



# **Enric Carcereny**

Institut Català d'Oncologia Badalona Badalona-Applied Research Group in Oncology (B-ARGO)

First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

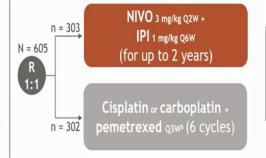
### Study Dresign

#### Key eligibility criteria

- · Unresectable MPM
- · No prior systemic therapy
- ECOG PS 0-1

#### Stratified by

Histology (epithelioid vs non-epithelioid) and sex



Until disease progression, unacceptable toxicity, or for 2 years for immunotherapy

#### Primary endpoint

#### · 05

#### Secondary endpoints

- ORR, DCR, and PFS by BICR
- · Efficacy by PD-L1c expression

#### Exploratory endpoints

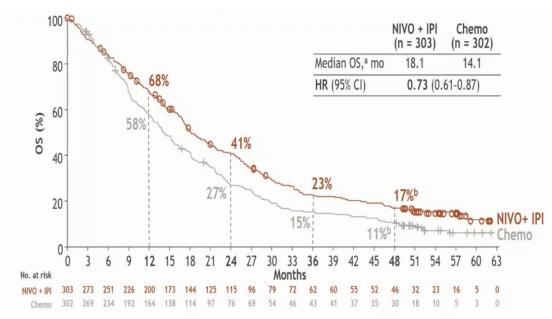
- Safety and tolerability
- Biomarkers

Database lock: May 6, 2022; minimum / median follow-up for OS: 47.5 months / 55.1 months.

Reprinted from The Lancet, Vol. 397, Baas P et al, First-line nivolumab plus ipilimumab in unresectable malignant pleural mesothelioma (CheckMate 743): a multicentre, randomised, open-label, phase 3 trial, p375-386, Copyright 2020, with permission from Elsevier.

<sup>a</sup>NCT02899299; <sup>b</sup>Cisplatin (75 mg/m²) or carboplatin (AUC 5) + pemetrexed (500 mg/m²), Q3W for 6 cycles; <sup>c</sup>Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). Baas P, et al. Lancet 2021;397:375-386.

### **Overall Survival**



- 4-year PFS rates were 9% vs 0% with NIVO + IPI vs chemo<sup>c</sup>
- ORR and DOR were consistent with previous database lockd; rate of ongoing responders at 4 years was 16% vs 0%, respectively

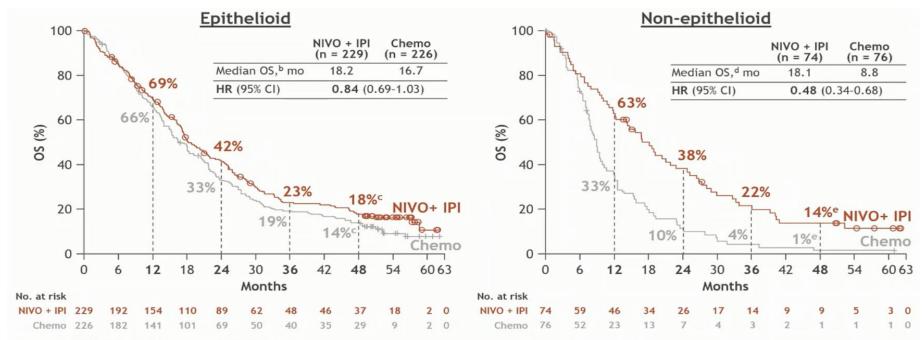
Minimum / median follow-up for OS: 47.5 months / 55.1 months.

Subsequent systemic therapy was received by 46% of patients in the NIVO + IPI arm and 43% in the chemo arm; subsequent immunotherapy was received by 5% and 23%; subsequent chemotherapy was received by 44% and 34%, respectively.

<sup>295%</sup> CIs were 16.8-21.0 (NIVO + IPI) and 12.4-16.3 (chemo); <sup>595%</sup> CIs were 12.7-21.5 (NIVO + IPI) and 7.5-14.7 (chemo); <sup>6</sup>Median PFS was 6.8 vs 7.2 months with NIVO + IPI vs chemo (HR, 95% CI: 0.93. 0.77-1.13); <sup>6</sup>ORR was 39.3% vs 44.4%, and median DOR was 11.6 vs 6.8 months.

First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

### Overall Survival by Histology



Minimum / median follow-up for OS: 47.5 months / 55.1 months.

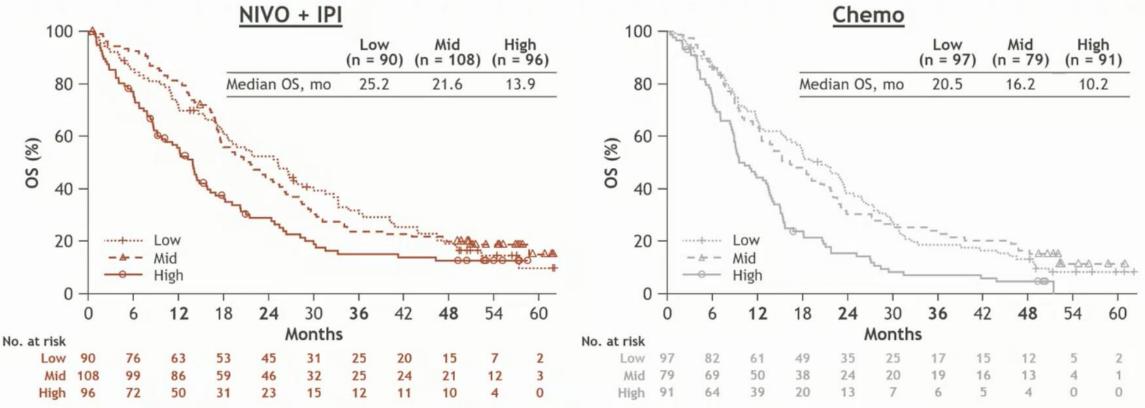
In patients with epithelioid histology, subsequent systemic therapy was received by 48% in the NIVO + IPI arm vs 45% in the chemo arm; subsequent immunotherapy was received by 46% vs 37%, respectively. In patients with non-epithelioid histology, subsequent systemic therapy was received by 40% in the NIVO + IPI arm vs 37% in the chemo arm; subsequent immunotherapy was received by 7% vs 20%; subsequent chemotherapy was received by 38% vs 26%, respectively.

"Histology per CRF; b95% CIs were 16.9-21.9 (NIVO + IPI) and 14.9-20.3 (chemo); c95% CIs were 13.0-23.2 (NIVO + IPI) and 9.6-18.9 (chemo); d95% CIs were 12.2-22.8 (NIVO + IPI) and 7.4-10.2 (chemo); c95% CIs were 6.9-23.3 (NIVO + IPI) and 0.1-6.8 (chemo).



First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

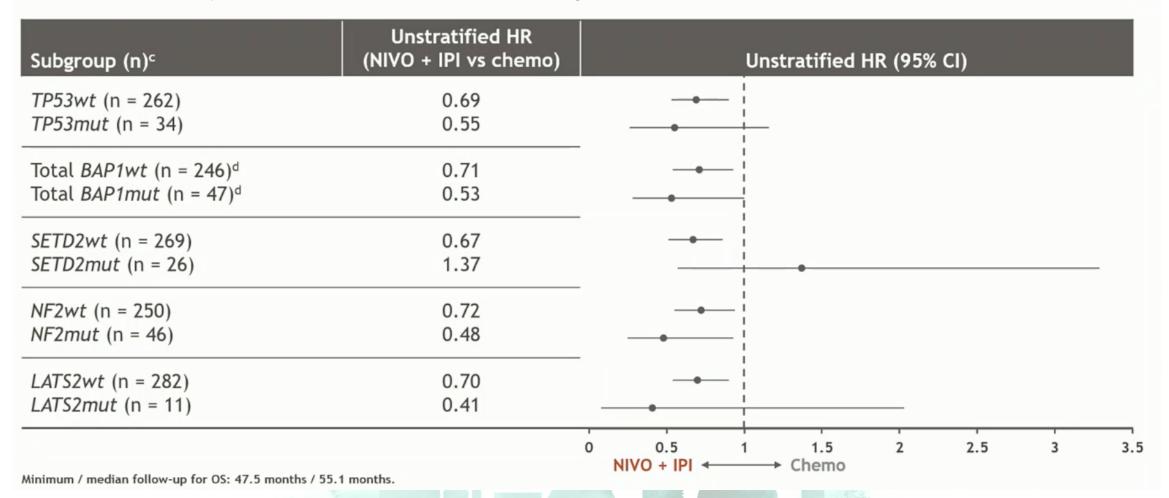
Overall Survival by baseline soluble mesothelin level



Similar trends in OS were seen in patients with epithelioid<sup>c</sup> and those with non-epithelioid histology,<sup>d</sup> although the non-epithelioid histology subgroups were small

First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

Overall Survival by MPM specific tumor suppressor gene mutations



### **Conclusiones**

- 1. La combinación de Nivolumab + Ipilimumab sigue demostrando beneficio en supervivencia a los 4 años de seguimiento frente a la quimioterapia.
- 2. El 16% de los respondedores a la inmunoterapia continúan respondiendo a los 4 años frente a ninguno en el brazo de quimioterapia.
- 3. Los niveles elevados de mesotelina basal se correlacionan con un peor pronóstico, independientemente del brazo de tratamiento.
- 4. .En el análisis exploratorio de biomarcadores, entre los distintos genes supresores analizados, el beneficio es mayor para el brazo de inmunoterapia.
- 5. No aparecen nuevos datos seguridad con este mayor seguimiento