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Number needed to treat (NNT) and cost of preventing an event (COPE) analysis for pembrolizumab in non-squamous metastatic non–small-cell lung cancer (NSCLC) in Colombia

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Background

- Lung cancer is the leading cause of cancer-related deaths worldwide, with an estimated global mortality of 1.8 million annually[1]
- In Colombia, 6,876 new cases of lung cancer and 6,090 deaths due to lung cancer were reported in 2020[5]
- There are two types of lung cancer: small-cell lung cancer (SCLC) and non–small-cell lung cancer (NSCLC), the latter accounting for 85% of lung tumors[2,3,4]
- Due to high incidence and mortality rates, together with late-stage diagnosis and treatments required, the financial burden of NSCLC is high in Colombia and worldwide[3,6]
- Results from the KEYNOTE-189 trial demonstrated that first-line pembrolizumab plus pemetrexed-platinum significantly improved overall survival (OS) and progression-free survival (PFS) compared with pemetrexed-platinum alone in patients with metastatic non-squamous non–small-cell lung cancer (NSCLC), irrespective of tumor programmed death-ligand 1 (PD-L1) expression

Objective

- This study aimed to calculate the number needed to treat (NNT) and cost of preventing an event (COPE) using PFS and OS data from the KEYNOTE-189 protocol-specified final analysis and Colombian costs[7]

Methods

- A cost-per-responder model was developed considering 24-month time horizons for OS and PFS. NNT based on restricted mean survival time (RMST) and COPE were calculated for the ITT population and PD-L1 TPS ≥50%, PD-L1 TPS = 1%-49%, and PD-L1 TPS <1% subgroups
- Modeled costs reflected Colombian drug acquisition costs and were reported in local currency and converted to US dollars (USD)
- The model input parameters are listed in **Table 1**
- The model calculates NNT, which is the additional number of patients that need to be treated to prevent an outcome, and COPE is the additional cost of preventing that outcome[4,8]
  - This model uses RMST instead of absolute risk ratio (ARR), as RMST overcomes the limitations associated to ARR
  - Limitations associated with ARR include failure to capture treatment effect and misinterpretation of treatment benefit when observed event rates are low or survival curves cross

Table 1. Model parameters

Input parameter	Value			Source
Dosing schedule				
	Dosage	Doses per cycle	Cycle length (wks)	
Pembrolizumab	200 mg	1	3	https://clinicaltrials.gov/ct2/show/NCT02578680
Pemetrexed	500 mg/m^2	1	3	https://clinicaltrials.gov/ct2/show/NCT02578680
Cisplatin	75 mg/m^2	1	3	https://clinicaltrials.gov/ct2/show/NCT02578680
Carboplatin	5 AUC	1	3	https://clinicaltrials.gov/ct2/show/NCT02578680
% of platinum chemotherapy that is carboplatin	80			
Resource use				
	Physician visits per cycle			
Pembrolizumab + pemetrexed + platinum	1			Assumption
Pemetrexed + platinum	1			Assumption
Unit size and cost				
	Unit size	Unit cost (USD, $)		
Pembrolizumab	100	2,387		SISMED Q2 2022
Pemetrexed	100 500	50 251		SISMED Q2 2022
Cisplatin	10 50	1 4		SISMED Q2 2022
Carboplatin	150 450	6 17		SISMED Q2 2022

95% CI, 95% confidence interval; COP, Colombian peso; ITT, intention-to-treat; NNT, number-needed-to-treat; PD-L1, programmed death-ligand 1; TPS, tumor proportion score; wks, weeks.

- In the base-case analysis, the calculated COPE considers only drug acquisition costs, with a scenario that includes the following costs
  - Administration costs, monitoring costs, and adverse events costs

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Results

Base case

- Over a 24-month period, 3.13 patients (NNT_{RMST} OS = 3.13 - 95% CI 2.18, 5.17) needed to be treated with pembrolizumab combination to prevent an additional death in comparison with chemotherapy and 1.48 patients (NNT_{RMST} PFS = 1.48 - 95% CI 1.08, 2.17) needed to be treated to prevent an additional disease progression or death (**Figure 1** and **Table 2**)
- COPE to prevent death or progression in the ITT population was USD $112,634 (95% CI: 82,192-165,145) and USD $238,205 (95% CI: 165,906-393,457) for PFS and OS, respectively
- Across PD-L1 subgroups, NNT ranged from 1.02-2.49 for PFS and 2.74-4.23 for OS, with COPE ranging from USD $77,626-$189,499 for PFS and $208,524-$321,919 for OS

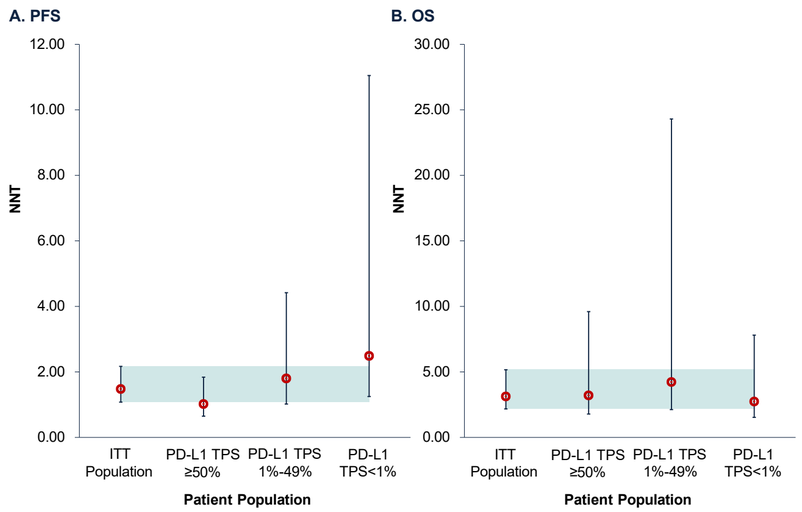
Table 2. NNT_{RMST} and COPE for PFS and OS through the 24-month period according to PD-L1 expression level

	NNT_{RMST}		COPE	
	NNT	95% CI	USD ($)	95% CI
Progression-free survival				
ITT population	1.48	1.08-2.17	112,634	82,192-165,145
PD-L1 TPS ≥50%	1.02	0.65-1.84	77,626	49,467-140,031
PD-L1 TPS 1%-49%	1.80	1.02-4.42	136,987	77,626-336,379
PD-L1 TPS <1%	2.49	1.25-11.05	189,499	95,130-840,947
Overall survival				
ITT population	3.13	2.18-5.17	238,205	165,906-393,457
PD-L1 TPS ≥50%	3.21	1.79-9.61	244,293	136,226-731,358
PD-L1 TPS 1%-49%	4.23	2.13-24.31	321,919	162,101-1,850,084
PD-L1 TPS <1%	2.74	1.54-7.81	208,524	117,200-594,371

95% CI, 95% confidence interval; COP, Colombian peso; COPE, cost of preventing an event; ITT, intention-to-treat; NNT, number-needed-to-treat; PD-L1, programmed death-ligand 1; RMST, restricted mean survival time; TPS, tumor proportion score.

Note: Base-case analysis only included drug acquisition costs, additional costs due to administration, disease monitoring and adverse events (AEs) were included in the scenario analysis.

Figure 1. NNT_{RMST} for PFS and OS through the 24-month period according to PD-L1 expression level



NNT, number-needed-to-treat; OS, overall survival; PFS, progression-free survival; RMST, restricted mean survival time.

Note: Base-case analysis only included drug acquisition costs, additional costs due to administration, disease monitoring and adverse events (AEs) were included in the scenario analysis.

Scenario analysis

- The incorporation of other cost categories resulted in the following for preventing a disease progression event (PFS) (**Table 3**)
  - The drug acquisition was the largest component impacting the COPE value for the ITT population, followed by administration, which resulted in a COPE value of $1,853
  - Next, the adverse events and monitoring, with an estimated COPE value of $124 and $28, respectively
- The incorporation of other cost categories for preventing a death event (OS) followed the same trend as the PFS
  - Drug acquisition cost made up the highest proportion of COPE value, followed by administration, AEs, and monitoring (**Table 3**)
- The COPE associated with additional costs was consistent between the ITT population and the subgroups

Table 3. COPE for PFS and OS through the 24-month period according to cost type (ITT population)

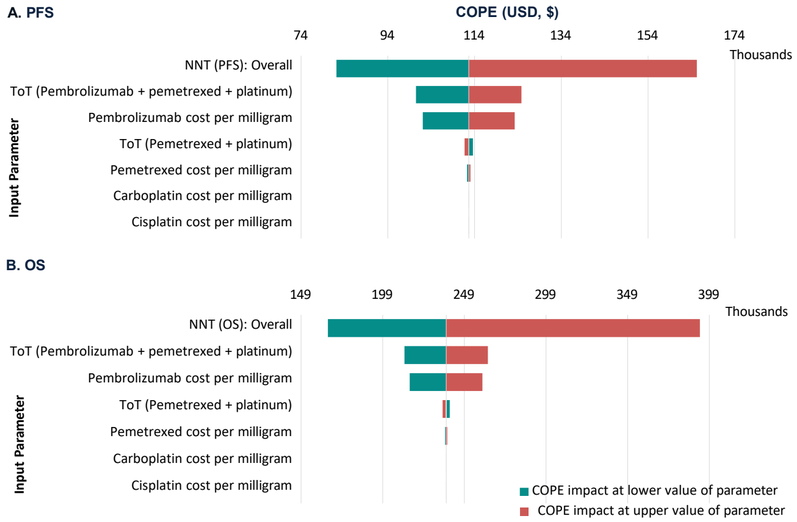
	COPE	
	USD ($)	95% CI
Progression-free survival		
Drug acquisition	110,628	80,729-162,205
Administration	1,853	1,352-2,717
Monitoring	28	21-41
Adverse events	124	91-182
Overall survival		
Drug acquisition	233,964	162,952-386,452
Administration	3,918	2,729-6,472
Monitoring	60	42-98
Adverse events	263	183-435

95% CI, 95% confidence interval; COP, Colombian peso; COPE, cost of preventing an event; ITT, intention-to-treat.

Deterministic sensitivity analysis

- The one-way deterministic sensitivity analysis (DSA) results were most sensitive to changes in the NNT_{RMST} input values used to calculate COPE, followed by time-on-treatment data (**Figure 2**)
- This trend was consistent in both PFS and OS input data

Figure 2. Tornado diagram illustrating COPE results for PFS and OS through the 24-month period



COP, Colombian peso; NNT, number-needed-to-treat; OS, overall survival; PFS, progression-free survival; ToT, time-on-treatment.

Conclusions

- Traditional health economic analyses can often be complex and can be misinterpreted when assessed outside of HTA analyses to make clinical decisions, due to the use of specific technical measures, for example QALYs. However, NNT provides a simple, clinically relevant assessment of the clinical value of an intervention[4,9,10]
- The NNT_{RMST} values obtained in this model for the ITT population are below the median NNT values reported in literature for PFS, OS, and reduction in risk of lung cancer (3.2), not specific to lung cancer type, histology, stage, or treatment modality[10]
- The low NNT_{RMST} observed in the ITT population and across PD-L1 subgroups highlights the clinical effectiveness of pembrolizumab combination for patients with NSCLC regardless of PD-L1 expression level. Additionally, the COPE in the ITT population and among PD-L1 level subgroups indicates a manageable per-patient financial impact in Colombia

References

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