



LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019



Con la colaboración de:



Iniciativa científica de:



CPNM avanzado: Quimioterapia / Inmunoterapia

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Con la colaboración de:



A phase III randomized study of Nivolumab/Ipilimumab vs Nivolumab for prev. treated st. IV SqNSCLC

(OA04.01 Bazhenova L, et al.)

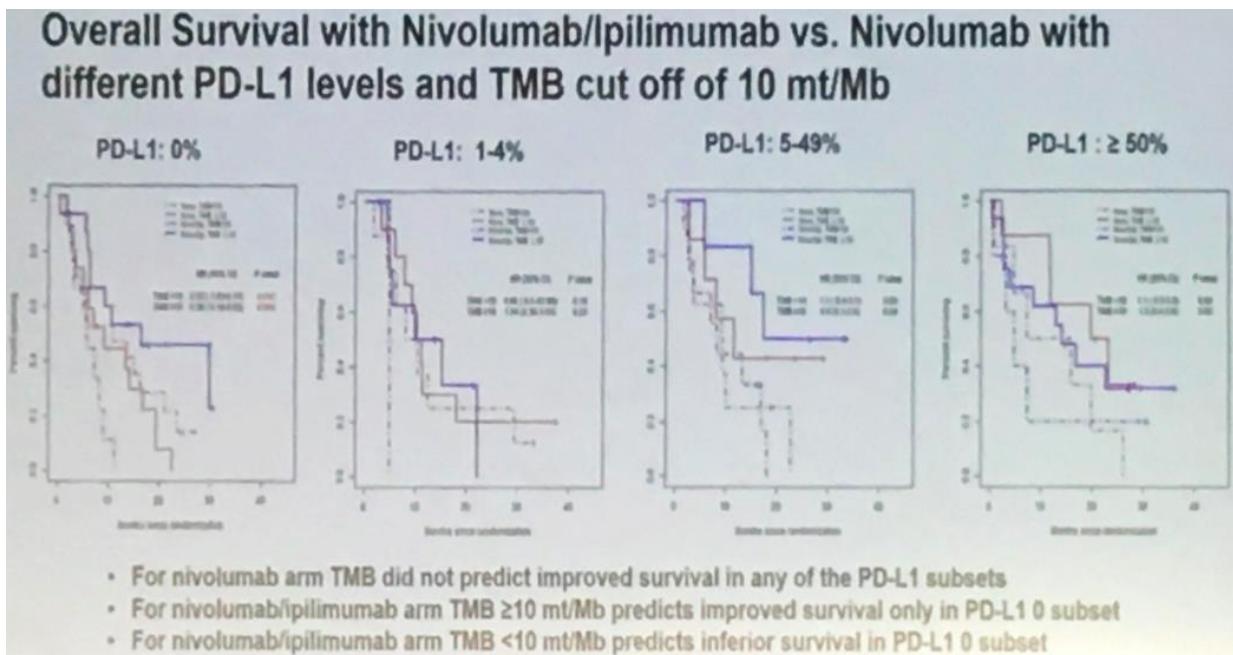
- 252 immunotherapy-naive SqNSCLC: **N+I** (125 p) vs **N** (127 p)
- **OS** (1ry objective): 10.0 mo. vs 11.0 mo. HR 0.97, p 0.82
- **PFS**: 3.8 mo. vs 2.9 mo. HR 0.84, p 0.19
- **RR**: 18% vs 17%
- Most AEs were low grade. G \geq 3: 39% vs 31%
- Discontinuation due to AEs: 25% vs 16%
- Outcomes similar across TMB subgroups and PD-L1 expression levels

	N+I Median in months	N Median in months	HR	p
OS PD-L1 \geq 5	14.1 (5.8-17.5)	12.0 (8.2-19.8)	1.06 (0.58-1.92)	0.86
OS PD-L1 <5	8.3 (6.0-10.7)	10.3 (6.3-13.5)	1.01 (0.62-1.65)	0.97
OS TMB \geq 10	13.1 (9.3-17.0)	11.4 (8.2-16.1)	0.86 (0.56-1.32)	0.48
OS TMB <10	7.6 (5.7-10.2)	10.0 (6.3-15.2)	1.08 (0.68-1.71)	0.74



Closed for futility at interim analysis

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- TMB score and PD-L1 do **not** correlate (expected)
- Different levels of PD-L1 or TMB itself do **not** differentiate OS between the treatment regimens
- In the subgroup PD-L1 neg/TMB ≥ 10 there is a signal for **improved** OS in the combination-arm
- In the subgroup PD-L1 neg/TMB < 10 there is a signal for a **detrimental** OS in the combination arm
- PD-L1 negative subset is 56 pts and 46 events

A Randomized Phase 3 Study of Camrelizumab plus CT as 1st-Line Therapy for Adv./Metastatic Non-Sq NSCLC (OA04.03 Zhou C, et al.)

- 419 patients (205 vs 207) – Asian patients nonSq NSCLC
- Carbo-Pemetrexed ± Camrelizumab followed by Peme ± Camrelizumab
- Grade 3-4 AEs: 66.3% vs 45.9%
- Discontinuation due to AEs: 13.7% vs 12.2%
- **PFS** by BICR (1ry objective) 11.3 mo. vs 8.3 mo. HR 0.61, p=0.0002

Table 1. Responses per blinded independent central review and overall survival in the total study population

	Camrelizumab plus chemotherapy (n=205)	Chemotherapy alone (n=207)	p-value
RR	60.0% (53.0–66.8)	39.1% (32.4–46.1)	p<0.0001
DCR	87.3% (82.0–91.6)	74.4% (67.9–80.2)	p=0.0009
DoR (mo)	17.6 (11.6–NR)	9.9 (8.5–13.8)	p=0.0356
OS (mo)	NR (17.1–NR)	20.9 (14.2–NR)	p=0.0272

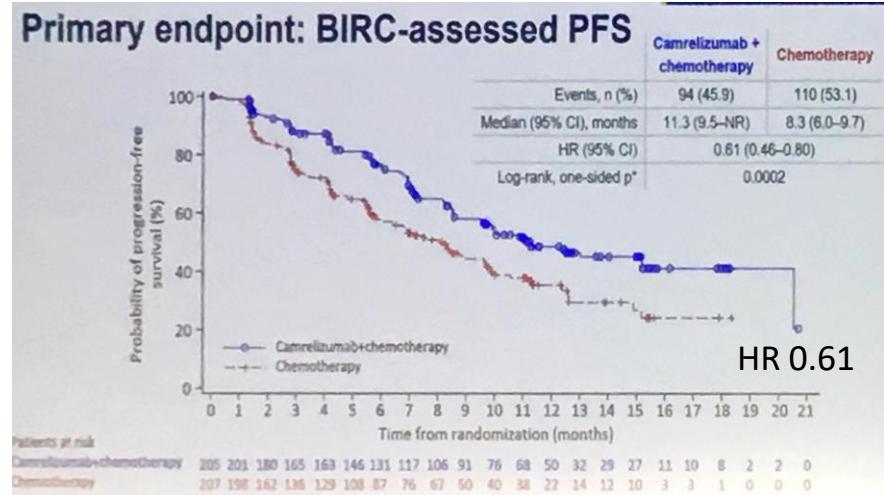
in % (95% CI) or median (95% CI). NR: not reached.



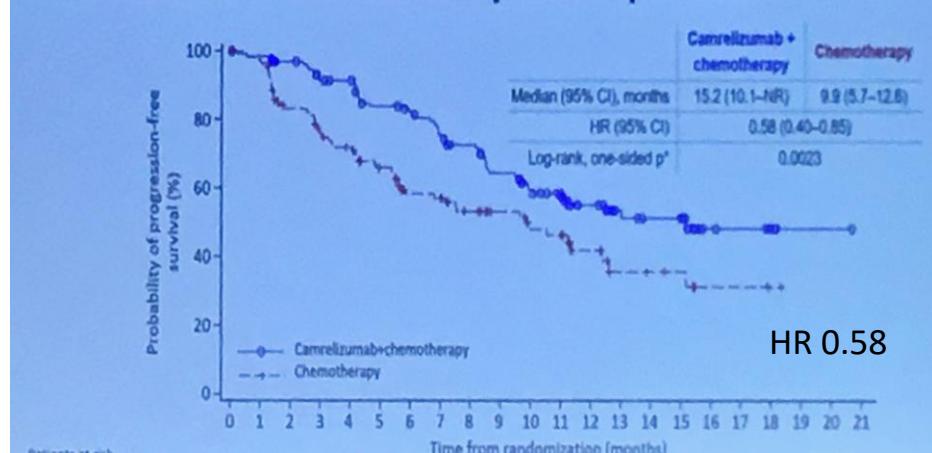
Iniciativa científica de:

A Randomized Phase 3 Study of Camrelizumab plus CT as 1st-Line Therapy for Adv./Metastatic Non-Sq NSCLC (OA04.03 Zhou C, et al.)

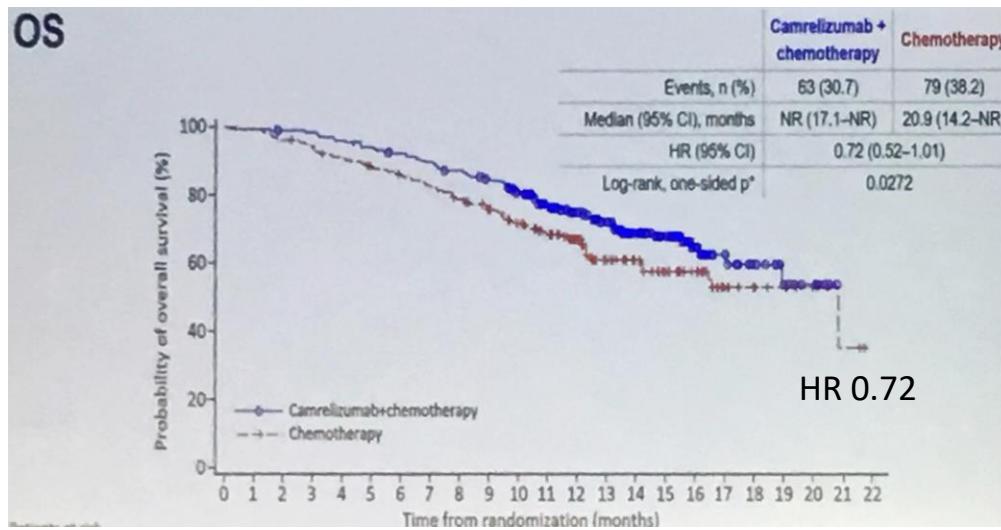
Primary endpoint: BIRC-assessed PFS



BIRC-assessed PFS in PD-L1 positive patients



OS



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KEYNOTE-021 & KEYNOTE-189: TMB and Outcomes for Carboplatin-Pemetrexed ± Pembrolizumab for NonSq NSCLC (OA04.05 Langer CJ, et al) (OA04.06 Garassino MC, et al)

Association of tTMB (\log_{10}) With Efficacy

Nominal P Value (one sided) ^a	Pembro + PC (n = 44)	PC Alone (n = 26)
ORR	0.180	0.861
PFS	0.187	0.795
OS	0.081	0.763

No association between tTMB as a continuous variable and efficacy for pembrolizumab + PC or PC alone based on $\alpha = 0.05$ significance level

Keynote-021

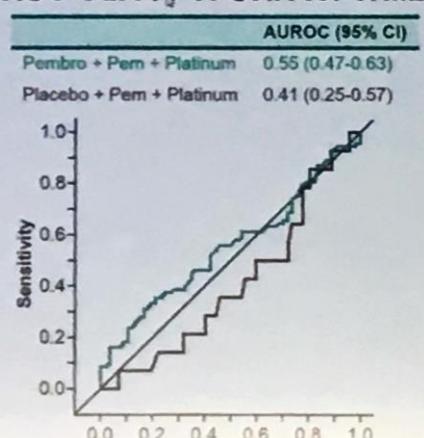
Association of tTMB (\log_{10}) With Efficacy

Nominal P Value ^a	Pembro + Pem + Platinum (n = 207)	Placebo + Pem + Platinum (n = 86)
OS	0.174 (one sided)	0.856 (two sided)
PFS	0.075 (one sided)	0.055 (two sided)
ORR	0.072 (one sided)	0.434 (two sided)

No association between tTMB as a continuous variable and efficacy in either arm based on $\alpha = 0.05$ significance level and AUROC analysis

^atest. P values are one-sided for pembrolizumab + carboplatin + pemetrexed because the a priori hypothesis was that pembrolizumab was positively associated with improved outcomes of pembrolizumab + carboplatin + pemetrexed. P values are two-sided for placebo + carboplatin + pemetrexed because there was no a priori hypothesis regarding the direction.

ROC Curves of ORR for tTMB



Keynote-189