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Budget impact analysis of bevacizumab biosimilars for cancer treatment in adult patients in Spain

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ABSTRACT

Objective To assess the economic impact of introducing biosimilars of bevacizumab for the management of cancer patients receiving systemic bevacizumab in the National Health System (SNHS) of Spain.

Methods A 3-year budget impact analysis model was adapted to estimate the cost of introducing biosimilars of bevacizumab in the SNHS for the adult population who were candidates to receive treatment with bevacizumab. Values for the estimation of the population were obtained from the literature and were validated by an expert panel. In this analysis only pharmaceutical costs (€, year 2021) obtained from official databases were considered. A sensitivity analysis was performed to examine the robustness of the model.

Results The introduction of bevacizumab biosimilars would generate an annual cost saving of €11 558 268 (−5.1%) for the first year with a penetration share of biosimilars from 30.0%, €29 126 373 (−8.5%) for the second year with a share of 50.0% and €52 361 778 (−13.6%) for the third year with a share of 80.0%. The total pharmaceutical costs of the scenario without biosimilars are €227 033 352 for the first year, €342 663 209 for the second year and €385 013 076 for the third year. In contrast, the pharmaceutical costs of the scenario with bevacizumab biosimilars are €215 475 084, €313 536 836 and €332 651 297 for years 1, 2 and 3, respectively.

Conclusions The introduction of biosimilars in the Spanish Health System would generate saving costs in the pharmacological budget to boost biological drugs from the first year.

INTRODUCTION

Cancer is the second leading cause of death in Europe and one of the diseases with the greatest impact on public health.[1] Advances in the knowledge of tumour biology in recent years have allowed the development of new systemic therapies based on the use of biological agents, whose purpose is to modify or enhance the patient's immune defence against the tumour.[1] Unlike conventional chemotherapeutic agents, biological agents have a more selective antitumor action, such as the ability to interfere with tumour cell angiogenesis, which causes a decrease in tumour growth.[1]

Bevacizumab was the first approved angiogenesis inhibitor and thus expanded the line of biological treatments against cancer.[2] It is a monoclonal antibody that acts as an inhibitor of vascular endothelial growth factor, whose main function is the formation of new blood vessels and promoting the maturation of dendritic cells, which can increase the infiltration of T cells to create a tumour-permissive immune microenvironment.[3 4]

It is estimated that, in Europe, approximately 30% of the pharmaceutical budget is allocated to the acquisition of biological drugs, and it is expected that this percentage will increase in coming years.[5] The expiration of patents for the originator biological drugs has given rise to biosimilar drugs as alternatives, which has allowed health systems to reduce their pharmaceutical expenditures without reducing the available therapeutic options.[6]

The bevacizumab biosimilars Zirabev (Pfizer), MVASI (Amgen) and Aybintio (MSD) have clinical profiles similar to that of the originator bevacizumab in terms of safety and efficacy.[2–4 7] They have also been approved by the European Medicines Agency (EMA) and the Spanish Agency of Medicines and Medical Products (AEMPS) for the treatment of adult patients, either alone or in combination with other chemotherapeutic agents for metastatic colorectal cancer (mCRC); metastatic breast cancer (mBC); metastatic, unresectable or relapsed non-small cell lung cancer (mNSCLC), except for squamous cell histological type; advanced and/or metastatic renal cell carcinoma (mRCC); stage IIIB, IIIC and IV epithelial ovarian, Fallopian tube or peritoneal cancer (mOC); and persistent, recurrent or metastatic cervical cancer (mCC).[2–4 7]

The global economic crisis, which has increased as a result of the pandemic caused by SARS-CoV-2, has highlighted the relevance of incorporating economic criteria into healthcare decision-making to increase the efficiency of health systems.[8 9]

Budget impact analysis (BIA) is a type of economic evaluation that allows the financial implications of the introduction and use of new alternatives for the treatment of a particular disease to be estimated, and its results are an additional tool to consider in the decision-making process.[10]

The objective of the present analysis is to determine the economic impact on the Spanish Health System (SNHS) of including bevacizumab biosimilars in the systemic treatment of patients with cancer.

METHODS

For the BIA, Microsoft Excel was used to develop a model that estimates the financial impact of the use of bevacizumab biosimilars in patients with cancer in Spain by comparing two different scenarios:

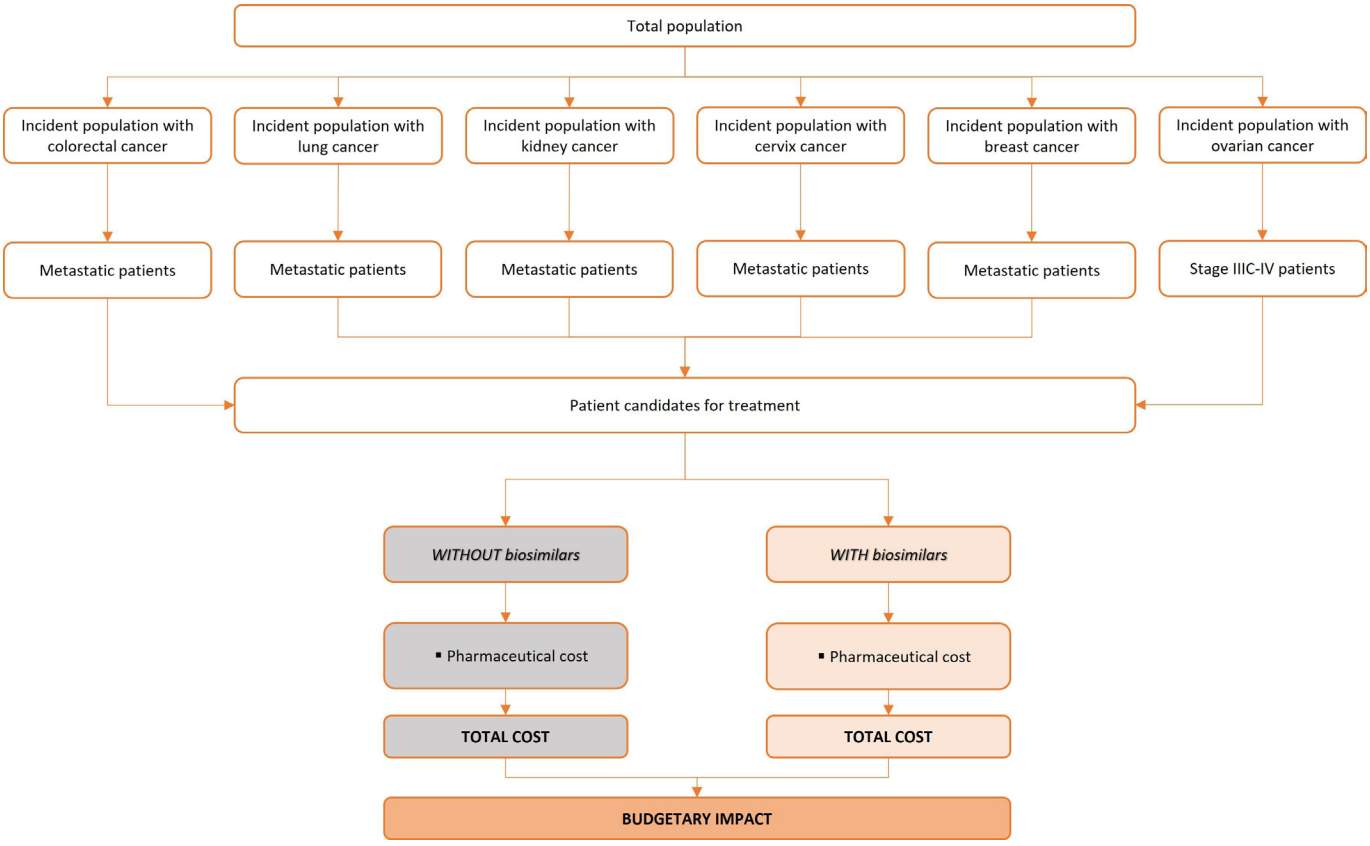

Figure 1 Structure of budget impact analysis (BIA) model.

a scenario without the availability of bevacizumab biosimilars in which only bevacizumab (Avastin, Roche) is available and a scenario with the availability of bevacizumab biosimilars (figure 1).

All the parameters used to feed the model were extracted from the literature and validated by a panel of seven experts (oncologists and hospital pharmacists) based in clinical practice in Spain.

Therapeutic alternatives

The therapeutic alternatives considered in the model were bevacizumab and bevacizumab biosimilars (Zirabev, MVASI and Aybintio).

In line with the indications authorised by and included in the healthcare system's financing scheme, the present analysis included the use of bevacizumab in adult patients for the indications described in table 1.

Both bevacizumab and its biosimilars are administered intravenously according to specified cycle lengths or until disease progression.

Population

The population considered in the analysis included patients with some of the tumours that can be treated with bevacizumab based on the total population at the national level reported by the National Institute of Statistics corresponding to the adult Spanish population on 1 January 2020 (39 006 054 adults), except for cancers that affect only or mainly females (mCC, mBC and mOC), for which a total of 20 099 852 adult women was considered[11] (table 1).

The incidence rates of the different cancer entities were obtained from data published by the Spanish Network of Cancer Registries (REDECAN) for 2020.[12] Of these parameters, data on advanced or metastatic disease, the proportion of patients treated per line and the proportion of patients eligible to receive bevacizumab according to the summary of products characteristics (SmPC) were applied (table 1, figure 1).

Time horizon and discount rate

In accordance with the perspective, only the pharmaceutical costs of the acquisition of bevacizumab were considered in the model. The cost of intravenous administration was not included because it is the same for all drugs.

The time horizon established for the BIA was 3 years, between 2021 and 2023. No discount rate was considered, as recommended in the BIA best practices guidelines of the International Society for Pharmacoeconomics and Outcomes Research.[10]

Resources and costs

The acquisition costs were calculated based on the dosages established in the SmPC (table 1). Because bevacizumab is administered according to patient weight, a standard average weight of 70 kg was established for both men and women.[13]

The analysis was calculated based on the ex-factory prices, which were obtained from the database of the General Council of Official Colleges of Pharmacists,[14] after applying the mandatory deductions.[15] The ex-factory price of original bevacizumab was €316.08 (100 mg) and the ex-factory price of biosimilars was €262.43 (100 mg).

Estimation of the pharmaceutical cost for each cancer considered the duration of treatment for each case, which was obtained from the literature[16 17] and validated by the expert panel. For the treatment durations of mCRC and mCC, an average was calculated based on the durations of each treatment line and

Table 1 Indication, posology and parameters used to obtain the flow of patients according to indication

Neoplasm	mCRC	mBC	mNSCLC	mRCC	mOC	mCC
Indication	In combination with fluoropyrimidine-based chemotherapy	In combination with first-line paclitaxel. In combination with capecitabine as first-line or as an alternative to treatment with taxanes or anthracyclines. Patients who have treatment with bevacizumab in combination with capecitabine in the last 12 months must be excluded	In combination with first-line platinum-based chemotherapy and in combination with first line, except in patients with squamous cells. In combination with erlotinib in patients with activating mutations in epidermal growth factor receptor	In combination with first-line interferon α–2a	In combination with first-line carboplatin and paclitaxel in patients with advanced cancer (stages IIIB, IIIC and IV). In combination with carboplatin and gemcitabine (during 6–10 cycles) or in combination with carboplatin and paclitaxel (during 6–8 cycles) in patients sensitive to platinum after first relapse who have not received a previous treatment of bevacizumab or VEGF inhibitors. In combination with paclitaxel, topotecan or liposomal pegylated doxorubicin in patients resistant to platinum after relapse and who have not received more than two previous treatments of bevacizumab or VEGF inhibitors	In combination with paclitaxel and cisplatin or paclitaxel and topotecan in patients who cannot tolerate platinum therapy
Posology (mg/kg)	5 mg/kg every 2 weeks (with Folfox and Folfiri)* 7.5 mg/kg every 3 weeks (with CAPOX or capecitabine)*	10 mg/kg every 2 weeks	15 mg/kg every 3 weeks	10 mg/kg every 2 weeks	7.5 mg/kg every 3 weeks† 15 mg/kg every 3 weeks†	15 mg/kg every 3 weeks
Treatment duration (months)	9‡	6[23]	6[16]	8.5[17]	8§	4.7‡[19 20]
Base population[11]	39 006 054	20 099 852	39 006 054	39 006 054	20 099 852	20 099 852
Crude incidence rate (100 000 person-year)[12]	113.40	163.95	75.98	18.72	18.13	9.81
Histology with indication	NA	Triple negative (15.0%)¶[24]	Non-microcytic (85.0%)[25] Adenocarcinoma (63.8%)[26]	Renal cell carcinoma (85.0%)[27]	Epithelial ovarian (90.0%)[28]	NA
% metastatic	50.0%[29]	30.0%[23]	70.0%[30]	55.0%[31]	Stage IIIC–IV (55.0%)§	30.0%[32]
% first-line systemic treatment	NA	94.0%§	80.0%[30]	90.0%§	90.0%§	90.0%§
% second-line systemic treatment	NA	NA	NA	NA	70.0%§	70.0%§
% third-line systemic treatment	NA	NA	NA	NA	50.0%§	NA
% treatment patients with bevacizumab	25.6%[18]	30.0%§	5.0%§	1.0%§	60.0%§	20.0%§
Total no of patients who received bevacizumab	5653	308	450	31	1997	181

*The Advisory Board determined that 20.0% of patients received 5 mg/kg Folfox and Folfiri and 80.0% received CAPOX or capecitabine.
†The Advisory Board determined that 20.0% of patients received a dose of 15 mg/kg every 3 weeks and 80.0% received a dose of 7.5 kg/mg every 3 weeks.
‡The duration was calculated based on posology and the mean durations of all lines.
§Advisory Board value.
¶Only the triple negatives have been considered for this analysis.
mBC, metastatic breast cancer; mCC, metastatic cervical cancer; mCRC, metastatic colorectal cancer; mNSCLC, metastatic, unresecable or relapsed non-small cell lung cancer; mOC, metastatic epithelial ovarian, fallopian tube or peritoneal cancer.; mRCC, metastatic renal cell carcinoma; NA, not available; VEGF, vascular endothelial growth factor.

the proportion of patients who were treated in each line[18–20] (table 1).

All costs are expressed in euros for the year 2021 (€, 2021).

Estimation of bevacizumab biosimilar use

The incorporation of bevacizumab biosimilars into the SNHS will change the proportions of use of bevacizumab and its biosimilars over the years. Based on the experts' experience, the estimated biosimilar penetration proportions were 30.0% in the first year, 50.0% in the second year and 80.0% in the third year.

No difference in use was established among the bevacizumab biosimilars, assuming that their ex-factory prices are equal and would not affect the results of the BIA.

Sensitivity analysis

To check the robustness of the model, a sensitivity analysis (SA) was performed by analysing different scenarios in which the values of the following parameters were changed: the estimated use of bevacizumab biosimilars in the different analysis years (SA1, SA2 and SA3) and the ex-factory price of both bevacizumab and bevacizumab biosimilars. For the latter analysis, scenarios were proposed in which price reductions of 20.0% (SA4), 30.0% (SA5) and 40.0% (SA6) were applied to all alternatives and both scenarios.

In addition, the price of original bevacizumab was compared with the price of bevacizumab biosimilars in the scenario with biosimilars (SA7).

Lastly, an analysis was performed in which the difference in ex-factory prices between original bevacizumab and bevacizumab biosimilars was changed (SA8).

RESULTS

After applying epidemiological data, it was estimated that the total number of current patients who are candidates for treatment with bevacizumab would be 7004, 10 622 and 11 973 over the 3-year study period. The indication with the greatest number of candidates receiving bevacizumab was mCRC (5653 patients), and the one with the fewest recipients was mRCC (31 patients) (table 1).

The introduction of bevacizumab biosimilars at the estimated shares would equate to the treatment of 2100 patients with biosimilar bevacizumab in the first year, 5311 in the second year and 9579 in the third year, as shown in table 2.

Figure 2 shows the pharmaceutical acquisition drug cost per patient per year for each of the cancers treated with bevacizumab. The cost of mNSCLC without biosimilars is €57 687 compared with €47 948 with biosimilars. In contrast, mCRC has a pharmaceutical cost per patient of €29 207 per year without biosimilars compared with €24 245 with biosimilars. These neoplasms generated cost differences of €9740 for mNSCLC and €4963 for mCRC.

The total pharmaceutical costs without biosimilars are €227 033 352 for the first year, €342 663 209 for the second year and €385 013 076 for the third year. In contrast, the acquisition drug costs of the scenario with bevacizumab biosimilars are €215 475 084, €313 536 836 and €332 651 297 for years 1, 2 and 3, respectively. This results in a decrease in the budgetary impact of 5.1% in the first year, 8.5% in the second year and up to 13.6% in the third year after the introduction of biosimilars (table 2).

Sensitivity analysis

The SA confirmed the results obtained in the base case (table 3). The savings generated by biosimilars ranged from €15 411 024 for the first year assuming 40% use of biosimilars, to €21 190 158 assuming 55% use of biosimilars. In the third year, at which point it is assumed that the use of biosimilars in the hospital environment will have stabilised at its maximum, savings could range between €55 634 389 at a share of 85.0% and €63 376 617 at a share of 97.0%.

In the analysis that raised the possibility of ex-factory price matching between original bevacizumab and its biosimilars, the cumulative savings for the Spanish SNHS in the 3 years of analysis would be up to €162 014 225 (17.0%) compared with the current situation with bevacizumab.

Taking into account the existence of trade agreements involving variations in the prices for both alternatives, an analysis was performed in which the difference between both ex-factory prices was varied (figure 3). The cumulative savings percentage over 3 years would increase as the price difference between the ex-factory prices increased as a result of greater reductions in the price of bevacizumab biosimilars.

DISCUSSION

The present analysis was conducted to estimate the financial impact of the introduction of bevacizumab biosimilars in the Spanish healthcare setting for the treatment of oncological patients who are candidates for treatment with bevacizumab, showing the pharmacological savings resulting from their use.

The cancers associated with the highest use of bevacizumab were mCRC (5653 treated patients) and mOC (1997 treated patients), due in large part to the number of treatment lines for which bevacizumab is indicated. This contrasts with other cancers, such as mRCC, for which almost no patients in Spain are indicated for bevacizumab treatment.

One of the limitations of the analysis was the absence of certain data in the literature that are necessary for estimating populations who are candidates for treatment with bevacizumab. It was therefore necessary to make certain assumptions; however, these assumptions were validated by the participating experts.

Table 2 Results of cost by indication, number of patients and budget impact

		mCRC		mBC		mNSCLC		mRCC		mOC		mCC		Total	
		No of patients	Cost	No of patients	Cost	No of patients	Cost	No of patients	Cost	No of patients	Cost	No of patients	Cost	No of patients	Cost
Year 1															
	Without biosimilars	Original	4607	€134 552 572	314	€9 046 010	338	€19 482 624	25	€1 430 348	1592	€55 141 009	128	€7 380 788	7004	€227 033 352
	With biosimilars	Original	3225	€127 702 501	220	€8 585 477	236	€18 490 764	17	€1 357 529	1114	€52 333 781	90	€7 005 032	4902	€215 475 084
		Biosimilar	1382		94		101		7		478		38		2100	
	Incremental cost			**–€6 850 071**		**–€339 719**		**–€991 860**		**–€72 819**		**–€2 807 229**		**–€375 756**		**–€11 558 268**
	Budget impact															**–5.1%**
Year 2	Without biosimilars	Original	7094	€207 192 952	444	€12 815 181	478	€27 600 384	38	€2 178 292	2396	€82 971 757	172	€9 904 642	10 622	€342 663 209
	With biosimilars	Original	3547	€189 581 552	222	€11 725 890	239	€25 254 352	19	€1 993 137	1198	€75 919 158	86	€9 062 748	5311	€313 536 836
		Biosimilar	3547		222		239		19		1198		86		5311	
	Incremental cost			**–€17 611 401**		**–€1 089 290**		**–€2 346 033**		**–€185 155**		**–€7 052 599**		**–€841 895**		**–€29 126 373**
	Budget impact															**–8.5%**
Year3	Without biosimilars	Original	8081	€236 020 306	477	€13 757 473	513	€29 629 824	43	€2 459 408	2680	€92 811 413	179	€10 334 651	11 973	€385 013 076
	With biosimilars	Original	1616	€203 921 545	95	€11 886 457	103	€25 600 168	9	€2 124 929	536	€80 189 061	36	€8 929 138	2395	€332 651 297
		Biosimilar	6465		382		411		34		2144		143		9579	
	Incremental cost			**–€32 098 762**		**–€1 871 016**		**–€4 029 656**		**–€334 480**		**–€12 622 352**		**–€1 405 513**		**–€52 361 778**
	Budget impact															**–13.6%**

mBC, metastatic breast cancer; mCC, metastatic cervical cancer; mCRC, metastatic colorectal cancer; mNSCLC, metastatic, unresecable or relapsed non-small cell lung cancer; mOC, metastatic epithelial ovarian, fallopian tube or peritoneal cancer; mRCC, metastatic renal cell carcinoma.

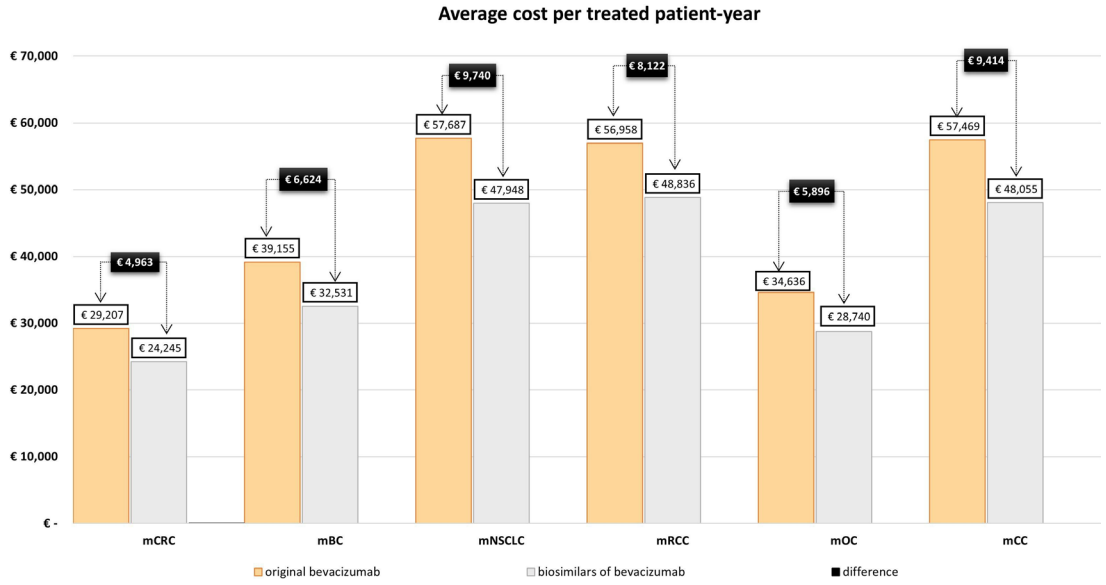

Figure 2 Average cost for patients treated with original bevacizumab versus biosimilar for different indications. mCRC, metastatic colorectal cancer; mCC, metastatic cervical cancer; mBC, metastatic breast cancer; mNSCLC, metastatic, unresecable or relapsed non-small cell lung cancer; mRCC, metastatic renal cell carcinoma; mOC, metastatic epithelial ovarian, fallopian tube or peritoneal cancer.

Regarding pharmaceutical costs per patient, a decrease in the costs of all cancers treated with bevacizumab was observed after the introduction of biosimilars. This finding results from two factors. On the one hand, for indications that required higher doses there was a greater impact due to the lower price of biosimilars compared with bevacizumab; this phenomenon was observed for indications such as mNSCLC and mRCC. On the other hand, indications for which a greater number of patients are candidates for treatment with either bevacizumab or its biosimilars, such as mOC and mCRC, showed high cost differences.

It is therefore clear that the use of biosimilars can generate certain savings in the treatment of patients with cancer. The analysis suggests that, for some indications, these savings may be approximately €9500 per treated patient-year. Even for indications with a lower cost difference between the scenarios such as mCRC, biosimilars can save €4900 per patient-year, which translates into a decrease in the pharmacological budget due to the large number of patients who can benefit from the use of biosimilars.

Nonetheless, these data are not free from possible bias since the yearly pharmaceutical cost was calculated by estimating the duration of treatment by indication. Because of this limitation of the model, it was not possible to calculate the pharmaceutical cost per line for each of the indications.

In breast cancer, the main use of bevacizumab is in triple negative patients and we focused the current analysis in this population. However, bevacizumab is also approved by EMA for patients with HR+/HER2− advanced breast cancer after exhausting hormone therapy options or in patients with visceral crisis. However, due to the lower use in these patients and the difficulties in obtaining an accurate estimation of the proportion of affected persons, this was not included in the calculations. Furthermore, the EMA approval of atezolizumab and nab-paclitaxel in PD-L1+ metastatic triple negative patients, which account for 40% of the cases, might also change the current estimations of the impact of bevacizumab biosimilars in breast cancer in the near future.

With these limitations in mind, the results of this analysis showed the impact on the budget. In the first year, and with

Table 3 Sensitivity analysis

			Year 1		Year 2		Year 3	
Parameters	Value		Difference scenario with vs without	%	Difference scenario with vs without	%	Difference scenario with vs without	%
Base case			−€11 558 268	−5.1%	−€29 126 373	−8.5%	−€52 361 778	−13.6%
Biosimilar shares (base case 30%/50%/80%)	SA1	40%/60%/85%	−€15 411 024	−6.8%	−€34 951 647	−10.2%	−€55 634 389	−14.5%
	SA2	50%/80%/95%	−€19 263 780	−8.5%	−€46 602 196	−13.6%	−€62 179 612	−16.2%
	SA3	55%/85%/97%	−€21 190 158	−9.3%	−€49 427 455	−14.4%	−€63 376 617	−16.5%
Reduction of bevacizumab original price and biosimilars (before and after introduction of biosimilars)	SA4	−20%	−€9 248 549	−5.1%	−€23 264 846	−8.5%	−€41 824 250	−13.6%
	SA5	−30%	−€8 093 558	−5.1%	−€20 359 450	−8.5%	−€36 601 091	−13.6%
	SA6	−40%	−€ 6 936 412	−5.1%	−€ 17 448 634	−8.5%	−€31 368 188	−13.6%
Bevacizumab original ex-factory price equal to biosimilars ex-factory prices in scenario with bevacizumab biosimilars	SA7	€262.43	−€38 527 560	−17.0%	−€58 149 947	−17.0%	−€65 336 719	−17.0%

SA, Sensitivity analysis.

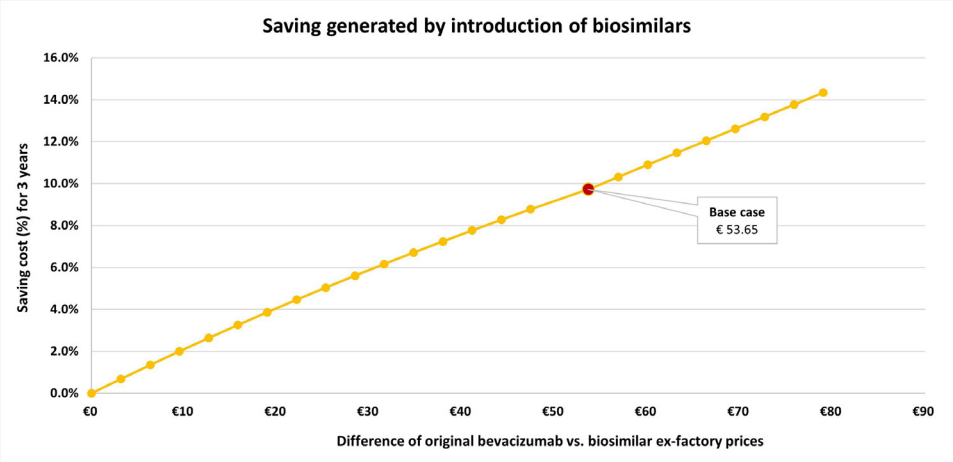

Figure 3 Results of variation in ex-factory prices of original bevacizumab versus biosimilars.

a penetration rate of 30.0% for the bevacizumab biosimilars, a savings of 5.1% (−€11 558 268) was estimated. Due to the increase in the market share of bevacizumab biosimilars compared with the original, it was estimated that in years 2 and 3 the budgetary impact would include decreases of 8.5% (−€29 126 373) and 13.6% (−€52 361 778), respectively, in the pharmaceutical costs derived from the treatment of oncological patients with bevacizumab. These savings are due to the difference in price between original bevacizumab and its biosimilars and also to the market access policies for biosimilars and the confidence of clinicians in their implementation in the hospital setting, where their demand is greatest.[5]

These savings were based on the listed prices although, in practice, these prices may vary due to decentralised purchasing by hospitals. Therefore, to facilitate the evidence of the savings arising from the introduction of biosimilars, different analyses were performed in which discounts were applied to the prices of both bevacizumab and its biosimilars in the scenarios without and with the availability of biosimilars. Thus, although the percentage of the budgetary impact was equal to that of the base case, the generated savings varied—that is, in the scenario with a 20% reduction in the ex-factory prices the savings generated for the first year were €9 248 549 while, in the scenario with a 40% reduction, the savings were only €6 936 412.

It is foreseeable that the penetration rates of bevacizumab in particular and of biosimilars in general could increase in importance over a relatively short period such as 3 years. Therefore, analyses of different scenarios were also performed in which the usage of bevacizumab biosimilars compared with bevacizumab were varied.

In the first scenario, the first- and second-year shares were increased by 10% and in the third year they were increased by 5% compared with the base case. Thus, with shares of 40%, 60% and 85% for each year, savings of €15 411 024 (first-year), €34 951 647 (second-year) and €55 634 389 (third-year) were seen.

The literature on the budgetary impact of biosimilars in Spain is scarce. A BIA of biosimilar drugs in the SNHS was recently published that included a retrospective analysis (2009–2019) and a prospective study (2020–2022) in which the impact of bevacizumab biosimilars was determined, along with 17 active principles for the hospital setting.[5] The bevacizumab biosimilars were analysed over a prospective period of 2 years, with savings of €23 600 000 with a usage rate of 50% for the first year and €48 600 000 for the second year with a usage rate of 80%.

In accordance with that report, an analysis was performed based on a biosimilar penetration rate of 50% that increases to 80% in the second year and to 95% in the third year. The savings for each year were €19 263 780, €46 602 196 and €62 179 612.

The obtained results differed somewhat from those of the cited report, mainly due to two limitations. The first is a possible overestimation of the number of patients treated with bevacizumab, as described above. Another possible limitation is related to the price differences used in the two analyses, since the cost of bevacizumab may be subject to certain discounts at the time of purchase by hospitals, which is not reflected in the results.

The availability of biosimilars leads to a regularisation in the reference price of the original drugs, which leads to an equalisation of prices between the original biological drugs and their biosimilars.[5] Therefore, two analyses were conducted to consider this factor.

In the first case, the price of bevacizumab was equal to that of its biosimilars after the introduction of the biosimilars, which had a budgetary impact of 17% reflecting the difference in the drug prices. This result showed a savings of €162 014 225 for the 3 years, which contrasts with analyses based on the starting price of other biosimilars, which differ by approximately 20–30% from the price of the original drug.[5 21] However, according to estimates using data from Spain, the price difference between biosimilars and their original drugs is on average 19%.[22] The savings produced by the price differences are largely due to two situations: (1) the entry of biosimilars allows access to drugs that are less expensive than the original biological but have similar efficacy and safety; and (2) the price of bevacizumab relative to its biosimilars must be adjusted so that it can compete with them. Thus, both scenarios produce a decrease in pharmaceutical expenditures.

Additionally, an analysis was carried out in which the price of the biosimilars was fixed and the margin of difference from the original bevacizumab was varied to determine the budgetary impact based on the differences between the ex-factory prices. This analysis showed that, with a difference in price of only €3.16 between the original bevacizumab and the biosimilars, savings of €5 473 135 could be obtained for the 3 years of the analysis.

These savings will increase as the difference between the prices of the biosimilars and original drug increases, thus increasing the

competition between them. In contrast, if this competition is not favoured, the savings tend to decrease to the point that the use of biosimilars would mean a budgetary increase.

In conclusion, the inclusion of bevacizumab biosimilars in the Spanish healthcare system will lead to a decrease in budget allocations for the acquisition of biological medicines that will be notable after the first year.

Key messages

What is already known on this subject?

⇒ Biosimilars have been shown to generate savings for health systems and improve access to biological medicines.
⇒ The impact on the heath budget of biological medicines is growing
⇒ Budgetary impact studies of biosimilars are limited

What this study adds?

⇒ The introduction of bevacizumab biosimilars can generate cost savings for the national health system in Spain

Contributors IO and LSO adapted the model, reviewed the scientific literature, performed the analyses and drafted the manuscript. MAC, JA, EA, JGF, AF, FR and JS validated the model structure and the inputs and provided information about the clinical management of cancer patients receiving bevacizumab in Spain. All the authors contributed to interpretation of the results and reviewed and approved the final version of the manuscript. LSO is the guarantor and accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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Competing interests IO and LSO are employees of Pharmacoeconomics & Outcomes Research Iberia (PORIB), a consultant company specialising in health technology assessment, which has received financial support from Pfizer to conduct the development of the present work. JS is an employer of Pfizer Spain. MAC has received payment from Amgen, Roche and Samsung Bioepis for educational events and has participated in Advisory Boards for these companies. JA has received payment from Amgen, Roche and MSD and has received support for attending meetings for MSD and Amgen. EA has participated in Advisory Boards for Amgen, Bayer, Merck Serono, Roche and Sanofi. JGF has contracts with Biocartis, Bayer, Janssen, Merck Serono, Roche, Sanofi, Servier and Sysmex and has also received payment for lectures, presentations, speakers bureaus, manuscript writing or educational events, support for attending meetings and consulting fees from AstraZeneca, Biocartis, BMS, Bayer, Celgene, GSK, Janssen, Lilly, Merck Serono, MSD, Novartis, Pfizer, Foundation Medicine, Roche, Sanofi, Servier, Sysmex and tesaro. FR has received payment for lectures, presentations, speakers bureaus, manuscript writing or educational events and support for attending meetings from Amgen, Merck Serono, MSD, BMS, Servier, Roche, Sanofi and Lilly. MAC, JA, EA, JGF, AF and FR have received payment from Pfizer for consultant activities related to validation of the parameters and results. None of them received financial compensation for review and co-authorship of this manuscript. AF declares no conflicts of interest.

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