#ESMOUPDATES

Iniciativa científica de:

GECP lung cancer research

# LUNG CANCER UPDATES

## ESMO HIGHLIGHTS

**27 SEPTIEMBRE - 1 OCTUBRE 2019**


Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

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BARCELONA

Iniciativa científica de:

GECP lung cancer research

# Inmunoterapia (II)

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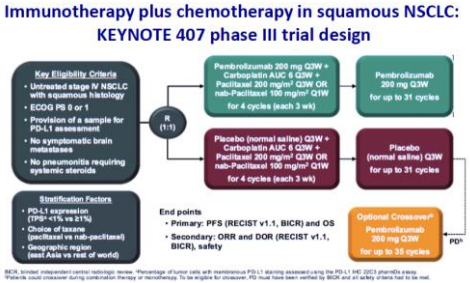
Con la colaboración de:

Bristol-Myers Squibb

illumina

Lilly

# Inmunoterapia en 1L: ¿Es el lugar apropiado?



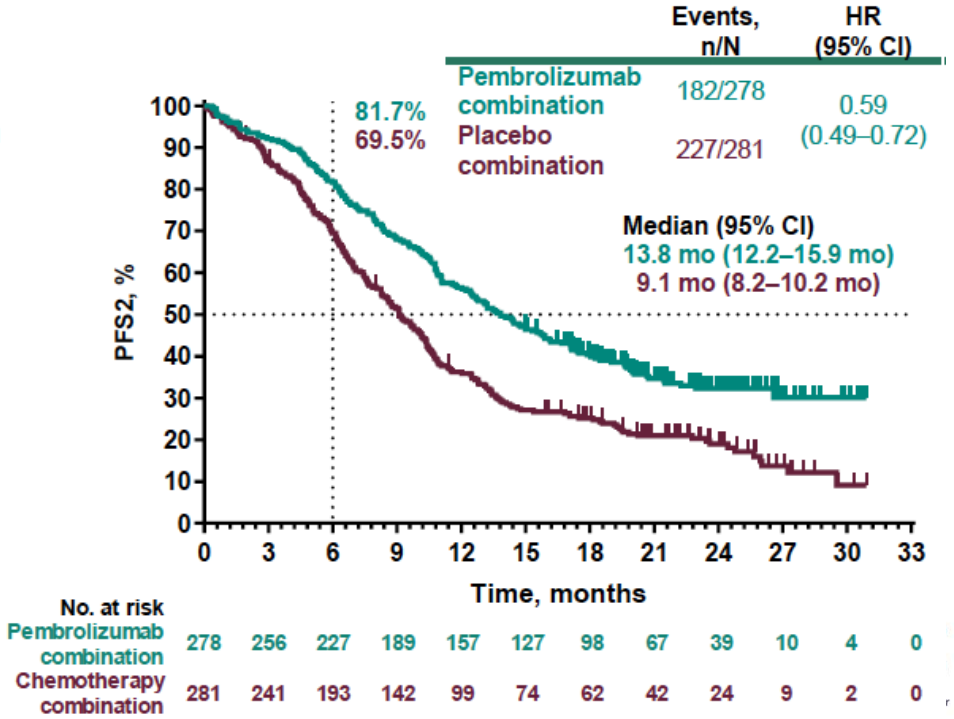

## KEYNOTE_407

# Kaplan-Meier Estimates of PFS2

## Overall Study Population[a]

- PFS2 defined by EMA as time from randomization to objective tumor progression on next-line treatment or death from any cause[1]
- Can be used to assess impact of crossover on OS and whether therapy in one line positively or negatively affects efficacy of the next line of therapy

**Representation of PFS, OS, and PFS2**

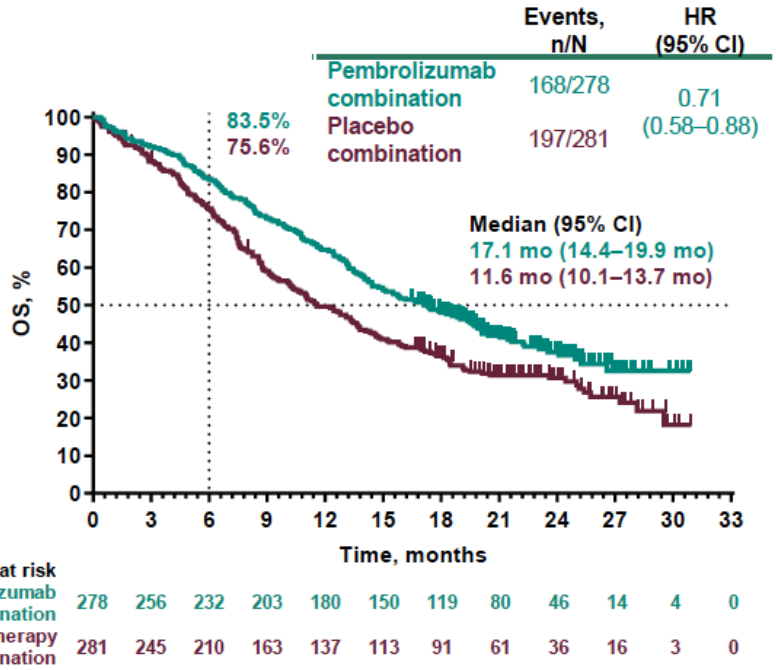



# Inmunoterapia en 1L: ¿Es el lugar apropiado?



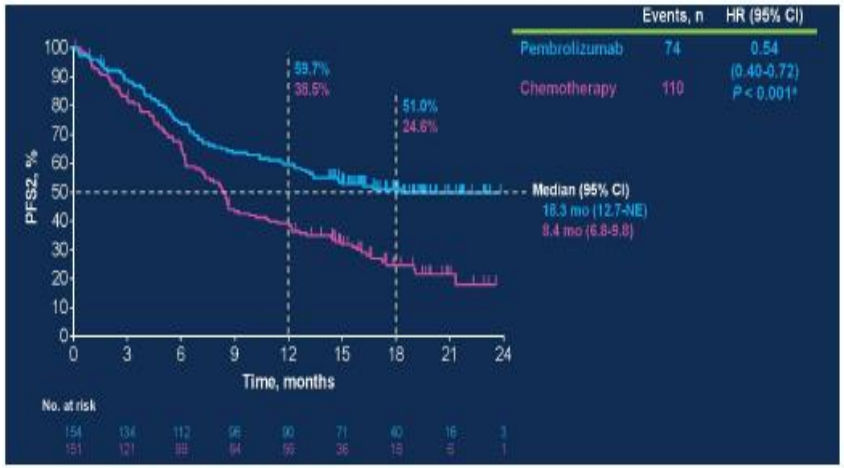
## KEYNOTE_407

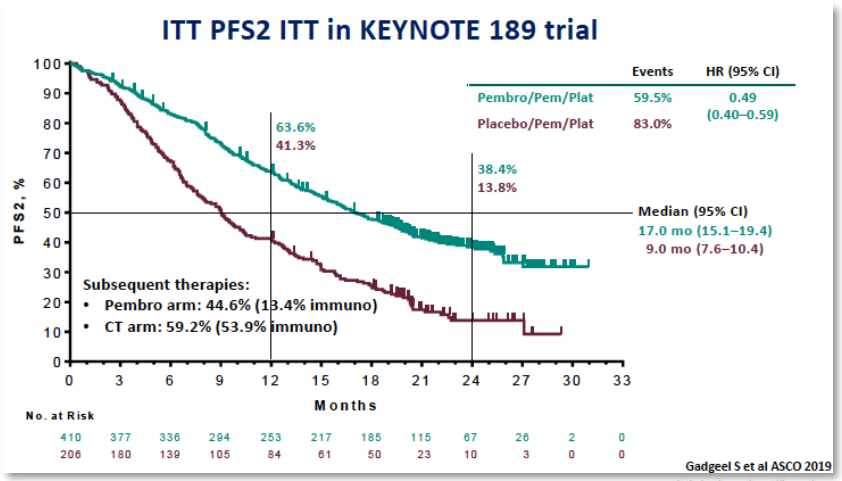
### Overall Study Population




Median follow-up 14.3 months

## KEYNOTE 024



# KEYNOTE_407

**Table 2. Summary of OS, PFS, ORR, DOR, and PFS2 in the Total Population (ITT) and Across PD-L1 TPS Groups**

| End Point | Total N = 559 | TPS ≥50% N = 146 | TPS 1–49% N = 207 | TPS <1% N = 194 |
|---|---|---|---|---|
| OS, HR (95% CI) | 0.71 (0.58–0.88) | 0.79 (0.52–1.21) | 0.59 (0.42–0.84) | 0.79 (0.56–1.11) |
| PFS, HR (95% CI) | 0.57 (0.47–0.69) | 0.43 (0.29-0.63) | 0.52 (0.38–0.71) | 0.67 (0.49–0.91) |
| ORR, pembrolizumab combination vs placebo combination | 62.6% vs 38.4% | 64.4% vs 30.1% | 55.3% vs 42.3% | 67.4% vs 41.4% |
| DOR, median (range), mo, pembrolizumab combination vs placebo combination | 8.8 (1.3+ to 28.4+) vs 4.9 (1.3+ to 28.3+) | 9.2 (2.7 to 25.8+) vs 4.6 (1.3+ to 28.3+) | 10.4 (1.3+ to 28.4+) vs 4.8 (2.0 to 22.8+) | 6.9 (1.4+ to 25.4+) vs 5.7 (1.4+ to 25.6+) |
| PFS2, HR (95% CI) | 0.59 (0.49–0.72) | 0.61 (0.40–0.91) | 0.51 (0.37–0.72) | 0.61 (0.44–0.85) |

+, no progressive disease as of last disease assessment before data cutoff date.

# TAIL study design

**Key eligibility criteria**

- Stage IIIb or IV NSCLC that progressed following 1-2 lines of prior chemotherapy
- Squamous or non-squamous histology
- ECOG PS 0-2
- Any PD-L1 status
- Sensitizing *ALK/EGFR*+ NSCLC requires prior TKI therapy

N = 600

→ Atezolizumab 1200 mg IV q3w → Until loss of clinical benefit, unacceptable toxicity, investigator/ patient decision to withdraw, loss of follow-up or death → Survival follow up

**Special populations:**
**-ECOG-PS 2**
**-Prior anti-PS-1 therapy**
**-Untreated/treated asymptomatic CNS metastases**
**-Autoinmune disease**
**-HBV/HCV/HIV+**
**-Severe renal impairment**

**Primary endpoint (readout ≈ 6 mo after LPI):**

- Incidence of SAEs related to atezolizumab[a]
- Incidence of irAEs related to atezolizumab[b]

# TAIL study design

| Characteristic | All Patients (N = 615) |
|---|---|
| Median age (min-max), y | 64.0 (24-88) |
| Male, n (%) | 370 (60.2) |
| ECOG PS, n (%) | |
| 0-1 | 554 (90.1) |
| 2 | 61 (9.9) |
| Stage IV at diagnosis, n (%) | 581 (94.5) |
| Histology, n (%)[a] | |
| Non-squamous | 462 (75.1) |
| Squamous | 152 (24.7) |
| Prior lines of NSCLC therapy, n (%) | |
| 1 | 398 (64.7) |
| 2 | 177 (28.8) |
| > 2 | 40 (6.5) |

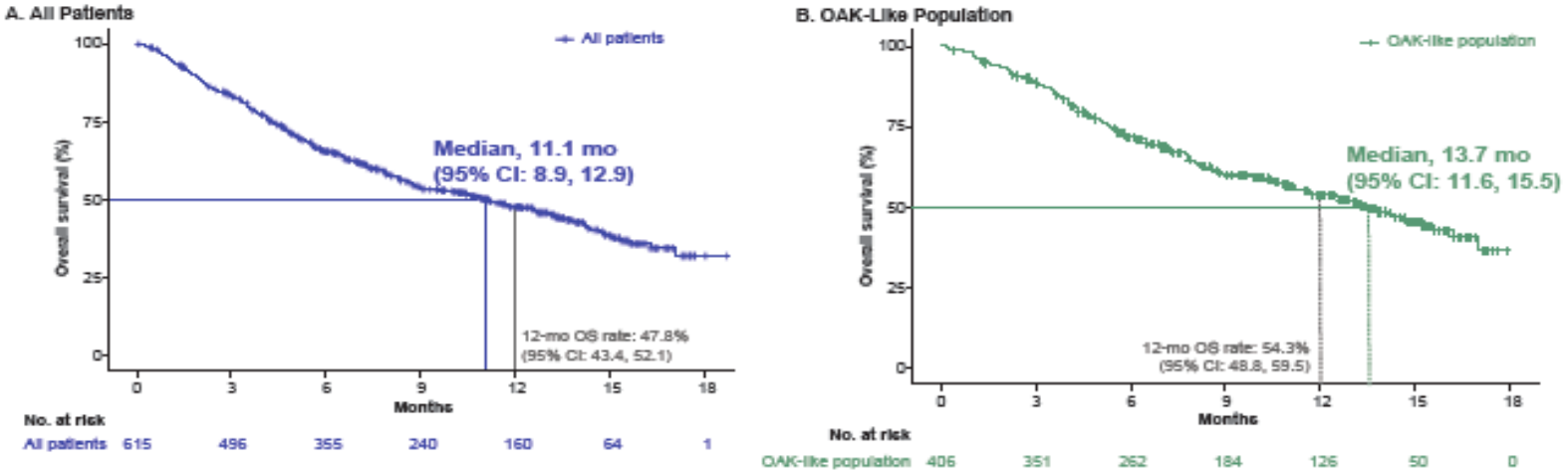
| Characteristic | All Patients (N = 615) |
|---|---|
| Prior chemotherapy, n (%)[b] | 611 (99.3) |
| Prior anti–PD-1 therapy, n (%)[c] | 39 (6.3) |
| ≥ 2 prior lines of NSCLC therapy | 35 (89.7) |
| *EGFR* mutation, n (%) | 40 (6.5) |
| *EML4-ALK* rearrangement, n (%) | 5 (0.8) |
| PD-L1 expression on TC, n (%)[d] | |
| Positive (≥ 1%) | 213 (34.6) |
| Negative (< 1%) | 168 (27.3) |
| Unknown | 234 (38.1) |
| CNS metastases, n (%) | 89 (14.5) |
| Renal impairment, n (%)[e] | 78 (12.7) |
| History of autoimmune disease, n (%) | 30 (4.9) |
| OAK-like population, n (%)[f] | 406 (66.0) |

*Ardizzoni et al. ESMO 2019*

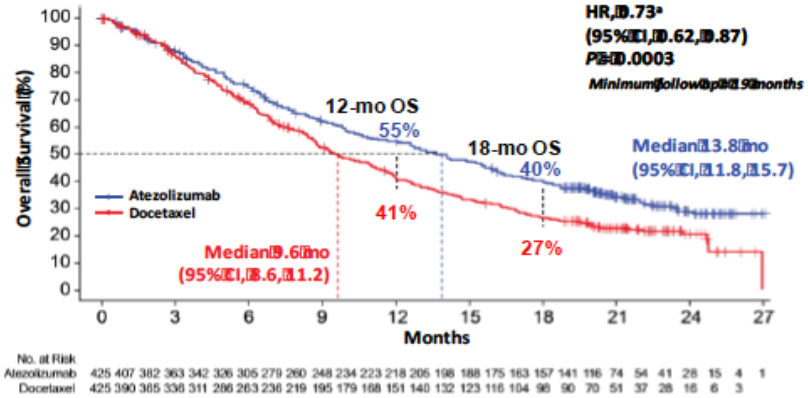
# Inmunoterapia en poblaciones especiales

## TAIL study

### Overall Survival




### OS in OAK trial




*Ardizzoni et al. ESMO 2019*

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# TAIL study

**Table 4.** Efficacy in All Patients and Key Subgroups

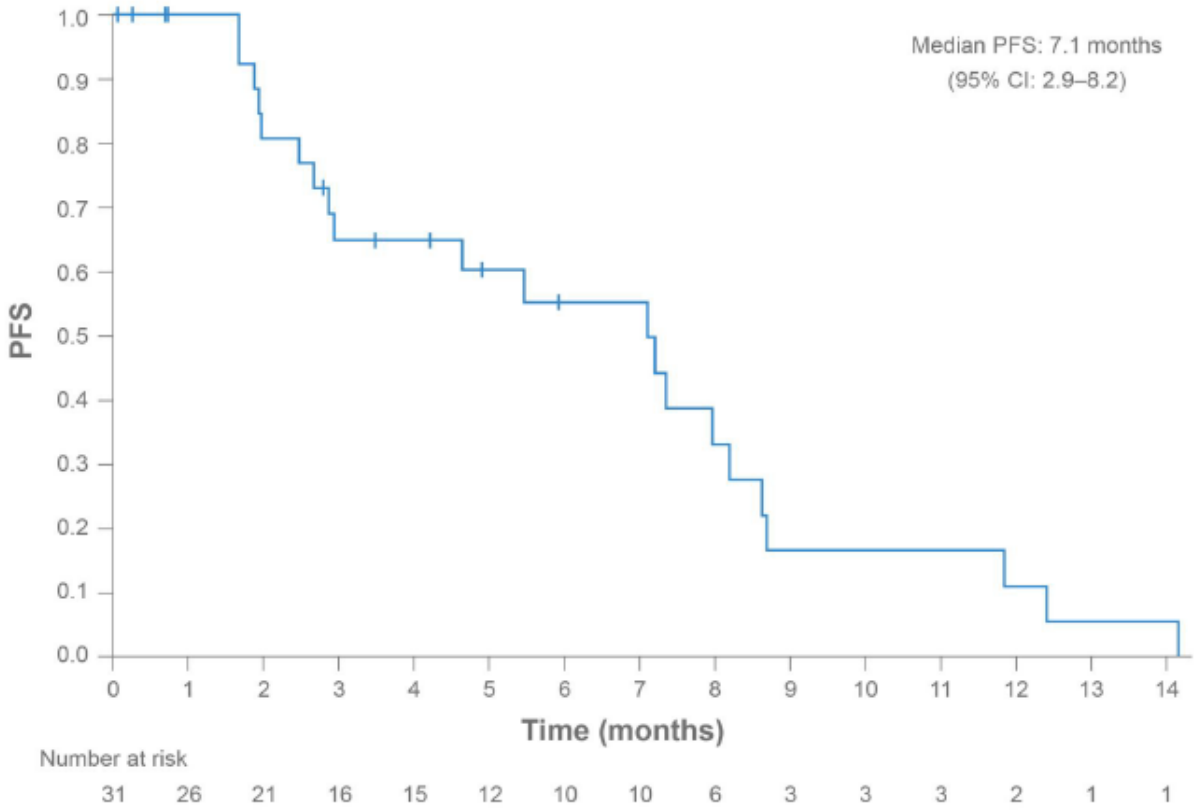
| Patient Subgroup | n | CR, n (%) | PR, n (%) | ORR (95% CI), % | mPFS (95% CI), mo | OS events, n | mOS (95% CI), mo |
|---|---|---|---|---|---|---|---|
| All patients | 615 | 3 (0.5) | 65 (10.6) | 11.1 (8.7, 13.8) | 2.7 (2.1, 2.8) | 312 | 11.1 (8.9, 12.9) |
| OAK-like population | 406 | 3 (0.7) | 52 (12.8) | 13.5 (10.4, 17.3) | 2.8 (2.7, 3.9) | 181 | 13.7 (11.6, 15.5) |
| CNS metastases | 89 | 0 | 5 (5.6) | 5.6 (1.8, 12.6) | 1.4 (1.3, 1.5) | 58 | 5.1 (4.1, 8.5) |
| Renal impairment | 78 | 0 | 9 (11.5) | 11.5 (5.4, 20.8) | 3.1 (2.6, 5.2) | 38 | 13.0 (8.5, 17.0) |
| ECOG PS 2 | 61 | 0 | 2 (3.3) | 3.3 (0.4, 11.3) | 1.7 (1.4, 2.8) | 46 | 3.5 (1.9, 5.1) |
| Prior anti–PD-1 therapy | 39 | 0 | 1 (2.6) | 2.6 (0.1, 13.5) | 1.6 (1.3, 2.9) | 23 | 6.2 (3.5, 15.0) |
| Autoimmune disease | 30 | 0 | 3 (10.0) | 10.0 (2.1, 26.5) | 2.9 (1.4, 4.2) | 18 | 10.1 (6.5, 14.1) |

CR, complete response; mPFS, median progression-free survival; PR, partial response.

*Ardizzoni et al. ESMO 2019*

# VARGADO study: Docetaxel + Nintedanib

## Figure 3. PFS by investigator assessment (n=31)




*Grohe et al. ESMO 2019*

# Inmunoterapia en MTS cerebrales



## Pembrolizumab Plus Platinum-Based Chemotherapy in NSCLC With Brain Metastases: Pooled Analysis of KEYNOTE-021, 189, and 407

S.F. Powell[1]; D. Rodríguez-Abreu[2]; C.J. Langer[3]; A. Tafreshi[4]; L. Paz-Ares[5]; H.-G. Kopp[6]; J. Rodríguez-Cid[7]; D. Kowalski[8]; Y. Cheng[9]; T. Kurata[10]; M.M. Awad[11]; J. Lin[12]; B. Zhao[12]; M.C. Pietanza[12]; B. Piperdi[12]; M.C. Garassino[13]

## Outcomes With Pembrolizumab Monotherapy in Patients With PD-L1–Positive NSCLC With Brain Metastases: Pooled Analysis of KEYNOTE-001, 010, 024, and 042

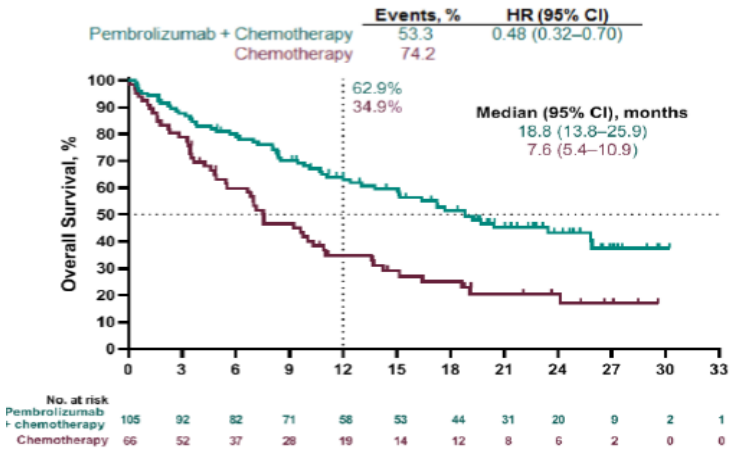
Aaron S. Mansfield,[1] Roy S. Herbst,[2] Gilberto Castro Jr,[3] Rina Hui,[4] Nir Peled,[5] Dong-Wan Kim,[6] Silvia Novello,[7] Miyako Satouchi,[8] Yi-Long Wu,[9] Edward B. Garon,[10] Martin Reck,[11] Andrew G. Robinson,[12] Ayman Samkari,[13] Bilal Piperdi,[13] Victoria Ebiana,[13] Jianxin Lin,[13] Tony SK Mok[14]

# Inmunoterapia en MTS cerebrales

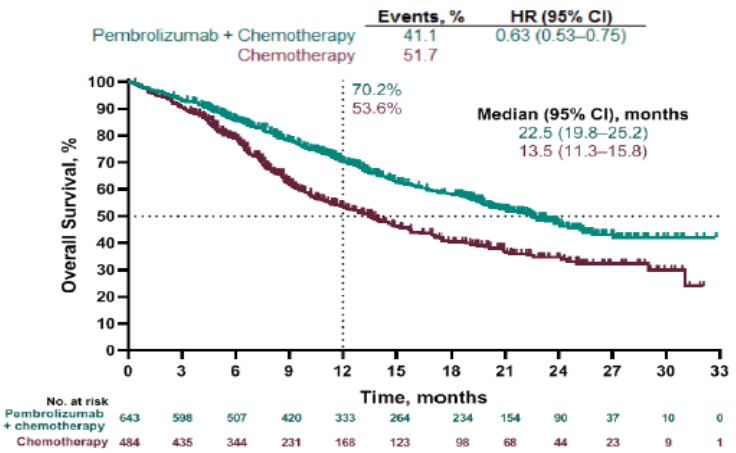


## KN 021, 189 y 407

### With Brain Metastases

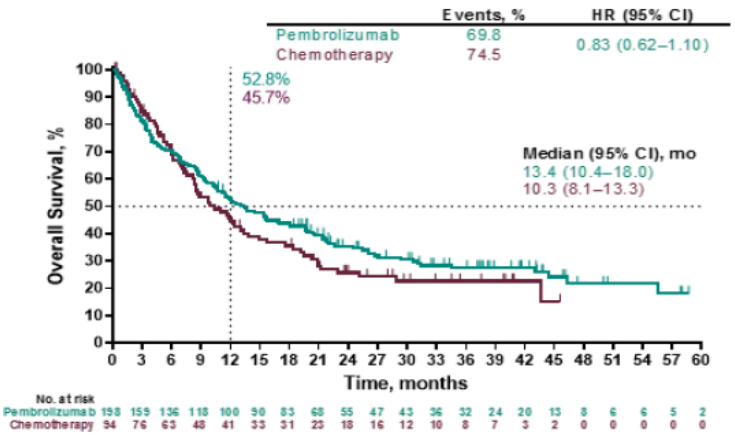



### Without Brain Metastases

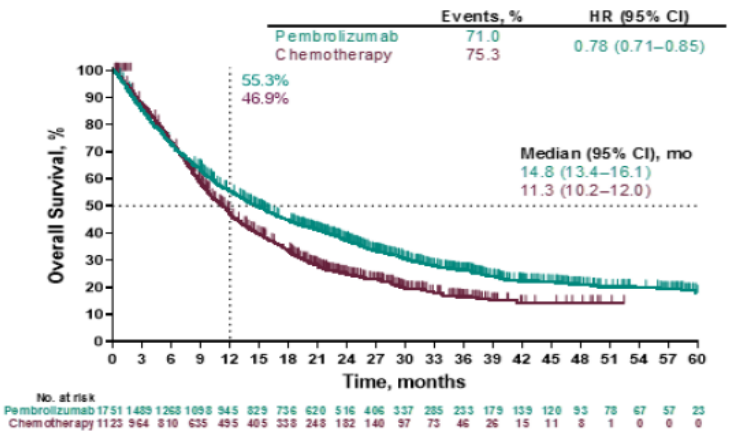



## KN 001, 010, 24 y 42

### PD-L1 TPS ≥1% With Brain Metastases




### PD-L1 TPS ≥1% Without Brain Metastases

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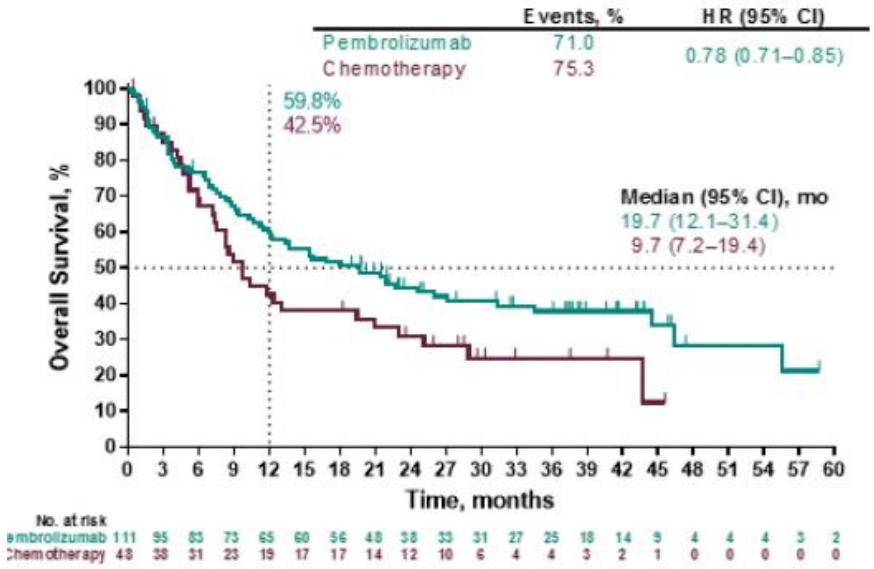
## KN 001, 010, 24 y 42

# OS in Patients With or Without Brain Metastases

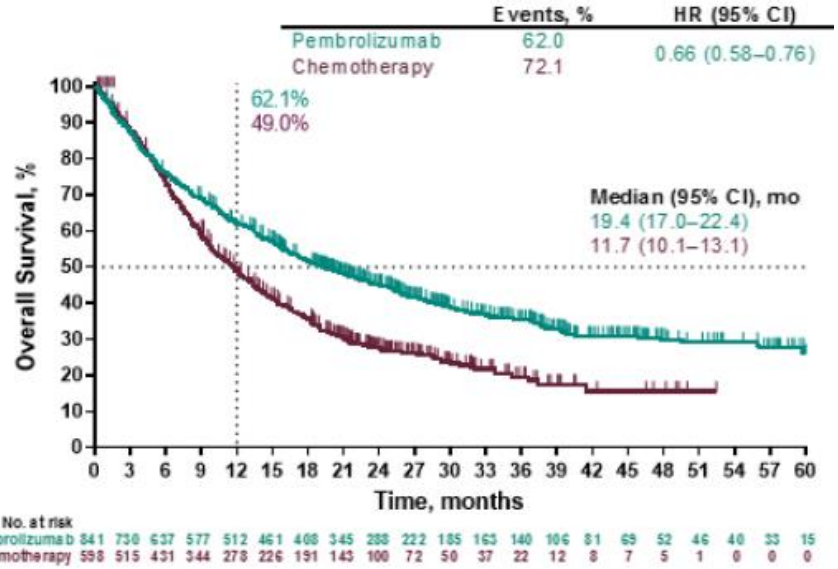
Mansfield. ESMO 2019.

## Pooled Analysis Population[a]

### PD-L1 TPS ≥50% With Brain Metastases




### PD-L1 TPS ≥50% Without Brain Metastases



# Valor predictivo de TMB

## B-F1RST study design

Stage IIIB-IVB[a] locally advanced or metastatic NSCLC (any histology; N = 152[b]) → Atezolizumab 1200 mg IV q3w → Until PD, unacceptable toxicity or loss of clinical benefit

**Inclusion criteria**
- Measurable disease per RECIST 1.1
- ECOG PS of 0 or 1
- Immunotherapy naive
- PD-L1 unselected
- Provision of blood[c]

**Exclusion criteria**
- Sensitizing *EGFR* mutations or *ALK* rearrangements
- Active brain metastases requiring treatment

**Final analysis**
- All enrolled patients with ≥ 18 months of follow-up

**Co-primary endpoints**
- Efficacy endpoint: INV-assessed ORR per RECIST 1.1
- Biomarker endpoint: INV-assessed PFS per RECIST 1.1 at the prespecified bTMB cutoff of 16

**Secondary objectives**
- Safety and assessment of efficacy by INV-assessed DOR, OS

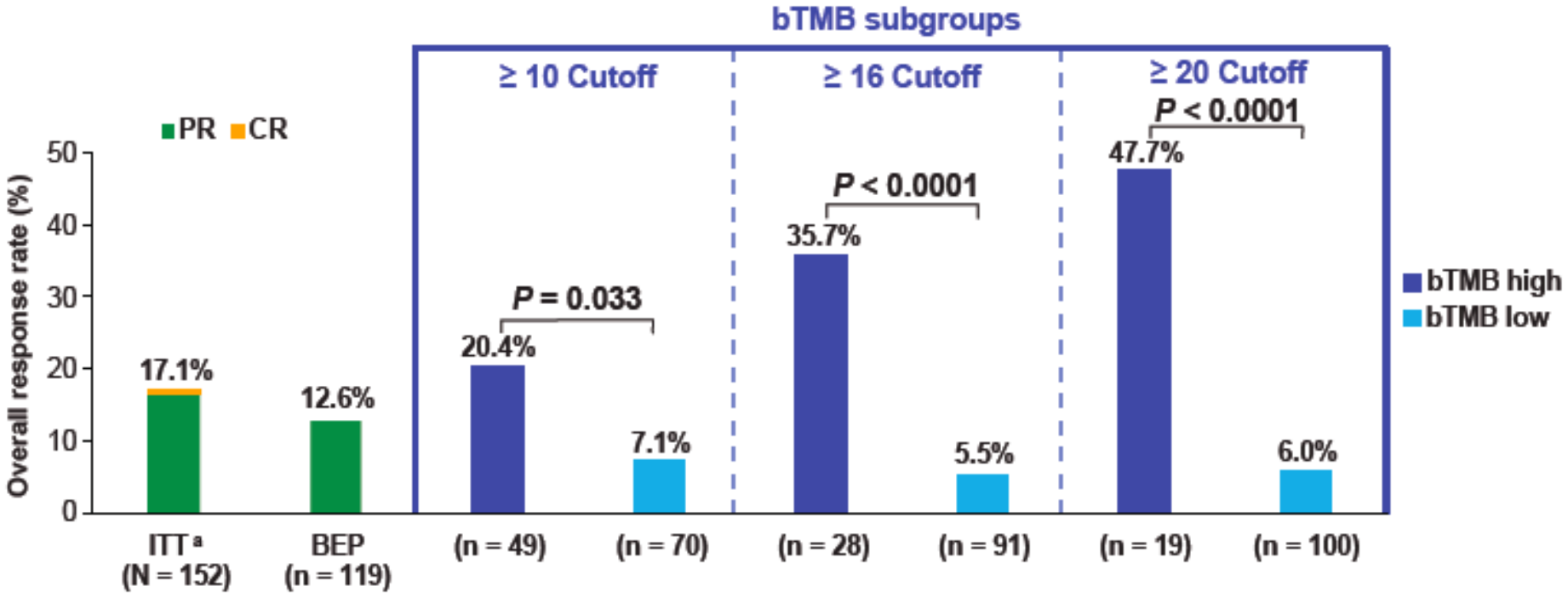
**Exploratory endpoint**
- OS at various bTMB cutoffs
- OS according to CRP ratio

*Socienski et al. ESMO 2019*

# Valor predictivo de TMB



## B-F1RST study design

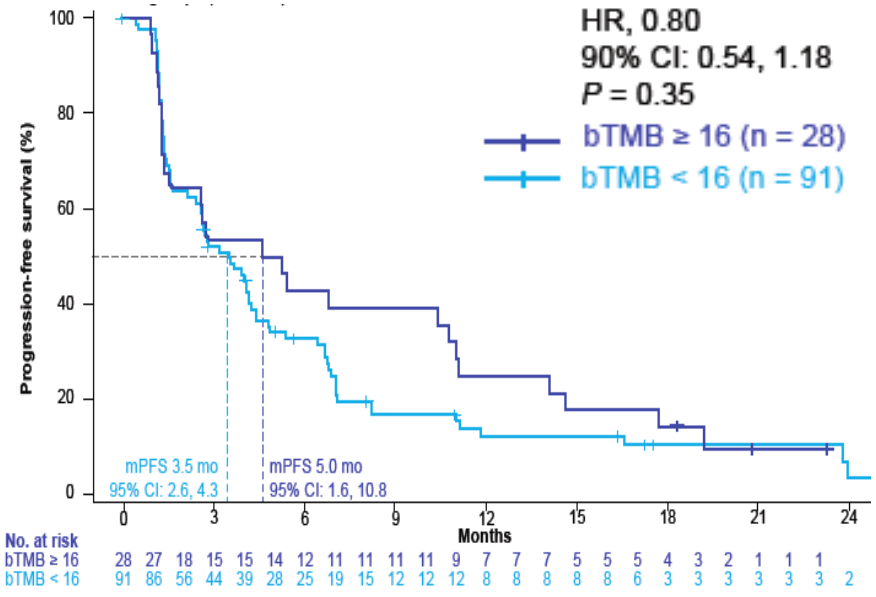



Socienski et al. ESMO 2019

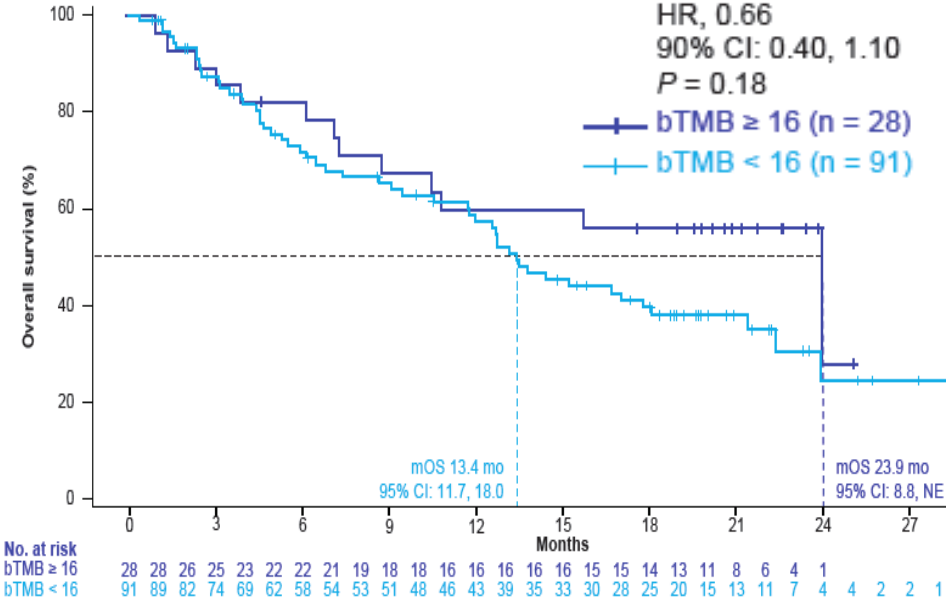
# Valor predictivo de TMB

## B-F1RST study design

### Progression-free Survival




### Overall Survival




mPFS y OS fue superior en pacientes con TMB alto

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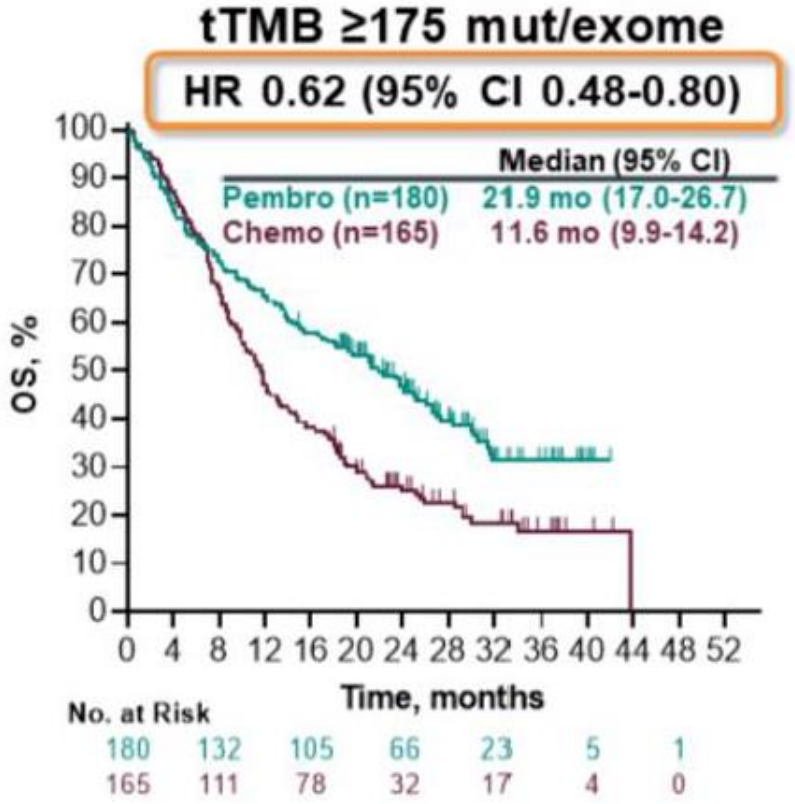
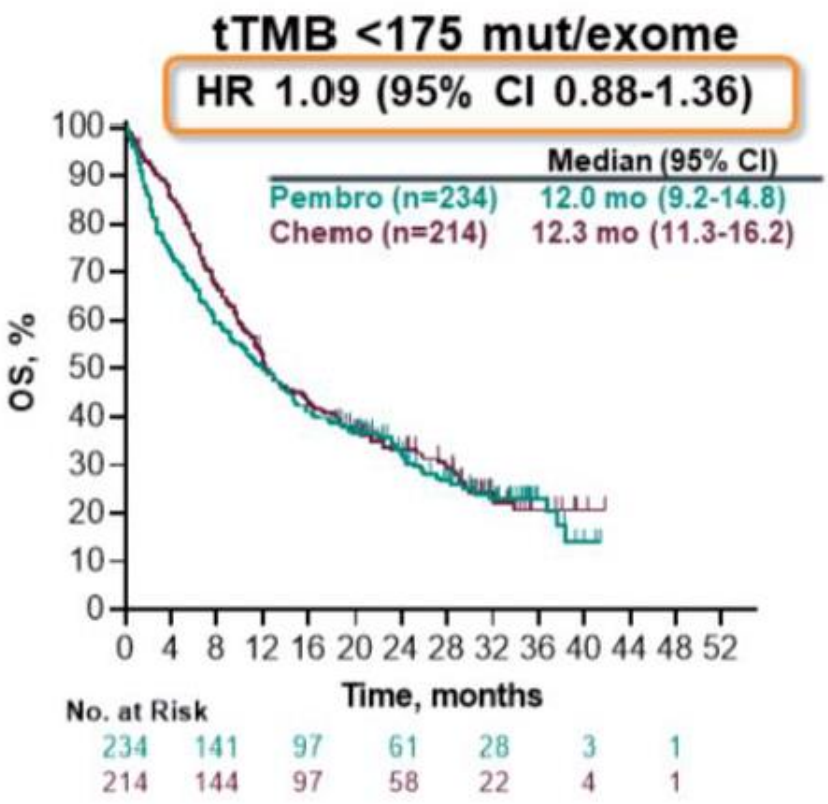
# Valor predictivo de TMB



## KEYNOTE 024

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*Herbst R et al. ESMO 2019*