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Nancy: Conroy T). The Northwest Data Center is acknowledged for managing the study data. It is supported by grants from the French National League Against Cancer and the French National Cancer Institute. We are also indebted to the Clinical Research Associates from Lille (France) for onsite data monitoring.

ABSTRACT

Objectives: Continuous chemotherapy has been used to treat patients with metastatic oesophageal squamous cell carcinoma (mESCC), despite weak evidence supporting a clinical benefit, associated side effects for the patients, and unjustified medical costs. In the French setting, we conducted a cost-utility analysis alongside the randomised E-DIS trial (NCT01248299), which compared first-line fluorouracil/platinum-based chemotherapy continuation (CT-CONT) to CT discontinuation (CT-DISC) in progressive-free patients after an initial 6-week treatment phase.

Methods: A partitioned survival analysis was performed using patient-level data collected during the trial for survival outcomes, quality of life (EQ-5D-3L), and medical costs. The mean quality-adjusted life years (QALYs) and medical costs were estimated over an 18-month period to assess the incremental net monetary benefit (INMB) and incremental cost-effectiveness ratio (ICER). Uncertainty was handled using the non-parametric bootstrap and univariate analysis. Sixty-seven mESCC patients were randomised and included in the cost-utility analysis.

Results: On average, CT-CONT slightly decreased the number of QALYs (-0.038) and increased the cost per patient (+ €1,177). At a willingness-to-pay threshold of €50,000/QALY (Quality-Adjusted Life-Years) the INMB was negative (-€3,077 [95% confidence interval: -6,564; 4,359]), and the ICER was -30,958€/QALY (CT-CONT dominated). The probability of the CT-CONT treatment option being cost-effective at a willingness-to-pay threshold of €50,000/QALY, as compared to CT-DISC, was 29%.

Conclusion: CT-DISC may be considered as an alternative therapeutic option to CT-CONT in mESCC patients who have stable disease after an initial chemotherapy treatment phase. A

continuous chemotherapy could indeed reduce the number of QALYs because of the disutility associated with the continuous treatment.

Highlights

- The efficacy of continuous chemotherapy in the treatment of metastatic oesophageal squamous cell carcinoma has not been demonstrated
- The cost-utility of continuing chemotherapy in patients with non-progressive metastatic oesophageal squamous cell carcinoma is uncertain
- Chemotherapy discontinuation may be considered as an alternative therapeutic option to patients with stable disease after 6 weeks of initial treatment

INTRODUCTION

Worldwide, oesophageal cancer is the eighth most common cancer and the sixth most common cause of cancer-related death (400,000 deaths representing 4.9% of cancer deaths) [1]. The survival rate of oesophageal cancer is poor, with a 5-year survival of around 15–25% [2]. The presence of metastases, which is observed at the time of diagnosis in many patients [3], is an additional factor of poor outcome, with a median survival of around 6 months in unselected patients [4].

The two main histological sub-types of oesophageal cancer are adenocarcinoma and squamous cell carcinoma (SCC). Even though SCC is the predominant histological sub-type worldwide, the incidence of adenocarcinoma now exceeds that of SCC [2,5] in North America and Europe.

The role of chemotherapy has not yet been fully established in the treatment of metastatic oesophageal SCC (mESCC) [4,6] and the European Society of Medical Oncology guidelines recommend supportive care or chemotherapy as clinical options [7]. However, in clinical practice, most patients with mESCC are treated with continuous chemotherapy despite unproven treatment benefit, associated side effects, and unjustified medical costs. To overcome this situation and to better estimate the benefit of chemotherapy in the setting of mESCC, our group initiated the E-DIS trial, which is a phase 2, randomised discontinuation trial [8]. This trial aimed at estimating the efficacy, safety, quality-of-life, medical costs, and cost-utility of chemotherapy continuation (CT-CONT) treatment versus chemotherapy discontinuation (CT-DISC) in mESCC patients, who were progression-free after a 6-week selection-phase of a fluorouracil/platinum-based chemotherapy regimen. The clinical results of the E-DIS trial have been previously reported [8]. Briefly, CT-CONT provided a 9-month overall survival rate that was similar to that of CT-DISC. However, we observed a

numerically extended time until definitive deterioration of the quality of life related to some symptoms in the CT-CONT arm compared to the CT-DISC arm [8].

Cost-utility combines survival endpoints, preferences from a societal perspective regarding health-related quality-of-life, and medical costs. The availability of experimental data on both costs and effects provides the opportunity to conduct, to our knowledge, the first economic evaluation alongside a randomised clinical trial in patients with metastatic oesophageal squamous cell carcinoma with prospective collection of costs and utilities. As shown in a Cochrane review by Janmaat et al [9], only five randomized controlled trials in 750 participants with oesophageal or gastroesophageal junction cancer contributed data to the comparison of palliative therapy versus best supportive care. Among these studies, only two were first-line therapy regimens in a total of 118 patients [10, 11] but did not evaluate cost-effectiveness. Our objective was to perform a cost-utility analysis, in the French setting, of CT-CONT in progressive-free patients after 6 weeks of initial chemotherapy, compared to CT-DISC.

PATIENTS AND METHODS

E-DIS study design

The E-DIS trial is a multicenter, phase 2 trial involving two phases. In the selection phase, mESCC patients were treated by chemotherapy for 6 weeks. Patients were selected before starting a first-line fluorouracil/platinum-based chemotherapy (the choice of the regimen was made by the physician). Prior chemotherapy was permitted only if it was delivered as a neoadjuvant treatment. The main selection criteria included histologically confirmed mESCC, measurable disease, age greater than 18 years, and an ECOG performance status of 0, 1 or 2.After the selection phase, progressive-free patients with Eastern Cooperative Oncology Group (ECOG) performance status ≤2 were randomly allocated into a CT-CONT

or a CT-DISC arm. Progression was assessed according to RECIST 1.1. Patients were observed until death or until 48 months after study entry. In total, 105 patients from 13 centers were included in the selection phase. In the CT-CONT arm, the study treatment continued until disease progression, unacceptable toxicity, or a patient or physician decision to terminate the treatment. In the CT-DISC arm, chemotherapy could be resumed after disease progression. In case of disease progression, treatment options were left to the discretion of the referring oncologist. Sixty-seven patients were randomised between 2011 and 2015: 34 and 33 patients in the CT-CONT and CT-DISC arms, respectively. In the cost-utility analysis, all randomised patients were considered on an intent-to-treat basis.

Overview of the partitioned survival analysis

To take into account censored patients, we used a partitioned survival analysis (area under the survival curves) to estimate the mean number of quality-adjusted life years (QALYs) in each treatment arm [12,13]. In the partitioned survival analysis, all patients are directly included in the survival analysis (taken into account the censors) and the mean utility values are used to weight the mean survival time without progression and mean survival time after progression. Three health states are therefore defined: before the first instance of disease progression, after the first instance of disease progression, and death.

The mean duration before and after progression was estimated in each arm using the area under the Kaplan-Meier survival curve. A time horizon of 18 months was defined based on the survival of the patients in the trial, this time horizon allows to take into account all the differences in terms of costs and QALYs between the two strategies [8]. Survival probabilities were estimated in each treatment arm for OS and PFS. The area under the PFS curve corresponds to the mean survival time before the first instance of disease progression

and the area between OS curve and PFS curve corresponds to the mean survival time after the first instance of disease progression, but before death.

To obtain utility values, the Euroqol-5D (EQ-5D-3L) questionnaire was used in the trial and the formula estimated in a sample of the general population in France was used to convert the results into utility values [14]. In the E-DIS trial, the EQ-5D-3L questionnaire was administered to the patients every 6 weeks from the randomization to 42 weeks after the randomization. For each patient, a mean utility value was calculated before and after the first instance of metastatic disease progression. Then, the mean utility value was calculated by treatment arm, before progression. The mean utility value after first progression was calculated using all the questionnaires completed by the patients who experienced a progression, regardless of treatment arm. It was therefore assumed that the quality of life after the first instance of disease progression would not differ between the two treatment arms. This assumption was based on the observed individual patient data of the E-DIS trial and on clinical experts' opinion. To obtain QALYs, these utility values were applied to the mean duration in each health state and distinguishing between the two arms. The calculation of the mean utility value by health state implied that missing utility values were implicitly imputed by the mean value stratified on the health state.

Costs

Medical costs were assessed from the perspective of the French national health insurance. Healthcare resource use was prospectively collected every 6 weeks. Health resources included all hospitalizations (in-patient and day admissions), chemotherapy sessions, hospitalizations at home, radiation therapy, out-patient visits, and imaging procedures. All the costs before and after progression were included in both arms. Unit costs (Table 1) were extracted from activity-based payment tariffs for hospitals, common classification for

medical procedures, and the list of professional fees from the French national health insurance. Costs are expressed in 2018 Euros.

Cost-utility analysis

For the cost utility analysis, the CT-CONT arm was compared to the CT-DISC arm. Due to the short time horizon, neither costs nor QALYs were discounted in the base case analysis. To take into account uncertainty, a bootstrap procedure was used with 1,000 replicates, resampled from the original dataset. The 95% confidence intervals (95% CIs) for the difference in QALYs and in cost per patient were computed from the 1,000 replicates using the percentile method. Since we expected a small difference in QALYs, we used the net monetary benefit framework [15] as a primary measure. This framework allows to overcome the limitations of the incremental cost-effectiveness ratio (ICER) [16]. The ICER was also reported as a secondary measure because it is the most common measure to report cost-effectiveness results. The Incremental Net Monetary Benefit (INMB) between the CT-CONT and CT-DISC arms was calculated:

$$INMB = \lambda \cdot \Delta QALYs - \Delta C,$$

where $\Delta QALYs$ and ΔC are the incremental QALYs and cost between the two treatment arms, respectively, and λ is the willingness-to-pay for an additional QALY. A positive INMB means that CT-CONT in progressive-free patients after 6 weeks of chemotherapy is cost-effective, as compared to CT-DISC. The ICER was estimated as the ratio of the difference in costs and the difference in QALYs between the two strategies. The ICER has to be compared to the willingness to pay for an additional QALY. The cost-effectiveness probability was calculated as the empirical proportion of the 1,000 replicates with a positive INMB. The acceptability curve representing the cost-effectiveness probability at different willingness-to-pay thresholds was plotted. A one-way sensitivity analysis was conducted to assess the

impact of the key parameters on the results. A specific sensitivity analysis was performed on the cost of chemotherapy. Moreover, a sensitivity analysis was conducted to adjust for the difference, even if not statistically significant, in utility value at baseline between the two treatment arms.

This study complies with the good research practices for cost-effectiveness analysis alongside clinical trials [16]. The checklist items from the Consolidated Health Economic Evaluation Reporting Standards [17] (CHEERS) were used to report this study.

RESULTS

Included patients

Median age was 64.5 and 63 in the CT-CONT and in the CT-DISC arm, respectively. The proportion of male was 74% and 88% in the CT-CONT and in the CT-DISC arm, respectively. The estimated 9-month survival rate was 50% (85% CI: 37-62%) and 48% (85% CI: 35-60%) in the CT-CONT and the CT-DISC groups, respectively. The median OS rate was 8.5 months (95% CI: 6.6 to 12 months) and 8.8 months (95% CI: 5.9 to 13.4 months) and the median PFS was 4 months (95% CI: 2.8 to 5.8 months) and 1.4 months (95% CI: 1.4 to 2.7 months) for CT-CONT and CT-DISC, respectively.

Health-related quality of life (EQ-5D-3L questionnaire)

The proportion of missing EQ-5D-3L questionnaires was relatively high, from 9% (6/67) at randomisation to 70% (19/27) at the last follow-up visit (supplementary Table 1). The main reason for a missing questionnaire was an omission of the healthcare team (53%).

The proportion of respondents reporting severe problems on the EQ-5D-3L questionnaire was higher for the dimensions pain/discomfort (up to 21.4%) and anxiety/depression (up to

14.3%), as compared to the other dimensions (supplementary Table 2 and supplementary Figure 1).

Healthcare resource use and costs

Healthcare resource use was missing for 3 patients (1 patient in the CT-CONT arm and 2 patients in the CT-DISC arm). Mean costs were subsequently calculated based on 64 patients and imputed by the mean for 3 patients. Healthcare resource use was collected for five cost items, corresponding to the perspective of this cost-utility analysis (Table 2).

First, from the time of randomisation to the end of the study, 584 hospitalizations were recorded (366, CT-CONT arm; 218, CT-DISC arm), with 76% due to chemotherapy administration (78%, CT-CONT arm; 72%, CT-DISC arm). More chemotherapy sessions were administered in patients in the CT-CONT arm (284 sessions, corresponding to an average of 8.6 sessions per patient) compared to patients in the CT-DISC arm (157 sessions, corresponding to an average of 5.1 sessions per patient). The number of hospitalizations at home was similar between the two arms. The reasons for hospitalization at home were parenteral nutrition (3 hospitalizations), heavy nursing care (2 hospitalizations), and palliative care (1 hospitalization). A large majority of outpatient visits were with a medical oncologist (326, CT-CONT arm, representing 78% of the total number of visits; 211, CT-DISC arm, representing 71% of the total number of visits).

The main cost driver was hospitalization (supplementary Table 3). Mean cost per patient over an 18-month time horizon was higher in the CT-CONT arm (€11,858) compared to the CT-DISC arm (€10,682). The cost difference amounted to €1,177 [95% CI: -4,249; 6,298].

Cost-utility analysis

The cost-utility results are shown in Table 3. CT-CONT increased the time before progression or death from 4.77 to 7.18 months. However, OS appeared similar in both treatment arms. The mean utility value before the first instance of disease progression was lower in the CT-CONT arm, as compared to the CT-DISC arm (0.75 [95% CI: 0.67; 0.82] versus 0.83 [95% CI: 0.77; 0.88]), but the confidence intervals for both arms overlapped. On average, CT-CONT slightly decreased the number of QALYs (-0.038) and increased the cost per patient (€1,177). At a willingness-to-pay threshold of €50,000/QALY (quality-adjusted life years), the INMB was negative (- €3,077 [95% CI: -6,564; 4,359]), meaning that CT-CONT was not cost-effective when compared to CT-DISC. The incremental cost-effectiveness ration (ICER) was -30,958€/QALY (CT-CONT dominated).

The cost-utility plane and the acceptability curve are shown in Figure 1. The probability that CT-CONT was less effective and more costly than CT-DISC was 48% (proportion of points in the North-West quadrant of the cost-utility plane). At a willingness to pay for a QALY of €50,000 and €100,000, the probability of CT-CONT being cost-effective compared to CT-DISC was 29% and 32%, respectively. In the one-way sensitivity analysis, the utility value after progression in the CT-CONT arm was the parameter with the biggest impact on the ICER (Figure 2). The CT-CONT strategy was still dominated when varying the parameters, except when the utility value before progression for CT-CONT was increased (ICER of 171,886€/QALY). In the sensitivity analysis of the cost of a chemotherapy session, the higher the cost of chemotherapy, the lower the probability of CT-CONT being cost-effective when compared to CT-DISC (Table 4). In the sensitivity analysis adjusting for the difference in utility value at baseline, the difference in terms of QALYs was still in favor of CT-DISC but was reduced (-0.014 QALYs compared to -0.038 QALYs), and the corresponding ICER was -84,071€/QALY (CT-CONT still dominated).

DISCUSSION

To our knowledge, the assessment of medical costs and the cost-utility analysis that were conducted in this work were the first to be done within a prospective randomised study of first-line treatment in the mESCC setting. Not surprisingly, CT-CONT was associated with extra costs in chemotherapy administration, as compared to CT-DISC, even though most patients in the CT-DISC arm resumed chemotherapy after having disease progression. We showed that CT-CONT seems to delay the time to disease progression, but it does not increase the mean number of QALYs due to the disutility associated with this treatment. The results suggest that chemotherapy does not affect the utility similarly before and after progression. A possible explanation is that a treatment with chemotherapy before progression impacts more the utility compared to after progression, because the quality of life is better before progression. The INMB at a willingness-to-pay threshold of €50,000/QALY was negative, meaning that CT-CONT is not cost-effective when compared to CT-DISC. However, the uncertainty of the results was high, mainly due to the low number of patients.

Our study had both strengths and limitations. The major strengths of this work relate to the design of the economic evaluation alongside a randomised clinical trial using patient level data for efficacy, healthcare resource use, quality-of-life assessment, and utility values. This design avoids most selection bias and ensures homogeneity of the data collected alongside the clinical trial when comparing the use of different sources for the costs and the utility values. Moreover, in our study, we adopted the method of partitioned survival analysis, which is an appropriate and common method in oncology. Compared to an approach using directly the individual longitudinal EQ-5D data to estimate the QALYs, this method allowed us to use data on survival outcomes from all study patients, including those patients with missing quality-of-life questionnaires. We faced many challenges collecting the quality-of-

life questionnaires, especially after the first instance of disease progression. However, the rate of missing data was similar in both treatment arms. Further limitations in this study are related to the EQ-5D-3L questionnaire, which was shown to be relatively insensitive to changes in the health status of cancer patients [18]. This generic questionnaire may not fully capture quality-of-life impairment due to chemotherapy, especially in situations where the degree of vitality matters. This may explain why the improvement in time until a definitive deterioration in some specific symptoms of the QLQ-C30 questionnaire is not captured by the EQ-5D-3L questionnaire. Therefore, our study may underestimate the difference in QALYs. However, as patients received chemotherapy after the first instance of disease progression in the CT-DISC arm, the period of discontinuation was indeed quite short, and the impact on the quality of life was limited. Lastly, the small sample size of the E-DIS trial was also a limitation in our study. However, the bootstrap approach enabled to take uncertainty into account in this analysis.

Our economic evaluation provides valuable data in first-line mESCC, where economic data are scarce. These data could be reused in future cost-effectiveness studies. Few recent economic studies have been performed in this type of patient population. A cost analysis has been conducted based on a prospective population cohort of 1,100 Australian patients with a primary diagnosis of oesophageal cancer, where a quarter of the patients had metastatic cancer and 28% had SCC [15]. The authors concluded that the costs were dominated by chemotherapy-related expenses in patients treated without surgery. The mean total cost for metastatic cancer patients managed without surgery (including oesophageal adenocarcinoma, gastro-oesophageal junction adenocarcinoma, and SCC) was estimated to be €17,281 [15]. This cost per patient is higher than those estimated in our study (€11,858 in the CT-CONT arm and €10,682 in the CT-DISC arm). Indeed, in the E-DIS trial, healthcare resource use started at the date of randomisation, excluding costs incurred during the diagnosis phase and

the cost of chemotherapy during the selection phase (the E-DIS trial included patients with progression-free disease after 6 weeks of chemotherapy). A study assessed the cost-effectiveness of adding cetuximab to a palliative chemotherapy regimen in the Dutch healthcare setting [19]. This study was based on a phase II trial that included 62 patients with mESCC, randomly assigned to cetuximab, cisplatin, and fluorouracil or to cisplatin and fluorouracil regimens [20]. The addition of cetuximab was not found to be cost-effective. Unfortunately, neither quality-of-life, nor healthcare resource use, was collected in this trial. A median OS of 5.5 months was reported. In the E-DIS trial, median OS was higher, amounting to 9.9 months because patients were randomized after a selection phase during which they received 6 weeks of chemotherapy. Only responding patients were enrolled in the E-DIS trial. This study used utility values from a different patient population (symptomatic adenocarcinoma of the oesophagus) [21, 22] because no data were available in mESCC. This study is the only previous economic evaluation assessing palliative chemotherapy in mESCC [23]. Few other economic evaluations were conducted in oesophageal cancer in different settings (patients eligible for surgery and/or patients with adenocarcinoma) [23].

Treatment options in patients with mESCC are limited to chemotherapy and best supportive care. Literature on the efficacy of systemic treatment in patients with mESCC is scarce [9]. Guidelines from the European Society for Medical Oncology state that chemotherapy is less effective for ESCC than for adenocarcinoma [24]. Best supportive care or palliative monotherapy is recommended as a possible option [24]. All these treatment options were combined in the E-DIS trial either in the experimental arm (continuing palliative chemotherapy after 6 weeks in non-progressive patients) or in the control arm (interrupting chemotherapy). Patients in the E-DIS trial could be offered radiation therapy and supportive care. Most of the patients (72.7%) received subsequent chemotherapy after progression. Our economic evaluation failed to demonstrate a gain in QALYs with CT-CONT compared to

CT-DISC. Therefore, the consequence of pursuing chemotherapy might be to add unnecessary costs for the healthcare system without a clear evidence of benefits for the patients since chemotherapy is associated with adverse effects. However, our study relies on data gathered on 64 patients only and there was a substantial uncertainty. Our results need to be confirmed in further studies including prospective data collection. However, randomized controlled trials comparing chemotherapy versus best supportive care in first-line setting are difficult to conduct because patients and physicians are reluctant to randomisation [9, 25].

In conclusion, based on this cost-utility analysis, CT-DISC may be considered as an alternative therapeutic option to CT-CONT in mESCC patients who have stable disease after an initial chemotherapy treatment phase.

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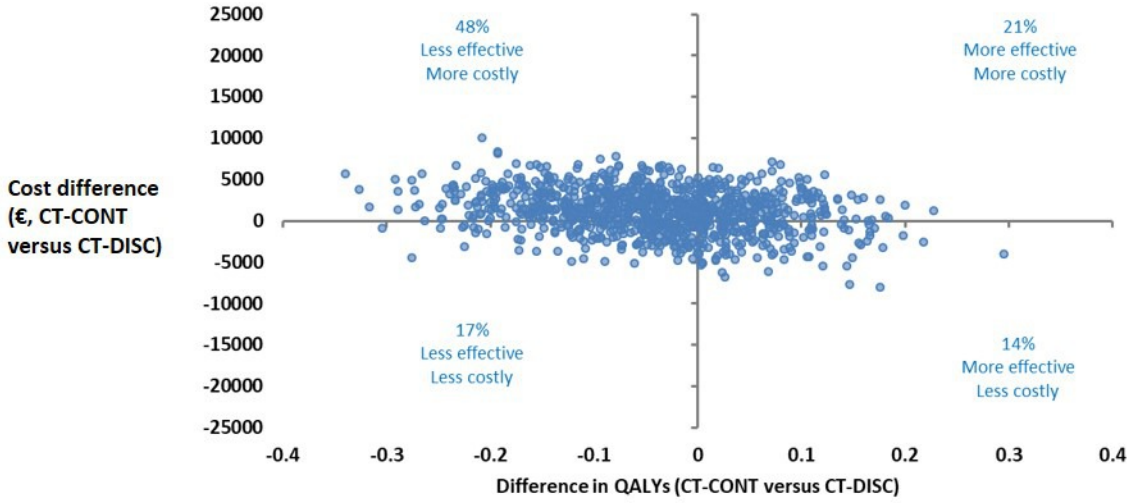
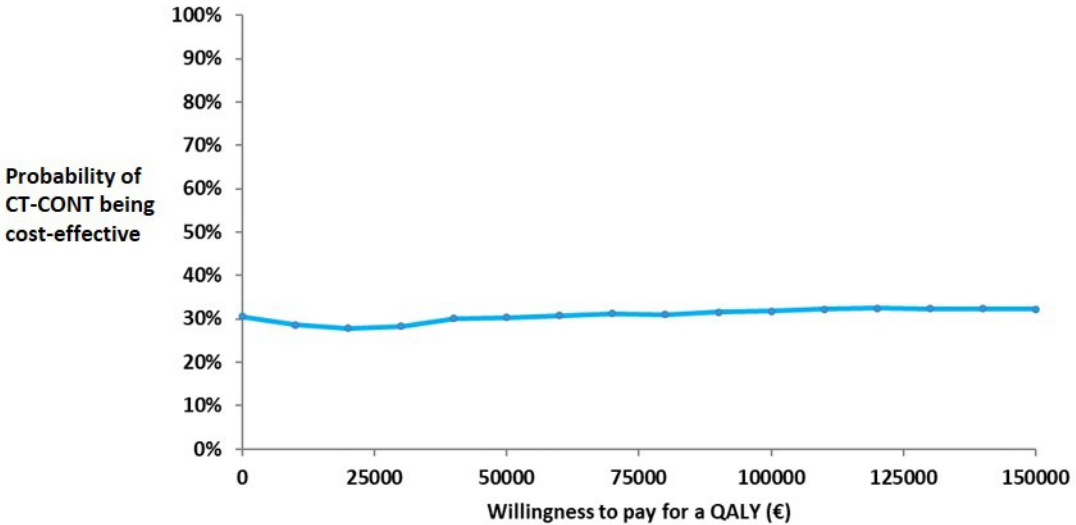

Cost difference (€, CT-CONT versus CT-DISC)
25000
20000
15000
10000
5000
0
-5000
-10000
-15000
-20000
-25000
48%
Less effective
More costly
21%
More effective
More costly
17%
Less effective
Less costly
14%
More effective
Less costly
-0.4
-0.3
-0.2
-0.1
0
0.1
0.2
0.3
0.4
Difference in QALYs (CT-CONT versus CT-DISC)


Probability of CT-CONT being cost-effective
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
25000
50000
75000
100000
125000
150000
Willingness to pay for a QALY (€)

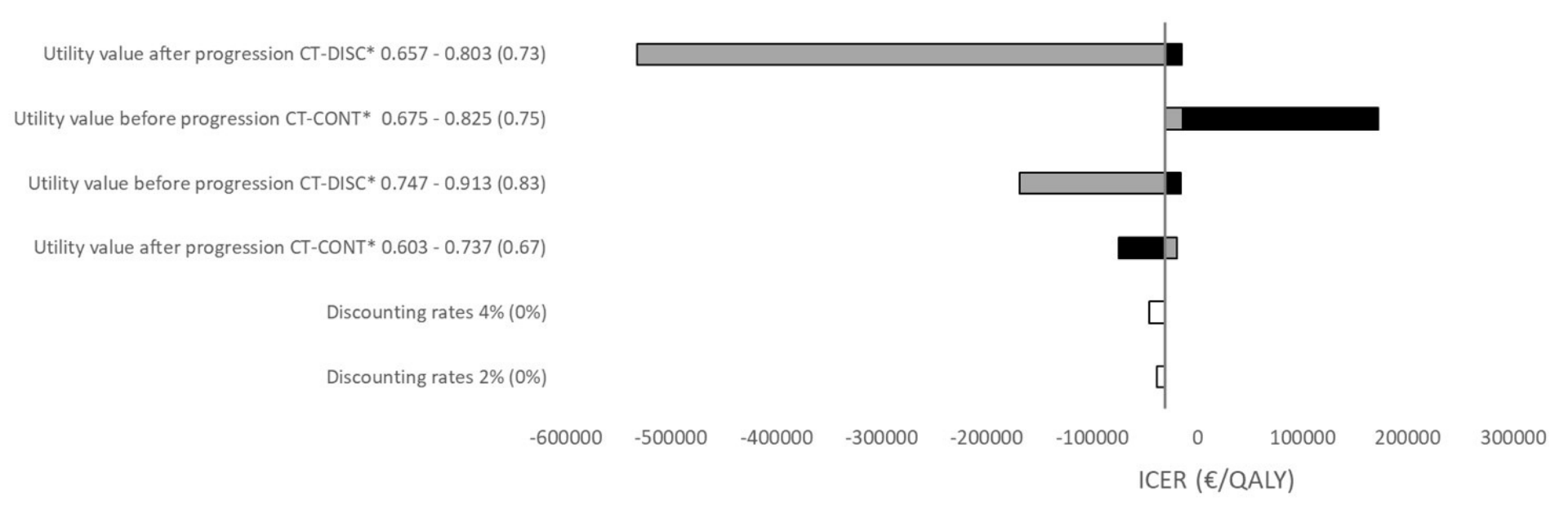

Utility value after progression CT-DISC* 0.657 - 0.803 (0.73)
Utility value before progression CT-CONT* 0.675 - 0.825 (0.75)
Utility value before progression CT-DISC* 0.747 - 0.913 (0.83)
Utility value after progression CT-CONT* 0.603 - 0.737 (0.67)
Discounting rates 4% (0%)
Discounting rates 2% (0%)
-600000
-500000
-400000
-300000
-200000
-100000
0
100000
200000
300000
ICER (€/QALY)

Table 1. Unit cost data

	Unit cost (in €)
Hospitalizations*	
Chemotherapy session	407
Hospitalizations at home (daily tariff)	
Parenteral nutrition	71
Palliative care	104
Heavy nursing care	267
Radiation therapy	
3-dimensional, initial set-up	991
3-dimensional, radiation session	170
2-dimensional, initial set-up	347
2-dimensional, radiation session	83
Outpatient visits	
General practitioner	22
Specialist practitioner	27
Imaging procedures†	
Technological fixed price for a computed tomography scan	42
Chest and abdomen computed tomography scan	25
Abdomen and pelvis computed tomography scan	51
Chest, abdomen and pelvis computed tomography scan	51
Chest x-ray	21

*Only the Diagnosis-Related Group (DRG) price per session of chemotherapy is listed in the table as it represented 76% of all hospitalizations. However, all hospitalizations are included in the analysis.

†Only the most performed imaging procedures are listed

Table 2. Healthcare resource use

	CT-CONT arm N=33*	CT-DISC arm N=31*
Hospitalizations		
Total number of chemotherapy sessions	284	157
Total number of other hospitalizations	82	61
Number of patients who were treated by chemotherapy	32	24
Number of patients hospitalized for other causes	23	22
Hospitalizations at home		
Total number of hospitalizations at home	3	3
Number of patients hospitalized at home	3	3
Radiation therapy		
Total number of patients who received radiation therapy	3	2
Outpatient visits		
Total number of outpatient visits	77	74
Number of patients who had at least one visit	32	31
Imaging procedures		
Total number of imaging procedures	77	68
Number of patients who had at least one imaging procedure	33	31

CT-CONT: chemotherapy continuation; CT-DISC: chemotherapy discontinuation

* Healthcare resource use was missing for 3 patients (1 in arm CT-CONT and 2 in arm CT-DISC) and was then collected for 33 patients in arm CT-CONT and 31 patients in arm CT-DISC

Table 3. Cost-utility analysis results

	CT-CONT arm	**CT-DISC arm**	**Difference CT-CONT versus CT-DISC** [95%CI]
Mean survival time without progression or death (Months)	7.18	4.77	2.40 [0.24 ; 4.36]
Mean survival time (Months)	11.14	11.05	0.09 [-2.53 ; 2.43]
Mean utility value before first progression	0.75	0.83	-0.07 [-0.17 ; 0.02]
Mean utility value after first progression	0.67	0.73	-0.06 [-0.20 ; 0.09]
Mean QALYs	0.670	0.708	-0.038 [-0.23 ; 0.15]
Mean Costs, €	11,858	10,682	1,177 [-4,249 ; 6,298]
INMB, € (€50,000/QALY), [95%CI]	-3,077 [-6,564 ; 4,359]		
Cost-utility probability (€50,000/QALY)	29%		
ICER	-30,958€/QALY (CT-CONT dominated)		

CT-CONT: chemotherapy continuation; CT-DISC: chemotherapy discontinuation; CI: Confidence Interval; INMB: Incremental net monetary benefit; QALY: Quality-adjusted life years

NA: not apply (same value in both arms)

Table 4. Sensitivity analysis on the cost of a chemotherapy session

Unit cost	**€1,000**	**€2,000**	**€3,000**
INMB, € (€50,000/QALY), [95%CI]	-3,435 [-9,170 ; 2,430]	-6,977 [-13,770 ; 76]	-10,518 [-19,232 ; -1,936]
Cost-utility probability (€50,000/QALY)	12.5%	2.7%	0.8%

CI: Confidence Interval; INMB: Incremental net monetary benefit; QALY: Quality-adjusted life years