Estimated Costs of Treatment-related Adverse Events For Recurrent or Metastatic Squamous Cell Carcinoma of the Head and Neck in the CheckMate 141 Trial in Spain

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Introduction

- Nivolumab is a fully human IgG4 antibody that targets the programmed death-1 immune checkpoint expressed on activated T cells to restore T-cell antitumor response[1–3]
- Nivolumab monotherapy is approved for adults In the United States, for the treatment of patients with recurrent or metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN) with disease progression on or after platinum-based therapy[4] and is approved in the United States and European Union[4,5] for adult patients with SCCHN progressing on or after platinum-based therapy[5]
- Nivolumab was also associated with fewer high-grade treatment-related adverse events (TRAEs) as well as better patient-reported outcomes compared with IC[1,7]. Grade 3–4 TRAEs occurred in was lower with nivolumab (13.1%) of patients treated with nivolumab and compared with IC (35.1%) of patients treated with IC[7]
- Nivolumab Patient-reported outcomes showed stable stabilized symptoms and functioning with nivolumab, whereas IC led to but clinically meaningful declines with IC
- Health care resource utilization benefits, including decreased rates of hospitalization, were observed with nivolumab in CheckMate 141[8]
- Only antibiotics and anti-infectives were the cause of more TRAEs at the time of admission (23.4%)
- The objective of this analysis was to estimate the healthcare costs in Spain of treating assess the frequency and associated estimated costs of grade 3–4 nivolumab TRAEs based on their frequencies observed in CheckMate 141

Methods

Study design and safety assessments

- All patients in CheckMate 141 who received at least 1 dose of nivolumab or IC (safety population) were included in this analysis
- Safety was assessed by monitoring the incidence of TRAEs, which were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v4.0 and then grouped by System Organ Class
- This analysis included all grade 3 and 4 TRAEs flagged as requiring intervention that occurred between the first day of treatment and 30 days after the last day of treatment
- For patients who experienced multiple TRAEs, each event was counted and costed separately in the analysis

Estimated costs of TRAEs

- All grade 3–4 TRAEs reported in CheckMate 141 were included in the analysis
- An *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code was identified for each TRAE
- Corresponding unit costs in euros for each TRAE-related *ICD-9-CM* code were identified from the Spanish Ministry of health, comsumer affairs and social services and eSalud database
- A cost of €0 was assigned to TRAEs for which the cost was negligible, uncertain, or unknown.
- The cumulative estimated cost related to each TRAE was calculated by multiplying the frequency of that TRAE (grade ≥3) reported in each arm of CheckMate 141 by its unit cost
- The average estimated cost per patient was calculated by dividing the cumulative estimated cost by the number of patients receiving treatment

Results

Frequency of TRAEs

- Of 361 patients randomized 2:1 to nivolumab or IC, 347 received study drug and are included in this analysis (236 received nivolumab; 111 received IC)
- The frequency of TRAEs was lower in patients who received nivolumab compared with those who received IC (Table 1 and Figure 1). Each patient could have had multiple grade 3–4 TRAEs
- In the nivolumab arm, 97 (41.1%) patients experienced no TRAEs. Among the 139 (58.9%) patients who experienced any grade TRAE, there were 28 grade 3–4 TRAEs. The most frequent grade 3–4 TRAEs in patients treated with nivolumab were hypophosphatemia (number of events: 4; anemia, 2; dehydration, 2; and pneumonitis, 2)
- In the IC arm, 25 (22.5%) patients experienced no TRAEs. Among the 86 (77.5%) patients who experienced a TRAE, there were 60 grade 3–4 TRAEs
- Frequency varied by agent received in the IC arm
- The most frequent grade 3–4 TRAEs in patients treated with IC were anemia (number of events: 6; neutropenia, 5; hyponatremia, 4; platelet count decreased, 4; and stomatitis, 3)
- On a per–treated patient basis, this represents a 4.5-fold lower rate of grade 3–4 TRAEs in the nivolumab arm compared with the IC arm

Table 1. Incidence of TRAEs

	Nivolumab (n=256)	IC total (n=111)
Number of patients with any grade TRAE, n (%)	139 (58.9)	86 (77.5)
Number of grade 3–4 TRAEs (average per treated patient), n (%)	28 (11.8)	60 (54.1)

Results

Cost of TRAEs

- Consistent with the lower rate of TRAEs per patient receiving nivolumab, the estimated cost of TRAEs 3-4 was also lower with nivolumab compared with IC (Figure 2)
- In CheckMate 141, the estimated total cost of managing grade 3–4 TRAEs was 107,853€ for the 236 treated patients in the nivolumab arm and 220,487€ for the 111 treated patients in the IC arm (Figure 2)
- Among patients receiving nivolumab, the greatest estimated cost burden was for the management of respiratory, thoracic, and mediastinal TRAEs 38,736 €), followed by investigations TRAEs (18,789 €) and general disorders (16,271 €) (Figure 2)
- Among patients receiving IC, the greatest estimated cost burden was for the management of thoracic and mediastinal TRAEs (53,089 €**)** and gastroinstestinal TRAEs (47,305 €**)**, followed by investigations (26,651 €) (Figure 2)
- The estimated average per-patient cost of managing grade 3–4 TRAEs was nearly 1500 € lower for patients who received nivolumab compared with those who received IC (1986 € vs 457 €)

Figure 2. Estimated total cost of TRAEs 3-4, by system organ class

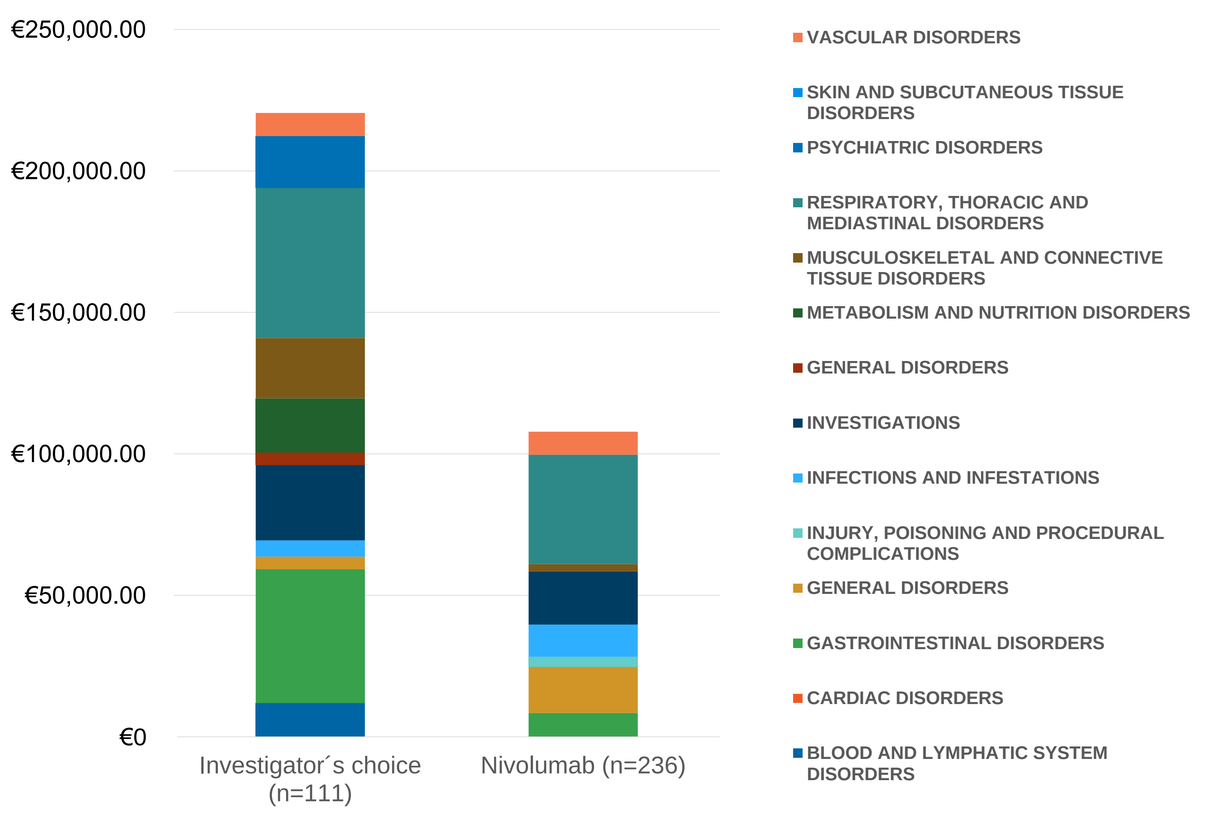
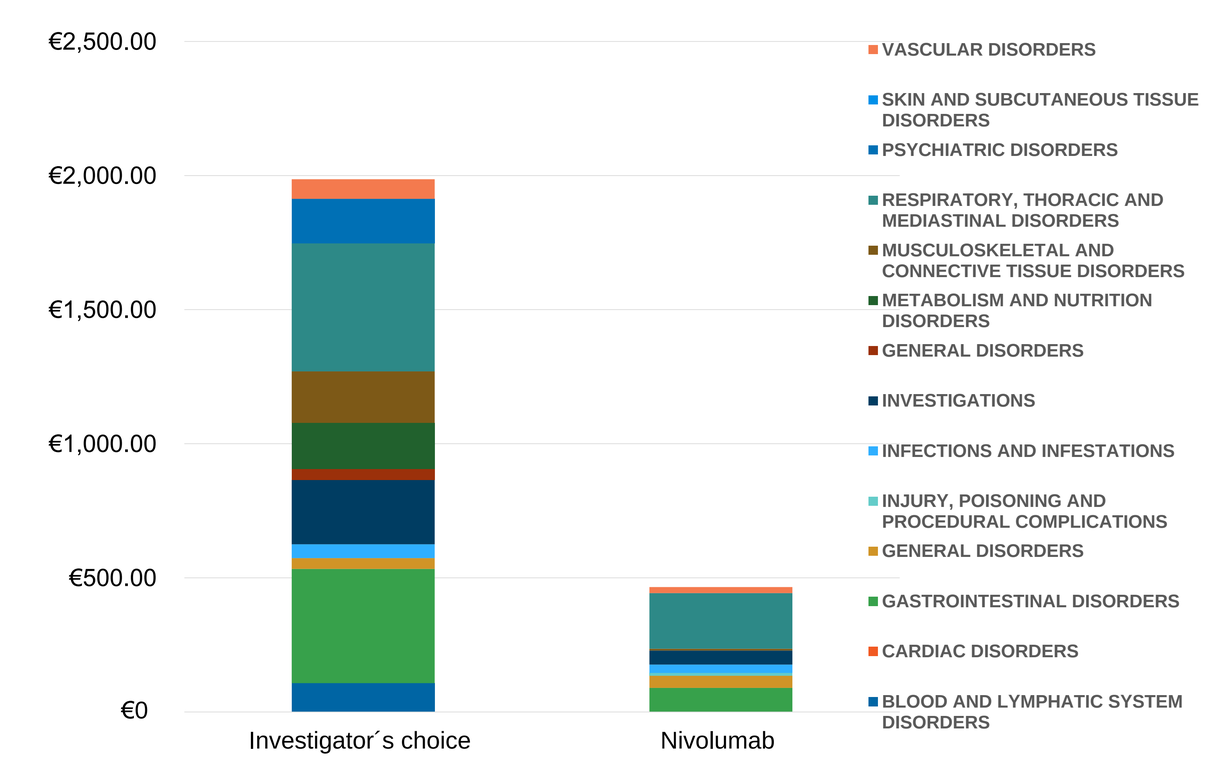


Figure 3. Estimated total cost by patient of TRAEs 3-4, by system organ class



Limitations

- The cost of TRAE management in this analysis may have been underestimated in the following ways: Grade 1 and 2 TRAEs were excluded from the analysis (intervention was not indicated), which had a higher per-patient incidence in the IC arm
- Some TRAEs had missing or unknown associated costs and thus were not included in the total
- Results are based on the assumption that TRAE frequency was patient- and treatment-specific and not country-specific
- Estimated costs used in this analysis are based on Spain cost data, and may not accurately reflect the cost of TRAE management in other countries

Conclusions

- As previously reported, in CheckMate 141, the frequency of TRAEs was lower among patients who received nivolumab than those who received IC for R/M SCCHN
- In this analysis, we found that there was an estimated 4.5-fold lower incidence of grade 3–4 TRAEs with nivolumab
- Consistent with the lower frequency of TRAEs, the cost of managing grade 3–4 TRAEs was estimated to be 4.6-fold lower in the nivolumab arm compared with the IC arm
- The estimated cost savings related to management of TRAEs was nearly 1500€ per patient treated with nivolumab vs IC
- In addition to the benefit of fewer TRAEs resulting in lower estimated costs in the nivolumab arm, data have shown that patients treated with nivolumab experience benefits in quality of life compared with IC,[7] which might further offset the cost of care
- The lower cost of TRAE management associated with nivolumab should be considered when assessing the value of nivolumab in patients with R/M SCCHN

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