Economic Evaluation of Tislelizumab for the Treatment of Second-Line Esophageal Squamous Cell Carcinoma: A Lifetime Partition Survival Model

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Conclusion

- **In this cost-effectiveness model, tislelizumab was a cost-effective treatment option for patients with previously treated esophageal squamous cell carcinoma (ESCC) at a willingness-to-pay (WTP) threshold of £30,000/quality adjusted life year (QALY) gained, when assuming price parity (acquisition cost per treatment cycle) with nivolumab**

Background

- ESCC is the most common subtype of esophageal cancer, which is the seventh highest cause of cancer-related death worldwide and is associated with poor prognosis (5-year survival is as low as 18% for disease stages I-IV).[1-3] A high proportion of patients with ESCC are diagnosed at an advanced stage of disease[3]
- In the first-line setting, advanced unresectable ESCC is typically treated with chemotherapy and immunotherapy (for patients who express high programmed cell death-ligand 1 [PD-L1] levels).[4] Patients who progress to second-line (2L) treatment typically receive further systemic chemotherapy or nivolumab[4,5]
- In the primary analysis of the RATIONALE-302 trial, the humanized immunoglobulin G4 anti-programmed death receptor-1 (PD-1) immune checkpoint inhibitor tislelizumab was associated with a statistically significant increase in overall survival (OS) versus investigator chosen chemotherapy (ICC) among patients with advanced unresectable or metastatic ESCC receiving 2L treatment (hazard ratio [HR]: 0.70 [95% confidence interval (CI), 0.57-0.85]; one-sided *P*=0.0001)[6]
- The objective of this analysis was to assess the cost-effectiveness of tislelizumab compared with nivolumab for the treatment of patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy, from a UK perspective

Methods

Model Structure

- A 3-state partitioned survival model was developed with health states defined as progression-free (PF), progressed disease (PD), and death. Time on treatment (ToT) was modelled separately from progression-free survival (PFS) to more accurately capture treatment duration and costs. An overview of the model is provided in **Table 1**

Model Inputs

- Health-state occupation for tislelizumab was based on extrapolations of OS and PFS from the RATIONALE-302 trial.[7] ToT for tislelizumab was also derived from RATIONALE-302.[7] Standard parametric and hazard spline extrapolations of OS, PFS, and ToT were derived in line with National Institute for Health and Care Excellence (NICE) guidance.[8] Base case extrapolation model choices were based on statistical fit, visual fit, and clinical plausibility (loglogistic, spline 2 hazard, and spline 3 hazard for OS, PFS, and ToT, respectively)
  - For nivolumab, health-state occupation was based on an indirect treatment comparison (ITC) of OS and PFS derived from the RATIONALE-302 and ATTRACTION-3 studies.[7,9] The ITC permitted assessment and adjustment for potential heterogeneity between the trials, facilitating a more accurate comparison between the 2 treatments
  - Nivolumab ToT was not explored in the ITC due to data limitations. It was considered reasonable to assume ToT would be equal to nivolumab PFS as a simplifying assumption
- Health-state specific utility values were derived for the PF and PD health states using RATIONALE-302 EQ-5D-5L data (mapped to EQ-5D-3L as recommended by NICE).[10] Utility values were assumed to be equal for nivolumab and tislelizumab within each health state due to their similar mechanisms of action
- All Grade ≥3 treatment-related adverse events that occurred in ≥5% of patients in at least 1 treatment arm of RATIONALE-302 or the nivolumab arm of ATTRACTION-3 were included in the model, with costs applied as one-off costs.[7,9] Utility decrements for adverse events were not included in the model base case to avoid double counting the utility impact of adverse events
- Drug acquisition and administration costs were sourced from the British National Formulary (BNF) and the 2021/2022 National Health Service (NHS) reference costs respectively.[11,12] Monitoring and disease management costs were sourced from previous NICE appraisals and the latest NHS reference costs.[5,12] Subsequent (third-line) treatment costs (chemotherapy, nivolumab, or best supportive care) were informed by clinical expert opinion, previous NICE appraisals, and costs derived from the BNF.[5,11] Adverse event costs were sourced from the literature and the NHS reference costs.[12] Costs were inflated to the 2022/2023 cost year where required

Table 1. Summary of Model Features

Model Characteristic	Specification
Perspective	Healthcare payer in the UK (NHS and personal social services)
Population	Patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy
Time horizon	Lifetime
Cycle length	1 week (half-cycle correction applied)
Discount rate (outcomes and costs)	3.5%
Baseline characteristics (derived from RATIONALE-302)[7]	
Mean age, years	61.80
Male, %	84.38
Mean BSA, m^2	1.65
Mean weight, kg	59.73

BSA, body surface area; NHS, National Health Service; ESCC, esophageal squamous cell carcinoma.

Results

Base Case

- **Table 2** summarizes the discounted base case results of the model. At a WTP threshold of £30,000/QALY gained, tislelizumab was cost-effective versus nivolumab (incremental cost-effectiveness ratio [ICER]: £16,589/QALY gained) when assuming price parity in terms of treatment acquisition costs per treatment cycle
  - Tislelizumab was associated with greater total discounted QALYs (tislelizumab: 1.02, nivolumab: 0.86)
- Absolute and proportional QALY shortfalls were also calculated following NICE guidance.[13] The appropriate QALY weight based on the shortfall results was 1.2, resulting in a severity modifier-adjusted ICER of £13,824/QALY gained

Scenario Analyses

- Decreasing or increasing the price per treatment cycle of tislelizumab by 10% whilst holding nivolumab price constant resulted in ICERs of £2715/QALY gained and £30,463/QALY gained, respectively

Table 2. Base Case Cost Effectiveness Results

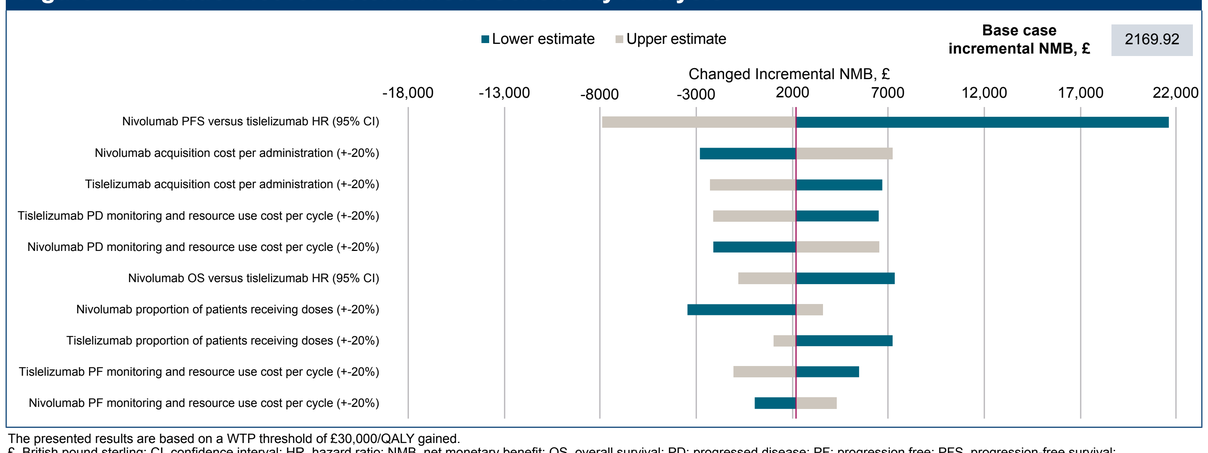
Outcome	Tislelizumab	Nivolumab	Incremental
Total discounted costs, £	75,874	73,190	2684
Acquisition	22,448	25,144	-2696
Administration	2626	2941	-315
Treatment-related adverse events	28	25	4
Monitoring	37,986	32,228	5757
Subsequent treatment	3668	3670	-2
Terminal care	9119	9182	-64
Total discounted LYs	1.34	1.14	0.20
Total discounted QALYs	1.02	0.86	0.16
ICER per QALY gained, £			16,589
ICER per QALY gained (with NICE severity modifier*), £			13,824

Total and incremental values reported in the table may not exactly align due to rounding. *A QALY modifier of 1.2 was applied based on QALY shortfall results, in accordance with the NICE health technology evaluations manual.[13]
£, British pound sterling; ICER, incremental cost-effectiveness ratio; LY, life years; NICE, National Institute for Health and Care Excellence; QALY, quality adjusted life year.

Sensitivity Analyses

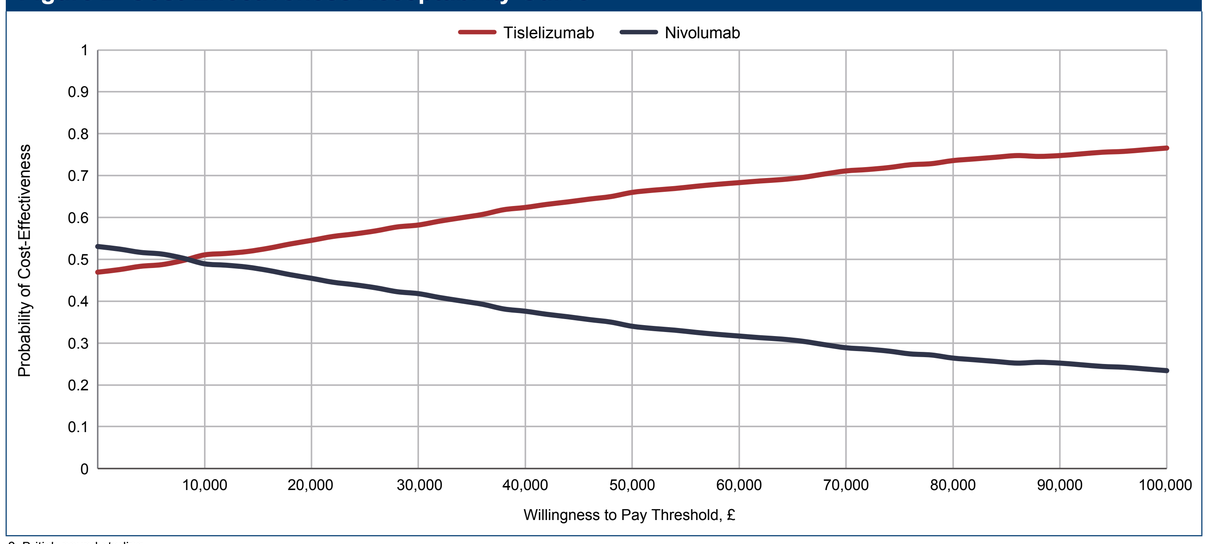
- Deterministic sensitivity analyses of incremental net monetary benefit at a WTP threshold of £30,000/QALY gained suggested that nivolumab efficacy relative to tislelizumab efficacy (particularly in terms of the PFS HR), drug acquisition costs, and PD resource use were the most influential model inputs (**Figure 1**)
- The probabilistic sensitivity analysis (1500 simulations) resulted in an estimated average ICER of £4133/QALY gained for tislelizumab versus nivolumab, and a 58% probability of tislelizumab being cost-effective at a WTP threshold of £30,000/QALY gained (**Figure 2**)

Figure 1. Tornado Plot for Deterministic Sensitivity Analysis



The presented results are based on a WTP threshold of £30,000/QALY gained.
£, British pound sterling; CI, confidence interval; HR, hazard ratio; NMB, net monetary benefit; OS, overall survival; PD: progressed disease; PF: progression free; PFS, progression-free survival; QALY, quality adjusted life year; WTP, willingness to pay.

Figure 2. Cost-Effectiveness Acceptability Curve



£, British pound sterling.

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Presenter Disclosures

Eugenia Priedane is employed by BeiGene and may hold stock or other ownership.

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