LUNG CANCER UPDATES

AACR HIGHLIGHTS

14-18 ABRIL 2018, CHICAGO

Combinación de inmunoterapia en primera línea de enfermedad avanzada

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Con el patrocinio de

Bristol-Myers Squibb

Iniciativa científica de:

GECP

Grupo Español de Cáncer de Pulmón

Spanish Lung Cancer Group

KEYNOTE-189: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab or Placebo plus Pemetrexed and Platinum as First-Line Therapy for Metastatic NSCLC

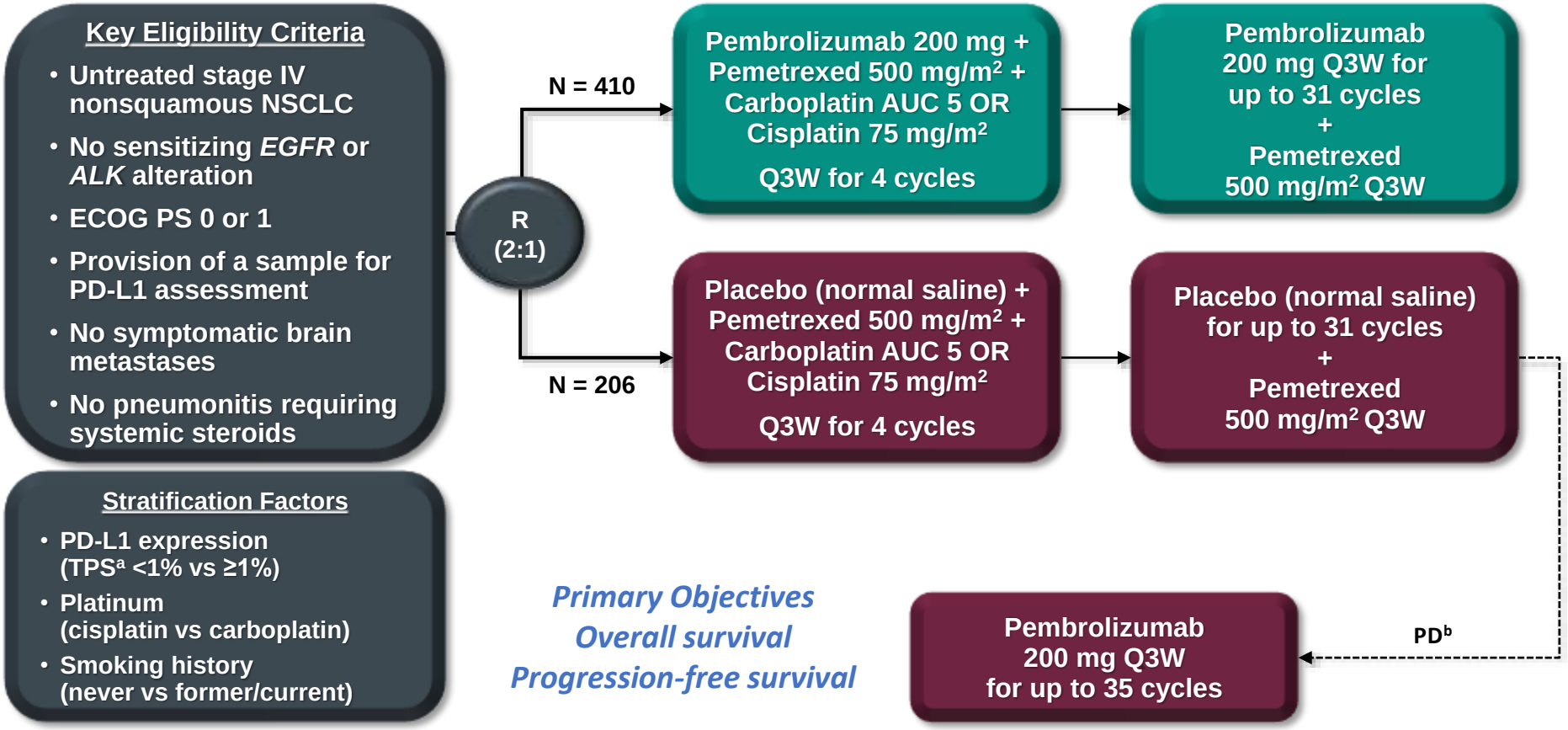
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer

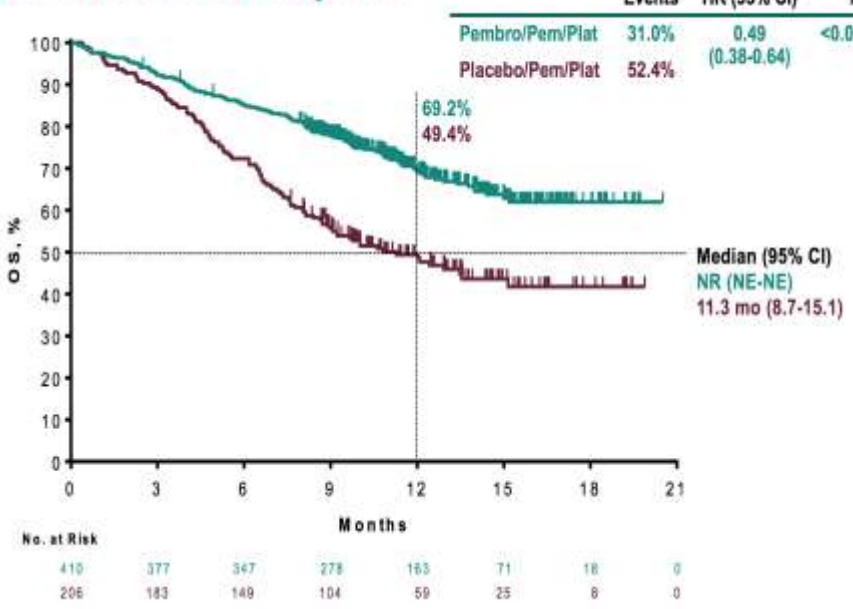
L. Gandhi, D. Rodríguez-Abreu, S. Gadgeel, E. Esteban, E. Felip, F. De Angelis, M. Domine, P. Clingan, M.J. Hochmair, S.F. Powell, S.Y.-S. Cheng, H.G. Bischoff, N. Peled, F. Grossi, R.R. Jennens, M. Reck, R. Hui, E.B. Garon, M. Boyer, B. Rubio-Viqueira, S. Novello, T. Kurata, J.E. Gray, J. Vida, Z. Wei, J. Yang, H. Raftopoulos, M.C. Pietanza, and M.C. Garassino, for the KEYNOTE-189 Investigators*

KEYNOTE-189 Study Design (NCT02578680)

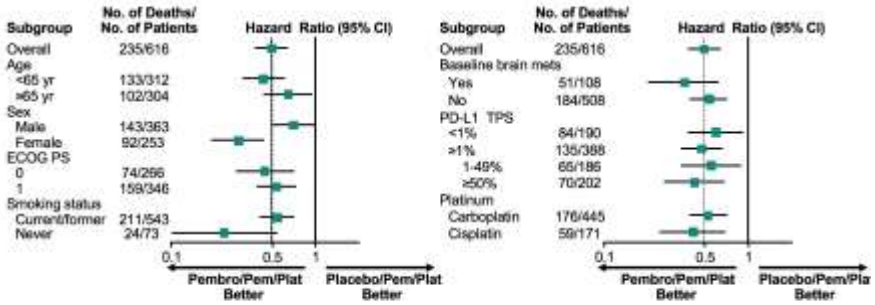


[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during the induction or maintenance phases. To be eligible for crossover, PD must have been verified by blinded, independent central radiologic review and all safety criteria had to be met.
aPercentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay.

Overall Survival, ITT

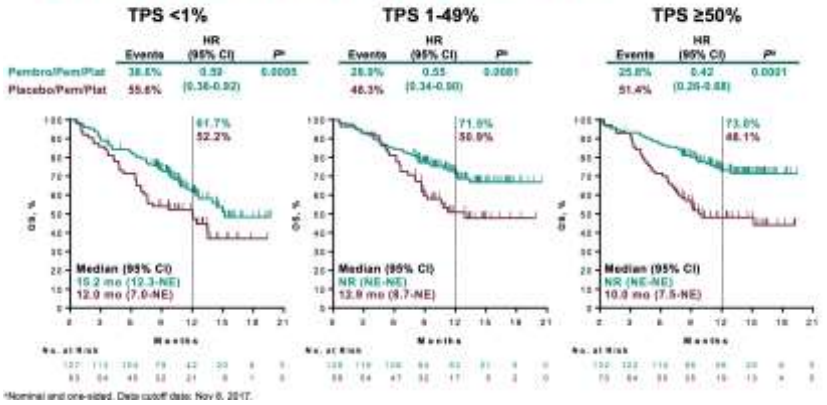


Overall Survival in Key Subgroups



Data cutoff date: Nov 8, 2017.

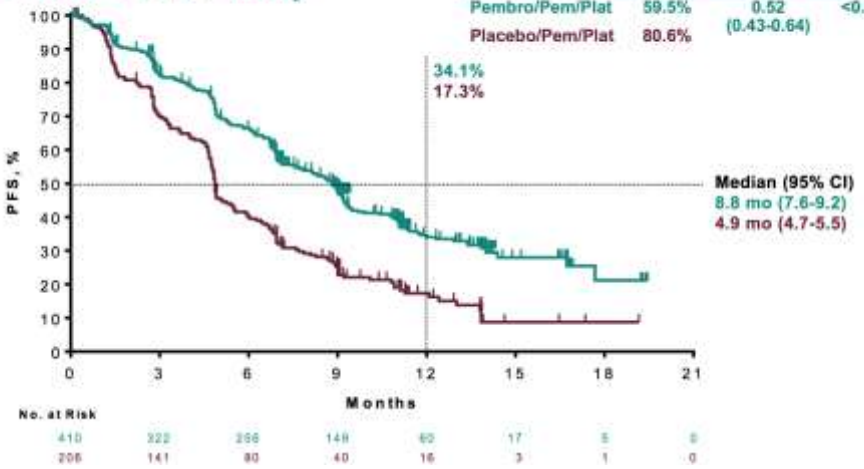
Overall Survival by PD-L1 TPS



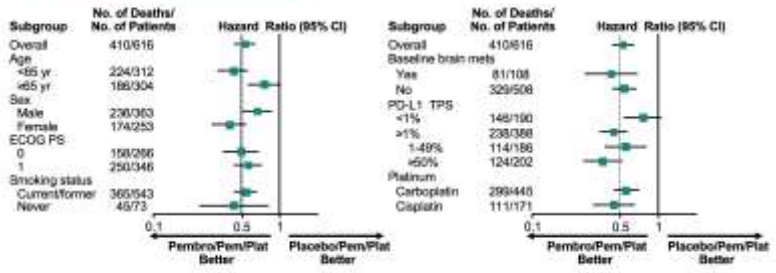
*Nominal and one-sided. Data cutoff date: Nov 8, 2017.

Progression-Free Survival, ITT
(RECIST v1.1, BICR)

	Events	HR (95% CI)	P
Pembro/Pem/Plat	59.5%	0.52 (0.43-0.64)	<0.00001
Placebo/Pem/Plat	80.6%		

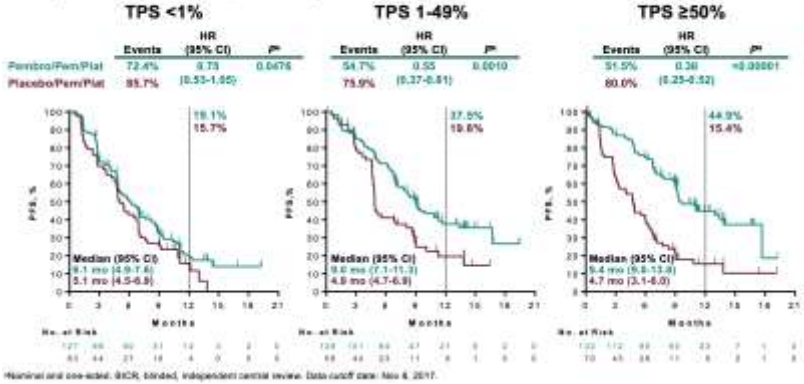


Progression-Free Survival in Key Subgroups
(RECIST v1.1, BICR)



BICR, blinded, independent central review. Data cutoff date: Nov 6, 2017.

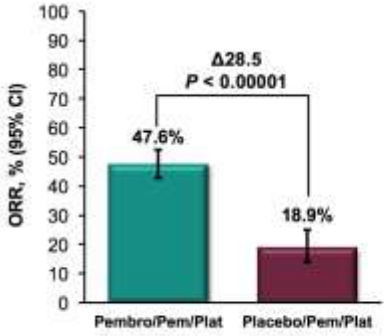
Progression-Free Survival by PD-L1 TPS
(RECIST v1.1, BICR)



*Nominal one-sided, BICR, blinded, independent central review. Data cutoff date: Nov 6, 2017.

Response Rate

Response Rate and Duration, ITT
(RECIST v1.1, BICR)

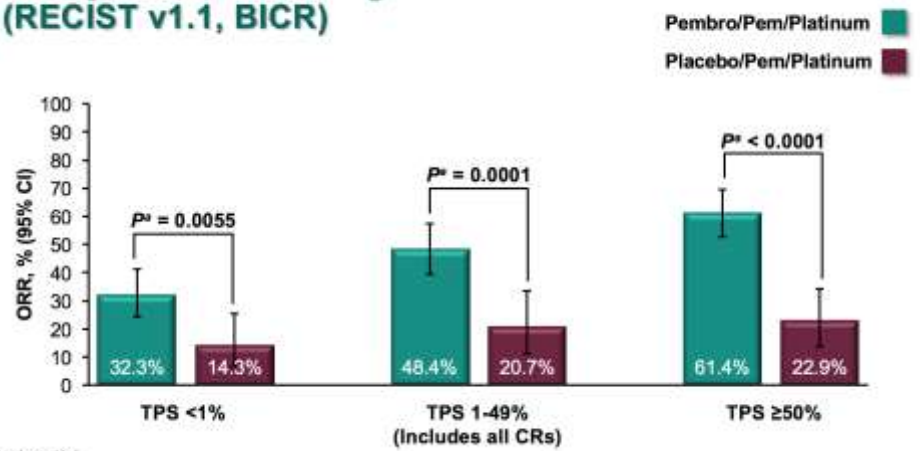


Best Response,* n (%)	Pembro/ Pem/Plat (N = 410)	Placebo/ Pem/Plat (N = 206)
CR	2 (0.5%)	1 (0.5%)
PR	193 (47.1%)	38 (18.4%)
SD	152 (37.1%)	106 (51.5%)
PD	36 (8.8%)	36 (17.5%)

Duration of response, mo	Pembro/ Pem/Plat (N = 195)	Placebo/ Pem/Plat (N = 39)
Median	11.2	7.8
Range	1.1+ to 18.0+	2.1+ to 16.4+

*An additional 27 (6.6%) patients in the pembro/pem/plat arm and 25 (12.1%) in the placebo/pem/plat arm had disease that was not evaluable for best response or did not have a post-baseline imaging assessment. BICR, blinded, independent central review. Data cutoff date: Nov 8, 2017.

Response Rate by PD-L1 TPS
(RECIST v1.1, BICR)



*Nominal and one-sided.
BICR, blinded, independent central review. Data cutoff date: Nov 8, 2017.

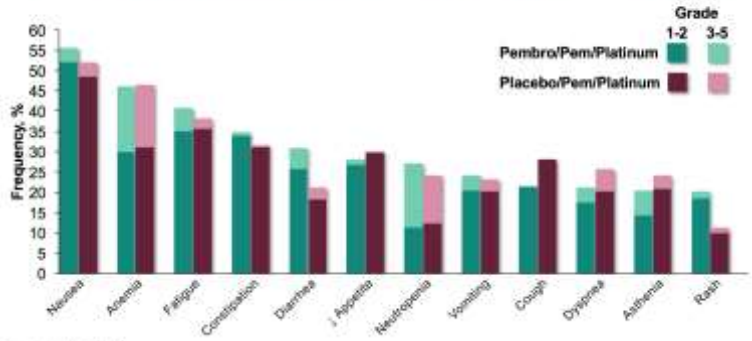
Adverse Events

Summary of Adverse Events (All Cause)

	Pembro/Pem/Platinum N = 405	Placebo/Pem/Platinum N = 202
Any	404 (99.8%)	200 (99.0%)
Grade 3-5	272 (67.2%)	133 (65.8%)
Led to death	27 (6.7%)	12 (5.9%)
Led to discontinuation		
All treatment[a]	56 (13.8%)	16 (7.9%)
Any treatment	112 (27.7%)	30 (14.9%)
Pembrolizumab or placebo	82 (20.2%)	21 (10.4%)
Pemetrexed	93 (23.0%)	23 (11.4%)
Platinum	31 (7.7%)	12 (5.9%)

[a]Includes patients who discontinued pembrolizumab or placebo, pemetrexed, and carboplatin for an adverse event at any time and patients who discontinued pembrolizumab or placebo and pemetrexed for an adverse event after completing 4 cycles of platinum.
Data cutoff date: Nov 8, 2017.

Adverse Events (All Cause): Frequency ≥20%



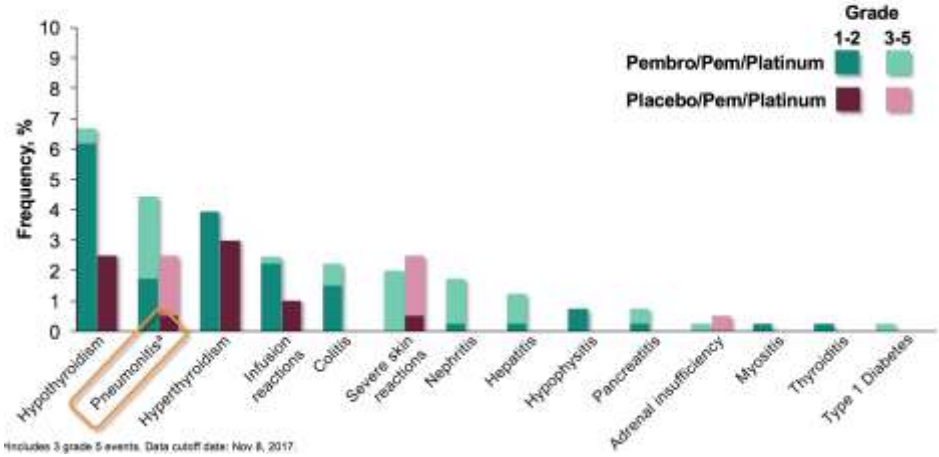
Data cutoff date: Nov 8, 2017.

Renal Events

- Acute kidney injury
  - Incidence: 5.2% in pembrolizumab/pemetrexed/platinum arm vs 0.5% in placebo/pemetrexed/platinum arm
  - Grade 3-5 incidence: 2.0% vs 0%
  - Grade 5 events: 2
- Nephritis[a]
  - Incidence: 1.7% in pembrolizumab/pemetrexed/platinum vs 0% in placebo/pemetrexed/platinum arm
  - Grade 3-5 incidence: 1.5% vs 0%
  - Grade 5 events: 0
- Events associated with pembrolizumab, pemetrexed, and platinum

[a]Includes preferred terms of autoimmune nephritis, nephritis, and tubulointerstitial nephritis.
Data cutoff date: Nov 8, 2017.

Immune-Mediated Adverse Events



[a]Includes 3 grade 5 events. Data cutoff date: Nov 8, 2017.

Conclusiones

Pembrolizumab + pemetrexed y platino reduce el riesgo de muerte en el 51% Median OS: NR vs 11.3 meses

- OS beneficio para pembrolizumab plus pemetrexed y platino es independiente de expresión de PDL-1.
- PD-L1 TPS: HR 0.59 en TPS <1%, 0.55 en TPS 1-49%, and 0.42 en TPS ≥50%

Riesgo de progresión o muerte se reduce en el 48% con pembrolizumab +pemetrexed y platino

- Median PFS: 8.8 vs 4.9 meses

RO y DOR superior con pembrolizumab + pemetrexed + platino

- ORR: 47.6% vs 18.9%
- Median DOR: 11.2 vs 7.8 meses

Efectos Adversos frequencia y severidad similar

- Pembrolizumab no exacerba los EA asociados a pemetrexed y platino
- Excepción de toxicidad renal

Pembrolizumab + pemetrexed y platino puede considerarse un nuevo estándar para el tratamiento de primera línea de los carcinoma de pulmón no escamosos metastásico independientemente de la expresión de PD-L1

- El punto principal de discusión es la decisión en pacientes TPS ≥50%: Pembro vs Pembro + QT: Individualización del tratamiento