EE215

Pharmacoeconomic analysis of adjuvant nivolumab for patients with resected esophageal or gastroesophageal junction cancer in Switzerland

César Oniangue-Ndza,[1] Gerhard Strittmatter,[1] Aaron Lucas,[2] Michele Wilson,[2] Sarah Kassahun,[3] Prianka Singh[4]

[1] Bristol Myers Squibb SA, Steinhausen, Switzerland; [2] RTI Health Solutions, Research Triangle Park, NC, United States; [3] Bristol Myers Squibb, Uxbridge, Middlesex, United Kingdom; [4] Bristol Myers Squibb, Lawrenceville, NJ, United States

Introduction

Disease background

- Esophageal cancer (EC) is specific to cancerous cells in the muscular tube, which connects the throat to the stomach
- The 5-year survival associated with EC is 22%, which indicates a relatively poor prognosis for patients and a high unmet need[1]
- In Switzerland, EC contributed to an estimated 685 new cases and 529 deaths in 2021[2]

Nivolumab

- In Switzerland, nivolumab alone or in combination with ipilimumab has already been approved and reimbursed for several other indications[3]
- CheckMate 577 is a randomised (2:1), double blind, phase 3 clinical trial that compares nivolumab with surveillance as adjuvant treatment in adults (aged ≥ 18 years) with resected EC or gastroesophageal junction cancer (GEJC)[4]
- From long-term follow-up data from CheckMate 577, nivolumab improved disease-free survival (DFS) with a hazard ratio of 0.67 (96.4% confidence interval [CI], 0.55-0.81) in the intention-to-treat population compared with surveillance. Median DFS for the intention-to-treat population was 22.4 vs. 10.4 months (95% CI, 17.68-36.93) for the nivolumab arm compared with the surveillance arm
- Based on the trial's results, Swissmedic granted nivolumab a marketing authorisation on 6 July 2021 and was received/granted reimbursement by the Swiss Federal Office of Public Health on 1 November 2021

Objective

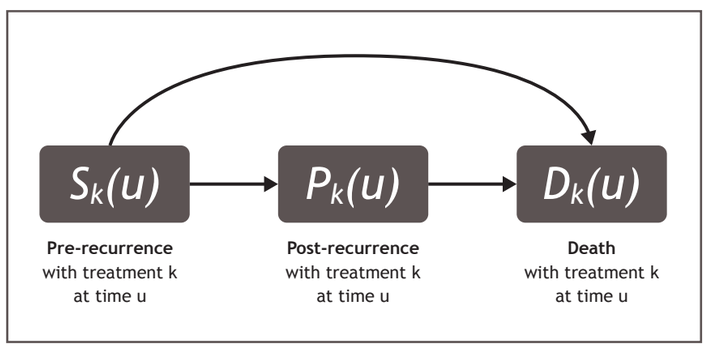
- To evaluate the cost-utility of nivolumab compared with surveillance as evaluated in the CheckMate 577 trial from a Swiss statutory health insurance system perspective

Methods

Model structure

- A 3-health state Markov model was used to estimate the cost-effectiveness of nivolumab compared with surveillance. The 3 health states in the model include prerecurrence, postrecurrence, and death as shown in **Figure 1**

Figure 1. Overview of the 3-health-state model



Efficacy and survival

- To determine the most appropriate parametric form to extrapolate DFS, multiple methods of parametric analyses were explored and presented to experts. Based on all parametric forms evaluated, the base-case extrapolation selected was the generalised gamma model for both nivolumab and surveillance
- The extrapolation of DFS is utilised to estimate the transition up to the point of cure (assumed to be 5 years). After 5 years, the model assumes that patients remain in the prerecurrence health state, and only transition from the prerecurrence health state to death
- The general population mortality with no adjustment is applied to estimate the transition from prerecurrence to death and included in the transition from prerecurrence to postrecurrence[5]
- Postrecurrence survival was estimated using a registry data set from the Netherlands Comprehensive Cancer Organisation (IKNL) obtained and matched to the CheckMate 577 population

Inputs and settings

- Grade ≥ 3 adverse events for nivolumab and surveillance were obtained from CheckMate 577
- All acquisition costs were incurred within the first year in line with treatment-stopping. Subsequent treatment was provided for 6 months and informed by CheckMate 577
- Based on expert opinions, patients in prerecurrence were assumed to incur disease management costs for the first 5 years. Following 5 years, no follow-up was assumed if patients maintained DFS. Postrecurrence disease management costs are incurred through the model time horizon
- The unit cost of terminal care is applied to patients up to the point of cure

Table 1. Base-case settings

Parameter	Base-case value
Model framework	3-state Markov model
Time horizon	25 years
Perspective	Swiss statutory health insurance system
Population	Per Swiss label for nivolumab: for the adjuvant treatment of completely resected oesophageal or GEJC in adult patients who have residual pathologic disease following prior neoadjuvant CRT
Cycle length	1 month (4 weeks-28 days)
Discount rate	3.0% (applied for outcomes and costs)
Patient characteristics	Based on the characteristics of patients enrolled in CheckMate 577
Survival extrapolation	DFS: Generalised gamma distribution for both nivolumab and surveillance. Based on expert consultation and visual inspection with Schoenfeld residual plots, hazards over time, and log-cumulative hazard plots PRS: Exponential model fitted to IKNL data set
Health state utilities	CheckMate 577 and French utility values[6]
Drug acquisition and administration costs[a]	Drug acquisition costs: Swiss FOPH[7] Administration costs: TARMED[8]
Resource use	Expert opinions
Unit costs for resource use	Disease management, pre- and post-recurrence, monitoring costs,[b] adverse event costs, and terminal costs sourced from TARMED,[8] Swiss inpatient tariffication system [DRG],[9] and Spitex[10]
Subsequent treatment	Informed by CheckMate 577

CRT = chemoradiotherapy; DRG = diagnosis-related group; FOPH = Federal Office of Public Health; PRS = postrecurrence survival

[a] 240 mg as an intravenous infusion over 30 minutes q2w for 16 weeks followed by 480 mg over 30 minutes q4w beginning at week 17 (2 weeks after the eighth dose)

[b] For nivolumab patients only, these costs are applied for the first year (as nivolumab has a maximum treatment duration of 1 year) and in pre-recurrence

Results

Base case

- Incremental survival was substantially higher for nivolumab than with surveillance, with a life-year (LY) gain of 1.90 (total LYs: 6.53 vs. 4.63, respectively) over a lifetime horizon (25 years) (**Table 2**)
- Treatment with nivolumab was associated with greater total quality-adjusted life-years (QALYs) compared with surveillance (total QALYs: 5.45 vs. 3.85, respectively), resulting in an incremental QALY gain of 1.60
- The total cost of nivolumab was CHF 96,077; in comparison, the total cost of surveillance was CHF 35,325 (incremental cost, CHF 60,751)
- The corresponding incremental cost-utility ratio (ICUR) of nivolumab compared with surveillance was CHF 37,896/QALY

Table 2. Base-case results

	Nivolumab (mean)	Surveillance (mean)
Discounted LYs		
Total LYs	6.53	4.63
LYs prerecurrence	6.08	4.09
LYs postrecurrence	0.45	0.55
Discounted QALYs		
Total QALYs	5.45	3.85
QALYs prerecurrence	5.12	3.45
QALYs postrecurrence	0.34	0.40
Discounted costs		
Total costs	CHF 96,076.68	CHF 35,325.41
Treatment costs (drug acquisition and administration)	CHF 60,446.96	N/A
Monitoring costs	CHF 4,179.66	N/A
Adverse event costs	CHF 128.55	CHF 69.45
Recurrence-free disease-related costs	CHF 10,794.21	CHF 8,160.35
Postrecurrence disease-related costs	CHF 2,056.44	CHF 2,472.86
Subsequent treatment costs	CHF 6,137.34	CHF 9,744.90
Terminal care costs	CHF 12,333.52	CHF 14,877.07
Incremental cost-utility of nivolumab vs. surveillance	**CHF 37,986**	

Scenario and sensitivity analyses

- Deterministic sensitivity analysis was undertaken. The parameters that lead to greater uncertainty in results included the cost of subsequent treatment for nivolumab and surveillance and the utility values for prerecurrence
  - Across the parameters tested, the ICUR varied within +/− 3% from the base case. All parameters tested generated an ICUR lower than the CHF 200,000/QALY threshold derived from the study by Beck et al.,[11] as no official willingness-to-pay threshold is defined in Switzerland
- The probabilistic sensitivity analysis showed nivolumab with a 100% probability of being cost-effective at a CHF 200,000/QALY threshold (**Figure 2**)
- Additional scenario analyses included: (1) altering the time horizon to 15 years; (2) a cure timepoint of 3 years; (3) postrecurrence survival based on a pooled overall survival data from first-line metastatic EC/GEJC from 2 studies in the first-line metastatic EC setting—CheckMate 649 and KEYNOTE590[12,13]; (4) use of German utility tariffs instead of French utility tariffs; and (5) transition from prerecurrence to postrecurrence estimates using TTR instead of DFS
- Of all scenarios tested, a 15-year time horizon showed the largest increase in ICUR (CHF 52,072/QALY gained). Across all scenarios tested, the ICUR remained under CHF 200,000/QALY gained

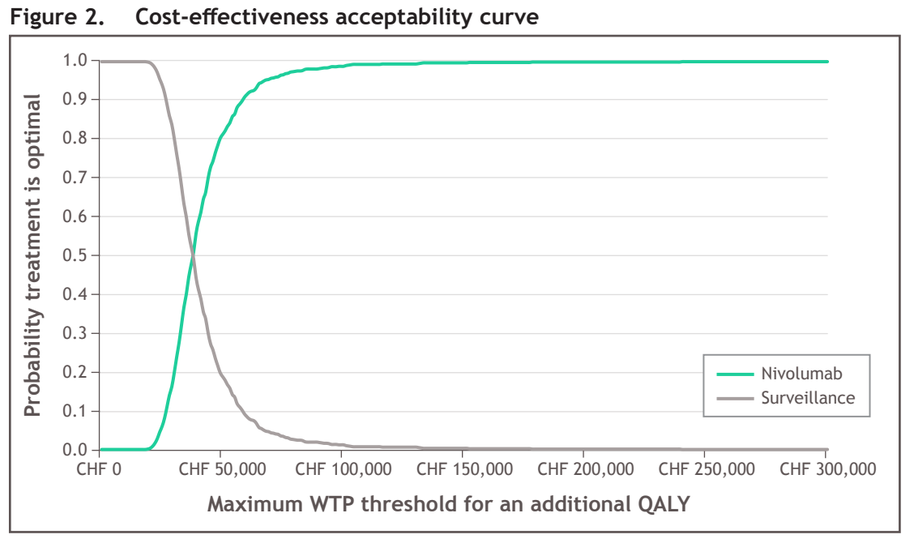
Table 3. Deterministic sensitivity analysis

Parameter	ICUR if parameter set to lower bound	ICUR if parameter set to upper bound
Cost of subsequent treatment surveillance	CHF 39,122/QALY	CHF 36,736/QALY
Cost of subsequent treatment, nivolulmab	CHF 37,271/QALY	CHF 38,774/QALY
Utility pre-recurrence (monthly)	CHF 38,548/QALY	CHF 37,437/QALY
Monitoring cost, nivolumab	CHF 37,499/QALY	CHF 38,523/QALY
Cost disease management pre-recurrence	CHF 37,679/QALY	CHF 38,324/QALY

Table 4. Scenario results

	ICUR	
	Value	% change
Base case	CHF 37,986/QALY	–
Time horizon, 15 years	CHF 52,072/QALY	37.1%
Cure timepoint at 3 years	CHF 34,289/QALY	−9.7%
Post-recurrence survival data set	CHF 37,115/QALY	−2.3%
German utility tariffs	CHF 34,799/QALY	−8.4%
Transition from prerecurrence to postrecurrence using TTR instead of DFS	CHF 34,290/QALY	−9.7%

Figure 2. Cost-effectiveness acceptability curve



Conclusions

- In Switzerland, patients with resected EC or GEJC who have completed preoperative chemoradiotherapy followed by surgery historically have had no systemic available treatment options. Nivolumab is the first systemic treatment option available for patients in the adjuvant setting
- Based on a CHF 200,000/QALY threshold, the results of this study show that nivolumab has the potential to generate significant survival benefits and be a cost-effective treatment option for patients in Switzerland

References

1. Ruhstaller T, et al., 2014. https://www.nicer.org/assets/files/publications/others/skb_03-2014_oesophageali_cancer_survival.pdf.
2. International Agency for Research on Cancer. 2021. https://gco.iarc.fr/today/data/factsheets/populations/756-switzerland-fact-sheets.pdf.
3. Bristol Myers Squibb. 2021. https://www.swissmedic.ch/dam/swissmedic/de/dokumente/marktueberwachung/rmp/nivolumab_nivolumabbmsopdivormpsummary.pdf.download.pdf/nivolumab_opdivo_ch-rmp-summary-v5.pdf.
4. Kelly RJ, et al. Ann Oncol. 2020;31:S1193-4.
5. Federal Statistical Office. 2020. https://www.bfs.admin.ch/bfs/en/home/search.html?dyn_search=su-d-01.04.02.02.04&dyn_tab=1&dyn_orderby=relevance.
6. Matter-Walstra K, et al. Pharmacoeconomics. 2014 Jun;32(6):591-9.
7. Federal Office of Public Health. Spezialitästlsit. 2021. http://www.spezialitaetenliste.ch/ShowPreparations.aspx.
8. TARMED online browser. 2021. https://www.tarmed-browser.ch/de.
9. Swiss DRG. 2022. https://www.swissdrg.org/de/akutsomatik/swissdrg-system-1002021/fallpauschalenkatalog.
10. SPITEX. 2021. https://www.spitexbe.ch/.
11. Beck K, et al. Kosten und Nutzen von medizinischen Behandlungen am Lebensende; Nationales Forschungsprogramm NFP 67. 2016.
12. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02872116.
13. Kato K, et al. Pembrolizumab plus chemotherapy versus chemotherapy as a first-line therapy in patients with advanced esophageal cancer: the Phase 3 KEYNOTE-590 study. Annual Meeting of the European Society of Medical Oncology; 2020.

Acknowledgments

This study was supported by Bristol Myers Squibb. All authors contributed to and approved the presentation.

Presented at ISPOR Europe 2022; 6-9 November 2022; Vienna, Austria

Email: Cesar.Oniangue-ndza@bms.com