LUNG CANCER UPDATES

ESMO HIGHLIGHTS

19-23 DE OCTUBRE 2018, MUNICH

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Dra. Virginia Calvo

Iniciativa científica de:

GECP

Grupo Español de Cáncer de Pulmón

Spanish Lung Cancer Group

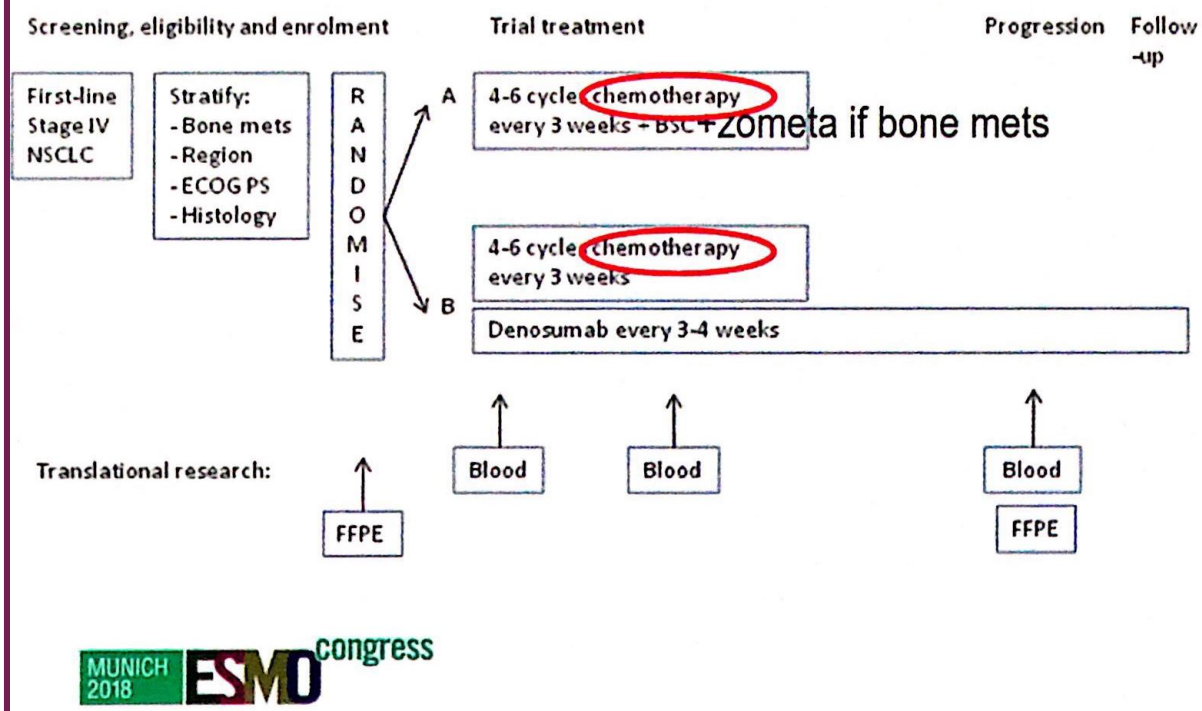
POSTERS DISCUSSED

ID	Lead Author	Title
1385PD	Peters et al.	A randomised phase III trial evaluating the addition of denosumab to standard first-line treatment in advanced NSCLC – the ETOP and EORTC SPLENDOUR trial
LBA64	Spigel et al.	nab-Paclitaxel + Carboplatin induction followed by nab-Paclitaxel maintenance in squamous non-small cell lung cancer (NSCLC): results from the ABOUND.sqm study
LBA65	Socinski et al.	Progression-free survival (PFS) and overall survival (OS) analysis of a randomised Phase III study of atezolizumab + carboplatin + paclitaxel or nab-paclitaxel vs carboplatin + nab-paclitaxel in 1L advanced squamous NSCLC
1386PD	Reck et al.	IMpower150: clinical safety, tolerability and immune-related adverse events in a Phase III study of atezolizumab (atezo) + chemotherapy (chemo) + bevacizumab (bev) vs chemo + bev in 1L nonsquamous NSCLC

1385PD. A randomised phase III trial evaluating the addition of denosumab to standard first-line treatment in advanced NSCLC- the ETOP and EORTC SPLENDOUR trial

PETERS ET AL. #1385PD

SPLENDOUR design



Open label
Primary endpoint: OS

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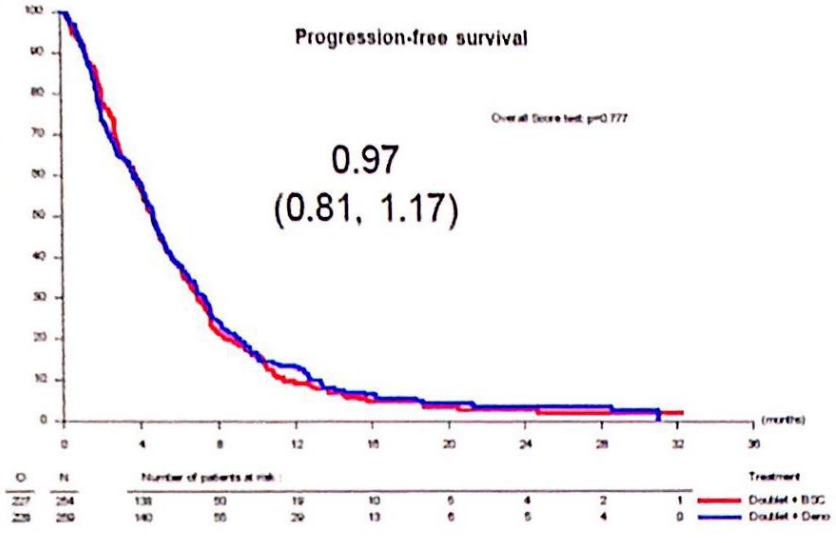
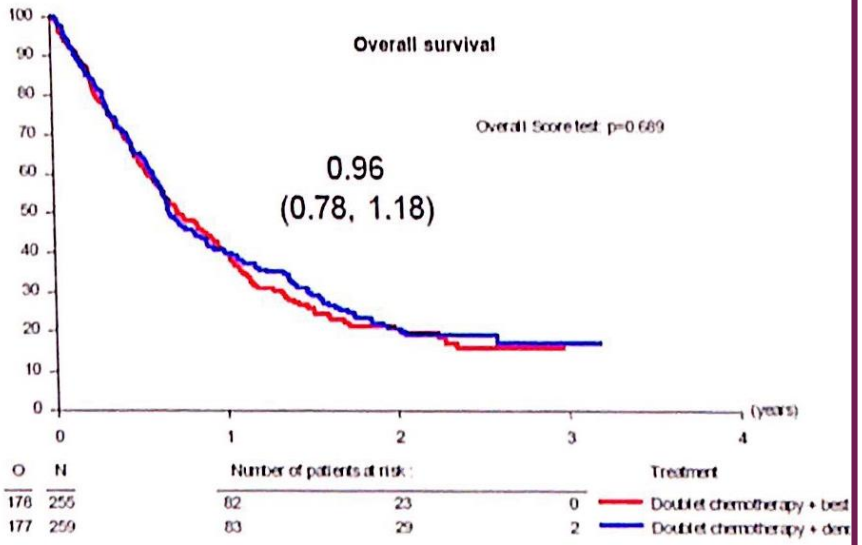
1385PD. A randomised phase III trial evaluating the addition of denosumab to standard first-line treatment in advanced NSCLC-the ETOP and EORTC SPLENDOUR trial

PETERS ET AL. #1385PD

SPLENDOUR outcomes: PFS & OS





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1385PD. A randomised phase III trial evaluating the addition of denosumab to standard first-line treatment in advanced NSCLC- the ETOP and EORTC SPLENDOUR trial

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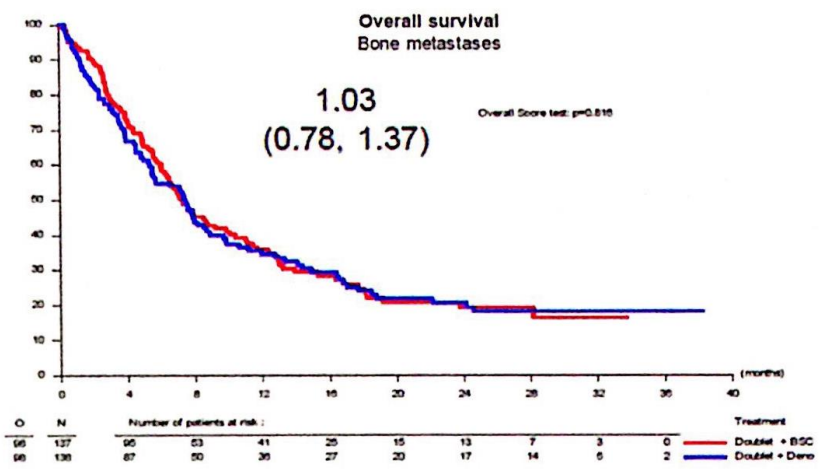
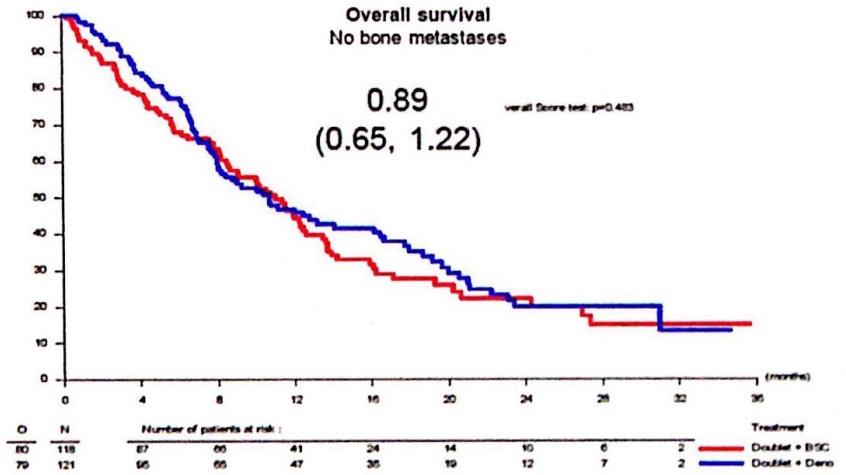
SPLENDOUR outcomes: OS (+/- bone mets)





Contrary to Scagliotti et al post hoc analyses

No obvious strong bone protective effect: CARE, power of dataset & effect of x-over

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SO...WHAT DOES SPLENDOUR MEAN IN 2018?

My interpretation

- Trial did not meet the primary endpoint (OS)
- Adding denosumab to 1st line CHEMOTHERAPY ALONE in advanced NSCLC with/without bone mets (the ITT population) does not improve OS.
- The OS suggestion of denosumab in NSCLC (the registration trial) was not identified: population biases.
- A heterogeneous population, ITT difficult to interpret, changing over life of trial.
- A victim of rapid systemic therapy changes in advanced NSCLC.
    - Oncogene addicted patients excluded: those most likely to benefit from long-term denosumab
    - Likely over-representation of PDL1 negative, 1-49%+ TPS patients, unsuitable for ICIs (hidden biases)
- I look forward to translational analyses

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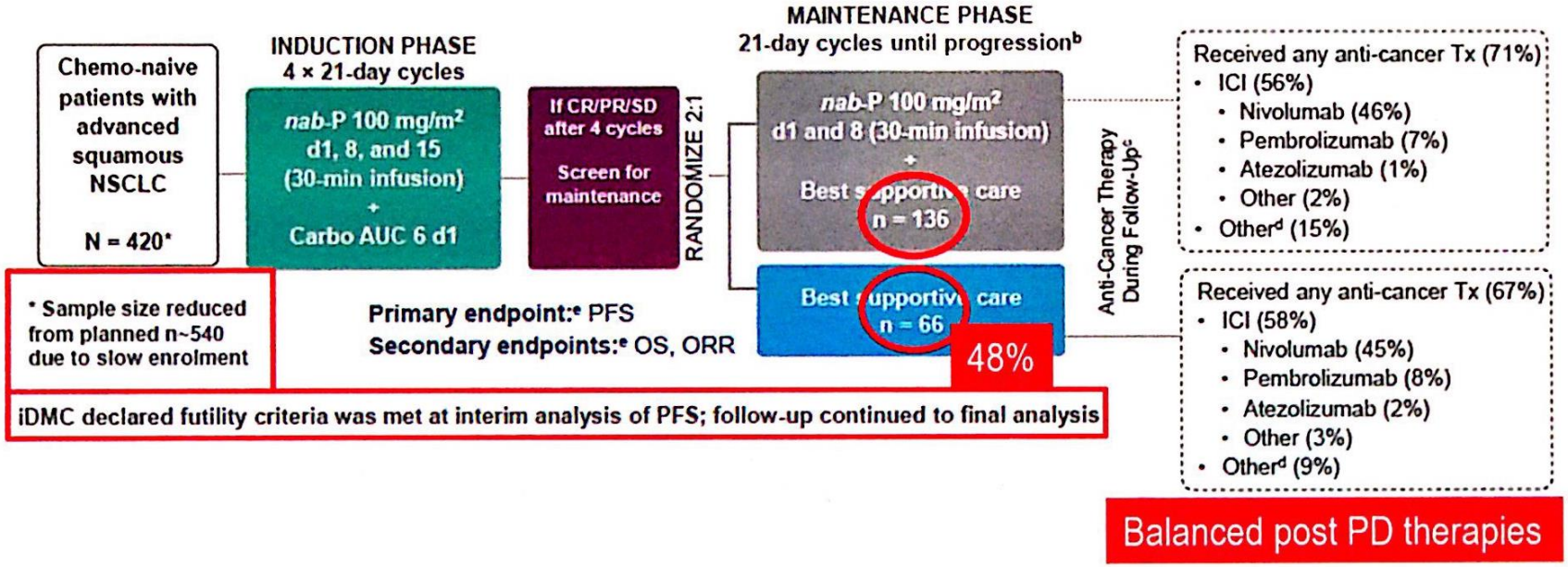
Invited Discussant: S. Popat

LBA64. Nab-Paclitaxel + Carboplatin induction followed by nab-Paclitaxel maintenance in squamous non-small cell lung cancer (NSCLC): results from the ABOUND.sqm study

SPIGEL ET AL. #LBA2936

ABOUND.sqm study



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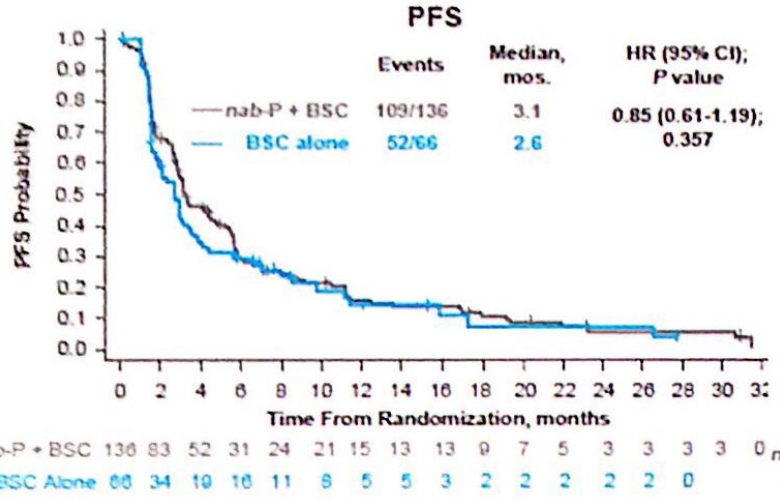
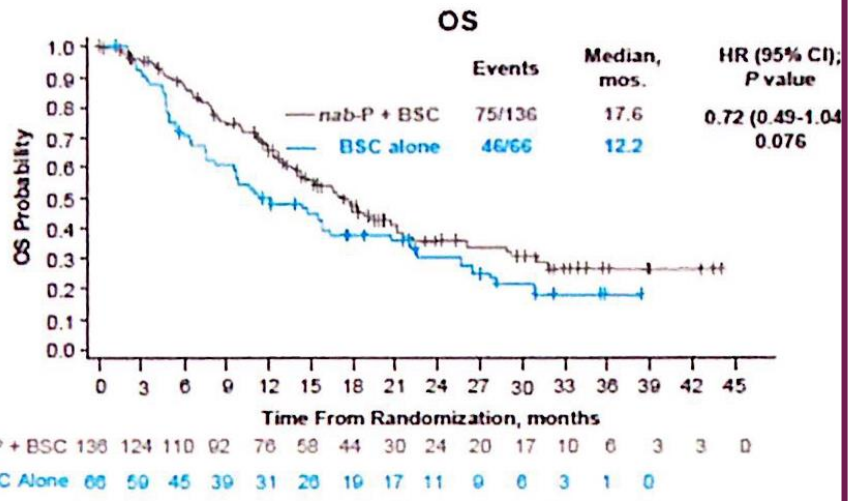
LBA64. Nab-Paclitaxel + Carboplatin induction followed by nab-Paclitaxel maintenance in squamous non-small cell lung cancer (NSCLC): results from the ABOUND.sqm study

SPIGEL ET AL. #LBA2936

PFS and OS: no statistically significant benefit





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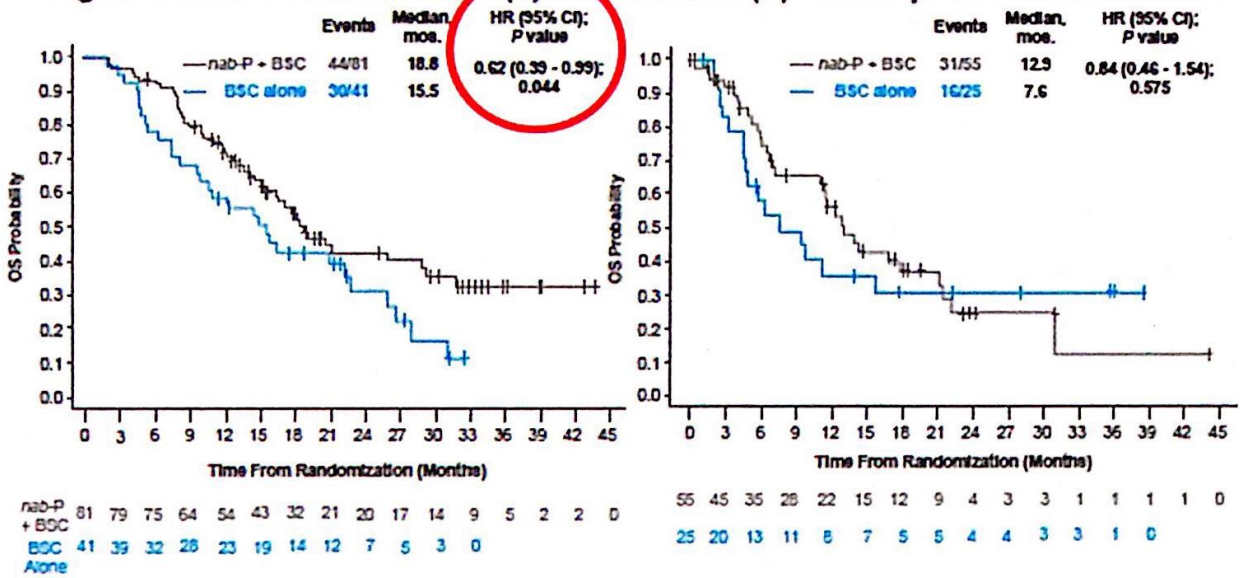
- ORR was 69.1% with maintenance *nab*-P + BSC vs 57.6% with BSC alone (RRR 1.20 [95% CI, 0.95-1.52]; *P* = .087)

ORR result may be due to lower power than registration trial

SPIGEL ET AL. #LBA2936

Differential benefit by subsequent ICI use: hypothesis generating

Figure 3. OS in Patients With (a) and Without (b) Subsequent ICI Treatment



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Is OS benefit in those receiving ICI confounded by imbalance in PDL1≥50%?

LBA64. Nab-Paclitaxel + Carboplatin induction followed by nab-Paclitaxel maintenance in squamous non-small cell lung cancer (NSCLC): results from the ABOUND.sqm study

SPIGEL ET AL. #LBA2936

Safety cf registration trial

Table 4. Safety[a,b]

Parameter	*nab*-P + BSC (n = 130)	BSC Alone (n = 62)
At least 1 grade ≥ 3 TEAE, n (%)	109 (83.8)	48 (77.4)
At least 1 serious TEAE, n (%)	55 (42.3)	22 (35.5)
Hematologic grade ≥ 3 TEAEs, n (%)[c]		
Neutropenia	69 (53.1)	20 (32.3)
Anemia	43 (33.1)	31 (50.0)
Thrombocytopenia	16 (12.3)	10 (16.1)
Leukopenia	14 (10.8)	9 (14.5)
Nonematologic grade ≥ 3 TEAEs, n (%)[c]		
Peripheral sensory neuropathy	18 (13.8)	0
Fatigue	8 (6.2)	1 (1.6)
Diarrhea	7 (5.4)	2 (3.2)
Hypokalemia	7 (5.4)	1 (1.6)
Time to improvement of grade ≥ 3 PN by ≥ 1 grade, median, days	21	NE

[a] Severity of AEs was graded using CTCAE v4.0. [b] Throughout entire study. [c] Occurring in ≥ 5% of patients in either arm.

Table 3. Most Common Treatment-Related Grade ≥ 3 AEs According to NCI-CTCAE

	nab-PC (%) (n = 514)		sb-PC (%) (n = 524)		
AE	Grade 3	Grade 4	Grade 3	Grade 4	*P*
Hematologic AEs					
Neutropenia	33	14	32	26	< .001*
Thrombocytopenia	13	5	7	2	< .001†
Anemia	22	5	6	< 1	< .001†
Febrile neutropenia	< 1	< 1	1	< 1	N/S
Nonhematologic AEs					
Fatigue	4	< 1	6	< 1	N/S
Sensory neuropathy	3	0	11	< 1	< .001*
Anorexia	2	0	< 1	0	N/S
Nausea	< 1	0	< 1	0	N/S
Myalgia	< 1	0	2	0	.011*
Arthralgia	0	0	2	0	.008*

Much higher neuropathy & neutropenia; likely exposure related

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Socinski et al. JCO (2012)

SO…WHAT DOES ABOUND.SQM MEAN IN 2018?

My interpretation

- No PFS benefit (primary endpoint): a negative trial.
- No significant OS benefit (negative); OS benefit identified by PD ICI use, may be confounded PDL1 strata.

AND

- More neutropenia: febrile neutropenia?
- More peripheral neuropathy
- + weekly vs q21 dosing

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What will happen when you add ICI to nab-paclitaxel?