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

# IMpower150: Efficacy of Atezolizumab Plus Bevacizumab and Chemotherapy in 1L Metastatic Nonsquamous NSCLC Across Key Subgroups

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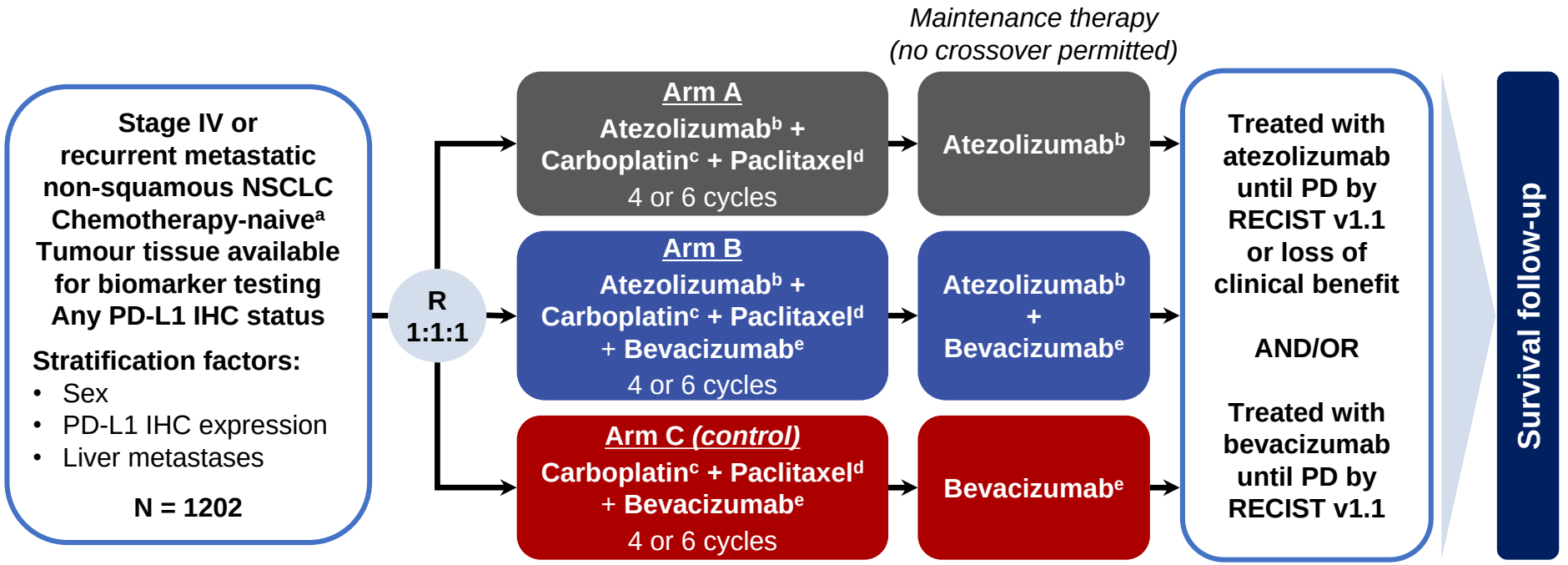
# IMpower150 study design



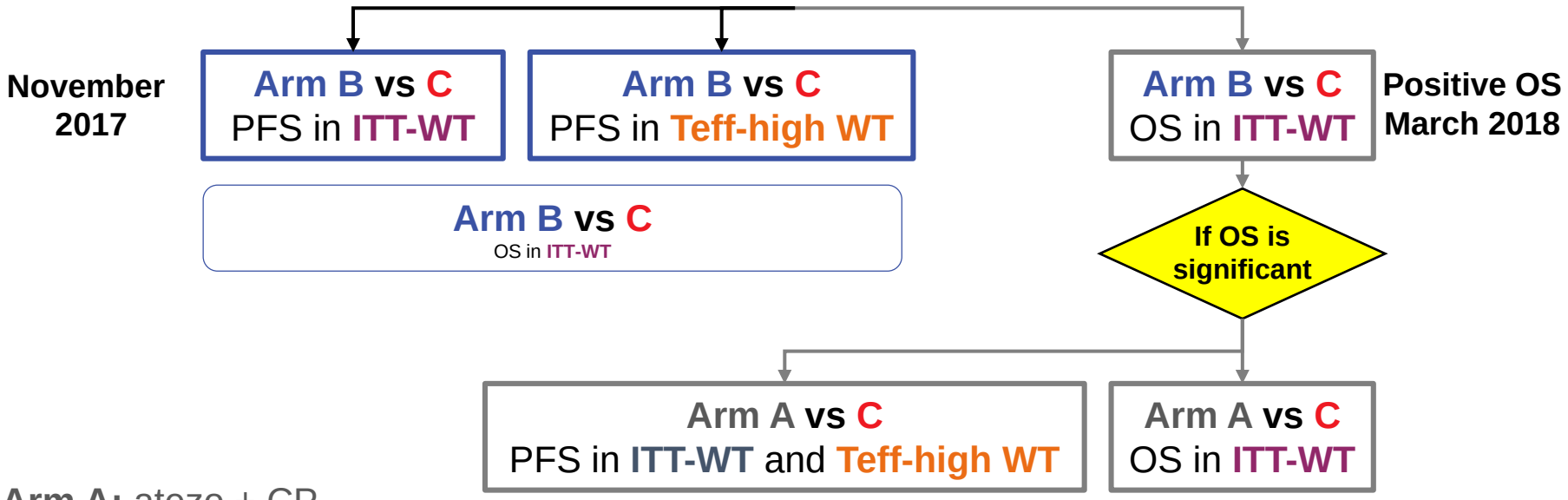



The principal question is to assess whether the addition of atezolizumab to Arm C provides clinical benefit

a Patients with a sensitising EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. b Atezolizumab: 1200 mg IV q3w. c Carboplatin: AUC 6 IV q3w.
d Paclitaxel: 200 mg/m2 IV q3w. e Bevacizumab: 15 mg/kg IV q3w.

# Statistical testing plan for the co-primary endpoints in IMpower150



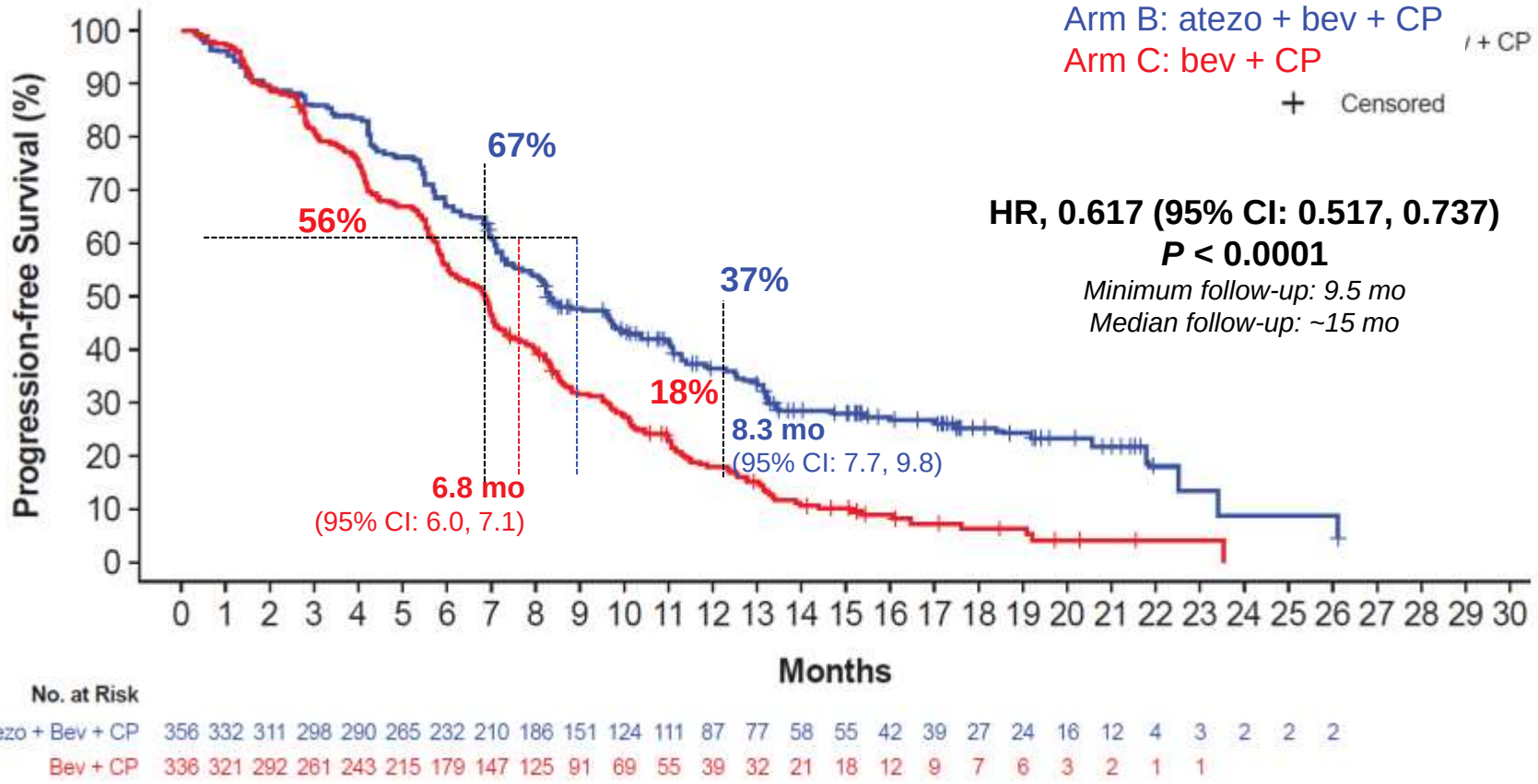



**Arm A:** atezo + CP
**Arm B:** atezo + bev + CP
**Arm C:** bev + CP *(control)*

Positive PFS results were presented in November 17
This presentation will provide a more in depth analysis of PFS results in key subgroups of patients

atezo, atezolizumab; bev, bevacizumab; CP, carboplatin + paclitaxel.

# INV-assessed PFS in ITT-WT (Arm B vs Arm C)




INV, investigator.

Data cutoff: September 15, 2017

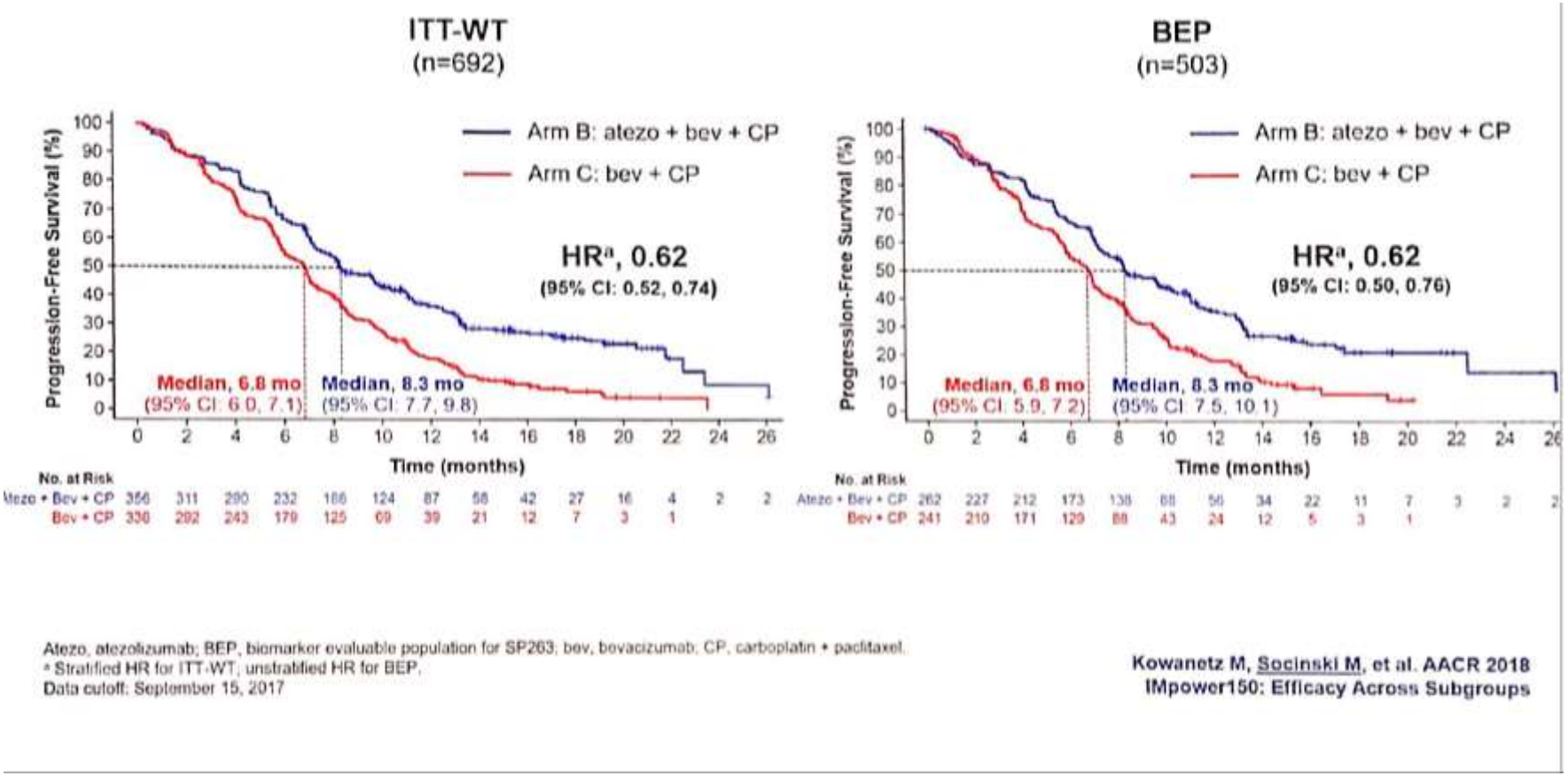
# Efficacy in key subgroups in the Impower 150 Study



- This analysis aims to further understand the PFS efficacy of atezolizumab + bevacizumab + chemotherapy in key patient populations in the IMpower150 study
  - PD-L1 IHC expression subgroups defined by the SP142 and SP263 assays (N= 503)
  - Patients with *EGFR/ALK* genetic alterations
  - Patients with liver metastases at baseline

# Similar PFS Benefit in ARM B vs C in IMpower150 ITT-WT and BEP






Atezo, atezolizumab; BEP, biomarker evaluable population for SP263; bev, bevacizumab; CP, carboplatin + paclitaxel.
[a] Stratified HR for ITT-WT; unstratified HR for BEP.
Data cutoff: September 15, 2017

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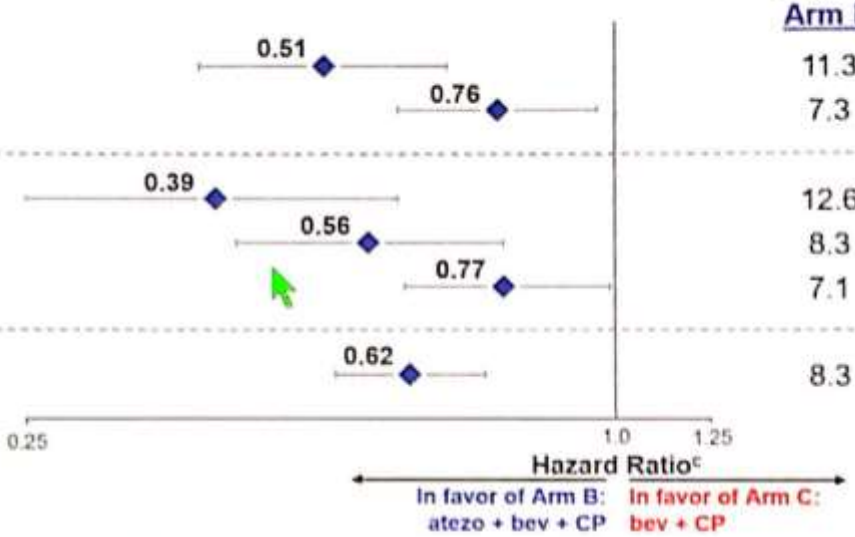
# PFS Benefit in Arm B was Observed Across All Biomarker Subgroups, Including PD-L1-Negative Patients (by SP142 IHC)



| Subgroup | n (%)[a] | Median PFS, mo Arm B | Median PFS, mo Arm C |
|---|---|---|---|
| Teff-high | 284 (43%) | 11.3 | 6.8 |
| Teff-low | 374 (57%) | 7.3 | 7.0 |
| PD-L1–High (TC3 or IC3) | 135 (20%) | 12.6 | 6.8 |
| PD-L1–Low (TC1/2 or IC1/2)[b] | 224 (32%) | 8.3 | 6.6 |
| PD-L1–Negative (TC0 and IC0) | 338 (49%) | 7.1 | 6.9 |
| ITT-WT | 692 (100%) | 8.3 | 6.8 |




- Teff gene signature enriches for PFS similarly to PD-L1 IHC, including biomarker–negative patients

Atezo, atezolizumab; bev, bevacizumab; CP, carboplatin + paclitaxel; IC, tumor-infiltrating immune cells; TC, tumor cells.
[a] Teff % prevalence out of those tested in ITT-WT (n = 658); PD-L1 IHC % prevalence out of ITT-WT (n = 692), using the SP142 assay.
[b] Mutually exclusive subgroup that excluded TC3 or IC3 patients.
[c] Stratified HRs for ITT-WT and Teff-high WT populations; unstratified HRs for all other subgroups.
TC3 or IC3 = PD-L1+ ≥ 50% of TC or ≥ 10% of IC; TC1/2/3 or IC1/2/3 = PD-L1+ ≥ 1% of TC or IC. TC0 and IC0 = PD-L1+ < 1% of TC and IC.
Data cutoff: September 15, 2017.
Reck M, et al. ESMO IO 2017 [LBA_PR1]

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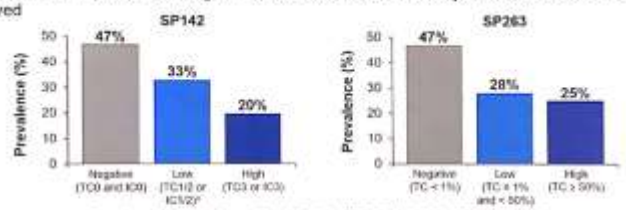
## Analysis of PD-L1 Subgroups Using the SP142 and SP263 IHC Assays

- The Blueprint analysis showed that the SP142 assay differed analytically from other PD-L1 IHC assays (SP263, 22c3, and 28-8)[1]; however SP263 and 22c3 were similar and highly concordant[1]
  - The SP142 assay was shown to be clinically equivalent with the 22c3 assay in OAK[2]
- PD-L1 prevalence in IMpower150 using the SP142 and SP263 IHC assays was similar and substantial overlap was observed




*Prevalence Analysis of Arms B and C in the BEP (Evaluable for SP263), n = 502ᵇ*

BEP, biomarker-evaluable population.
ᵃ Modularly exclusive subgroup that excluded TC3 or IC3 patients. ᵇ BEP from ITT-WT population.
TC3 or IC3 = PD-L1+ ≥ 50% of TC or ≥ 10% of IC. TC1/2 or IC1/2 = PD-L1+ ≥ 50% and < 1% of TC or ≥ 10% and < 1% of IC.
TC0 and IC0 = PD-L1+ < 1% of TC and IC.
Data cutoff: September 15, 2017.

1. Hirsch F, et al. J Thorac Oncol. 2017; 2. Badger BM, et al. ESMO 2017 [illegible]

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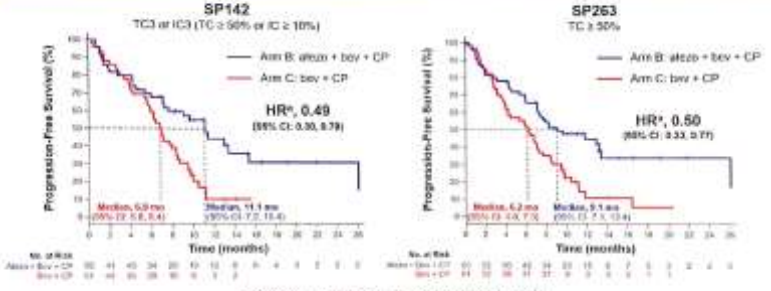
## PFS for Arm B vs C in SP142 and SP263 PD-L1–High Subgroups




*PFS Analysis in BEP of Arms B and C in ITT-WT (n = 503)*

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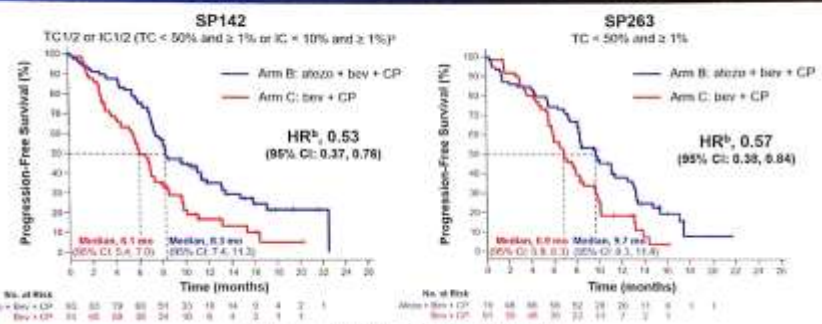
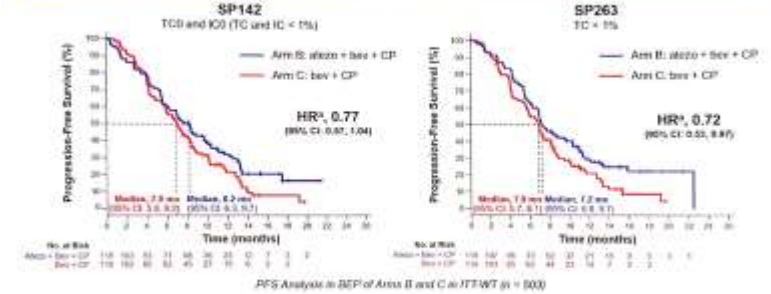
## PFS for Arm B vs C in SP142 and SP263 PD-L1–Low Subgroups




*PFS Analysis in BEP of Arms B and C in ITT-WT (n = 503)*

## PFS for Arm B vs C in SP142 and SP263 PD-L1–Negative Subgroups




*PFS Analysis in BEP of Arms B and C in ITT-WT (n = 503)*

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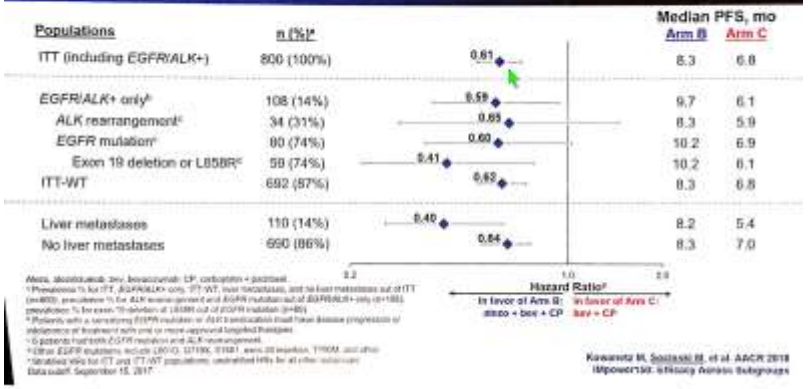
# Poblaciones Especiales: mutaciones de EGFR y ALK



## PFS Benefit in Arm B was Observed in Key Populations




| Populations | n (%)[a] | Arm B | Arm C | HR |
|---|---|---|---|---|
| ITT (including *EGFR/ALK*+) | 800 (100%) | 8.3 | 6.8 | 0.81 |
| *EGFR/ALK*+ only[b] | 108 (14%) | 9.7 | 6.1 | 0.59 |
| *ALK* rearrangement[c] | 34 (31%) | 8.3 | 5.9 | 0.85 |
| *EGFR* mutation[c] | 80 (74%) | 10.2 | 6.9 | 0.60 |
| Exon 19 deletion or L858R[c] | 59 (74%) | 10.2 | 6.1 | 0.41 |
| ITT-WT | 692 (87%) | 8.3 | 6.8 | 0.83 |
| Liver metastases | 110 (14%) | 8.2 | 5.4 | 0.40 |
| No liver metastases | 690 (86%) | 8.3 | 7.0 | 0.84 |

Kowanetz M, Socinski M, et al. AACR 2018
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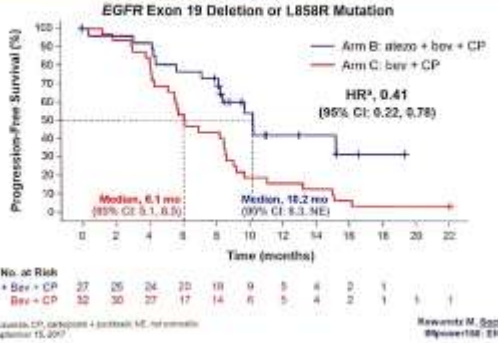
## PFS for Arm B vs C in Patients With Actionable *EGFR* Mutations (Exon 19 Deletion or L858R Mutation)

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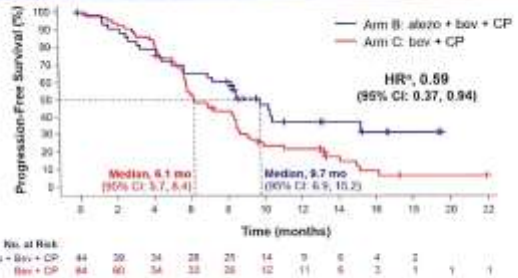
## PFS for Arm B vs C in *EGFR/ALK*+ Patients




- Anti–PD-L1/PD-1 monotherapy has not shown significant benefit in patients with *EGFR/ALK* genetic alterations
- Most other clinical trials of PD-L1/PD-1 inhibitors in 1L NSCLC exclude patients with *EGFR* mutations

Kowanetz M, Socinski M, et al. AACR 2018
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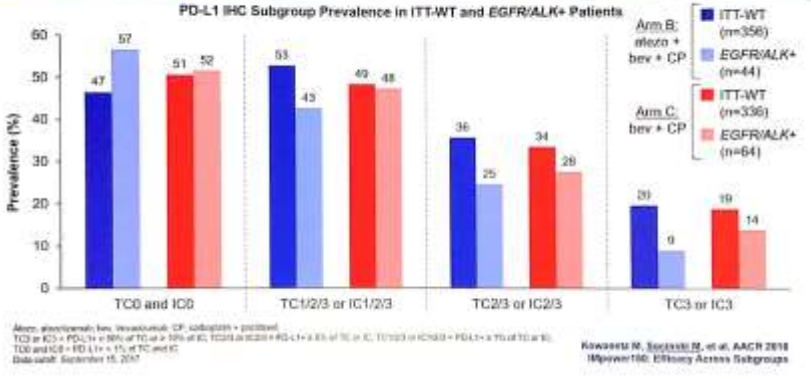
## PFS Benefit in *EGFR/ALK*+ Patients was Observed Despite Lower PD-L1 Expression in This Population




Kowanetz M, Socinski M, et al. AACR 2018
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# Pacientes con metástasis hepáticas

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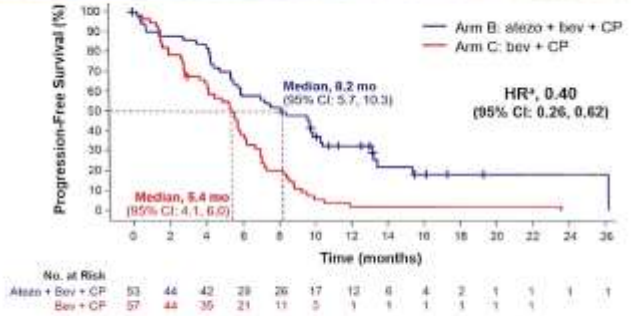
## PFS for Arm B vs C in Patients With Liver Metastasis at Baseline




- Patients with liver metastases at baseline, which is a known negative prognostic factor, demonstrated a clinically meaningful PFS benefit for Arm B vs Arm C

Kowanetz M, Socinski M, et al. AACR 2018
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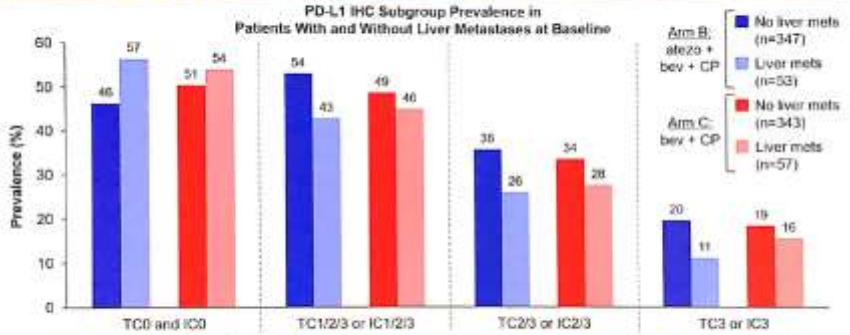
## PFS Benefit in Patients With Liver Metastases was Observed Despite Lower PD-L1 Expression in This Population

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# CONCLUSIONES



Atezolizumab + BVZ + QT ha demostrado un beneficio significativo en NSQ mNSCLC, en todos los subgrupos de expresión de PD-L1 independientemente del método de IHQ utilizado

El beneficio clínico en PFS se ha observado en todos los pacientes, incluidos los pacientes con mutaciones de EGFR, translocaciones de ALK y metástasis hepáticas.

- Este beneficio que no se había observado en los estudios de 2ª línea con anti PD-L1/ anti PD-1 puede deberse a la adición de BVZ a atezolizumab

- Esto sugiere que la combinación de Atezolizumab + BVZ + QT constituye un un nuevo tratamiento en estas poblaciones

IMpower 150 ha demostrado recientemente un beneficio significativo en supervivencia global los datos se presentaran en ASCO 2018

# Keynote 189 and IMpower150

| | Keynote 189[1] | IMpower150 |
|---|---|---|
| Populations | • Nonsquamous NSCLC<br>• EGFR and ALK+ patients excluded<br>• **Symptomatic CNS mets excluded**<br>• **Crossover permitted** | • Nonsquamous NSCLC<br>• **EGFR and ALK+ patients allowed[2]**<br>• Active/untreated CNS mets excluded<br>• **No crossover** |
| Sample Sizes | • N=616 | • N=692 (ITT WT; Arm B vs. C) |
| PFS[3] | • HR 0.52 (95% CI 0.43-0.64)<br>• Median PFS 8.8 vs. 4.9 months | • HR 0.617 (95% CI 0.52-0.74)<br>• Median 8.3 vs. 6.8 months |
| Overall Survival | • HR 0.49 (0.38-0.64)<br>• Median NR vs. 11.3 months | • Positive OS Benefit<br>• (Data awaited) |
| Impact of PD-L1 Expression | • OS improvement across all PD-L1 subgroups | • PFS improvement across all PD-L1 subgroups (OS data pending) |

Reck M, et al. IMpower150 PFS analysis.