Lung Cancer UPDATES
ASCO HIGHLIGTHS
29-31 MAYO 2020

Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón microcítico y otros tumores torácicos

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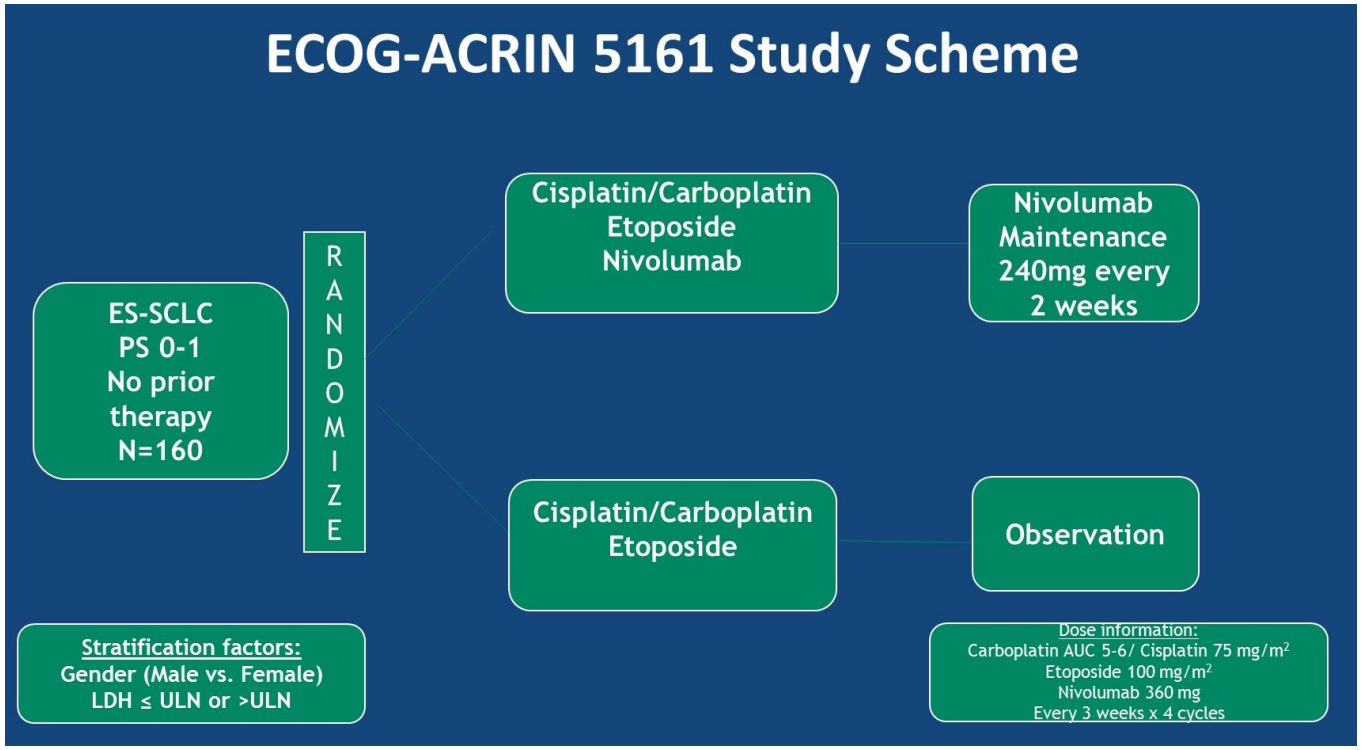
CÁNCER DE PULMÓN MICROCÍTICO

Abstract 9000 – Ticiana Leal et al.



Fase II randomizado
1L
M1 SNC tratadas

- SLP

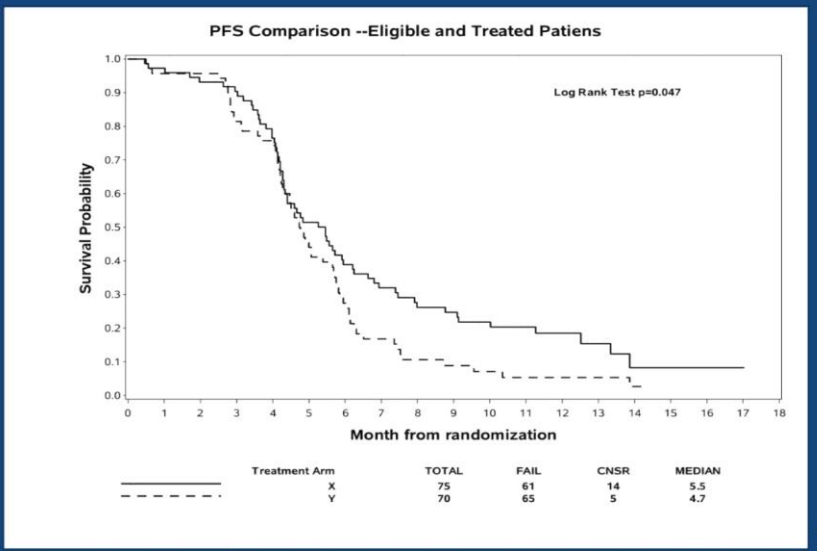
- SG
- TR RECIST 1.1
- Seguridad CTCAE v5

Reclutamiento: mayo a diciembre 2018 → 160 ptes
→ 145 elegibles/tratados

Baseline Characteristics

Parameter	Nivolumab + CE	CE
Number of pts	80	80
Number of eligible pts	75	70
Median age (yrs)	65	65
Female sex	45 (56%)	44 (55%)
PS 0	23 (49%)	24 (51%)

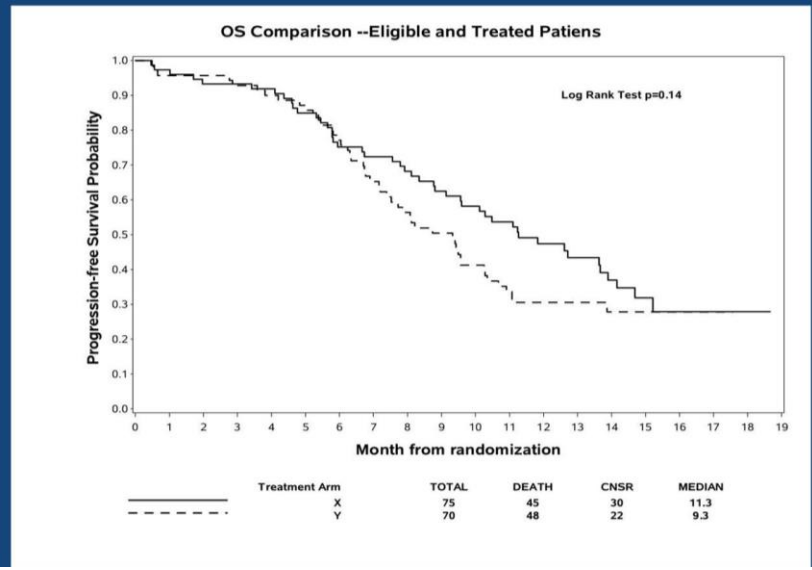
Progression-free Survival (Primary Endpoint)



	Nivolumab + CE	CE
mPFS, months	5.5	4.7
HR (95% CI)	0.68 (0.48-1.00)	
p=0.047		

X=Nivolumab + CE; Y=CE

Overall Survival (Secondary Endpoint)



	Nivolumab + CE	CE
mOS, months	11.3	9.3
HR (95% CI)	0.73 (0.49-1.1)	
p=0.14		

X=Nivolumab + CE; Y=CE

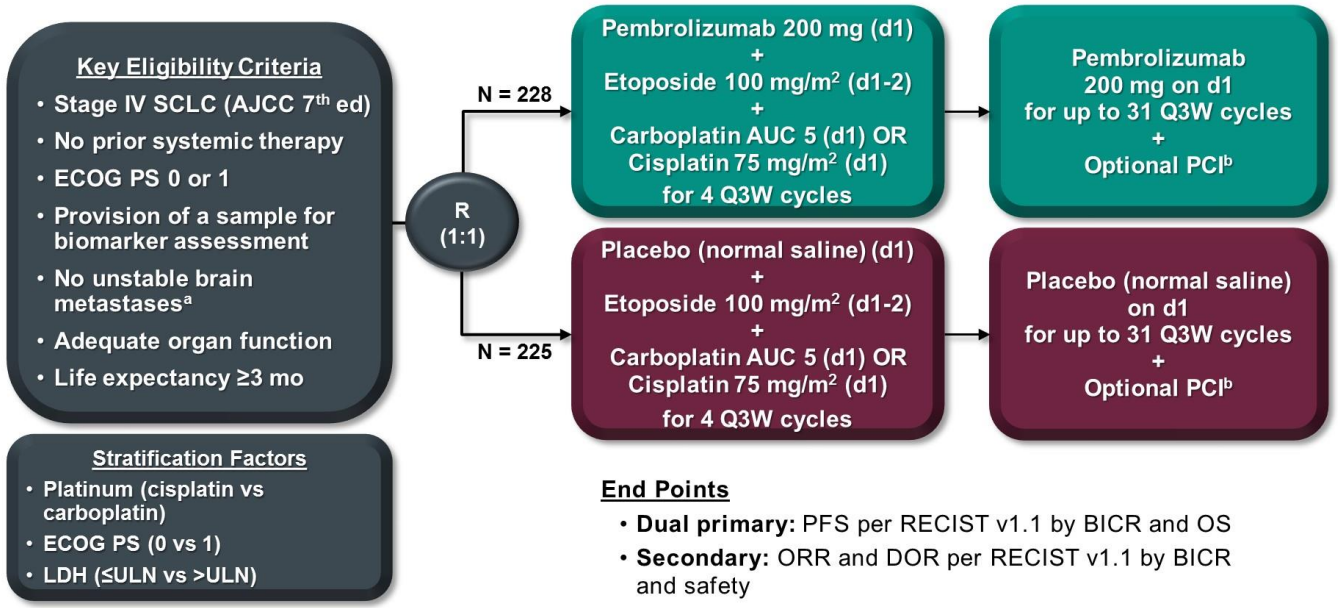
TR 52% vs 47%

Mediana de duración de respuesta: 5.6m vs 3.3m

CÁNCER DE PULMÓN MICROCÍTICO

Abstract 9001 – Charles Rudin et al.

KEYNOTE-604 Study Design N=453



End Points

- **Dual primary:** PFS per RECIST v1.1 by BICR and OS
- **Secondary:** ORR and DOR per RECIST v1.1 by BICR and safety

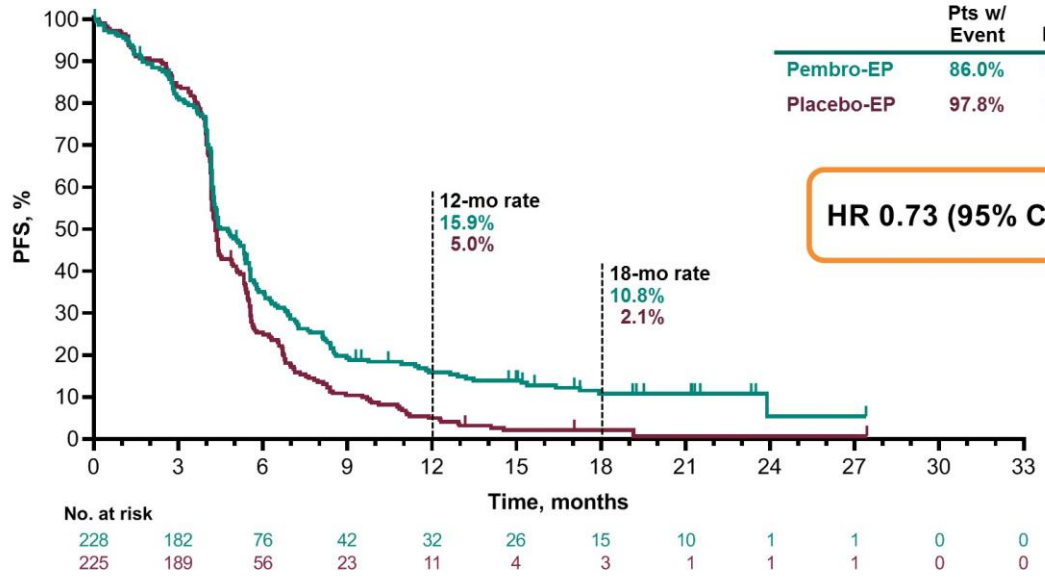
[a]All brain-targeted treatment completed ≥14 d before starting study, no new or enlarging brain lesions, and neurologically stable without steroids for ≥7 d before starting study.
[b]Participants with CR or PR after cycle 4 could receive up to 25 Gy of PCI in 10 fractions at investigator's discretion; PCI was to begin within 2-4 wk and no later than 6 wk after last dose of cycle 4; study treatment could continue during PCI. KEYNOTE-604 ClinicalTrials.gov identifier, NCT03066778. BICR, blinded independent central review.

Baseline Characteristics: FA

	Pembrolizumab-EP (N = 228)	Placebo-EP (N = 225)
Age, median (range), years	64 (24-81)	65 (37-83)
Men	152 (66.7%)	142 (63.1%)
ECOG PS 1	168 (73.7%)	169 (75.1%)
Former/current smoker	220 (96.5%)	217 (96.4%)
LDH >ULN	127 (55.7%)	129 (57.3%)
Brain metastases	33 (14.5%)	22 (9.8%)
Liver metastases	95 (41.7%)	92 (40.9%)
Sum of largest diameters of target lesions, median (range), mm	134.8 (24.4-431.7)	126.6 (20.8-408.8)
PD-L1 CPS ≥1[a]	88 (38.6%)	97 (43.1%)
Received carboplatin	161 (70.6%)	156 (69.3%)

[a]CPS was unknown for 43 (18.9%) in the pembrolizumab-EP arm and 50 (22.2%) in the placebo-EP arm.
Data cutoff date: Dec 2, 2019.

Progression-Free Survival, ITT: FA

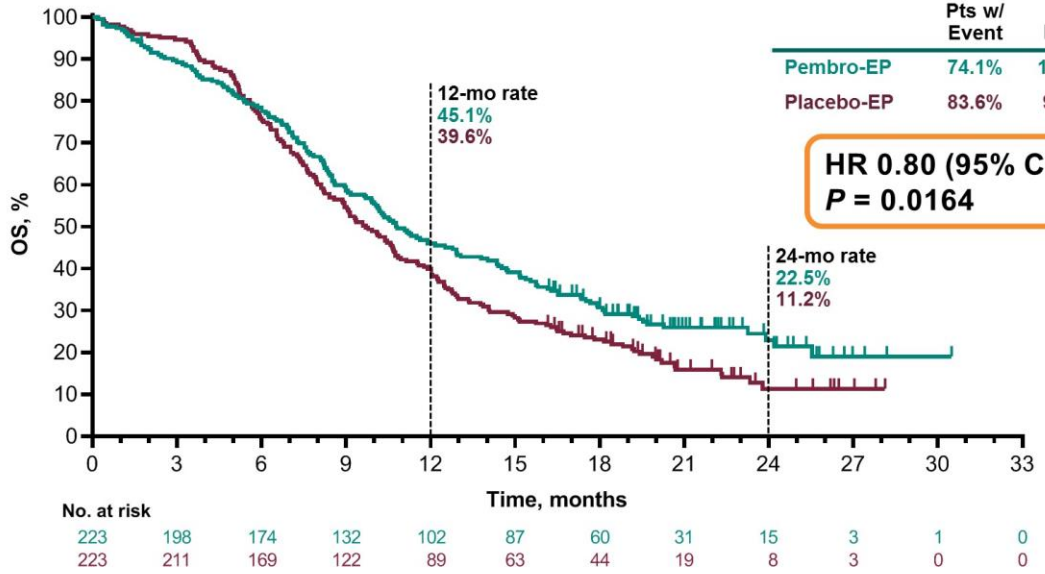


	Pts w/ Event	Median (95% CI)
Pembro-EP	86.0%	4.8 mo (4.3-5.4)
Placebo-EP	97.8%	4.3 mo (4.2-4.5)

HR 0.73 (95% CI 0.60-0.88)

Data cutoff date: Dec 2, 2019.

Overall Survival, ITT: FA



	Pts w/ Event	Median (95% CI)
Pembro-EP	74.1%	10.8 mo (9.2-12.9)
Placebo-EP	83.6%	9.7 mo (8.6-10.7)

HR 0.80 (95% CI 0.64-0.98)
***P* = 0.0164**

Superiority threshold: one-sided *P* = 0.0128.
Data cutoff date: Dec 2, 2019.

Final Analysis (FA)

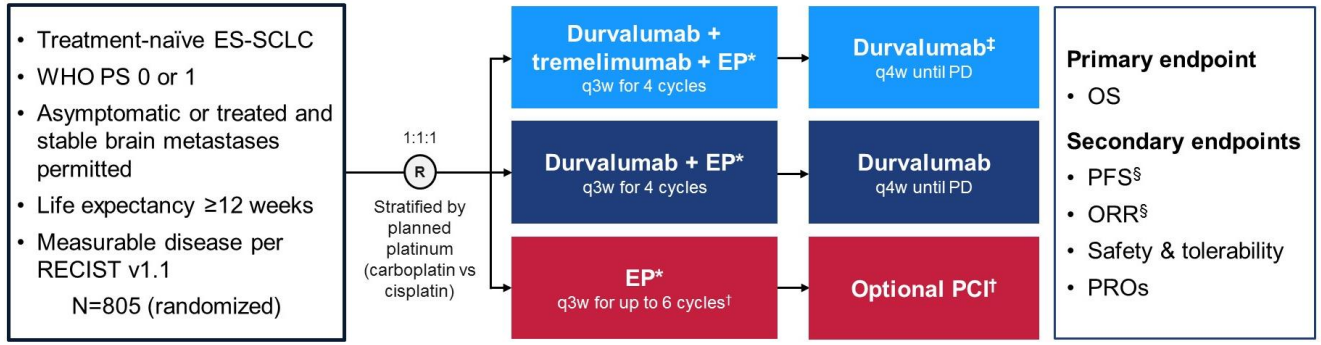
- Planned to occur ~31 mo after study start or when 294 deaths accrued, whichever was later
- Data cutoff date: December 2, 2019
  - No. of deaths: 357
  - OS superiority threshold: one-sided *P* = 0.0128

CÁNCER DE PULMÓN MICROCÍTICO

Abstract 9002 – Luis Paz-Ares et al.

CASPIAN Study Design

Phase 3, global, randomized, open-label, active-controlled, multicenter study



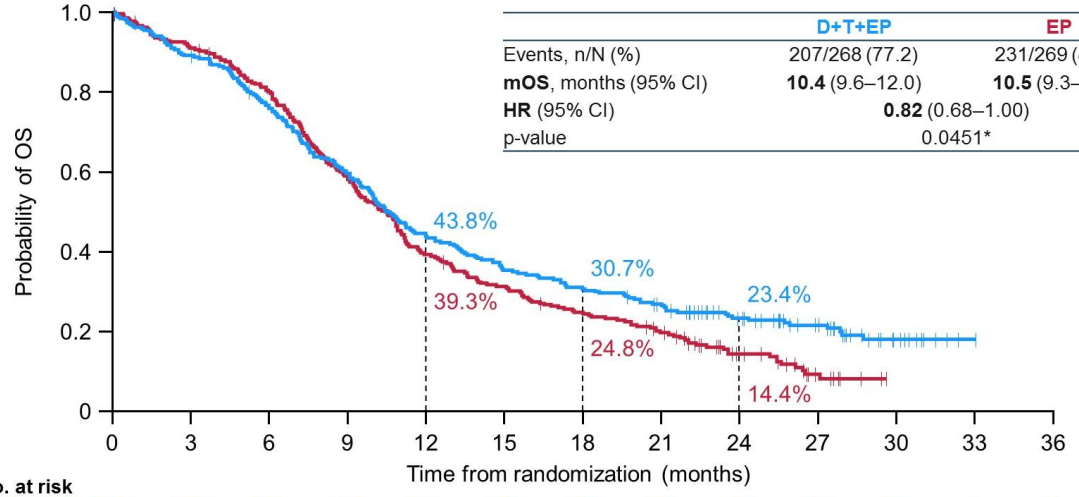
*EP consists of etoposide 80–100 mg/m2 with either carboplatin AUC 5–6 or cisplatin 75–80 mg/m2, durvalumab dosed at 1500 mg, tremelimumab dosed at 75 mg
†Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion
‡Patients received an additional dose of tremelimumab post-EP; §By investigator assessment per RECIST v1.1
AUC, area under the curve; ORR, objective response rate; PCI, prophylactic cranial irradiation; PD, disease progression; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

Baseline Characteristics

	D+T+EP (n=268)	D+EP (n=268)	EP (n=269)
Median age (range), years	63 (36–88)	62 (28–82)	63 (35–82)
Male, %	75.4	70.9	68.4
White / Asian / Other, %	80.2 / 17.5 / 2.4	85.4 / 13.4 / 1.1	82.2 / 15.6 / 2.2
WHO PS 0 / 1, %	40.7 / 59.3	36.9 / 63.1	33.5 / 66.5
Disease stage III / IV*, %	6.7 / 93.3	10.4 / 89.6	8.9 / 91.1
Current / Former / Never smoker, %	41.8 / 52.6 / 5.6	44.8 / 47.0 / 8.2	46.8 / 47.6 / 5.6
Brain or CNS metastases, %	14.2	10.4	10.0
Liver metastases, %	43.7	40.3	38.7

*All patients were confirmed as having ES-SCLC
CNS, central nervous system

Overall Survival: D+T+EP vs EP (Primary Endpoint)



	D+T+EP	EP
Events, n/N (%)	207/268 (77.2)	231/269 (85.9)
mOS, months (95% CI)	**10.4** (9.6–12.0)	**10.5** (9.3–11.2)
HR (95% CI)	**0.82** (0.68–1.00)	
p-value	0.0451*	

*p≤0.0418 required for statistical significance

HR 0.82 (0.68-1.00)

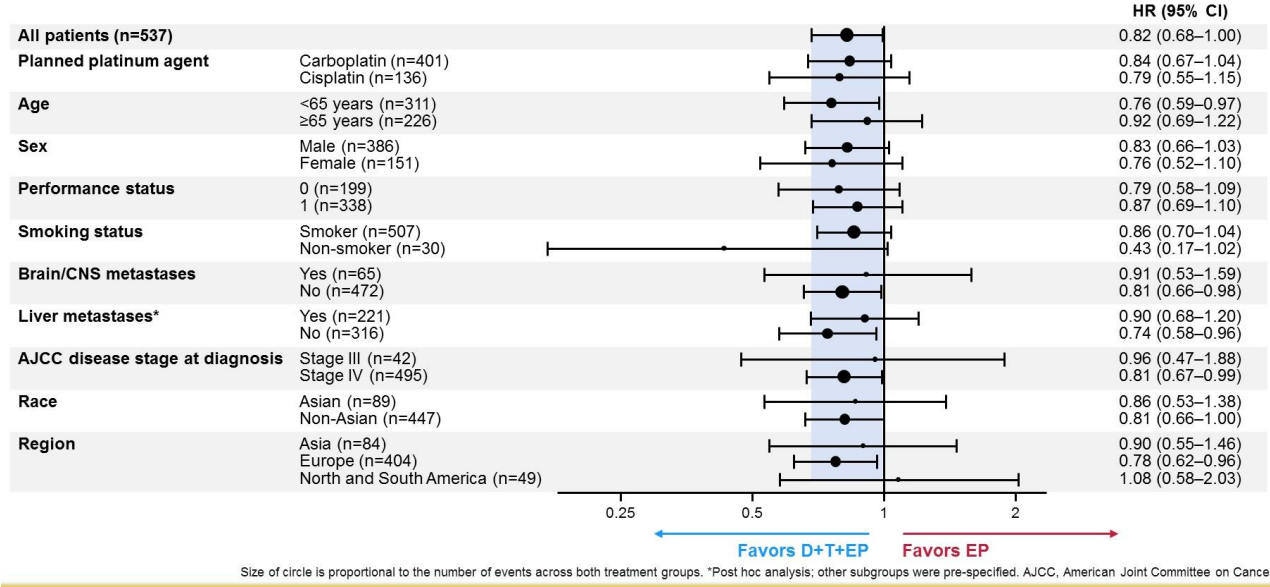
p 0.0451 → p ≤0.0418 para considerarse estadísticamente significativa

Safety Summary

	D+T+EP (n=266)	D+EP (n=265)	EP (n=266)
Any-grade all-cause AEs, n (%)	264 (99.2)	260 (98.1)	258 (97.0)
Grade 3/4 AEs	187 (70.3)	165 (62.3)	167 (62.8)
Serious AEs	121 (45.5)	85 (32.1)	97 (36.5)
AEs leading to treatment discontinuation*	57 (21.4)	27 (10.2)	25 (9.4)
Immune-mediated AEs†	96 (36.1)	53 (20.0)	7 (2.6)
AEs leading to death	27 (10.2)	13 (4.9)	15 (5.6)
Treatment-related AEs leading to death‡	12 (4.5)	6 (2.3)	2 (0.8)

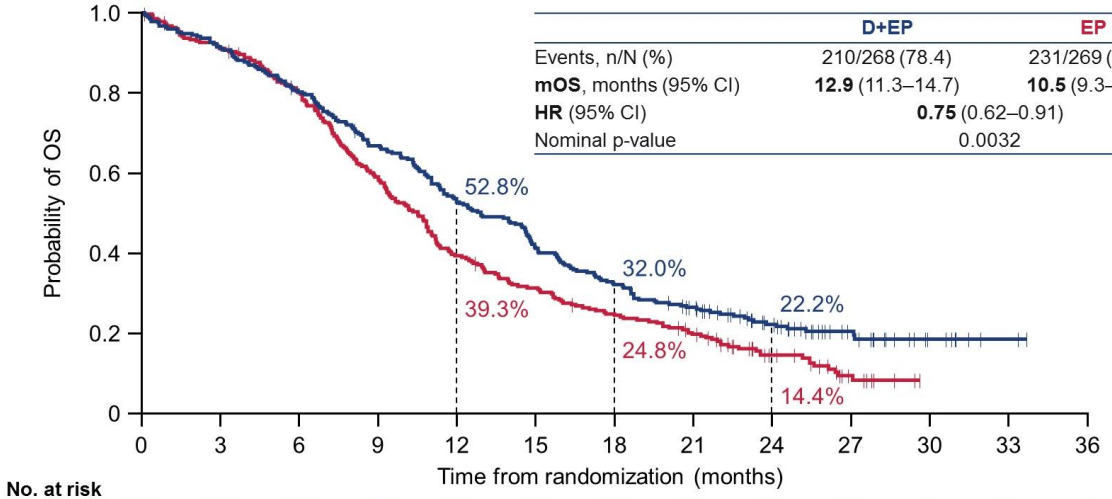
*Includes patients who permanently discontinued at least one study drug
†An event that is associated with drug exposure and consistent with an immune-mediated mechanism of action, where there is no clear alternate etiology and the event required treatment with systemic corticosteroids or other immunosuppressants and/or, for specific endocrine events, endocrine therapy; majority of immune-mediated AEs were low grade and thyroid related
‡AEs assessed by the investigator as possibly related to any study treatment. Causes of death were death, febrile neutropenia, and pulmonary embolism (two patients each), and enterocolitis, general physical health deterioration/multiple organ dysfunction syndrome, pneumonia, pneumonitis/hepatitis, respiratory failure, and sudden death (one patient each) in the durvalumab + tremelimumab + EP arm; cardiac arrest, dehydration, hepatotoxicity, interstitial lung disease, pancytopenia, and sepsis (one patient each) in the durvalumab + EP arm; pancytopenia and thrombocytopenia/haemorrhage (one patient each) in the EP arm

Overall Survival: D+T+EP vs EP Subgroup Analysis



Size of circle is proportional to the number of events across both treatment groups. *Post hoc analysis; other subgroups were pre-specified. AJCC, American Joint Committee on Cance

Updated Overall Survival: D+EP vs EP



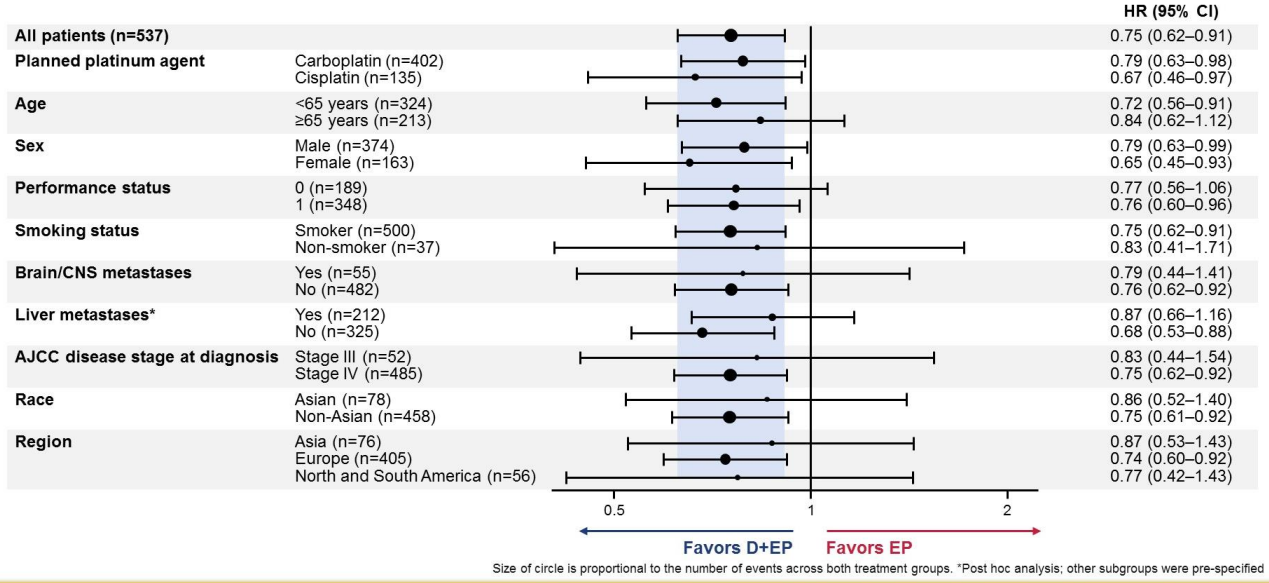
	D+EP	EP
Events, n/N (%)	210/268 (78.4)	231/269 (85.9)
mOS, months (95% CI)	**12.9** (11.3–14.7)	**10.5** (9.3–11.2)
HR (95% CI)	**0.75** (0.62–0.91)	
Nominal p-value	0.0032	

No. at risk												
D+EP	268	244	214	177	140	109	85	66	41	21	8	2	0
EP	269	243	212	156	104	82	64	48	24	8	0	0	0

HR 0.75 (0.62-0.91)

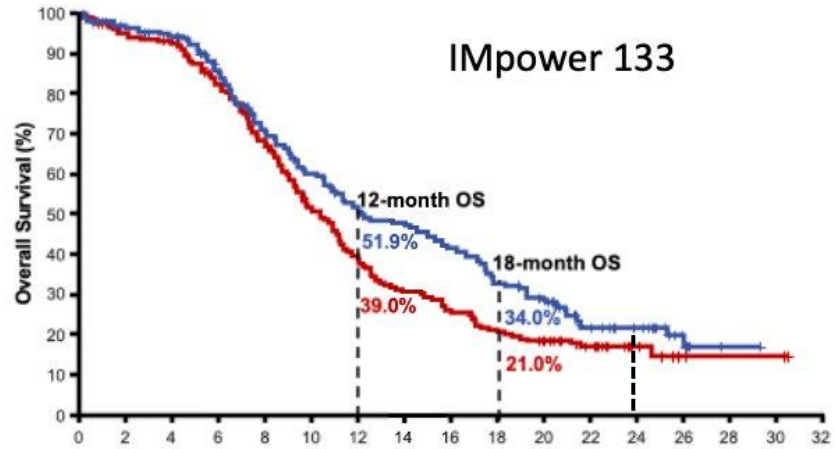
p 0.0032

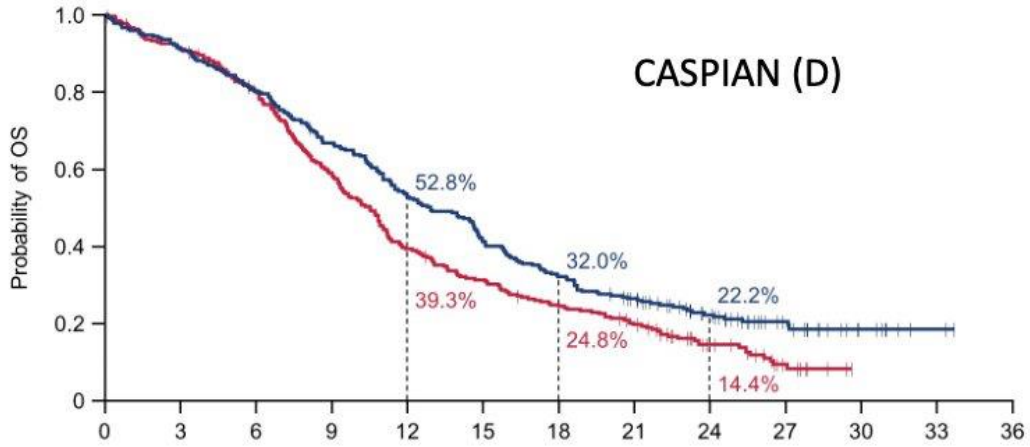
Overall Survival: D+EP vs EP Subgroup Analysis

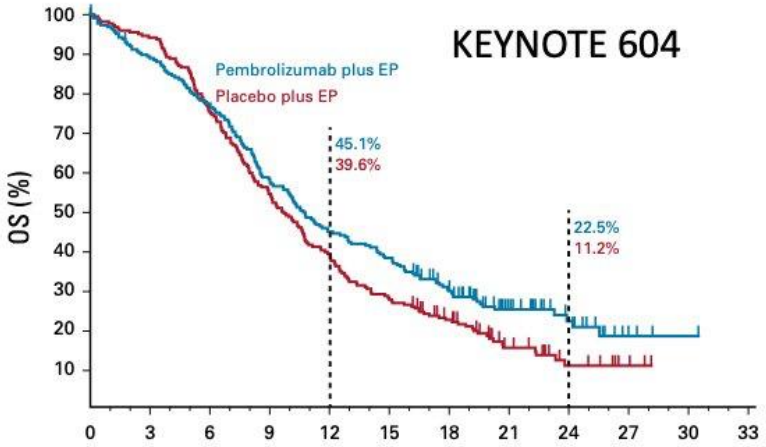


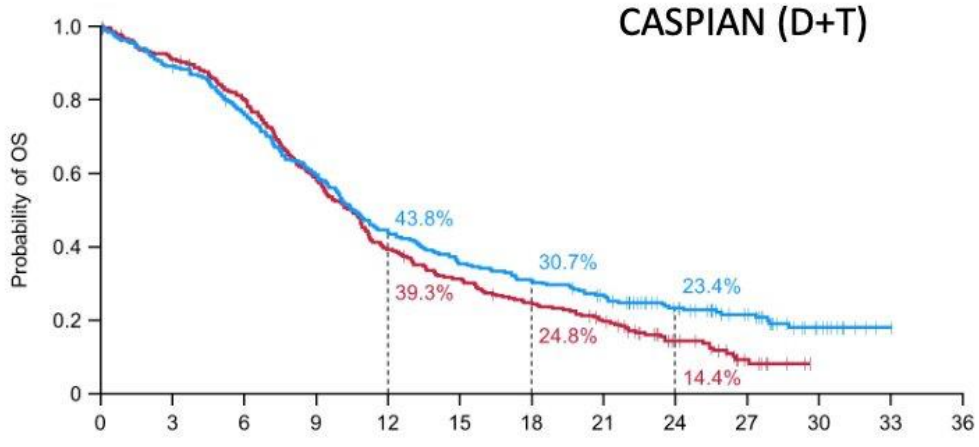
Size of circle is proportional to the number of events across both treatment groups. *Post hoc analysis; other subgroups were pre-specified

Comparación indirecta de la SG a los 24 meses - EC Fase III





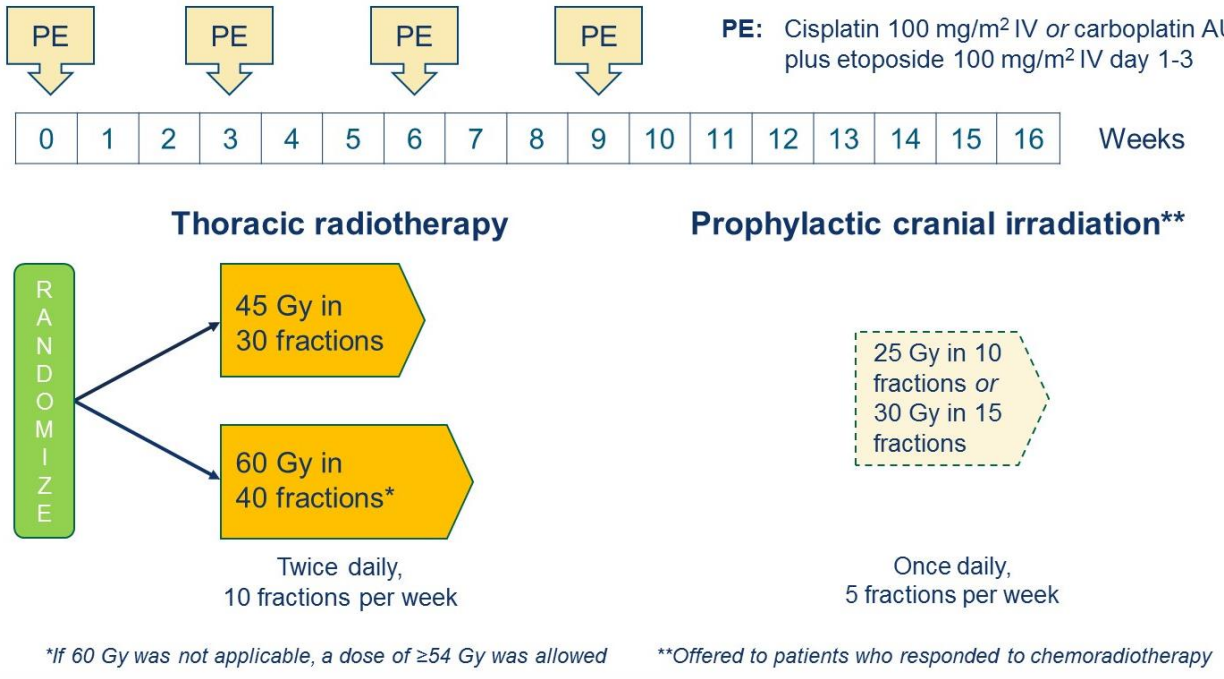




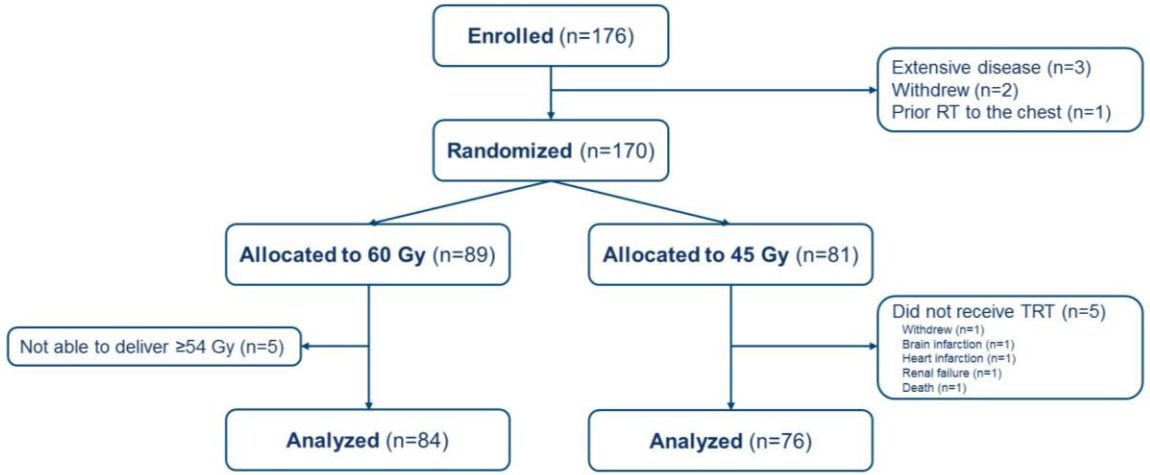
CÁNCER DE PULMÓN MICROCÍTICO – ENFERMEDAD LIMITADA

Abstract 9007 - Bjorn Henning Gronberg et al.

Study design



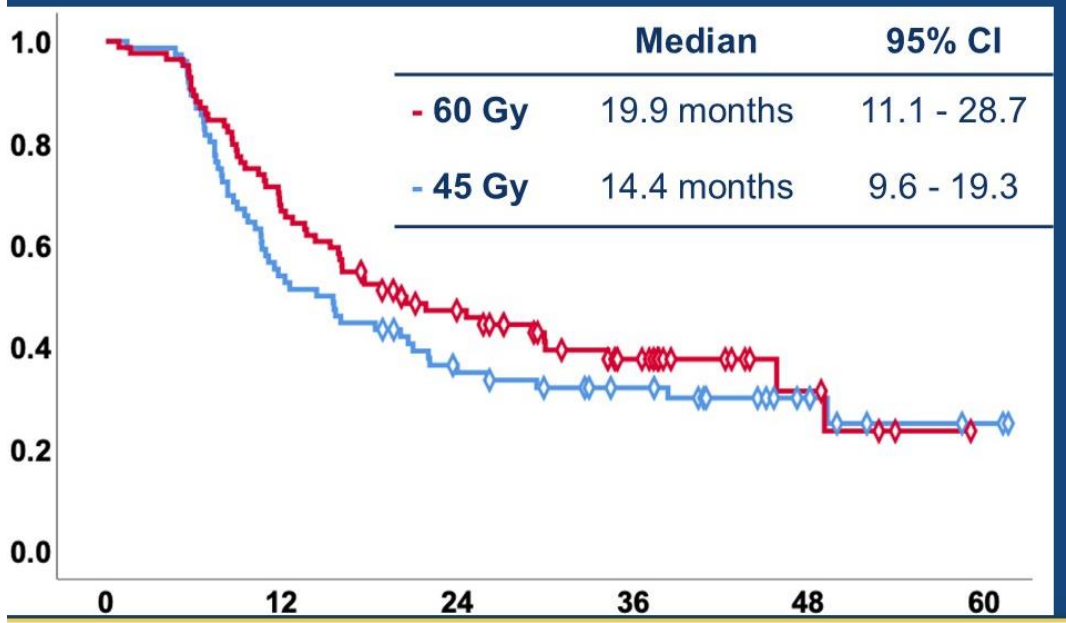
Patient selection



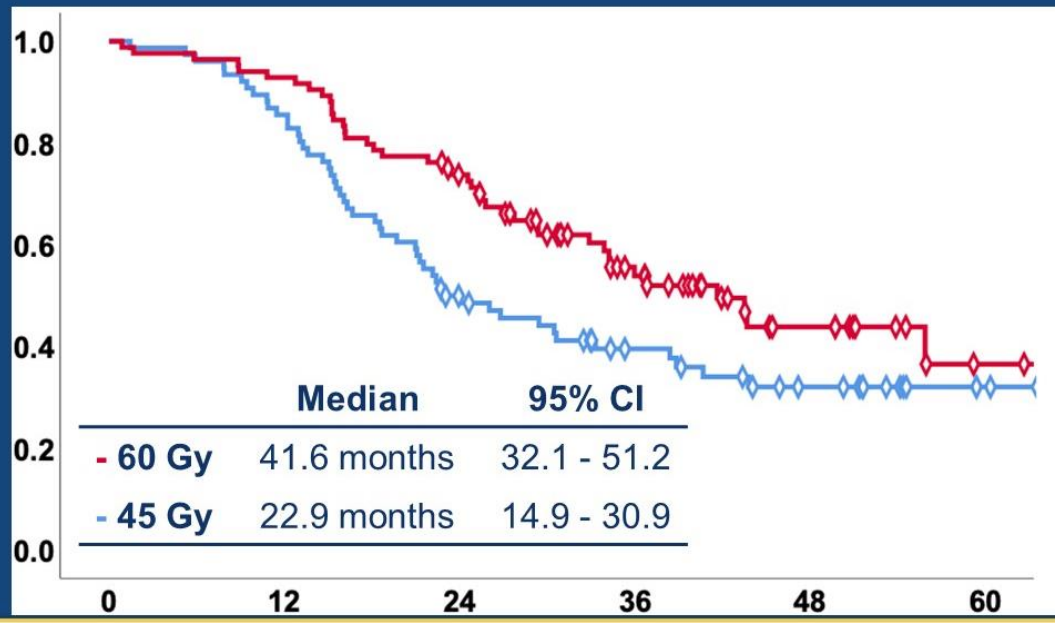
CTCAE grade 3-4 toxicity

	45 Gy (n=76)		**60 Gy** (n=84)		
	n	%	n	%	*p*
Anemia	18	23.7%	20	23.8%	*0.99*
Thrombocytopenia	19	25.0%	20	23.8%	*0.86*
Neutropenia	61	80.3%	67	80.7%	*0.94*
Neutropenic infections	27	35.5%	18	21.4%	*0.05*
Esophagitis	14	18.4%	16	19.0%	*0.92*
Pneumonitis	-	-	3	3.6%	*0.23*

PFS



OS



MESOTELIOMA – 1L

Abstract 9003 – Patrick Forde et al.

Patients and Methods

Between June 2017 and June 2018, 55 patients were enrolled at 15 US sites

- Unresectable MPM
- No prior therapy
- ECOG 0-1
- Baseline tumor specimen

→ Durvalumab 1120 mg + Pemetrexed 500 mg/m² + Cisplatin* 75 mg/m² every 3 weeks x 6 cycles → SD or PR → Durvalumab 1120 mg every 3 weeks until PD**

* Carboplatin was substituted if cisplatin was contraindicated, or due to toxicity during treatment

** Max duration 1 year from start of study

Study Objectives

Primary Objective

- Overall survival (vs. historical control[1])

Secondary Objectives

- Safety and tolerability
- Progression Free Survival (PFS)
- Objective Response Rate (ORR)*

Exploratory Objectives

- Baseline tumor PD-L1 expression and intra-tumoral CD8 T cell density, whole exome sequencing tumor-normal pairs, and immunologic analyses

*using modified RECIST 1.1 for mesothelioma

Demographics

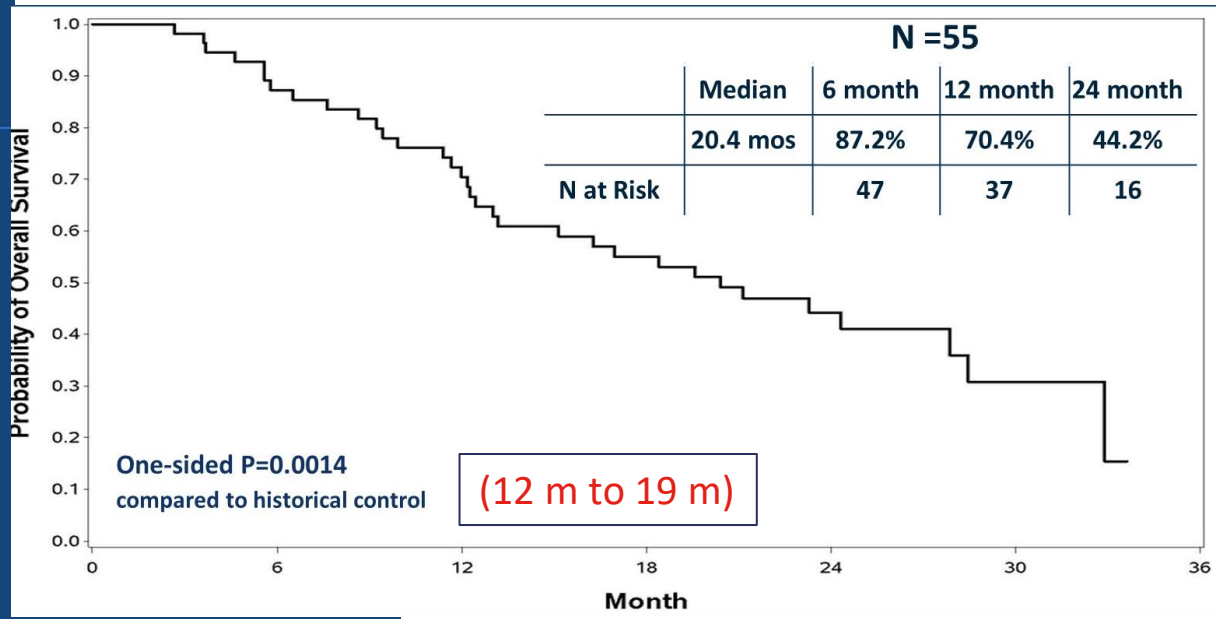
N=55

Characteristic	Number	Range or (%)
Age, years	68 (median)	35-83
Gender		
Female	10	(18.2)
Male	45	(81.8)
ECOG PS		
0	23	(41.8)
1	32	(58.2)
Histologic Subtype		
Epithelioid	41	(74.5)
Sarcomatoid	7	(12.7)
Biphasic	6	(10.9)
Desmoplastic	1	(1.8)

Results: Overall Survival

	N=55 % or months (95% CI)	
Median Overall Survival	20.4 mos	(13.0, 28.5)
	*One-sided P = 0.0014	
Overall Survival 6 mos	87.2 %	(75.1, 93.7)
Overall Survival 12 mos	70.4 %	(56.3, 80.7)
Overall Survival 24 mos	44.2 %	(30.2, 57.3)

* Calculated using the Kaplan-Meier method



Results: Best Objective Response

Variable€	N=55* N (%)
Partial Response	31 (56.4)
Stable Disease	22 (40.0)
Progressive Disease	1 (1.8)
Not Evaluable†	1 (1.8)

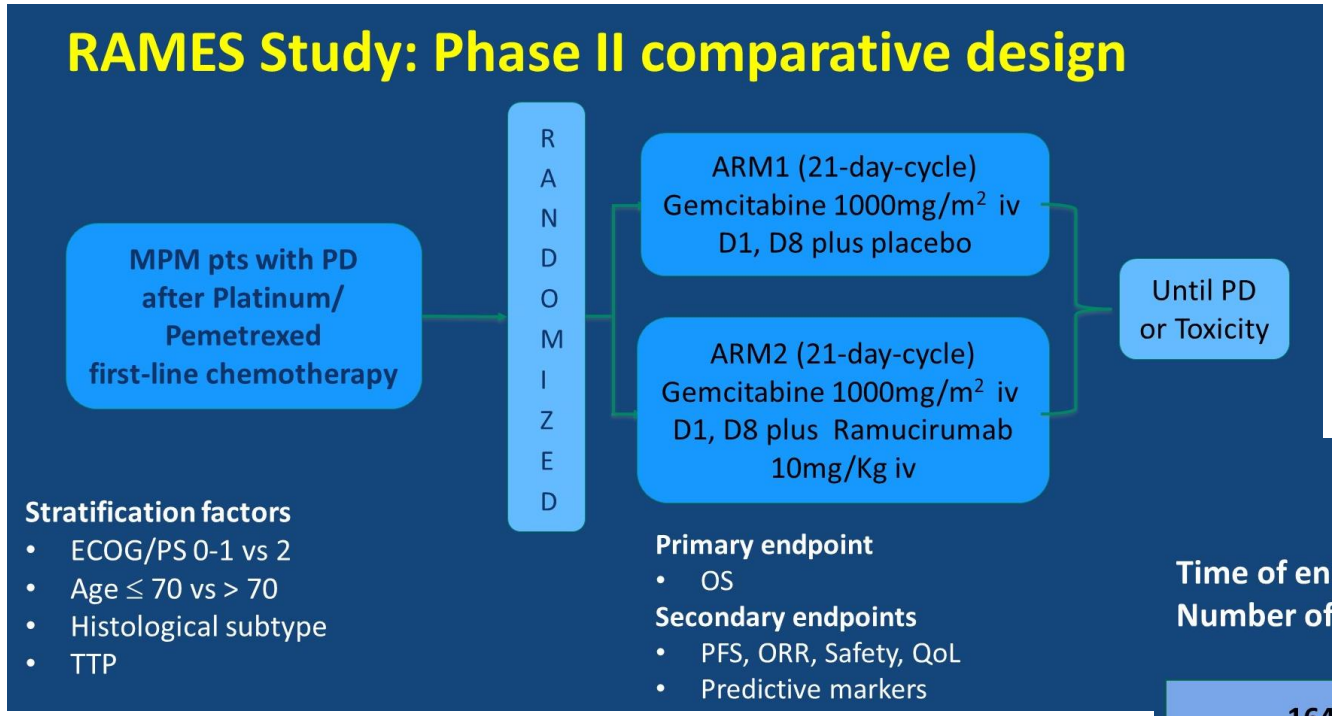
*Data cutoff date April 24, 2020
€Best Objective Response using RECIST 1.1 modified for mesothelioma
†One subject discontinued treatment before the first disease assessment

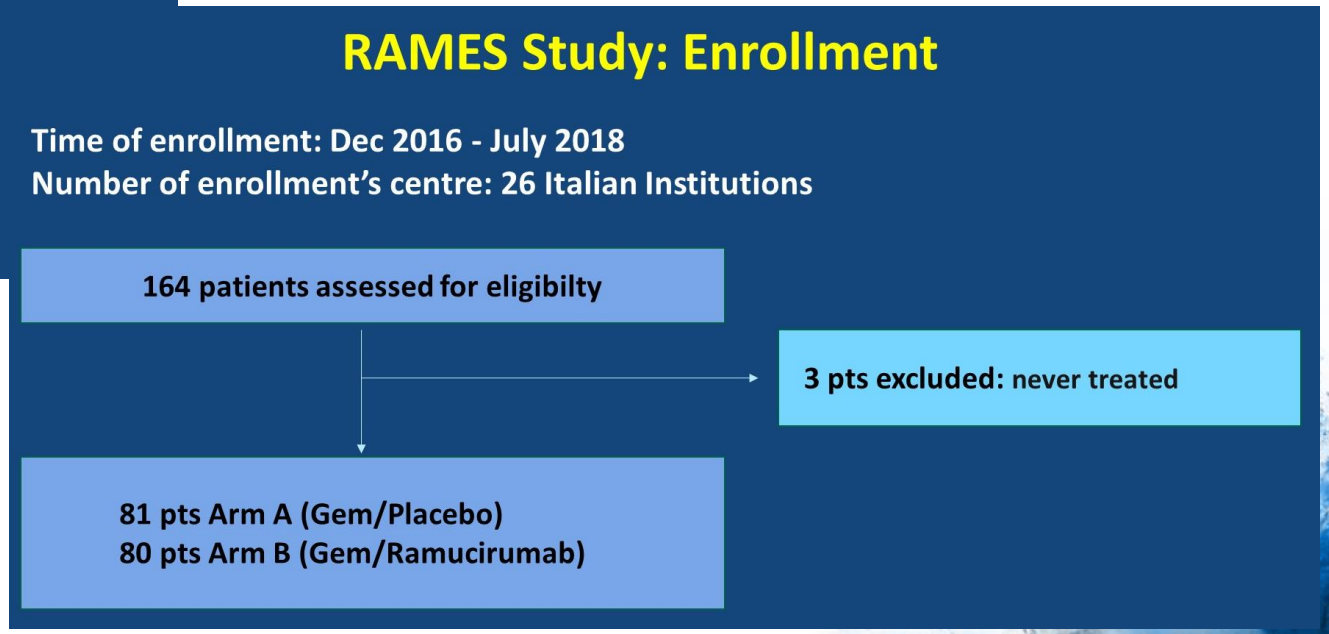
- Dual PD-L1/CD8 IHQ: 41/55
- WES: 42/55

No correlación con la expresión de PD-L1 o TMB

MESOTELIOMA – 2L

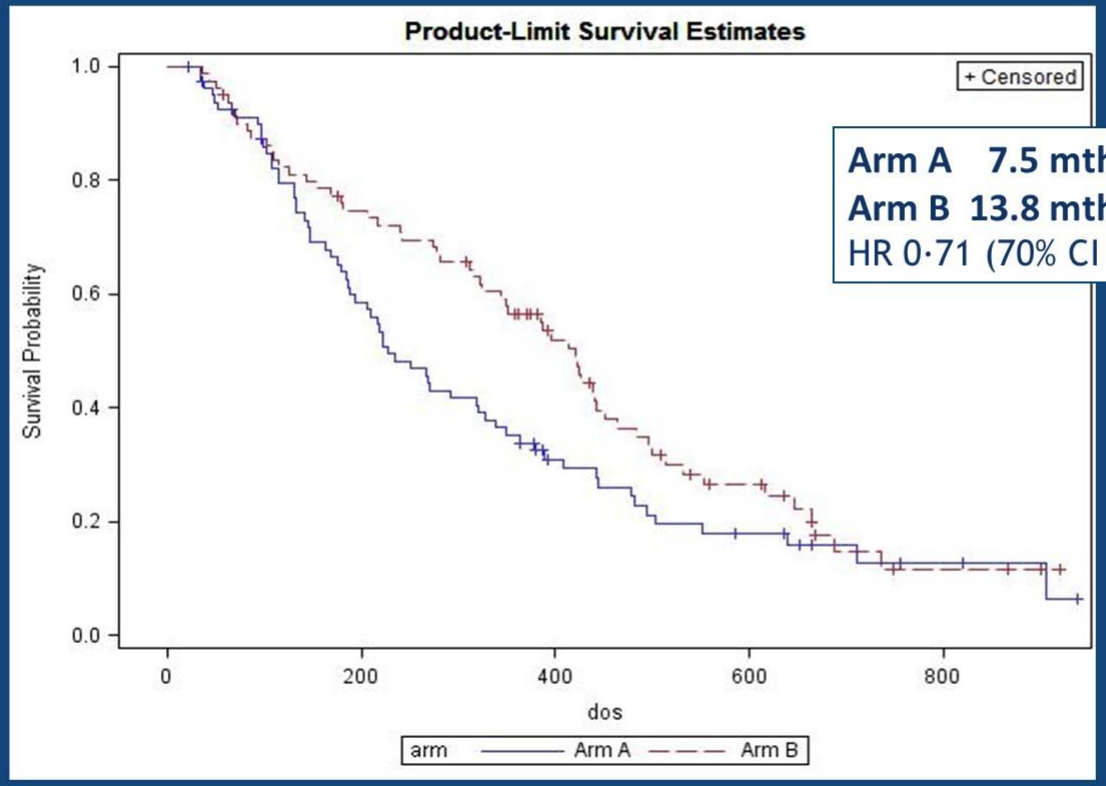
Abstract 9004 - María Pagano et al.





Mediana edad: 69 años
~74% varones
% similar en cuando a exposición a asbesto vs no
85% epitelioides
Localmente avanzado > metastásico

RAMES Study: OS ITT



Arm A 7.5 mths (70% CI 6.9-8.9)
Arm B 13.8 mths (70% CI 12.7·14.4)
HR 0·71 (70% CI 0.59-0.85, p=0.057)

Overall Survival	Arm A Gem/Placebo	Arm B Gem/Ramucirumab
6 months	63.9 %	74.7 %
12 months	33.9 %	56.5 %

RAMES Study: Safety

	Arm A (Gem/Placebo)		Arm B (Gem/Ramucirumab)	
Toxicity	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Anemia	25 (30.87%)	4 (4.94%)	15 (18.75%)	0
Neutropenia	23 (28.39%)	1 (1.23%)	27 (33.75%)	3 (3.75%)
Febrile neutropenia	1 (1.23%)	1 (1.23%)	0	0
Thrombocytopenia	7 (8.63%)	1 (1.23%)	11 (13.75%)	2 (2.50%)
Nausea/Vomiting	13 (16.05%)	0	26 (32.5%)	1 (1.25%)
Fatigue		3 (3.70%)		4 (5.00%)
Diarrhea	5 (6.17%)	1 (1.23%)	11 (13,75%)	0
AST/ALT increase	5 (7.4%)	2 (2.47%)	19 (23.75%)	2 (2.50%)

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