#IASLCUPDATES

Iniciativa científica de:

GECP lung cancer research

LUNG CANCER UPDATES

IASLC HIGHLIGHTS

7-10 DE SEPTIEMBRE 2019

Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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BARCELONA
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CPNM avanzado: Quimioterapia / Inmunoterapia

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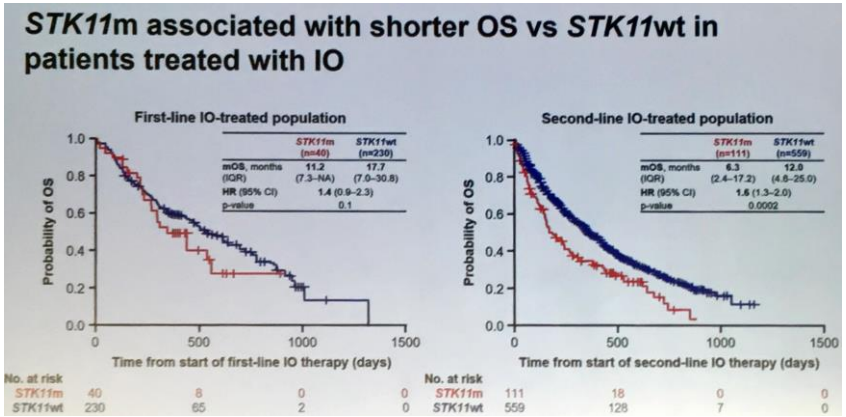
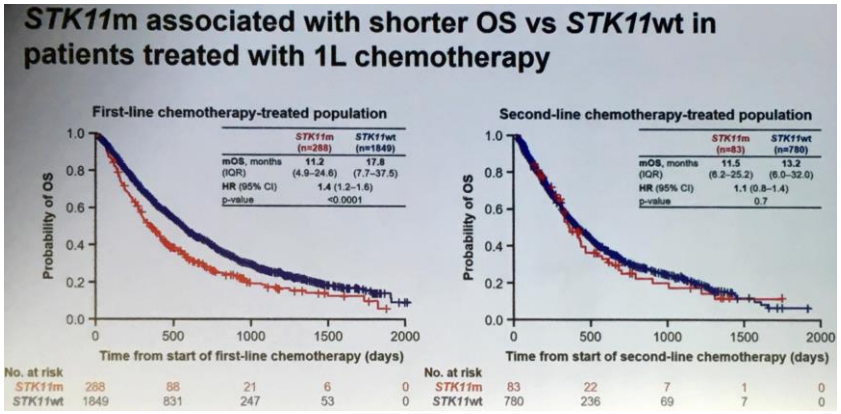
STK11/LKB1 Mutations in Metastatic NSCLC (mNSCLC): Prognostic Value in the Real World (OA07.02 Shire N, et al)

- *STK11 (STK11m)* mutations and co-occurring *KRAS* mutations/STK11 mutations (KRASm/STK11m) have been associated with poor outcomes in patients treated with immunotherapy
- The prognostic value is less understood among CT-treated patients
- Retrospective study examining *STK11m*, *KRASm/STK11m* (FoundationOne) and survival outcomes in patients receiving IO (as monotherapy or in combination) or CT in the real-world setting
- 2407 p (1847 nonSq), average age 66.1 years
  - 328/2047 (13.6%) p harbored *STKm*
  - 157/2047 (6.5%) p harbored *KRASm/STK11m*

- *STK11m* was associated with shorter OS and PFS versus wild-type in the 1st-L and 2nd-L setting irrespective of treatment
- All association were more pronounced among *KRAS/LKB1*

LKB1 Mutations in Metastatic NSCLC (mNSCLC): Prognostic Value in the Real World (OA07.02 Shire N, et al)





Outcomes in patients with non-squamous histology were generally consistent with the overall population

	IO therapy		Chemotherapy	
	First-line (n=187)	Second-line (n=498)	First-line (n=1,687)	Second-line (n=683)
mOS, months (IQR)				
*STK11*m	14.2 (7.3–NA)	6.6 (2.4–20.1)	11.7 (5.1–25.2)	13.1 (7.2–25.2)
*STK11*wt	20.1 (7.4–42.8)	13.6 (4.8–27.9)	18.9 (8.0–40.1)	15.2 (6.5–38.0)
HR (95% CI)*	1.4 (0.8–2.3)	**1.7 (1.3–2.2)****	**1.4 (1.2–1.7)****	1.1 (0.8–1.4)
mPFS, months (IQR)				
*STK11*m	4.1 (2.7–9.8)	2.2 (1.5–3.7)	4.5 (2.1–7.5)	4.2 (2.3–6.7)
*STK11*wt	5.4 (2.4–17.0)	3.1 (1.8–7.7)	6.1 (2.8–11.9)	4.5 (2.1–10.1)
HR (95% CI)†	1.4 (0.9–2.0)	**1.6 (1.2–2.0)****	**1.4 (1.2–1.6)****	1.1 (0.8–1.4)

*Hazard ratio for death comparing *STK11*m with *STK11*wt
†Hazard ratio for progression comparing *STK11*m with *STK11*wt
**P-value <0.001

Similar associations were observed in patients with *KRAS*m/*STK11*m

	*KRAS*m/*STK11*m	*KRAS*wt/*STK11*wt	*KRAS*m/*STK11*m	*KRAS*wt/*STK11*wt
	1L IO (n=17)	1L IO (n=149)	2L IO (n=56)	2L IO (n=371)
mOS, months (IQR)	10.0 (7.3–NA)	16.3 (6.0–29.7)	6.9 (2.4–21.9)	12.0 (4.3–26.9)
HR (95% CI)*	**1.5 (0.7–2.9)**		**1.6 (1.2–2.3)**	
mPFS, months (IQR)	4.1 (2.5–9.6)	4.4 (2.1–11.7)	2.2 (1.5–3.0)	2.8 (1.7–7.0)
HR (95% CI)†	**1.3 (0.8–2.2)**		**1.8 (1.4–2.4)**	
	1L chemotherapy (n=140)	1L chemotherapy (n=1,353)	2L chemotherapy (n=42)	2L chemotherapy (n=608)
mOS, months (IQR)	11.7 (5.2–23.5)	18.2 (8.1–38.4)	11.3 (7.2–25.2)	13.2 (6.2–33.5)
HR (95% CI)*	**1.6 (1.3–1.9)**		**1.3 (0.9–1.8)**	
mPFS, months (IQR)	4.5 (2.1–7.5)	6.0 (2.8–11.3)	4.4 (2.8–6.7)	4.3 (2.2–9.7)
HR (95% CI)†	**1.4 (1.2–1.7)**		**1.1 (0.8–1.5)**	

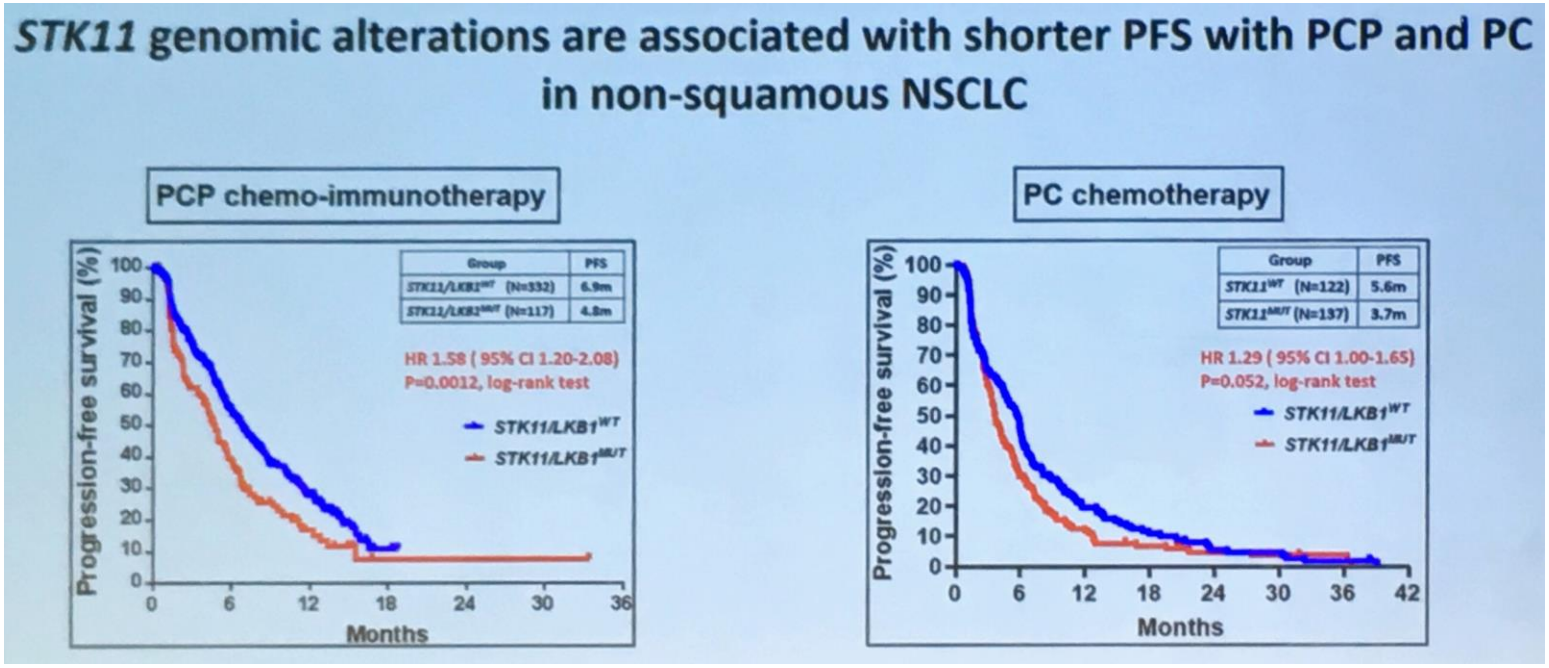
- These findings were generally consistent in the sub-population of patients with non-squamous histology

*Hazard ratio for death comparing *KRAS*m/*STK11*m with *KRAS*/*STK11*wt
†Hazard ratio for progression comparing *KRAS*m/*STK11*m with *KRAS*wt/*STK11*wt

STK11 mutations were prognostic of clinical outcomes in patients with mNSCLC

STK11/LKB1 Genomic Alterations Are Associated with Inferior Clinical Outcomes with Chemo-Immunotherapy in Non-Squamous NSCLC (MA11.11 Skoulidis F, et al)

- 620 p non-Sq patients from 21 institutions in the US and Europe (retrospective studio)
  - **Cohort A**: 468 p: Platinum-Pemetrexed-Pembrolizumab (CPP):
    - 118 (25%) *STK11/LKB1 alts*
  - **Cohort B**: 152 p *STK11/LKB1m* treated with Platinum-Pemetrexed (CP)



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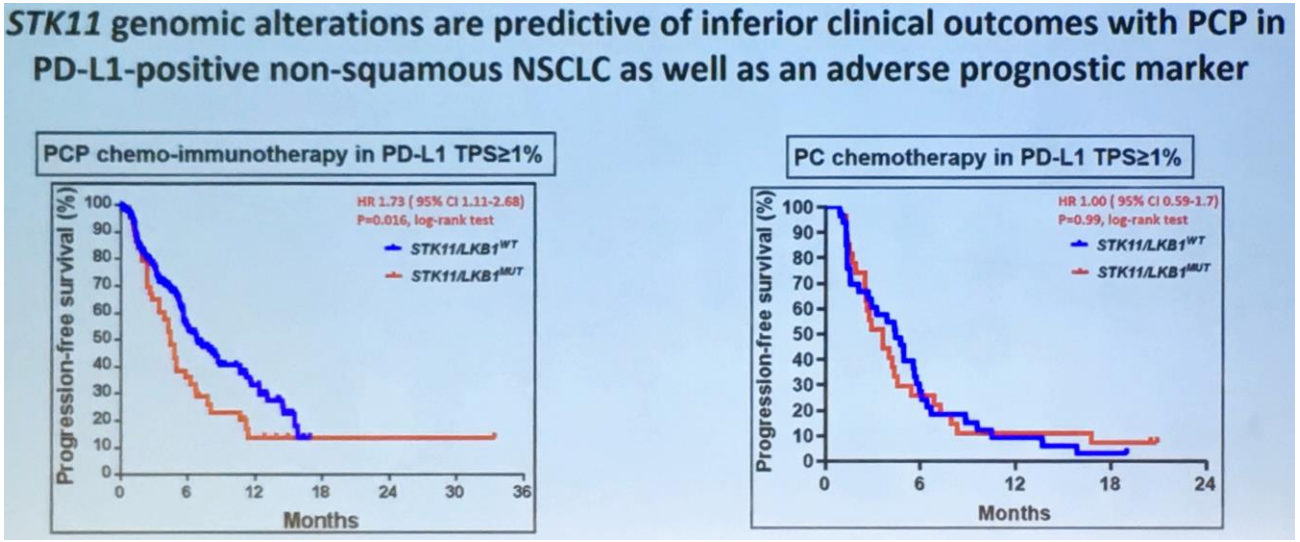

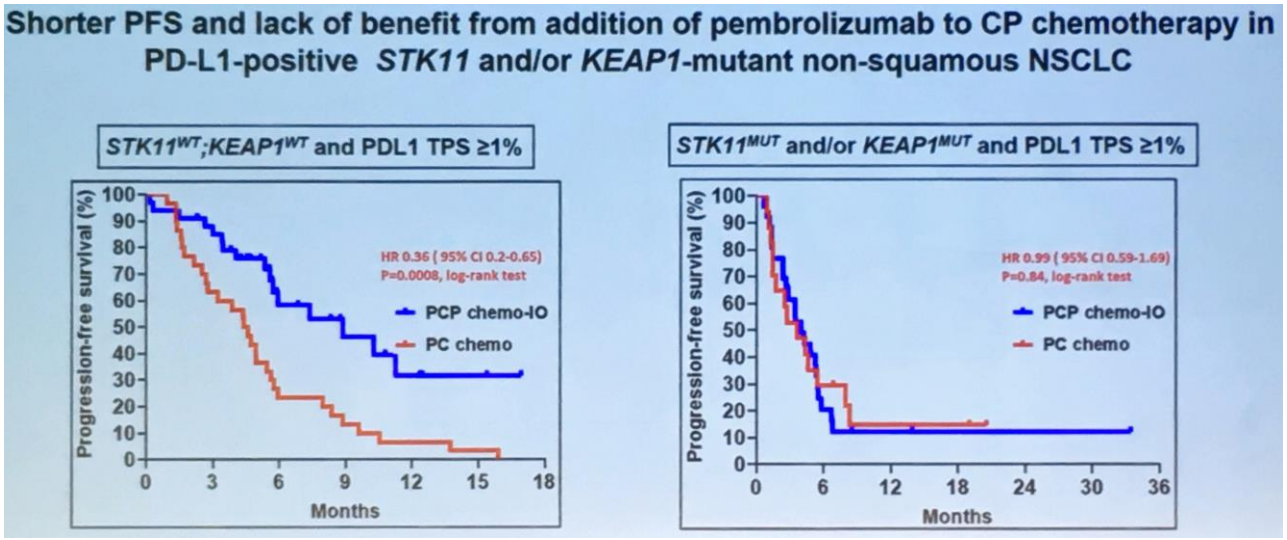

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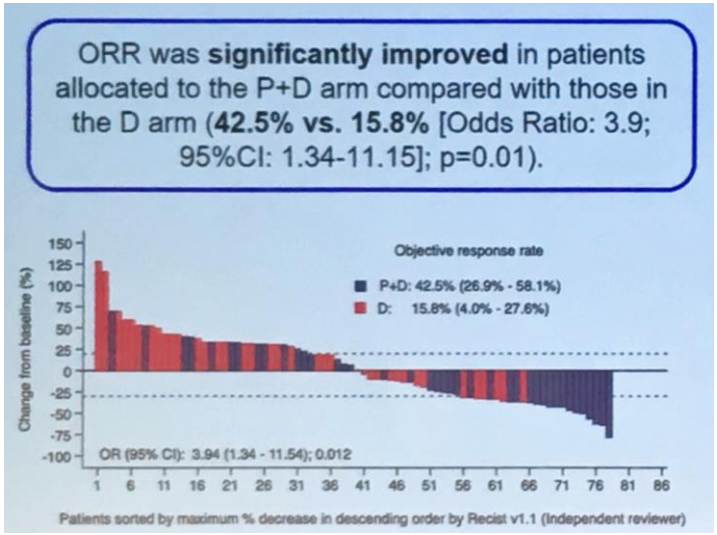
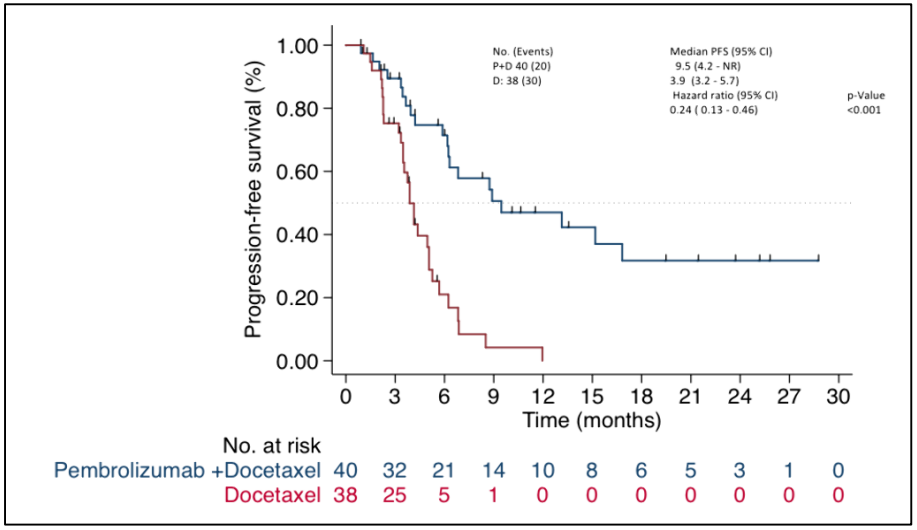
Pembrolizumab Plus Docetaxel Increases PFS Compared with Docetaxel Alone in Previously Treated Advanced NSCLC Patients (MA11.03 Arrieta OG, et al)

- 78 p progressed to previous lines of therapy, immuno-naive
- Phase 2, Randomized 1:1:
  - Pembrolizumab plus Docetaxel (40 p)
  - Docetaxel (38 p)
- RR (1ry endpoint): 42.5% vs 15.8%, OR 3.9, p=0.01 (DoR: 11.0 vs 5.2 m, p=0.0257)
- PFS: 9.5 mo. vs 3.9 mo., HR 0.24, p<0.001





- Grade 1-2 pneumonitis: 22.5% vs 5.3%, p=0.029
- Any-grade hypothyroidism: 27.5% vs 2.6%, p=0.002

Phase I expansion cohort of Ramucirumab plus Pembrolizumab in treatment-naive adv. NSCLC (JVDF)(MA14.07 Herbst RS, et al)

- Treatment-naive, PD-L1+, Sq or nonSq: 26 patients
- Ramucirumab 10 mg/kg plus Pembrolizumab 200 mg every 21 d
- No additive toxicities
- 11 (42.3%) grade ≥3 TRAES: hypertension (15.4%) and myocardial infarction (7.7%). No patient discontinued because of TRAES

Summary of efficacy endpoints with R+P in treatment-naïve NSCLC.

	All Patients (N=26)[a]	PD-L1 weakly positive (n=9)[b]	PD-L1 strongly positive (n=16)[c]
ORR, % (95% CI)	42.3 (23.4, 63.1)	22.2 (2.8, 60.0)	56.3 (29.9, 80.2)
CR, % (95% CI)	3.8 (0.1, 19.6)	0 (0, 33.6)	6.3 (0.2, 30.2)
PR, % (95% CI)	38.5 (20.2, 59.4)	22.2 (2.8, 60.0)	50.0 (24.7, 75.3)
SD, % (95% CI)	42.3 (23.4, 63.1)	66.7 (29.9, 92.5)	31.3 (11.0, 58.7)
PD, % (95% CI)	11.5 (2.4, 30.2)	11.1 (0.3, 48.2)	6.3 (0.2, 30.2)
NE, n (%)	1 (3.8)	0 (0)	1 (6.3)
mPFS, mo (95% CI)	9.3 (4.0, NR)	4.2 (1.2, NR)	NR (4.0, NR)
12-mo PFS, % (95% CI)	45.0 (24.4, 63.6)	33.3 (7.8, 62.3)	56.2 (26.9, 77.6)
18-mo PFS, % (95% CI)	45.0 (24.4, 63.6)	33.3 (7.8, 62.3)	56.2 (26.9, 77.6)
mOS, mo (95% CI)	NR (13.2, NR)	NR (3.2, NR)	NR (11.3, NR)
12-mo OS, % (95% CI)	72.5 (50.8, 85.9)	66.7 (28.2, 87.8)	75.0 (46.3, 89.8)
18-mo OS, % (95% CI)	68.0 (45.9, 82.6)	53.3 (17.7, 79.6)	75.0 (46.3, 89.8)
DCR, % (95% CI)	84.6 (65.1, 95.6)	88.9 (51.8, 99.7)	87.5 (61.7, 98.4)