

NIVOPOSTOP (GORTEC 2018-01)

A phase III randomized trial of adjuvant **nivolumab** added to radio-chemotherapy in patients with **resected head and neck squamous cell carcinoma** at **high risk** of relapse

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on behalf of GORTEC

Takeways

- **Background** : for high risk resected head and neck SCC cancers, the SOC cisplatin-radiotherapy did not change in the past decades
- **NIVOPOSTOP** phase III study tested the addition of nivolumab to SOC
- **Outcome** : the primary endpoint of improving DFS was met, with only a moderate increase in toxicity

INTRODUCCION

Background

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Resected locally advanced squamous-cell carcinoma of the head and neck (LA-SCCHN) with high risk of relapse:

High risk pathological features after surgery are **mainly** extra capsular extension in cervical nodes (ECE) and/or positive / close (< 1 mm) margin(s)

For over 20 years, the Standard of Care (SOC) has been adjuvant cisplatin-radiotherapy*

40-45% recurrence (local and/or distant)*: **unmet clinical need**

* Bernier J NEJM 2004 ; Cooper JS NEJM 2004

INTRODUCCION

Background (II)

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- Programmed death 1 (PD1) inhibitors are effective treatments in SCCHN and have been established as the **SOC in the recurrent / metastatic setting***
... but so far did not succeed in the locally advanced setting
- **NIVOPOSTOP (NCT03576417)** is a multicenter, open-label, randomized, phase 3 Investigator Sponsored Study, evaluating:
 - the addition of anti PD1 **nivolumab** to SOC versus SOC alone
 - in patients with **high risk resected LA-SCCHN**

*Burtness B et al. The Lancet 2019

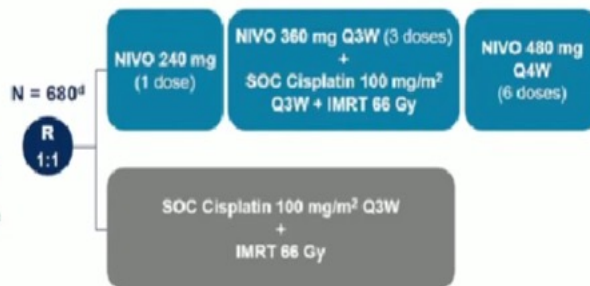
DISEÑO DEL ESTUDIO

NIVOPOSTOP study design

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Key inclusion criteria:

- Adult patients <75 y/o
- ECOG PS 0-1
- SCC of the oral cavity, oropharynx, larynx, or hypopharynx with :
 - Complete macroscopic surgical resection
 - pStage III or IV^b (AJCC 8th edition)
 - High-risk pathological features of relapse^c



DISEÑO DEL ESTUDIO

Primary endpoint: Disease-free survival (DFS) per investigator assessments (with biopsy if needed)

Key secondary endpoints: Overall survival (OS) and safety

OS : planned to be tested only if DFS was significant and triggered by a pre-specified number of deaths.

Safety: assessed in patients who received at least 1 dose of any study treatment according to NCI-CTCAE v5.0

Baseline Characteristics

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N (%)	NIVO + CRT (n = 332 ^a)	CRT (n = 334 ^a)
Median age (IQR), y	59 (53–65)	59 (53–64)
Sex		
Male	250 (75)	257 (77)
Female	82 (25)	77 (23)
ECOG PS		
0	169 (51)	188 (50)
1	163 (49)	166 (50)
Smoking status		
Current	179 (54)	181 (48)
Former	108 (33)	109 (33)
Never	45 (14)	64 (19)
Median no. packs-years (IQR)	40 (25–50)	40 (25–45)
Tumor site and p16 status		
Oral cavity	192 (58)	193 (58)
Hypopharynx	43 (13)	40 (12)
Larynx	40 (12)	41 (12)
OPC p16-	41 (12)	43 (13)
OPC p16+	16 (5)	17 (5)

^aAnalysis was based on 666 patients randomized before the data cut off (April 30th 2024) when the required number of DFS events was reached.

RESULTADOS

Disease-free survival: (primary endpoint ; ITT)

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Analysis based on **252 DFS events**
at the data cutoff of April 30th 2024

Median follow-up: **30.3 months** (IQR 16-44.9)

3-years DFS

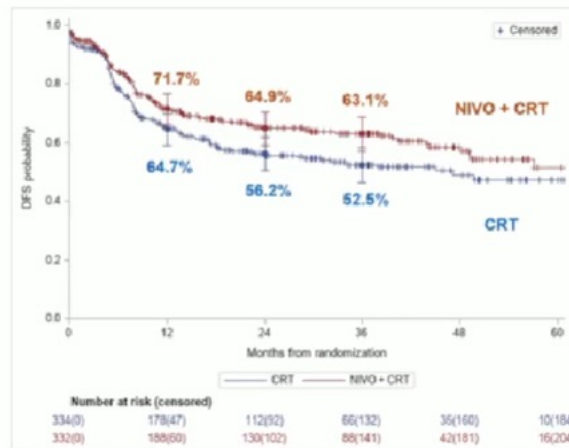
63.1% (95%CI 57.0%; 68.7%)
with NIVO + CRT

versus

52.5% (95%CI 46.2%; 58.4%)
with CRT

Stratified* HR (95%CI) = **0.76 (0.60; 0.98)**
Stratified log-rank p-value=0.034

*HR stratified for p16 status (OPC p16 positive versus OPC p16 negative and non-OPC) in Cox model



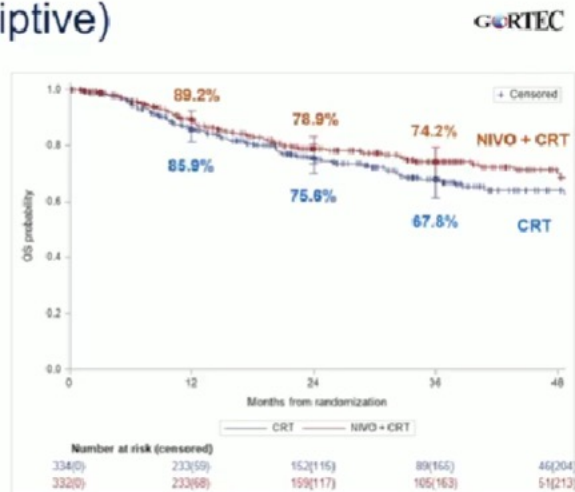
RESULTADOS

Overall survival (descriptive)

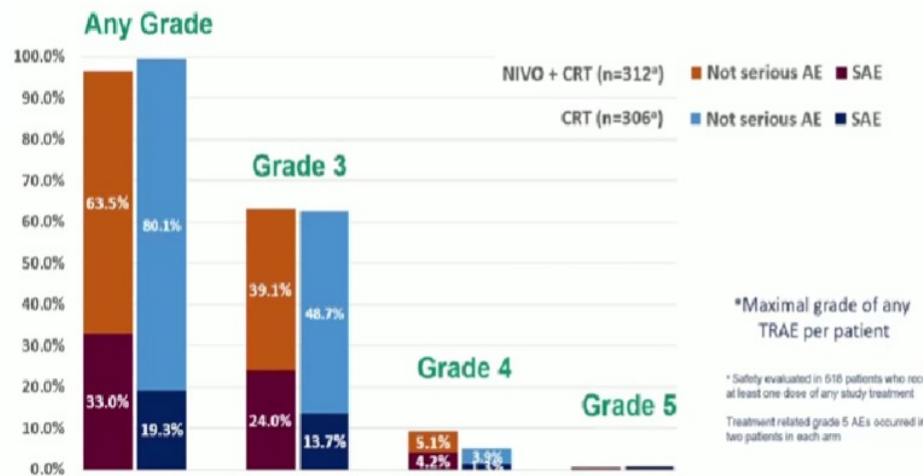
At the data cutoff, 158 patients died.

Results are in favor of NIVO + CRT
but OS could not be formally tested
since the pre-specified number of
deaths was not reached.

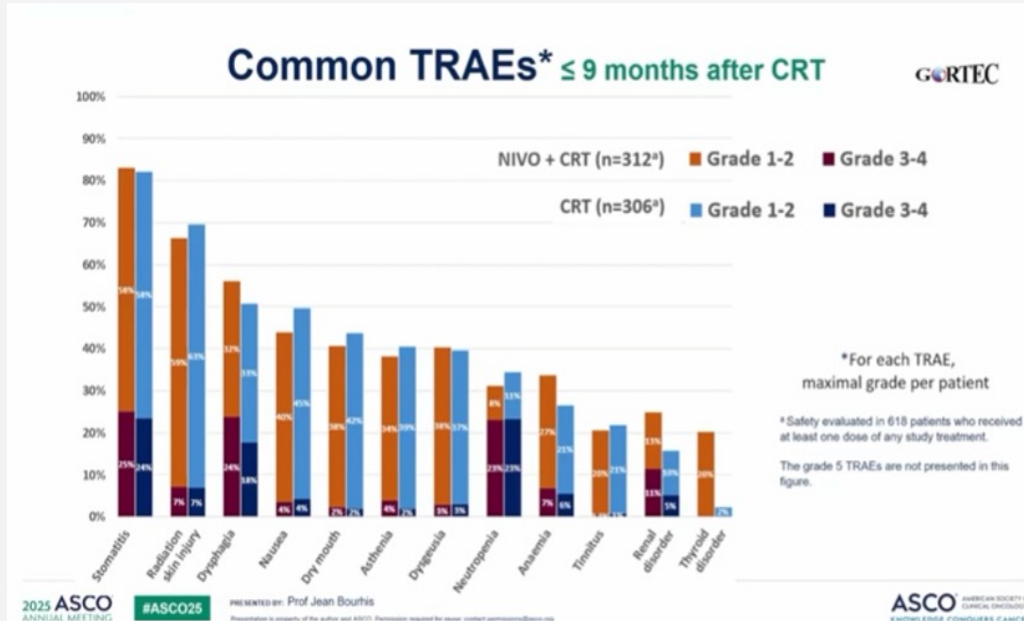
The statistical analysis of OS
requires more mature data according
to the statistical plan.



Treatment Related Adverse Events* ≤ 9 months after CRT



SEGURIDAD



CONCLUSIONES

Summary

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The benefit-risk ratio of adding nivolumab appeared favorable :

- The primary endpoint was met : DFS significantly improved (HR 0.76)
- Moderate increased toxicity, without increase in treatment-related deaths

Post-operative nivolumab added to SOC cisplatin-RT improved patient outcomes for resected high-risk LA-SCCHN, that could be proposed as a new standard treatment, ... for the first time in two decades...