# Comparing costs of immune checkpoint inhibitors for treatment of first-line non-small cell lung cancer in Colombia – a cost minimization analysis

EE512

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## Introduction

- Lung cancer is one of the most commonly diagnosed and deadly types of cancer[1]
- Non-small cell lung cancer (NSCLC) accounts for 84% of cases and is associated with short life expectancy[2]
- The Cuenta de Alto Costo estimated 2020 lung cancer prevalence and mortality in Colombia at 8.96 and 2.93 per 100.000, respectively[2]
- The recent introduction of immune checkpoint inhibitors (ICI) has substantially improved prognosis for patients with advanced NSCLC
- **Table 1** presents ICIs currently available to Colombian NSCLC patients in the first-line (1L) treatment setting

### Table 1. ICI regimens available to Colombian 1L NSCLC patients

| Treatment regimen | Pivotal trial | Licensed population |
|---|---|---|
| **NIVO+IPI+PDC**<br>Nivolumab<br>Ipilimumab<br>Cisplatin/carboplatin<br>Pemetrexed | CheckMate 9LA[3] | All 1L NSCLC patients, regardless of histology or PD-L1 levels |
| **Atezo+beva+plat+tax**<br>Atezolizumab<br>Bevacizumab<br>Paclitaxel<br>Carboplatin | IMpower150[4] | Non-squamous 1L NSCLC patients |
| **Pembro mono**<br>Pembrolizumab | KEYNOTE-024[5] | 1L NSCLC patients with PD-L1 > 50% |
| **Pembro+plat+pemx**<br>Pembrolizumab<br>Cisplatin / Carboplatin<br>Pemetrexed | KEYNOTE-189[6] | Non-squamous 1L NSCLC patients |
| **Pembro+plat+(nab)-tax**<br>Pembrolizumab<br>Carboplatin<br>(Nab-)Paclitaxel | KEYNOTE-407[7] | Squamous 1L NSCLC patients |

Atezo, atezolizumab; Beva, bevacizumab; Mono, monotherapy; NIVO+IPI+PDC, nivolumab plus ipilimumab plus platinum doublet chemotherapy; PD-L1, programmed death ligand 1; Pembro, pembrolizumab; Pemx, pemetrexed; Plat, platinum; (nab)-tax, (Nab)paclitaxel

## Objectives

- The objective of this study was to evaluate the total cost of available ICI therapies for treatment of patients with untreated stage IV or recurrent NSCLC in the Colombian setting
- In absence of formal assessment by the Colombian HTA agency (IETS), the analysis was conducted in accordance with published outcomes by HTA bodies in Sweden and the Netherlands.[8-11] These agencies assumed that the above ICIs have similar efficacy and that a cost minimization analysis (CMA) is therefore an appropriate method
- A CMA was conducted to estimate the total cost of nivolumab plus ipilimumab plus 2 cycles of platinum doublet chemotherapy, compared with alternative systemic therapies for treatment of patients with untreated stage IV or recurrent NSCLC in the Colombian setting

## Methods

### Cost minimization analysis

- The analysis was conducted from a Colombian payer perspective
- It is based on 2021 cost data and considers a 2-year time horizon
- Five different cost categories have been taken into account in the CMA, including:
  - Treatment acquisition costs
  - Drug administration costs
  - Monitoring costs
  - Costs for management of adverse events (AEs)
  - Costs for subsequent (second line; 2L) treatments
- A CMA inherently assumes that comparators are noninferior and have equal treatment efficacy. So-called health state costs have not been considered because these would have been equal across comparators

### Treatment duration/number of doses

- The number of doses administered is an important input parameter affecting treatment acquisition, treatment administration, and patient monitoring costs
- The mean number of doses administered to patients in the CheckMate 9LA trial was used to inform treatment duration for NIVO+IPI+PDC[3]
- Dosing information for the other ICIs was not reported in a consistent manner in the respective clinical trial papers. Therefore, the area under the PFS curve for the CheckMate 9LA all-comer population up to 2 years was used as a proxy to inform treatment duration for the other ICIs
- The underlying rationale for this assumption is that:
  - Patients are generally treated until progression
  - For the few ICIs they are publicly available, progression-free survival (PFS) and duration of therapy (DoT) curves are generally very similar
  - A CMA approach assumes that all treatments have equal efficacy (hence equal PFS curves)
  - A 2-year stopping rule is applied to ICI therapy in Colombian clinical practice
- The maximum number of treatment cycles, as per the respective clinical trial protocol, was taken into account for chemotherapy (ie, up to 4 cycles for pembrolizumab and 4-6 cycles for atezolizumab regimens)
- The resulting number of doses assumed in the CMA for each of the treatment regimens are presented in **Table 2**

### Table 2. Number of doses assumed in the CMA

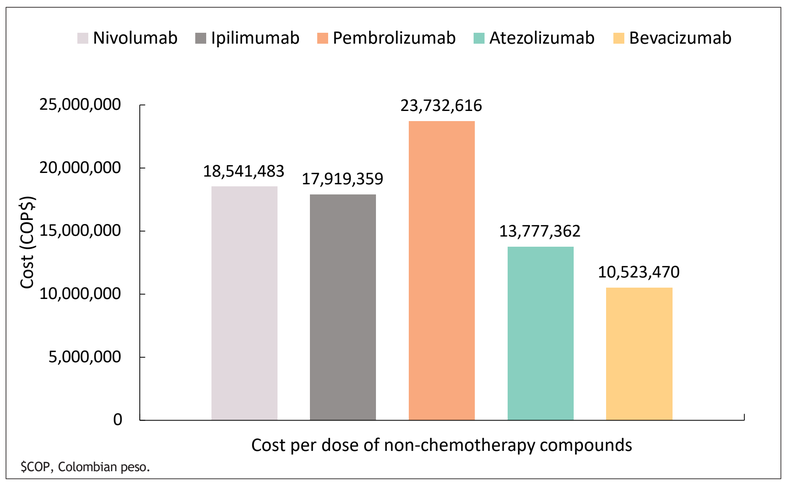
| Treatment | Number of doses | Source/method |
|---|---|---|
| **NIVO+IPI+PDC** | | Mean number of doses administered to patients in CheckMate 9LA |
| Nivolumab (Q3W) | 13.3 | |
| Ipilimumab (Q6W) | 6.7 | |
| Cis-/carboplatin (Q3W) | 1.9 | |
| Pemetrexed (Q3W) | 1.9 | |
| **Pembro+plat+pemx** | | Estimated number of doses based on dosing frequency and treatment duration<br>CheckMate 9LA PFS was used as a proxy to inform treatment duration for ICIs<br>Maximum number of cycles as per the respective clinical trial protocol was taken into account for chemotherapy |
| Pembrolizumab (Q3W) | 15.2 | |
| Cis-/carboplatin (Q3W) | 3.7 | |
| Pemetrexed (Q1W) | 15.2 | |
| **Pembro mono** | | |
| Pembrolizumab (Q3W) | 15.2 | |
| **Pembro+plat+(nab)-tax** | | |
| Pembrolizumab (Q3W) | 15.2 | |
| Carboplatin (Q3W) | 3.7 | |
| Paclitaxel (Q3W) | 3.7 | |
| Nab-paclitaxel (Q1W) | 11.0 | |
| **Atezo+beva+plat+tax** | | |
| Atezolizumab (Q3W) | 15.2 | |
| Bevacizumab (Q3W) | 15.2 | |
| Paclitaxel (Q3W) | 3.7 | |
| Carboplatin (Q3W) | 3.7 | |

Q×W, every × weeks.

### Drug acquisition costs

- Official drug prices were obtained from regulation list prices issued by the Colombian government[12,13]
- In the base-case analysis, the cost per dose for each treatment is calculated by assuming no vial sharing, except for the use of ipilimumab where it was confirmed that vial sharing is commonly used in Colombia
- The cost per dose for non-chemotherapy compounds is presented in **Figure 1**

**Figure 1. Drug acquisition costs per dose per non-chemotherapy compounds**

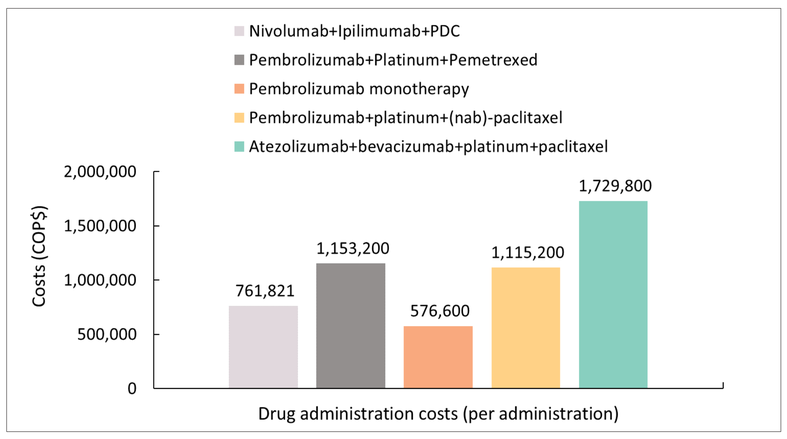



$COP, Colombian peso.

### Administration costs

- Administration costs are independent of the time required for infusion. Multiple drugs can be administered during the same session, resulting in only a single administration fee
- Cost per administration for each ICI regimen is summarized in **Figure 2**[13]

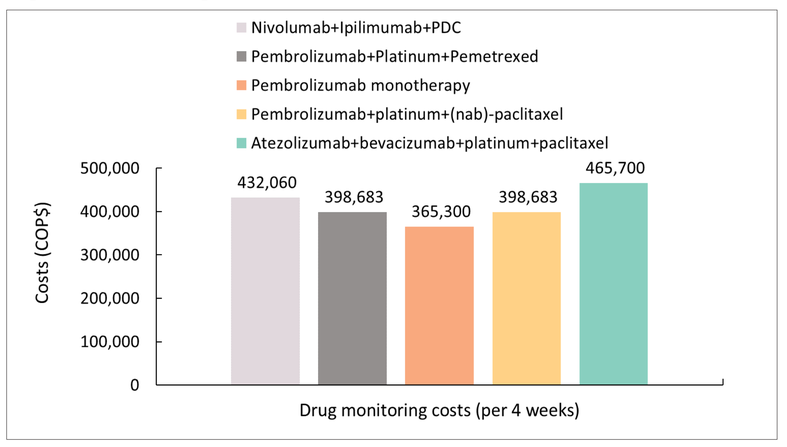
**Figure 2. Administration costs**




### Monitoring costs

- Monitoring costs reflect treatment-specific resource use such as laboratory and scans as required to ensure patients are tolerating the treatment well
- **Figure 3** shows a summary of monitoring costs included in the CMA

**Figure 3. Monitoring costs**




### Management of adverse events

- It is assumed that AE costs are primarily driven by grade 3-5 AEs; therefore, the AEs included in the analysis refer to grade 3-5 treatment-related AEs experienced by ≥ 5% of patients in either treatment arm of CheckMate 9LA or any of the external comparator arms (based on safety results reported for respective trials listed in **Table 1**)

### Subsequent treatments

- On failure of 1L treatment of NIVO+IPI+PDC or a comparator therapy, a proportion of the initial cohort moves on to a subsequent treatment
  - The proportion of patients receiving any subsequent treatment for NIVO+IPI+PDC was 30.75%, and 40.22% for PDC based on CheckMate 9LA data[3]
  - For other immuno-oncology (IO) regimens, the proportion receiving any subsequent treatment was assumed the same as for NIVO+IPI+PDC
- The distribution of 1L NIVO+IPI+PDC patients receiving subsequent therapy across the various treatment options was based on CheckMate 9LA data[3]
- For the other 1L IO regimens, this distribution was informed by local expert opinion and based on Colombian medical practice (**Table 3**). For patients receiving first-line treatment with pembro+plat+pemx, atezo+bev+plat+tax, and pembro mono, 2L treatment mainly consists of docetaxel and bevacizumab. The latter treatment option is generally only used in patients with non-squamous disease.

### Table 3. Subsequent treatment distribution[3,14]

| Drug | NIVO+IPI+PDC | Pembro+plat+(nab)-tax | Other ICIs |
|---|---|---|---|
| **Nivolumab** | 2.6% | 0.0% | 0.0% |
| **Pembrolizumab** | 1.6% | 0.0% | 0.0% |
| **Atezolizumab** | 2.1% | 0.0% | 0.0% |
| **Carboplatin** | 27.5% | 29.3% | 0.0% |
| **Cisplatin** | 5.7% | 6.1% | 0.0% |
| **Docetaxel** | 23.8% | 25.4% | 100.0% |
| **Gemcitabine** | 11.4% | 12.2% | 0.0% |
| **Paclitaxel** | 11.4% | 12.2% | 0.0% |
| **Pemetrexed** | 14.0% | 14.9% | 0.0% |
| **Bevacizumab** | 0.0% | 0.0% | 50.0% |

The subsequent treatment proportions reported in Paz-Ares et al. 2021 were adjusted to equal 100% in each treatment arm.

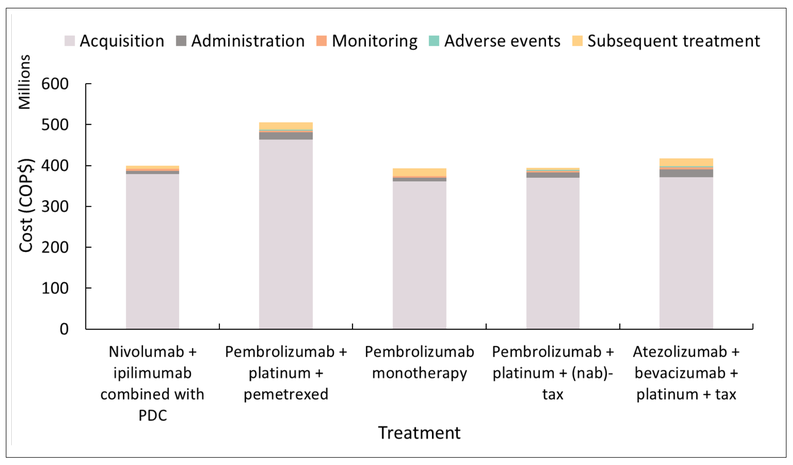
## Results

- The main results of the analysis are presented in **Figure 4** and **Table 4**
  - Total costs for the NIVO+IPI+PDC, pembrolizumab monotherapy, and pembro+plat+(nab)-tax regimens are very similar and range between 390M-400M COP$
  - Total costs for pembro+plat+pemx are ~$COP 100M higher. This is mainly driven by higher acquisition costs
  - While the acquisition costs for the atezo+beva+plat+tax regimen are slightly lower, all other costs are estimated to be higher, leading to an incremental cost of ~$COP 20M

### Disaggregated cost results

- Disaggregated cost results show the impact of the cost categories on the general results
- The disaggregated results are presented in **Figure 4**

**Figure 4. Disaggregated costs**




- From the cost breakdown, it is evident that drug acquisition costs are the key driver of results for each of the treatment options
- Costs for monitoring and administration, managing AEs, and subsequent treatments contribute relatively little to total costs (5%-11%)
- For pembro+plat+pemx, a stopping rule at 2 years was assumed for pemetrexed maintenance; however, the cost of pemetrexed is relatively high, accounting for 22% of the total acquisition costs
- Detailed disaggregated results are presented in **Table 4**

### Table 4. Disaggregated costs by treatment

| Regimen | Total cost | Treatment acquisition | Treatment admin. | Treatment monitoring | Adverse events | Subsequent treatments |
|---|---|---|---|---|---|---|
| **NIVO+IPI+PDC** | 399,795,693 | 379,121,571 (95%) | 8,040,115 (2%) | 4,103,413 (1%) | 917,598 (0%) | 7,612,995 (2%) |
| **Pembro+plat+pemx** | 506,120,035 | 463,221,197 (92%) | 17,552,263 (3%) | 4,551,111 (1%) | 2,207,500 (0%) | 18,587,965 (4%) |
| **Pembro mono** | 392,801,855 | 361,221,914 (92%) | 8,776,131 (2%) | 4,170,032 (1%) | 45,812 (0%) | 18,587,965 (5%) |
| **Pembro+plat+(nab)tax** | 394,205,067 | 370,182,016 (94%) | 12,190,096 (3%) | 4,551,111 (1%) | 2,755,700 (1%) | 4,526,144 (1%) |
| **Atezo+beva+plat+tax** | 416,842,103 | 371,021,231 (89%) | 19,704,323 (5%) | 5,316,135 (1%) | 2,212,450 (1%) | 18,587,965 (4%) |

Costs are in $COP. The numbers within parentheses indicate the percentage of total cost
Admin, administration; NIVO+IPI+PDC, nivolumab plus ipilimumab plus platinum doublet chemotherapy

- Drug administration and monitoring costs constitute around 2% to 5% and 1% of total costs for each of the treatment regimens, respectively
- The impact of costs included for the management of AEs on total costs is minor (0%-1%) for all treatment regimens

## Conclusions

- ICIs provide new first-line treatment options and improve overall survival for patients with advanced NSCLC
- In the base-case analysis, acquisition costs over the duration of treatment were shown to be the key driver to the total cost associated with all IO regimens
- Total cost for treatment of a previously untreated patient with advanced NSCLC with the CheckMate 9LA, KEYNOTE-024 and KEYNOTE-407 regimens ranged between 390M-400M COL$, 417M COL$ for the IMpower150, and 506M COL$ for the KEYNOTE-189 regimen
- The main limitation of this study is the assumption of PFS as a proxy for DoT for all IO external comparators. DoT directly influences the costs associated with treatment regimens through driving total acquisition costs, which make a large contribution to total costs for all treatment regimens

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