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PRELIMINARY COMMUNICATION

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Cost-effectiveness of cetuximab-containing regimens for squamous cell carcinoma of the head and neck in Italy

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ABSTRACT

Aims: To investigate the differences in clinical outcomes and costs for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN) with a combined positive score (CPS) of 1–19, with pembrolizumab ± chemotherapy or a cetuximab-containing regimen (CCR) in Italy.
Methods: A naïve indirect treatment comparison was conducted, and outcomes were incorporated into a newly developed cost-utility model. Inputs were derived from clinical trials, technology appraisal reports, and published literature. Scenario analyses were undertaken to explore key areas of uncertainty.
Results: Across the comparisons of pembrolizumab ± chemotherapy versus CCRs, incremental life-years ranged from – 0.502 to 0.155, while incremental quality-adjusted life years (QALYs) ranged from – 0.379 to 0.085. In some scenarios, CCRs dominated pembrolizumab ± chemotherapy (i.e. more QALYs at lower costs). In others, CCRs yielded similar estimates of QALYs at lower costs.
Conclusion: CCRs are likely to represent a comparable or more effective treatment option compared to pembrolizumab ± chemotherapy. Model results consistently demonstrated that CCRs are a cost-effective treatment strategy. CCRs remain a relevant treatment option for R/M SCCHN and a CPS of 1–19, for whom a targeted, patient-focused approach is warranted.

PLAIN LANGUAGE SUMMARY

This study looked at different treatment options for people in Italy with a specific type of head and neck cancer called recurrent and/or metastatic squamous cell carcinoma (R/M SCCHN). We focused on a group of people with a combined positive score (CPS) between 1 and 19. CPS is a measure related to how likely a person is to respond to immunotherapy. There is limited information concerning the costs and health outcomes for different treatment options specifically in the R/M SCCHN CPS 1–19 population.

We compared two types of immunotherapy treatment: pembrolizumab (with or without chemotherapy), and treatment regimens that include a drug called cetuximab (referred to as cetuximab-containing regimens, or CCRs). Instead of a head-to-head clinical trial, we used existing published data and built a health economic model to estimate the health benefits and costs of each approach. We also tested different scenarios to explore how certain assumptions might affect the results.

The findings showed that, in some cases, CCRs gave patients better health outcomes at a lower cost compared to pembrolizumab (with or without chemotherapy). In other cases, the health outcome results were similar, but the CCRs still cost less. Overall, our study suggests that CCRs are likely to be a cost-effective option for people in Italy with this type of cancer, supporting their continued use in clinical practice.

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KEYWORDS
Head and neck cancer; cost-effectiveness analysis; cetuximab

1. Introduction

Squamous cell carcinoma of the head and neck (SCCHN) is derived from the mucosal epithelium in the oral cavity, pharynx, and larynx [1]. SCCHN is the seventh most common cancer globally, with an estimated 890,000 new cases and 450,000 deaths per year, accounting for approximately 4.5% and 4.6% of global cancer diagnoses and deaths, respectively [2]. In addition to impacting survival, the consequences of SCCHN and its treatments have a large influence on patients' quality of life in general, in particular, health-related quality of life (HRQoL).

About 50% of patients with localized disease will develop recurrent and/or metastatic (R/M) SCCHN, either following

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Article highlights

- Cetuximab-containing regimens (CCRs) have been used for the treatment of people with R/M SCCHN for over a decade.
- More recently, pembrolizumab was recommended in this patient population, either as monotherapy or in combination with chemotherapy.
- For people with a combined positive score (CPS) of 1–19, it is unclear whether a CCR or pembrolizumab ± chemotherapy represents the most clinically-effective or cost-effective treatment option.
- An indirect treatment comparison was performed, alongside a cost-utility analysis, with the primary outcome being the cost per quality-adjusted life-year (QALY) gained.
- Estimates of clinical effectiveness were similar for all treatments compared, depending on the sources of data used for CCRs.
- CCRs were consistently shown to be cost-effective, either by providing more or similar QALYs at lower costs.
- CCRs therefore remain a relevant treatment option for R/M SCCHN with a CPS of 1–19, for whom a targeted, patient-focused approach is warranted.

diagnosis with metastatic disease or after experiencing local recurrence after initial treatment [3]. R/M SCCHN is a difficult "systemic" disease to treat, with poor prognosis, which is why "recurrent" and "metastatic" SCCHN are grouped in the same (poor) prognostic category [3]. Treatment options for patients with R/M SCCHN, for which local therapies are not amendable, include cytotoxic chemotherapy, targeted therapy (such as epidermal growth factor receptor [EGFR] inhibitors), and immunotherapy (immune checkpoint inhibitors).

Cetuximab is an EGFR inhibitor approved for the treatment of patients with R/M SCCHN in combination with platinum-based chemotherapy, as well as monotherapy [4]. The cetuximab-containing regimen (henceforth referred to as "CCR") initially approved in 2008 to treat patients with R/M SCCHN was the "EXTREME" regimen [5]. This regimen includes 5-fluorouracil (5FU), cisplatin/carboplatin, and cetuximab, followed by a cetuximab maintenance therapy, and has been used in several studies. The first-line treatment with the EXTREME regimen has been the standard of care in the European Medicines Agency (EMA) region, specifically in Italy, since 2010.

Other than the EXTREME regimen, an alternative CCR has gained increasing use internationally, known as the TPEx regimen, where 5FU is substituted with docetaxel, which has been shown to reduce 5FU-related toxicity while maintaining efficacy in tumor response. The TPEx regimen was investigated in phase II trials, including the GORTEC 2008–03 single-arm study and the randomized TPEXTREME trial [6,7].

More recently, pembrolizumab received EMA approval as monotherapy or in combination with platinum/5FU-based chemotherapy based on the KEYNOTE-048 (KN-048) trial, as a first-line treatment for R/M SCCHN in patients whose tumors express programmed cell death-ligand 1 (PD-L1) with a combined positive score (CPS) ≥1 [8]. Initial results from the KN-048 trial demonstrated increased median overall survival (OS) for pembrolizumab ± chemotherapy compared to the EXTREME regimen across several subgroups. However, the results for the EXTREME arm were notably different from those in earlier trials, including TPEXTREME, as well as more contemporary trials such as CHECKMATE-651 (CM-651). Additionally, no data are currently available on the direct comparison of pembrolizumab ± chemotherapy and the TPEx regimen.

Furthermore, larger effect sizes for programmed cell death-protein 1 (PD-1) inhibiting approaches have been observed in populations with higher CPS in the KN-048 trial. For example, the hazard ratios and corresponding 95% confidence intervals (CIs) for OS with pembrolizumab + chemotherapy compared to the EXTREME regimen across CPS subgroup were: CPS < 1, 1.21 (0.76, 1.94); CPS 1–19, 0.71 (0.54, 0.94); CPS ≥ 20, 0.60 (0.45, 0.82) [9]. Consequently, there remains uncertainty regarding the most clinically effective regimen (pembrolizumab ± chemotherapy or a CCR) for patients with a CPS of 1–19. It is important to note that this subgroup analysis of the KN-048 trial was *post-hoc*, involved a relatively small sample size, and did not account for differences in potentially important baseline patient characteristics. Moreover, owing to the differences in costs, it is unclear which regimen is likely to represent the most cost-effective option for patients with CPS 1–19.

The assessment of relative costs and outcomes between existing treatment options using economic models (i.e., cost-effectiveness analyses) plays a pivotal role in informing healthcare reimbursement decisions across several jurisdictions. The purpose of this study was to investigate the differences in outcomes and costs for the first time in patients with R/M SCCHN and a CPS of 1–19, treated in the first line with either pembrolizumab ± chemotherapy or a CCR, such as EXTREME or TPEx, from the perspective of the Italian National Health Service.

2. Methods

A naïve indirect treatment comparison using extrapolated progression-free survival (PFS) and OS data from identified prospective trials, followed by a cost-utility analysis, was performed. The primary outcomes of interest were differences in estimated life-years (LYs), quality-adjusted life years (QALYs), direct healthcare costs, and the incremental cost-effectiveness ratio (ICER, or cost per QALY gained) of pembrolizumab ± chemotherapy versus CCRs (EXTREME and TPEx).

The eligible patient population included people with untreated R/M SCCHN, who were suitable for treatment with platinum-based chemotherapy (i.e., Eastern Cooperative Oncology Group [ECOG] Performance Status of 0 or 1). Registered Phase II and III clinical trials of CCRs for the treatment of R/M SCCHN were eligible for data extraction. In addition to KN-048, four trials were identified through a targeted literature search: EXTREME, TPEXTREME, CM-651, and GORTEC 2008–03 [5–7,10]. Full details of the search strategy and the reasons for including each study are provided in the Supplementary Appendix. Studies were primarily selected to capture a range of survival estimates for CCRs, ensuring a representative set of outcomes was incorporated into the model.

Although the CM-651 trial reported outcome data for CPS subgroups, no specific data were available for the CPS 1–19 subgroup [10]. Similarly, the other three trials did not report data across CPS subgroups, as CPS was not considered

Table 1. Clinical trials informing the model and survival landmarks.

Trial	Arm	n	Median PFS (95% CI), months	Median OS (95% CI), months	12-month OS (%)‡	24-month OS (%)‡
KEYNOTE-048 [8,9]	P	124	2.2 (2.1 to 2.9)	10.8 (9.0 to 12.6)	44.0%	22.0%
(CPS 1–19)	P+CT	116	4.7 (3.4 to 6.2)	12.7 (9.4 to 15.3)	52.6%	26.3%
	EXTREME	133	4.9 (3.8 to 6.0)*	10.1 (8.7 to 12.1)*	38.6–	14.9–
		125	6.2 (5.0 to 7.3)†	9.9 (8.6 to 11.5)†	41.4%	16.7%
EXTREME [5]	EXTREME	222	5.6 (5.0–6.0)	10.1 (8.6–11.2)	39%	17%
TPEXTREME [7]	EXTREME	270	6.2 (5.8–6.7)	13.4 (12.2–15.4)	56%	24%
	TPEx	269	6.0 (5.7–6.4)	14.5 (12.5–15.7)	59%	30%
GORTEC 2008–03 [6]	TPEx	54	6.2 (5.4–7.2)	14.0 (11.3–17.0)	61%	20%
CHECKMATE-651 [10]	EXTREME	475	6.7 (5.8–7.0)	13.5 (12.6–15.2)	56%	30%

CI, confidence interval; CPS, combined positive score; CT, chemotherapy; ITT, intention to treat; OS, overall survival; P, pembrolizumab; PFS, progression-free survival. *comparison with P; †comparison with P+CT; ‡where not explicitly reported, values were obtained from digitized Kaplan-Meier estimates.

a relevant variable for subgroup analysis prior to the introduction of immunotherapy for SCCHN, especially in CCR-based regimens [5–7]. A summary of the treatment arms and corresponding survival landmarks (median PFS and OS, 12-month OS, and 24-month OS) from each of the included trials is provided in Table 1.

Median PFS and OS data from each trial were used to estimate survival extrapolations based on fitted standard parametric models, which ultimately represent the area under the entire survival curve, rather than estimates restricted to the observed period of trial follow-up, as provided by the Kaplan-Meier estimate [11]. Specific parametric models were selected based on visual inspection of the Kaplan-Meier estimates, goodness-of-fit statistics (Akaike Information Criterion [AIC] and Bayesian Information Criterion [BIC]), and the long-term plausibility of each extrapolation. Background mortality was incorporated within the final survival extrapolations to ensure that the survival estimates were plausible and did not exceed those of the age- and sex-adjusted general population.

In the base-case analysis, the TPEXTREME trial was chosen to inform the efficacy of both CCRs, as it is the only trial that provided results for both CCRs (EXTREME and TPEx). Further details on the survival analyses are provided in the Supplementary Appendix. Therefore, in our analysis, we explicitly considered the variation in PFS and OS between the different studies reporting outcomes for patients with R/M SCCHN treated with a CCR. This allowed for an investigation into the external validity of single-study based estimates of outcomes for decision-making. Following the generation of the survival extrapolations, a three-state partitioned survival analysis (PartSA) model was constructed to assess the cost-effectiveness of pembrolizumab ± chemotherapy versus CCRs (Figure 1).

The PartSA model structure has been widely used in economic evaluations of cancer drugs [12], and includes three health states: progression-free disease, progressed disease, and death. Transitions between the health states were not explicitly modeled using transition probabilities, but instead were inferred by calculating the area under the extrapolated PFS and OS curves.

The analysis was conducted from the perspective of the Italian National Health Service, considering direct payer costs and direct health effects for patients. A lifetime horizon of up to 40 years was used, with a cycle length of one week. Costs

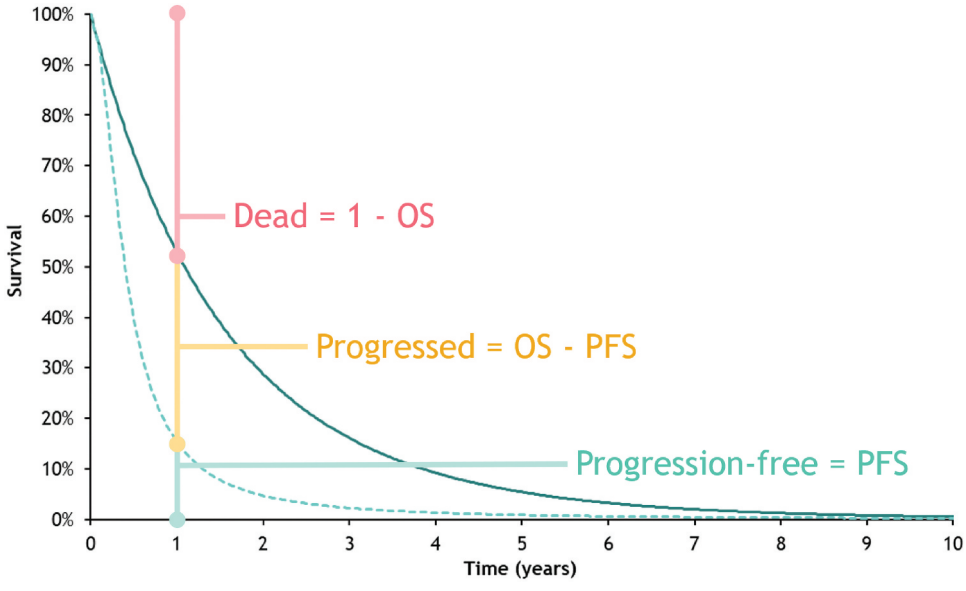


Figure 1. Model diagram.
OS, overall survival; PFS, progression-free survival.

and QALYs were discounted at 3% per annum, in accordance with Italian guidelines [13]. The willingness-to-pay threshold (λ) of €30,000 per QALY gained was applied, based on convention in Italian Health Technology Assessment which typically adopts a value of λ between €30,000 and €50,000. However, Russo et al. (2023) recently reported an average λ value of approximately €33,004, which may serve as a benchmark in Italy [14].

In addition to survival estimates, the model also required inputs related to HRQoL, dosing, and costs. Full details of the inputs used for the model are provided in the Supplementary Appendix.

For HRQoL, published utility values were sourced from the NICE appraisal for pembrolizumab in untreated R/M SCCHN (TA661) [15]. The utility values used in the model were 0.8192 and 0.7046, for the progression-free and progressed disease health states, respectively. Utility values were adjusted using general population norms for Italy to account for the natural decline in HRQoL associated with aging over time [16].

In accordance with the Italian National Health Service perspective, direct costs were captured within the model. The following cost categories were considered: treatment acquisition, administration, subsequent therapy, medical resource use, adverse event management, and end-of-life care. Unit costs were obtained from Italian databases, including Software Tunnel by Farmadati Italia (for list prices of pharmaceutical agents) and national tariffs (for medical resource use) [17]. Medical resource use frequencies were sourced from the NICE appraisal for pembrolizumab in untreated R/M SCCHN (TA661) [15].

For subsequent therapy, feedback was sought from two Italian clinical experts. The experts highlighted the availability of nivolumab as a second-line treatment option, which is expected to be the standard of care for patients progressing after CCR. For patients treated with pembrolizumab (either alone or in combination with chemotherapy), subsequent treatment options could include various regimens, such as CCRs, taxanes, or enrollment in a clinical trial. Given the lack of clear consensus on second-line treatment options, patients in the pembrolizumab ± chemotherapy were assumed to receive the corresponding selected comparator CCR (i.e., EXTREME or TPEx), while those in the CCR arm received subsequent nivolumab.

Based on the included survival estimates, and HRQoL and cost inputs, model results could be generated. Headline model results were total costs and QALYs, incremental costs and QALYs between treatment arms, and the ICER. Several sensitivity analyses were performed, including deterministic scenario analysis and probabilistic sensitivity analysis (PSA). Deterministic scenario analyses were conducted to test alternative model settings and assumptions, primarily focused on the use of different input data for the efficacy of CCRs. PSA was performed by randomly sampling inputs with associated uncertainty from a pre-specified probability distribution over 1,000 model iterations, to explore the impact of parameter uncertainty on the model results.

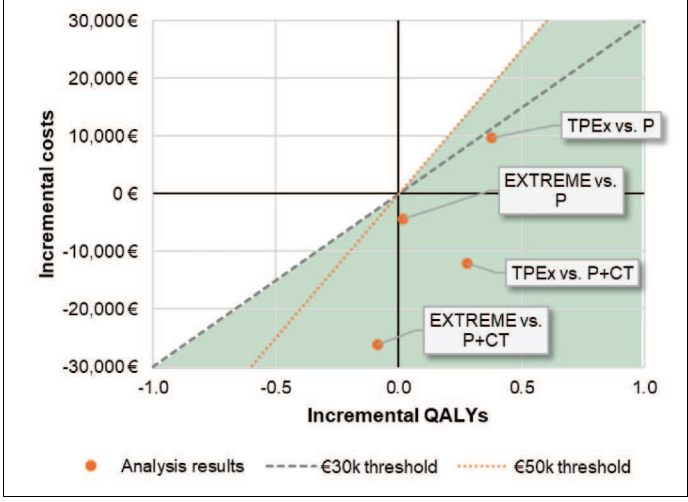
3. Results

The base-case results provided comparisons of pembrolizumab ± chemotherapy versus EXTREME and TPEx, using PFS and OS estimates for CCRs from the TPEXTREME trial, as

	EXTREME							
P+CT	Arm	Total			Incremental			
		Costs (€)	QALYs	LYs	Costs (€)	QALYs	LYs	ICER (€)
	EXTREME	85,315	1.122	1.518				
	P+CT	111,433	1.207	1.673	26,118	0.085	0.155	308,725
P	Arm	Total			Incremental			
		Costs (€)	QALYs	LYs	Costs (€)	QALYs	LYs	ICER (€)
	EXTREME	85,315	1.122	1.518				
	P+CT	89,599	1.105	1.579	4,284	-0.017	0.061	Dominated

TPEx							
Arm	Total			Incremental			
	Costs (€)	QALYs	LYs	Costs (€)	QALYs	LYs	ICER (€)
TPEx	106,773	1.483	2.081				
P+CT	118,813	1.207	1.673	12,040	-0.277	-0.409	Dominated
Arm	Total			Incremental			
	Costs (€)	QALYs	LYs	Costs (€)	QALYs	LYs	ICER (€)
TPEx	106,773	1.483	2.081				
P+CT	96,998	1.105	1.579	-9,775	-0.379	-0.502	25,822*

P±CT versus CCR†



CCR versus P±CT†

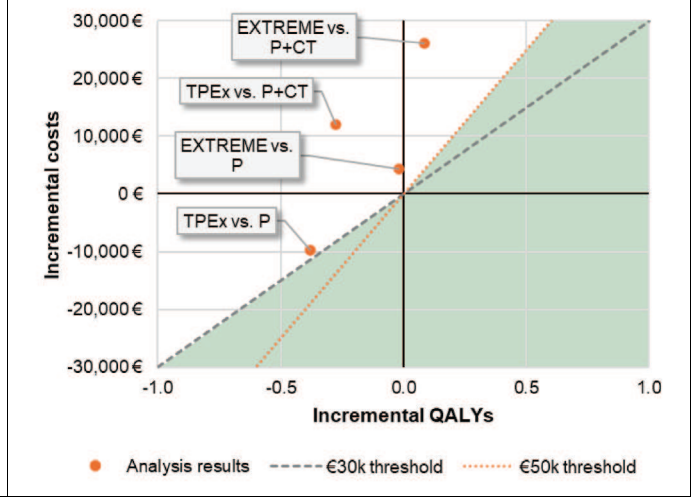


Figure 2. Full base-case results.

ICER, incremental cost-effectiveness ratio (cost per QALY gained); k, thousand(s); LY, life-year; P, pembrolizumab; P+CT, pembrolizumab + chemotherapy; QALY, quality-adjusted life year. *This ICER is TPEx versus P (i.e., P is associated with negative costs and negative QALYs); †Green shaded area shows where the intervention could be considered cost-effective (based on a conventional willingness-to-pay threshold of €30,000 to €50,000 per QALY gained). Results are presented with both P±CT and CCR as the intervention or comparator.

shown in Figure 2. Across the comparisons of pembrolizumab ± chemotherapy with CCRs, incremental LYs ranged from – 0.502 to 0.155, while incremental QALYs ranged from – 0.379 to 0.085.

In the comparisons of pembrolizumab + chemotherapy versus TPEx, and pembrolizumab versus EXTREME, CCRs dominated pembrolizumab ± chemotherapy, as they yield more QALYs at lower costs. The comparison of pembrolizumab versus TPEx showed an ICER of €25,822 per QALY gained, but this should be interpreted in reverse, as both costs and QALYs were negative (i.e., TPEx provided more QALYs with added costs). The comparison of pembrolizumab + chemotherapy versus EXTREME showed an ICER greater than €300,000 per QALY gained, making TPEx a cost-effective treatment option based on conventional willingness-to-pay thresholds.

Using the other external trials, the ICER for pembrolizumab + chemotherapy versus CCRs ranged from €132,408 to €437,920 per QALY gained, including one scenario where CCRs dominated pembrolizumab + chemotherapy (i.e., provided more QALYs at lower costs). Similarly, the ICER for pembrolizumab versus CCRs ranged from €14,193 to €38,447 per QALY gained, including one dominant result where CCRs provided more QALYs at lower costs versus pembrolizumab. Across all scenarios, CCRs remained a cost-effective treatment option based on conventional willingness-to-pay thresholds for Italy.

For simplicity, the PSA was focused on comparison between pembrolizumab + chemotherapy and CCRs. For the comparison of pembrolizumab + chemotherapy versus EXTREME, the majority of PSA iterations (Figure 3) clustered around the y-axis, suggesting that QALYs were similar for both treatment options. However, costs were nearly all greater than zero (99.8% of iterations), indicating that EXTREME was consistently less costly than pembrolizumab + chemotherapy. For the comparison of pembrolizumab + chemotherapy versus TPEx, most PSA iterations (Figure 3) clustered in the north-west quadrant (62.6% of iterations), indicating that CCRs dominate pembrolizumab + chemotherapy, providing more QALYs at a lower cost. The concentration of the scatterplot shows that, on average, the CCRs may provide more clinical benefit (i.e., QALYs) compared to pembrolizumab ± chemotherapy.

4. Discussion

Our analysis provides the first exploration of the cost-effectiveness of treatment options for patients with a CPS of 1–19, for whom there is currently limited evidence to guide decision-making. The results of the current analysis support the expectation of outcomes that are at least similar between pembrolizumab ± chemotherapy and the CCRs (i.e., EXTREME or TPEx) for patients with R/M SCCHN and a CPS of 1–19. Depending on the data used to inform the efficacy of CCRs, the QALY gain could plausibly favor either treatment arm. Additional findings from the authors' previous comparative effectiveness have been presented elsewhere [18,19]. However, across all scenarios, costs were either lower for CCRs or only slightly higher (with more QALYs), which supports the expectation that CCRs are likely to be considered a cost-effective treatment option for patients with a CPS of 1–19. Moreover, in several scenarios, the CCR was dominant over pembrolizumab, providing more QALYs at a lower cost.

Incorporating a broader patient cohort to inform the efficacy of CCRs provides more insights into the results of the *post-hoc* subgroup analysis from the KN-048 trial, allowing for an investigation into whether the KN-048 subgroup analysis, given its *post-hoc* design, reflects the expected effectiveness of CCRs. Our cost-effectiveness model provides alternative estimates that may be considered more realistic and have higher external validity.

The efficacy estimates in the identified external trials (e.g., TPEXTREME used in the base case) were not based on a strictly CPS 1–19 subgroup. Therefore, although CPS is not expected to influence outcomes in patients treated with CCRs, there remains a need to contextualize these findings with the results from the KN-048 trial. The use of external data for CCR efficacy relies on the notion that the within-trial comparison in the KN-048 subgroup analysis, specifically in the CPS 1–19 subgroup, has several drawbacks that may limit its external validity. This is challenging to substantiate due to the lack of outcomes data from trials other than the KN-048 trial for the CPS 1–19 subgroup. Additionally, as previously described, there are several limitations of the KN-048 *post-hoc* subgroup analysis, including the lack of a comparison to the TPEx regimen.

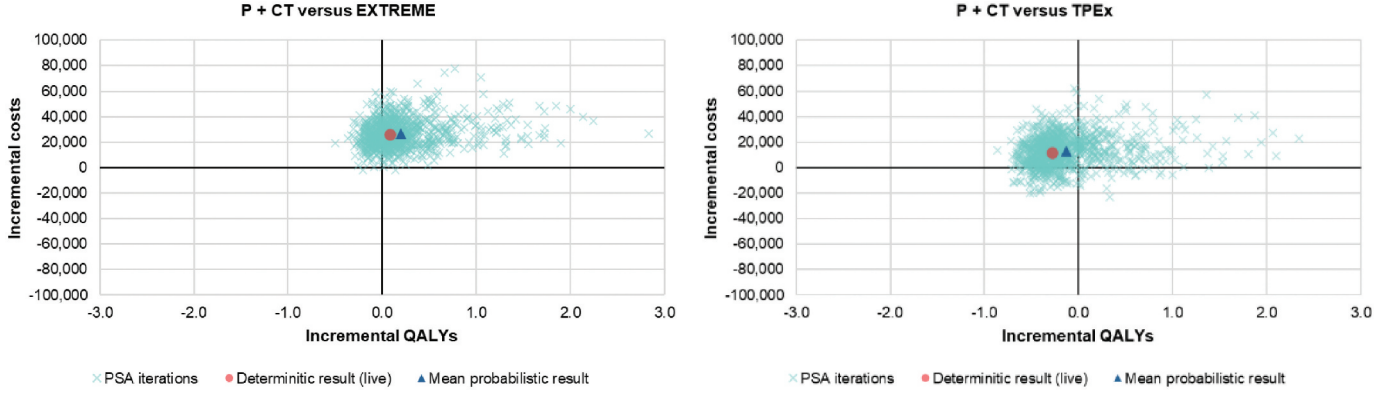


Figure 3. PSA scatterplot, P + CT versus EXTREME (left) and P + CT versus TPEx (right).

CT, chemotherapy; P, pembrolizumab; PSA, probabilistic sensitivity analysis; QALYs, quality-adjusted life years.

Our analysis focuses on a population for whom platinum-based chemotherapy is deemed suitable (based on the inclusion criteria of the trials eligible for this analysis, i.e., patients with an ECOG Performance Status of 0 or 1). Generalizations to the full population of R/M SCCHN patients should be made with this important distinction in mind. In addition, even within the CPS 1–19 subgroup, patient heterogeneity is expected to impact the potential benefits of any treatment strategy on an individual level. Further analyses of outcomes within the CPS 1–19 subgroups could yield differences based on a currently unpublished threshold.

Clinical outcome estimates generated by our model are dependent on the data source used to inform the efficacy of CCRs and are compared without any formal adjustment(s) to align the patient populations across trials, as the data were not publicly available. While the KN-048 trial provides a direct comparison of treatment options for patients with a CPS of 1–19, it was a *post-hoc* subgroup analysis that compared pembrolizumab ± chemotherapy only to the EXTREME regimen. Our analysis serves as an additional source of evidence for clinical decision-making, given the lack of robust evidence to conclusively determine the relative clinical and cost-effectiveness of pembrolizumab ± chemotherapy versus CCRs in patients with a CPS of 1–19.

As with all models, our model is not without limitations. A criticism of the PartSA model structure used in our analysis is that the disease course is simplified into two periods (pre- and post-progression), and that in reality there are changes in costs and HRQoL within each health state. Nevertheless, this structure was used in keeping with a large number of previous economic evaluations in R/M SCCHN, including the NICE assessment of pembrolizumab (TA661) [15]. In addition, the costs of subsequent therapies were captured using an assumption that patients would receive a single course of either nivolumab or a CCR (i.e., the treatment of a different class versus the first-line option). This choice was made due to a lack of robust data on subsequent therapy patterns in Italian National Health Service practice. In clinical practice, some patients may not receive a subsequent therapy, while others may receive multiple subsequent therapies. Therefore, although our approach to capturing the costs of subsequent therapy is simplified, it aims to represent the "average" use of subsequent therapy. However, the true costs of subsequent therapy could be higher or lower than the estimate reflected by our analysis.

5. Conclusion

In conclusion, based on our analysis, for patients with R/M SCCHN and CPS 1–19, CCRs are likely to represent a comparable or more effective treatment option compared to pembrolizumab ± chemotherapy. The cost-effectiveness results consistently demonstrate that CCRs are a cost-effective treatment strategy compared to pembrolizumab ± chemotherapy. Therefore, CCRs remain a relevant treatment option for managing patients with R/M SCCHN and a CPS of 1–19, for whom a targeted, patient-focused approach is warranted. Nevertheless, it should be noted that checkpoint inhibitors, although not frequently, are considered capable of altering the natural history of the disease in patients with R/M SCCHN. Further research is needed to conclusively determine the relative effectiveness of pembrolizumab ± chemotherapy versus CCRs in patients with a CPS of 1–19. As such, this analysis serves as an important source of evidence to inform decision-making in clinical practice.

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Author contributions

Conceptualization: Pescott
Methodology: Bullement, Naik, Gandola, Schlichting, Pescott
Software: Bullement, Naik, Gandola, Schlichting, Pescott
Writing – original draft: Bullement, Naik
Writing – review & editing: All authors
Data curation: Ivanyi, Botticelli, Perri, Annibali, Colombo
Investigation: Ivanyi, Botticelli, Perri, Annibali, Colombo
Resources: Ivanyi, Botticelli, Perri, Annibali, Colombo
Supervision: Pescott
Validation: Bullement, Naik, Gandola, Schlichting, Pescott

Disclosure statement

Philipp Ivanyi reports the following disclosures:

- Advisory Role or Expert Testimony: Bayer, Bristol Myers Squibb, Böhringer Ingelheim, ClinSol, Calliditas, Deciphera, EISAI, EMD-Serono, EUSA, Glaxo Smith Kline, H5-Oncology, Ipsen, Merck Serono (Global), Metaplan, MSD, Onkowissen, Pharma Mare, Pfizer, Roche
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Ethical disclosure statement

This study is a cost-effectiveness analysis based on data from published sources. No primary data collection involving human participants or animals were collected or analyzed. As such, ethical approval and informed consent were not required.

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Data availability statement

All data are either public domain, or have been included in the article or Supplementary Appendix.

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