Research Article

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Cost–effectiveness of cetuximab combined with radiotherapy versus radiotherapy alone in locally advanced head and neck cancer in Spain

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Aim: To estimate the cost–effectiveness of cetuximab in combination with radiotherapy compared with radiotherapy alone, for the treatment of locally advanced head and neck cancer patients in Spain. **Methods:** A probabilistic Markov model (second-order Monte Carlo simulation) with a 5-year time horizon and quarterly Markov cycles was performed from the perspective of the Spanish National Health System (NHS). **Results:** The additional cost and quality-adjusted life-year (QALY) gain per patient receiving radiotherapy in combination with cetuximab compared with radiotherapy alone was €4356 (95% CI: €4350-4,362) and 0.2380 (95% CI: 0.2370–0.2391) QALY, respectively. The incremental cost per QALY gain was €18,303 (95% CI: €18,243–18,354) with a probability of cost–effectiveness of 65.4% for a willingness to pay of €30,000 per QALY gained. **Conclusion:** According to the results of this analysis, the addition of cetuximab to radiotherapy would be a cost-effective alternative to radiotherapy alone in the treatment of locally advanced head and neck cancer in Spain.

Plain language summary: What was the aim of this research?: To analyze the cost–effectiveness of the locally advanced head and neck cancer treatment with cetuximab combined with radiotherapy compared with radiotherapy alone, from the Spanish National Health System (NHS) perspective.
How was the research carried out?: A probabilistic Markov model (second-order Monte Carlo simulation) with a 5-year time horizon and quarterly Markov cycles was performed. Data on disease control, recurrence and progression were obtained from the randomized clinical trials. Unit costs were obtained from Spanish official sources and from the existing literature. The use of health resources was estimated by a panel of Spanish clinical experts and from the literature. Utilities (quality-adjusted life years [QALY]) were obtained from a NICE report. Univariate sensitivity analyses (modifying one at a time all the variables of the model) were performed to confirm and provide robustness of the results.
What were the results?: The additional cost and QALY gain per patient receiving radiotherapy in combination with cetuximab compared with radiotherapy alone was €4356 and 0.2380 QALY, respectively. The incremental cost per QALY gain was €18,303 with a probability of cost–effectiveness of 65.4% for a willingness to pay of €30,000 per QALY gained. Most deterministic sensitivity analyses confirmed the cost–effectiveness of the combination of cetuximab and radiotherapy.
What do the results of the study mean?: Adding cetuximab to radiotherapy for the patient population diagnosed with locally advanced head and neck cancer could lead to additional clinical benefit for the patients at an acceptable cost for the healthcare system in Spain.

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Keywords: cetuximab • cost–effectiveness • locally advanced head and neck cancer • radiotherapy • Spain

Head and neck cancer is a malignant tumor, which represents 5% of oncological cases in adults in Spain. The squamous histology is present in more than 90% of these tumors [1]. Although most patients with early-stage head and neck squamous cell carcinoma (HNSCC) can be cured with surgery or radiotherapy [RT], those with aggressive or locally advanced disease, who account for two-thirds of new diagnoses, are more likely to recur, with an estimated 5-year overall survival rate of 50% [1]. In locally advanced disease (clinical stages III, IVA and IVB), the treatment recommended by the Spanish Society of Medical Oncology (SEOM) can be surgery (followed by adjuvant radiotherapy with or without chemotherapy if indicated) or concomitant RT with chemotherapy or cetuximab or RT alone, depending on the patient profile and decision of the multidisciplinary committee [1]. In patients who are not candidates or decline radical treatment with surgery, concomitant RT with high-dose cisplatin (100 mg/m^2 on days 1, 22 and 43) is the standard treatment. Weekly cisplatin and other combination therapies may not be considered equivalent to high-dose cisplatin, although this remains a subject of debate as shown in the existing literature [1]. Concomitance with cetuximab is recommended as one of the alternative treatments in patients with cisplatin contraindications, such as neuropathy, nephropathy, cardiovascular disease or hearing loss. Sequential therapy based on induction chemotherapy followed by RT (concomitant with chemotherapy or cetuximab or RT alone) is proposed as an option with a lower level of evidence than treatment with concomitant RT [1]. Cetuximab is a chimeric monoclonal IgG1 antibody explicitly targeting the epidermal growth factor receptor (EGFR) [2]. A randomized clinical trial comparing RT alone (N = 213) with the combination of RT + cetuximab (N = 211) in the treatment of patients with locally advanced HNSCC (LA HNSCC) is available and led to the approval of cetuximab in this indication [3]. The median duration of loco-regional control was 24.4 months among patients treated with RT + cetuximab and 14.9 months among those receiving RT alone (hazard ratio [HR] of loco-regional progression or death, 0.68; p = 0.005). RT + cetuximab significantly prolonged progression-free survival (PFS), with a median PFS of 17.1 months in the RT + cetuximab group and 12.4 months in the RT alone group (HR of disease progression or death: 0.70; CI 95% 0.54–0.90; p = 0.006) [3]. In addition, with a median follow-up of 5 years, the median overall survival was 49.0 months in patients treated with combination therapy and 29.3 months in those treated with RT alone (HR for death: 0.73; CI 95% 0.56–0.95; p = 0.018). The 5-year overall survival rate was 45.6% in the RT + cetuximab group and 36.4% in the RT alone group (p = 0.03) [4].

HNSCC has a considerable health economic impact. According to a study of the hospital burden of HNSCC in Spain over 12 years (1997–2008), the estimated cost per hospitalization would range from €8343 to €10,805. The estimated overall cost per year would be approximately 194 million euros [5], updated to 2023.

This study aimed to estimate the cost–effectiveness of cetuximab in combination with RT compared with RT alone for treating LA HNSCC in Spain.

Design & methods

Economic model

A probabilistic Markov model with five health states (patient with LA HNSCC on treatment; patient in response after treatment of LA HNSCC; patient progressing and treated to recurrent and/or metastatic stage (R/M HNSCC); patient on palliative treatment; death) was performed. (Figure 1).

Patients in a hypothetical cohort would evolve through the model according to transition probabilities (Tp) between the described states. These transitions would occur in quarterly periods (called Markov cycles). During a cycle of the model, patients can either remain in their current state or transition to another state. Each time a patient stays in or go into a Markov state, the costs and utilities (quality-adjusted life years, QALY) for that state and that patient are accounted for. The duration of the model (the time horizon) was 5 years (60 months), in line with the duration of patient follow-up in the randomized clinical trial by Bonner *et al.* [3,4].

Patients with LA HNSCC start treatment with an RT-based regimen, with or without cetuximab. During the first year of modelling, the patient is on treatment for 7 cycles of RT + cetuximab or RT alone. If the patient responds to treatment, they may remain responsive (with the usual follow-up) or suffer progression. In this case, the progressing patient would progress to R/M HNSCC during the following years and may undergo salvage treatment and/or surgery. In the post-treatment states (in response, R/M HNSCC on treatment and palliative treatment), the patient can be maintained in these states for successive cycles. Death is referred to as the "absorbent" state (Figure 1).

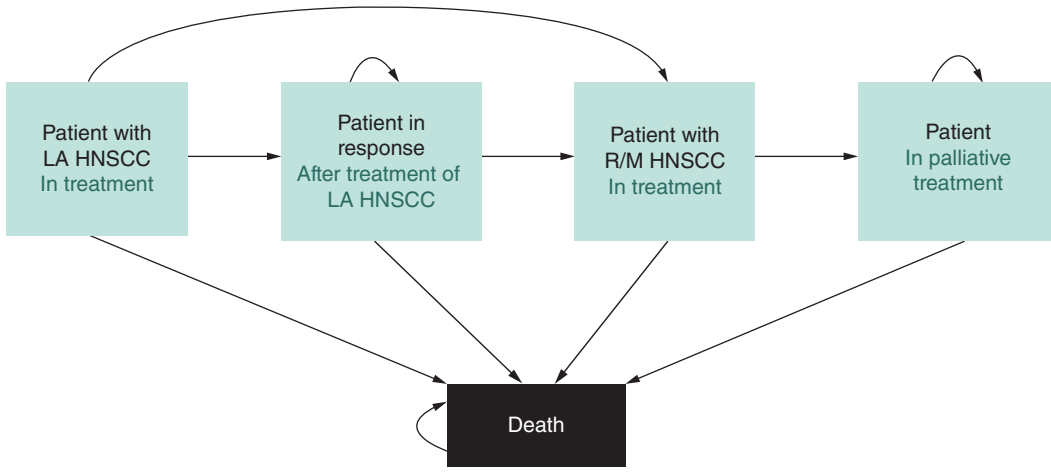

Figure 1. Markov model of locally advanced head and neck cancer.
LA HNSCC: Locally advanced head and neck squamous cell carcinoma; R/M HNSCC: Recurrent and/or metastatic head and neck squamous cell cancer.

All model assumptions (structure of the 5-state Markov model, annual transition probabilities between Markov states in patients with LA HNSCC, the utilities of each state, resource use and unit costs considered in the model) were validated by a panel of three Spanish clinicians with expertise in the management of LA HNSCC (JC, RAC, SRC). The model was run using TreeAge Pro Healthcare Software 2023 R2.0 [6]. The model was subjected to internal validation, defined as the degree to which the observed results represent the reality of the population studied and, therefore, not due to methodological errors.

Population

Since the efficacy results (response, progression, death) from the clinical trial [3] were used in the model, the model population would have the characteristics of the patients included in that study for RT + cetuximab and RT alone, respectively, regarding median age (56 and 58 years), gender (81 and 79% male), Karfnosky scale score (≤70 in 10% and 11% of patients), primary tumor location (56 and 63% in oropharynx) and tumor staging (26% and 24% and 74% and 76% of patients had stage III and IV, respectively) [3].

Perspective

The perspective is that of the Spanish National Health System (NHS). Therefore, only direct health costs were considered.

Transition probabilities

All transition probabilities between states were obtained from the clinical trial [3], except for the probability of death in each state. This was obtained from a retrospective Spanish study that reviewed data from 5,122 patients with HNSCC treated between 1985 and 2018 [7]. Table 1 shows the annual transition probabilities (model cycles were quarterly). The transition probabilities of the model were calculated according to the formula $Pt = 1 - e^{-rt}$, where r is the event rate, and t is the time at which the event rate takes place [8].

Unit costs & resources use

Table 2 presents the unit costs and health resource use considered in the model. The ex-factory selling price (LSP) of cetuximab was obtained from BotPlus [9] and included the official deduction of 15%. The unit cost of RT, intravenous (IV) administration in the day hospital, follow-up medical consultations, imaging techniques (CT, PET-CT and body CT) and surgery in R/M HNSCC (DRG 91) were obtained from the average public health prices of the autonomous communities.

The cost of full pharmacological treatment of the patient progressing after treatment with RT + cetuximab or RT alone was obtained from a cost analysis of R/M HNSCC treatment sequences in the Spanish NHS, published in 2023 [10]. Seven cycles of treatment with RT + cetuximab and RT alone were considered in the patient with LA

Table 1. Annual transition probabilities of the model.

RT + cetuximab							
Year 1							
From	**To**	**Tp**	**SD**	**Alpha†**	**Beta†**	**Study**	**Ref.**
LA HNSCC in treatment	LA HNSCC in response	0.4685	0.0477	50.79	57.62	Bonner, 2006	[3]
LA HNSCC in treatment	R/M HNSCC in treatment	0.5145	0.0523	46.47	43.86	–	
LA HNSCC in treatment	Death	0.0171	0.0015	121.99	7031.82	Lop, 2022	[7]
Palliative treatment	Palliative treatment	0.7993	0.0204	307.05	77.09	–	
Palliative treatment	Death	0.2007	0.0204	77.09	307.05	Bonner, 2006	[3]
Following years							
From	**To**	**Tp**	**SD**	**Alpha†**	**Beta†**	**Study**	**Ref.**
LA HNSCC in treatment	LA HNSCC in response	0.3953	0.0403	57.76	88.37	Bonner, 2006	[3]
LA HNSCC in treatment	R/M HNSCC in treatment	0.5877	0.0599	39.03	27.38	–	
LA HNSCC in treatment	Death	0.0171	0.0015	121.99	7031.82	Lop, 2022	[7]
Palliative treatment	Palliative treatment	0.5605	0.0446	68.71	53.88	–	
Palliative treatment	Death	0.4395	0.0446	53.88	68.71	Bonner, 2006	[3]
RT							
Year 1							
From	**To**	**Tp**	**SD**	**Alpha†**	**Beta†**	**Study**	**Ref.**
LA HNSCC in treatment	LA HNSCC in response	0.4284	0.0434	54.76	74.15	Bonner, 2006	[3]
LA HNSCC in treatment	R/M HNSCC in treatment	0.5582	0.0569	41.97	33.22	–	
LA HNSCC in treatment	Death	0.0171	0.0015	121.99	7031.82	Lop, 2022	[7]
Palliative treatment	Palliative treatment	0.7695	0.0237	241.71	72.40	–	
Palliative treatment	Death	0.2305	0.0237	72.40	241.71	Bonner, 2006	[3]
Following years							
From	**To**	**Tp**	**SD**	**Alpha†**	**Beta†**	**Study**	**Ref.**
LA HNSCC in treatment	LA HNSCC in response	0.3344	0.0342	63.34	126.11	Bonner, 2006	[3]
LA HNSCC in treatment	R/M HNSCC in treatment	0.6486	0.0661	33.21	17.99	–	
LA HNSCC in treatment	Death	0.0171	0.0015	121.99	7031.82	Lop, 2022	[7]
Palliative treatment	Palliative treatment	0.5185	0.0492	52.88	49.10	–	
Palliative treatment	Death	0.4815	0.0492	49.10	52.88	Bonner, 2006	[3]

†Calculated for beta distributions.
LA HNSCC: Locally advanced head and neck squamous cell carcinoma; R/M HNSCC: Recurrent and/or metastatic head and neck squamous cell cancer; RT: Radiotherapy; SD: Standard deviation; Tp: Transition probability.

HNSCC under treatment [3]. Treatment sequences, first and second line, in progressing patients, and percentages of use after RT + cetuximab and RT alone were estimated by the Spanish clinical expert panel (JC, RAC, SRC) according to SEOM clinical guidelines [1] and their clinical practice (Table 2).

The cost of managing adverse effects with RT + cetuximab and RT alone was calculated based on those observed in the clinical trial [3]. Annual adverse event rates were calculated for patient-years. Unit costs for adverse event management were obtained from Spanish public sources and prices [11–15] and the aforementioned panel of Spanish clinical experts. Adverse effect rates of drug treatments in patients with R/M HNSCC in treatment were obtained from their main clinical trials [16,17]. The methodology used to analyze the cost of adverse effects has been published previously [18].

In LA and R/M HNSCC, the following other health resource use was estimated, as agreed by the expert panel, respectively: 5 and 24 follow-up medical consultations per year [19]; 1.6 and 4 head and neck CT scans per year; finally, 1 PET-CT scan and a full body CT scan at the end of treatment, respectively. It was considered that 16% of patients with R/M HNSCC would undergo surgery [20].

Utilities

The utilities (patient-perceived quality of life, ranging from 0 [death] to 1 [perfect health]) of the patient with LA HNSCC (0.862) and R/M HNSCC (0.129) were obtained from the literature [21] (Table 2).

Table 2. Unit costs, use of resources and model utilities.

Resources	Unit costs	Study	Ref.
Cetuximab (Ex-factory price per vial, 15% discount)	€ 163.46	BotPlus, 2023	[9]
Radiotherapy (1 cycle)	€ 883	Public healthcare prices†	
IV administration (day hospital)	€ 308.62	Public healthcare prices†	
Complete pharmacological treatment in progression – After cetuximab + radiotherapy – After radiotherapy	 € 55,751 € 51,575	 Experts Panel Experts Panel	 [10]
Follow-up medical consultation	€ 115.00	Public healthcare prices†	
Computed axial tomography (CT)	€ 224.75	Public healthcare prices†	
PET-CT	€ 570.72 €	Public healthcare prices†	
Body CT	€ 662.87	Public healthcare prices†	
Adverse effects, cetuximab + radiotherapy – Locally advanced disease – In progression	 € 29.87 € 162.02	 Bonner, 2006; Public prices† Bonner, 2006; Public prices†	 [9]
Adverse effects, radiotherapy only – Locally advanced disease – In progression	 € 22.82 € 162.02	 Bonner, 2006; Public prices† Bonner, 2006; Public prices†	 [9]
Adverse effects in progression (Nivolumab, Pembrolizumab)	€ 162.02	Ferris, 2016; Harrington, 2022	[16,17]
Surgery in progression (DRG 91)	€ 17,475.93	Public healthcare prices†	
Resource utilization	**Values**	**Authors**	**Ref.**
Cycles (cetuximab and radiotherapy) – in response (n)	7 and 7	Bonner, 2006	[3]
Cycles of nivolumab and pembrolizumab – in progression (n)	4 and 6	Sisamón, 2023	[10]
Follow-up medical consultations per year (n) – Locally advanced disease – In progression	 5 24	 Experts Panel; Machiels, 2020 Experts Panel; Machiels, 2020	 [19]
Whole body CTs at the end of treatment (progression), n	1	Experts Panel	
PET-CT at the end of treatment (locally advanced), n	1	Experts Panel	
Annual body CT (locally advanced/progression), n	0/0.2	Experts Panel	
Surgery rate in progression	16%	Gandola, 2021	[20]

Treatment sequences in patients with recurrence				Ref.
First line	**Second line**	**RT+CET**	**RT**	
Erbitax‡	Nivolumab	25%	40%	Experts Panel
Pembrolizumab + platinum + 5FU	Erbitax‡	30%	25%	
Extreme§	Nivolumab	3%	3%	
Tpex¶	Nivolumab	2%	2%	
Pembrolizumab monotherapy	Erbitax‡	40%	30%	

Utilities	Values	Study	Ref.
Locally advanced disease	0.862	Greenhalgh, 2009	[21]
Progressing disease	0.129	Greenhalgh, 2009	[21]

†Average of the autonomous communities public prices.
‡Erbitax: combination of paclitaxel and cetuximab.
§Extreme: combination of platinum, 5FU and cetuximab.
¶Tpex: combination of cisplatin, docetaxel and cetuximab.
5FU: 5-fluorouracil; CT: Computed axial tomography; CET: Cetuximab; DRG: Diagnosis-related group; IV: Intravenous; PET: Positron emission tomography; RT: Radiotherapy.

Probabilistic analysis

In the base case study, two analyses were carried out: deterministic and probabilistic. The probabilistic analysis was performed using second-order Monte Carlo simulations with a cohort of 1,000 iterations (1,000 patients). This methodology allows the analysis of the uncertainty of the model variables [22]. Costs and utilities (continuous variables) were fitted to gamma distributions; probabilities (dichotomous variables) were fitted to beta distributions based on the minimum and maximum available values or the variability of 20% of the mean or available value of the variable [23,24]. The annual variables of the model are summarized in Table 1 (probabilities) and Table 3 (costs and utilities).

Table 3. Annual cost and utilities of the model.

Costs	Average	SD
Locally advanced disease (in treatment) – RT + cetuximab group	€ 26,392	€ 2693
Locally advanced disease (in treatment) – RT alone group	€ 9039	€ 922
Locally advanced disease and progression (post-treatment)	€ 2907	€ 297
Progression in treatment – RT + cetuximab group	€ 61,617	€ 6287
Progression in treatment – RT alone group	€ 57,440	€ 5861
Utilities	**Average**	**SD**
Locally advanced disease	0.862	0.044
Progression	0.129	0.007

RT: Radiotherapy; SD: Standard deviation.

Table 4. Deterministic analysis result.

Treatment	Costs	Cost difference	QALY	QALY difference	Cost per QALY gained
Radiotherapy	€ 46,607		1.1274		
RT + cetuximab	€ 51,271	€ 4664	1.3606	0.2331	€ 20,008

QALY: Quality adjusted life year; RT: Radiotherapy.

Table 5. Probabilistic analysis result.

Treatment	Costs			QALY			Cost per QALY gained			Cost–effectiveness probability
	Average	LL 95% CI	UL 95% CI	Average	LL 95% CI	UL 95% CI	Average	Minimum	Maximum	
Radiotherapy	€ 46,926	€ 46,663	€ 47,189	1.1272	1.1225	1.1318	€ 18,303	€ 18,243	€ 18,354	65.4%
RT + cetuximab	€ 51,282	€ 51,013	€ 51,551	1.3652	1.3595	1.3709				
Differences	€ 4,356	€ 4,350	€ 4,362	0.2380	0.2370	0.2391				

LL/UL 95% CI: Lower/upper limit of 95% CI; QALY: Quality adjusted life year; RT: Radiotherapy.

Deterministic sensitivity analysis

A univariate deterministic sensitivity analysis was performed for all model variables (probabilities, costs, utilities) to identify the individual variables determining the outcome (Tornado diagram).

Results

Deterministic analysis

For a 5-year time horizon, the cost and QALY per patient with RT + cetuximab and RT alone were calculated to be €51,271 and €46,607 and 1.3606 and 1.1274 QALY, respectively. Therefore, the combination resulted in an additional cost of €4664 and a gain of 0.2331 QALY per patient. The cost of gaining one QALY with RT + cetuximab versus RT alone was €20,008 (Table 4).

Probabilistic analysis

The additional cost and QALY gain per patient receiving RT in combination with cetuximab compared with RT alone were €4,356 (95% CI: €4,350-4,362) and 0.2380 (95% CI: 0.2370–0.2391) QALY, respectively. The incremental cost per QALY gained with RT + cetuximab was €18,303 (95% CI: €18,243-18,354) with a cost–effectiveness probability of 65.4% for a willingness to pay of €30,000 per QALY gained (Table 5 & Figure 2).

Deterministic sensitivity analysis

As can be seen in the tornado diagram in Figure 3, RT + cetuximab was cost-effective in most analyses. Exceptions were analyses in which the mean value of the probability of remaining in response (loco-regional control) was varied by +20% with both RT alone and RT + cetuximab, and in which this maximum value (+20%) of the costs in R/M HNSCC during treatment was used.

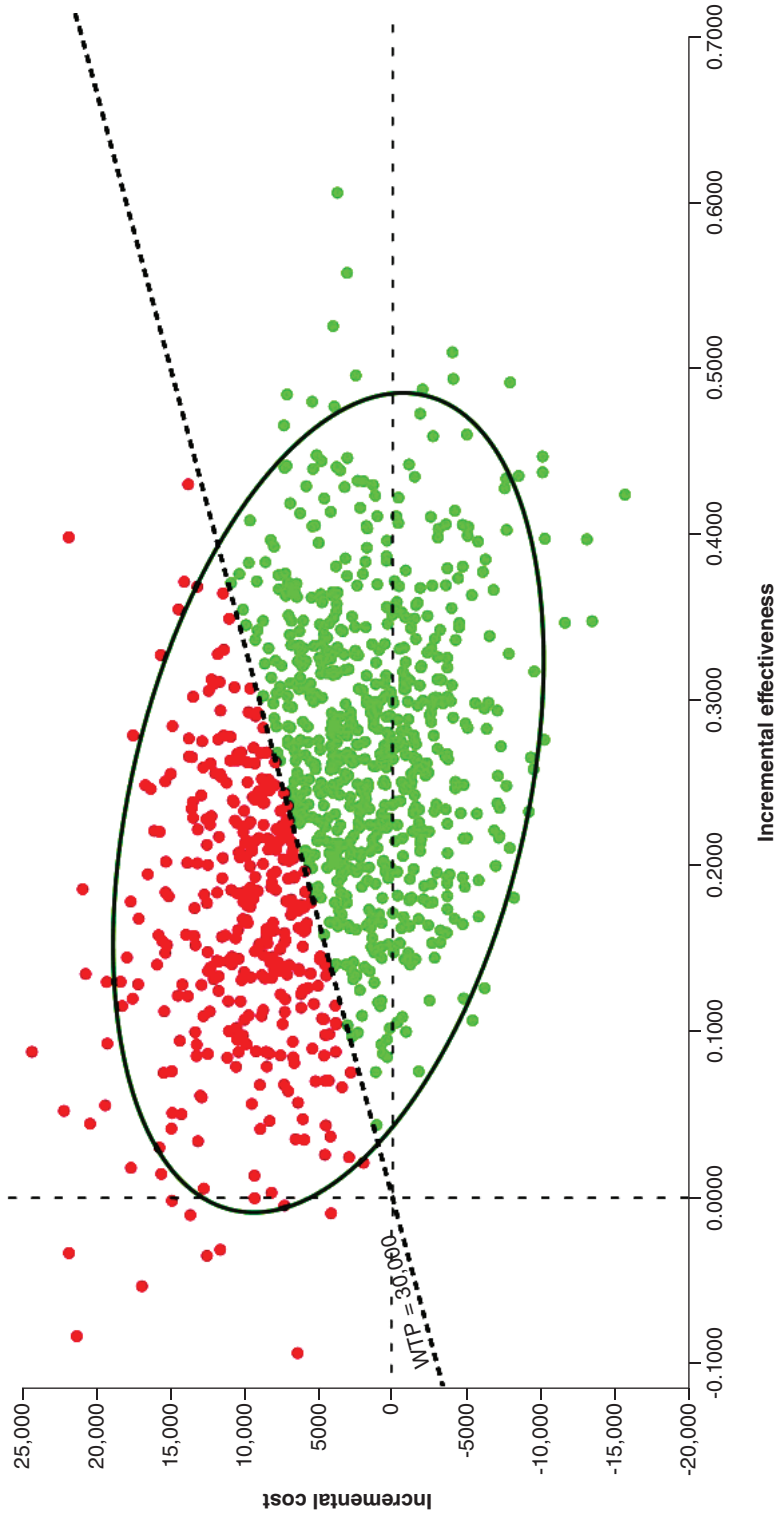

Figure 2. Probabilistic analysis result: cetuximab + RT vs RT.
RT: Radiotherapy; WTP: Willingness to pay (30,000 € per QALY gained).

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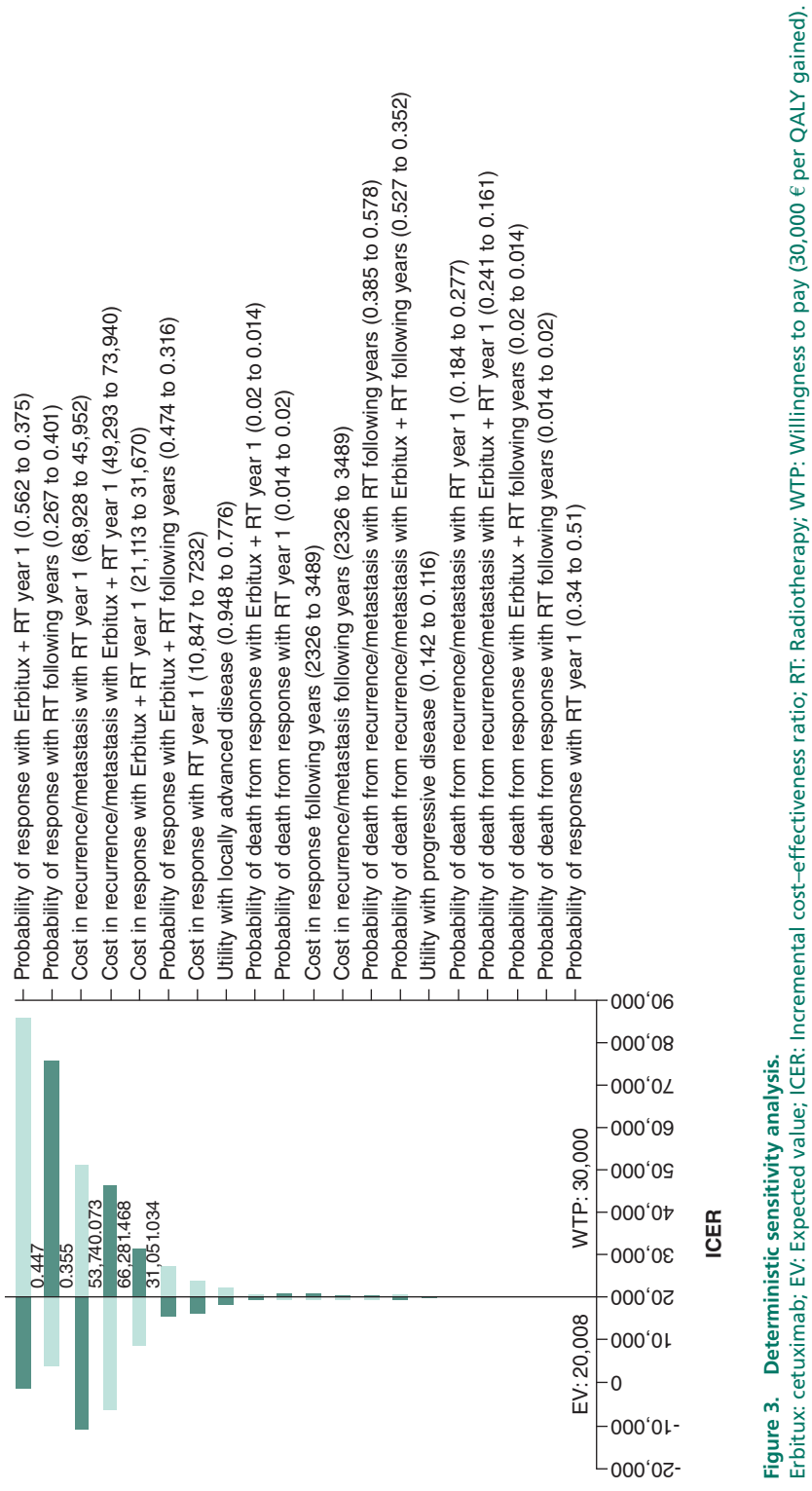

Figure 3. Deterministic sensitivity analysis.
Erbitux: cetuximab; EV: Expected value; ICER: Incremental cost–effectiveness ratio; RT: Radiotherapy; WTP: Willingness to pay (30,000 € per QALY gained).

Discussion

According to the present study, the cost of gaining one QALY in patients with LA HNSCC treated with the combination of RT + cetuximab would be cost-effective compared with RT alone, with a cost per QALY gained of €18,303. The probability of cost–effectiveness with the combination would be 65.4%. This study also showed a difference of 0.23 QALY in favor of the combination of RT + cetuximab over RT. This difference would be considered clinically relevant, according with the minimum clinically relevant difference in utility between two interventions observed with the EQ-5D, HUI2, HUI3 and SF-6D instruments that would be 0.074, 0.030, 0.030 and 0.033 QALY, respectively [25–28].

The probabilistic Markov model simulated the evolution of a cohort of patients with LA HNSCC, with transition probabilities obtained from the randomized clinical trial comparing the efficacy of the combination of RT + cetuximab and RT alone [3] and from a retrospective study of more than 5,000 Spanish patients [7]. The use of healthcare resources was obtained from the two studies mentioned above and other studies [18,19], considering the SEOM recommendations for the pharmacological treatment of HNSCC [1].

The study has some limitations. First, the study is limited due to the nature of economic models, which simplify clinical practice, and the need to make assumptions based on the literature. Second, the probability of surgery in LA HNSCC in recurrent and/or metastatic stage was obtained from Gandola *et al.* [20] and was validated using a panel of clinical experts which included experts in Medical Oncology and Oncologic Radiotherapy. This panel did not include a head and neck surgeon. However, the panel of experts was well acquainted with the surgical practice in their hospitals, since the surgeons are integrated into the work teams. This parameter was further validated using second-order Monte Carlo simulations. The utilities used in the model were obtained from the NICE report [21]. Regarding the validity of these utility data in comparison with the Spanish population, it is interesting to note that in a study based on 83,000 assessments of 44 health state values with EQ-5D, conducted in six European countries, including Spain, greater variability among individuals was recorded than among countries [29]. Finally, as is usual in cost–effectiveness analyses, one of the major limitations of this research is the model population, since the trial population could differ from the real-world population.

The strengths of this study rely on the fact that all assumptions of the economic model were validated by a panel of clinical experts from different specialties (medical and radiation oncology and hospital pharmacy), with experience in the management of patients with LA HNSCC, which is important to reflect as much as possible the clinical practice in Spain. Another strength of this study is the robustness of the economic model, as the direction of the base case result was maintained in most univariate sensitivity analyses and the probabilistic analysis.

Three economic analyses have been identified with a similar objective to the present study [30–32]. According to a Markov economic analysis published in 2008 [28], also based on the clinical trial by Bonner *et al.* [3], the incremental cost per QALY for patients receiving RT in combination with cetuximab compared with RT alone in all participating countries (Belgium, France, Italy, UK and Switzerland) was €7,538 to €10,836. Contrary to the present study, which had a 5-year time horizon, the 2008 study had a lifetime horizon. A decision analysis published in 2011 [31] concluded that the cost per QALY gained in patients treated with RT + cetuximab compared with RT alone was $36,992 in Taiwan. Finally, a study in the Netherlands [32] using a Markov model based on the clinical trial by Bonner *et al.* [3] concluded that over a 5-year time horizon, the cost per QALY gained with the combination versus RT alone would range from €36,985 to €38,543.

The different results of these models and the present study could be due to the structural differences in the models and the different costs, assumptions, and time horizons.

Conclusion

The following conclusion can be drawn from this study: (i) The cost of gaining one QALY in LA HNSCC patients treated with the combination of RT + cetuximab would be cost-effective compared with RT alone, with a cost per QALY gained of €18,303 (95% CI: €18,243-18,354), and the probability of cost–effectiveness with the combination is 65.4% for a willingness to pay of €30,000 per QALY gained; (ii) The difference of 0.23 QALY in favor of the combination over RT is clinically relevant, and above the difference that can be perceived by patients as observed with the main quality of life measurement instruments [25–28].

According to the present model, the use of RT + cetuximab in patients with LA HNSCC would reduce the costs associated with disease progression, compared with RT alone, due to loco-regional disease control and progression-free survival. This would mean fewer patients need to be treated at later stages of the disease, with the humanistic and economic burden that this would entail.

Summary points

- A probabilistic Markov model was performed to analyze the cost–effectiveness of the locally advanced head and neck cancer treatment with cetuximab combined with radiotherapy (RT) compared with RT alone, from the Spanish National Health System (NHS) perspective.
- For a 5-year time horizon, the cost per patient with RT + cetuximab and RT alone were calculated to be €51,271 and €46,607, respectively.
- For the same time horizon, QALY per patient with RT + cetuximab and RT alone were estimated to be 1.3606 and 1.1274 QALY, respectively.
- The QALY gain (0.2331) with RT + cetuximab versus RT alone was clinically relevant.
- The mean incremental cost per QALY gain was €18,303 (95% CI: €18,243-18,354).
- The probability of cost–effectiveness was 65.4% for a willingness to pay of €30,000 per QALY gained.
- Adding cetuximab to radiotherapy for the patient population diagnosed with locally advanced head and neck cancer could lead to additional clinical benefit for the patients at an acceptable cost for the healthcare system in Spain.
- These results serve as an important piece of evidence for policymakers, budget holders, and health advisers in decision-making when choosing among different treatment options for these patients.

Author contributions

C Rubio-Terrés, D Rubio-Rodríguez, H De los Santos, M Brines, J Cacicedo, R Álvarez, S Redondo made the conceptualization of the economic model. The methodology was performed by all authors. D Rubio-Rodríguez and C Rubio-Terrés built the original economic model and wrote the first draft. Supervision was made by H De los Santos. All authors interpreted the data, reviewed, edited and agreed on the final version.

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Competing interests disclosure

D Rubio-Rodríguez is a senior consultant of Health Value, a company that has received fees in relation to the present study. C Rubio-Terres is director of Health Value, a company that has received fees in relation to the present study. The authors have no other competing interests or relevant affiliations with any organization/entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Writing disclosure

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