:622. <https://doi.org/10.3332/ecancer.2016.622>.
 35. Li Y, Lin S, Zhong L, Luo S, Huang X, Huang X, Dong L, Xu X, Weng X. Is olaparib cost effective in metastatic castration-resistant prostate cancer patients with at least one favorable gene mutation in BRCA1, BRCA2 or ATM? *Pharmacogenomics*. 2021;22(13):809–19.
 36. Overview: Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer. Guidance, NICE [cited 2023 Jun 23]. <https://www.nice.org.uk/guidance/ta8>. Accessed 8 July 2024.

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