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Iniciativa científica de:
GECP
lung cancer research

INMUNOTERAPIA EN ENFERMEDAD AVANZADA

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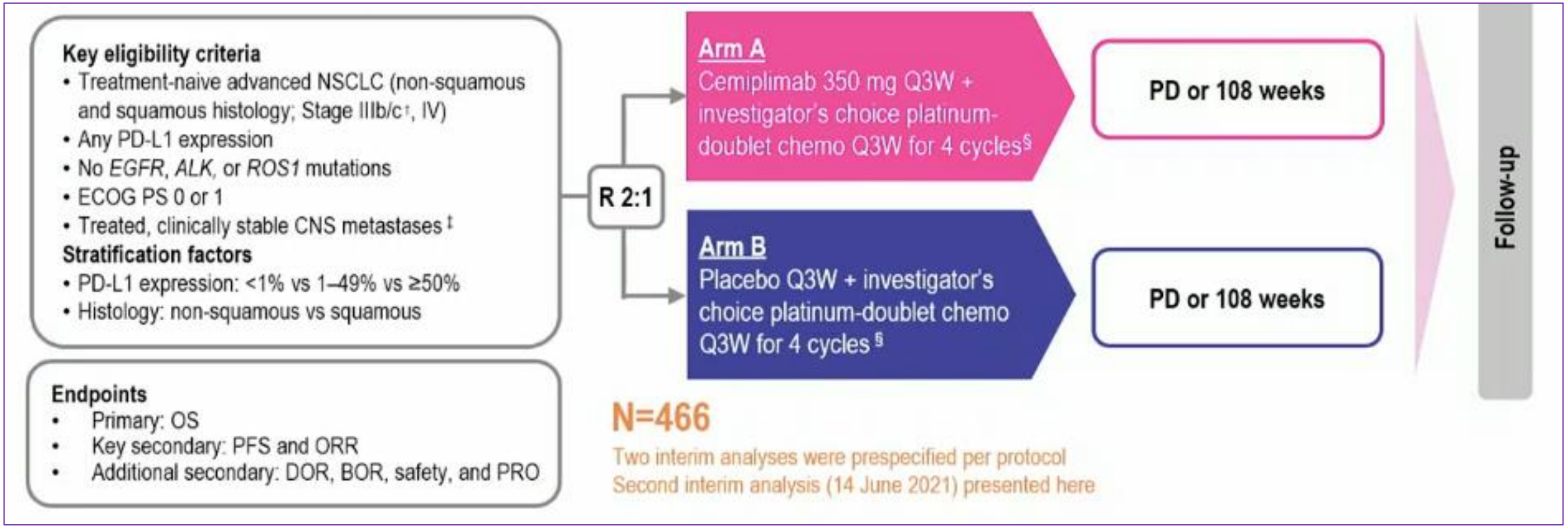
- PRIMERA LÍNEA
  - EMPOWER-Lung 3: cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)
  - Atezolizumab (atezo) vs platinum-based chemo in blood-based tumor mutational burden-positive (bTMB+) patients (pts) with first line (1L) advanced/metastatic (m)NSCLC: results of the Blood First Assay Screening Trial (BFAST) Phase 3 Cohort C

EMPOWER-Lung 3: cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)

LBA51. Miranda Gogishvili

- Cemiplimab is a high-affinity, fully human anti-PD-1. It is approved as first-line monotherapy for advanced NSCLC with PD-L1 ≥50% (EMPOWER-Lung 1 study)



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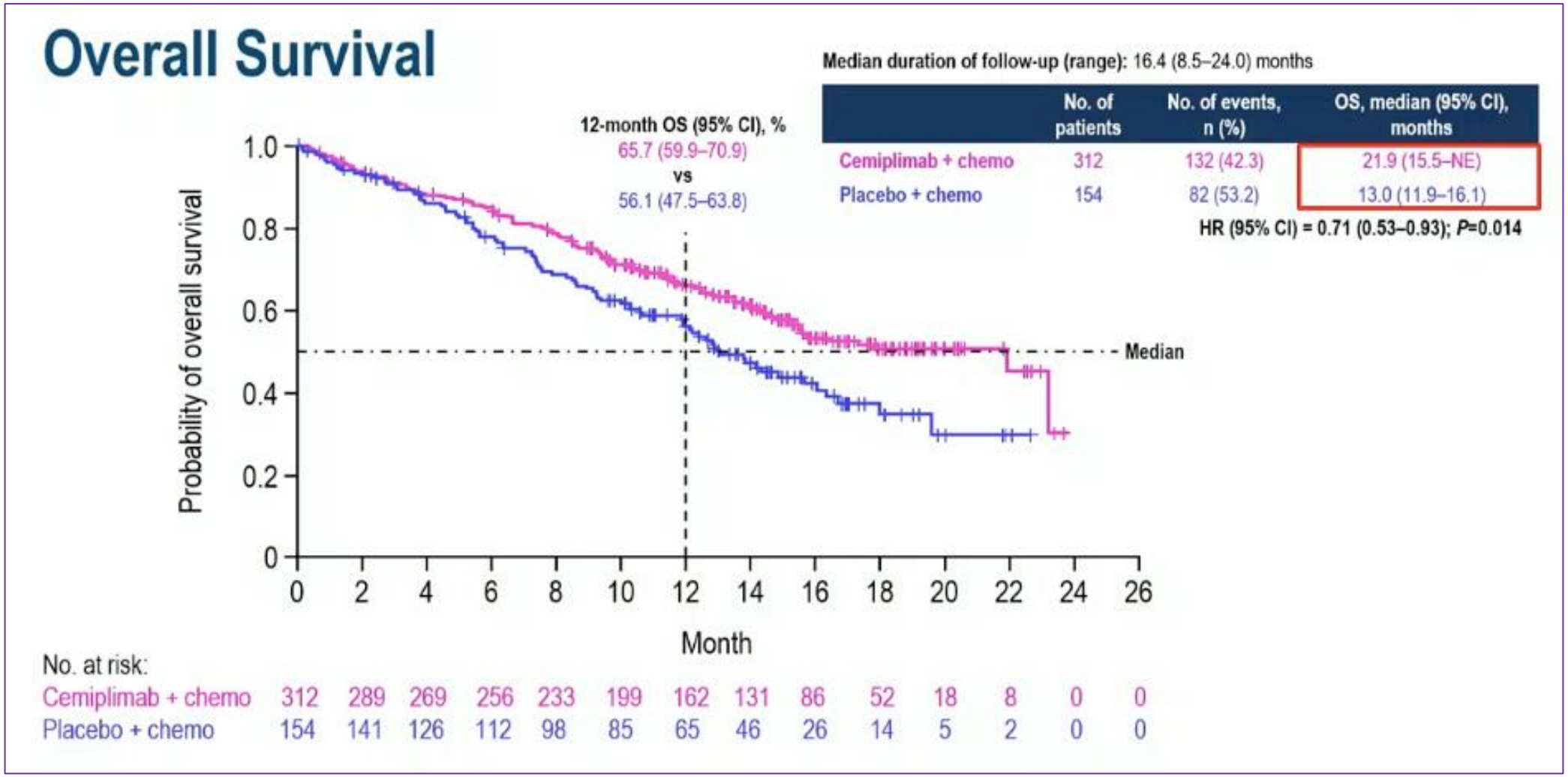

EMPOWER-Lung 3: cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)

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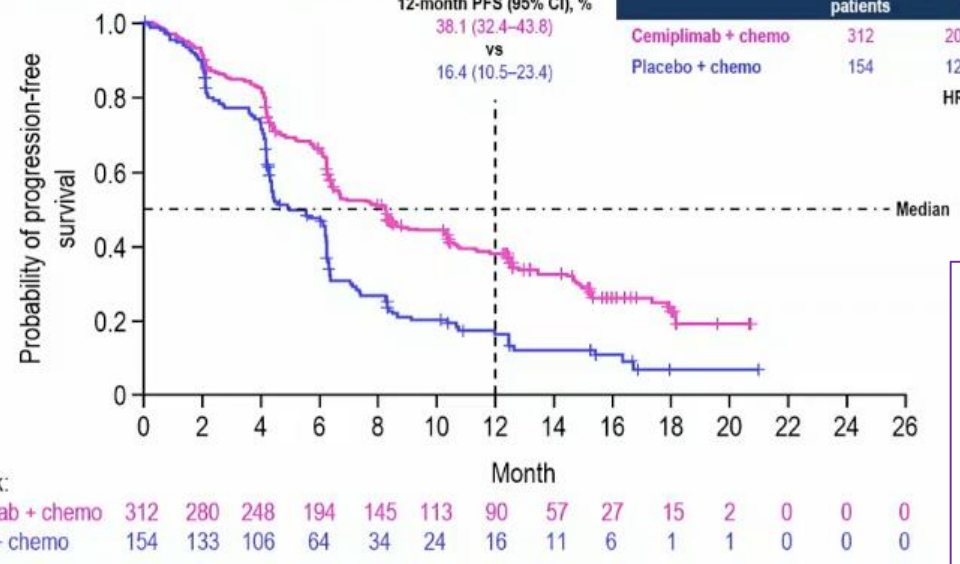
Progression-Free Survival

Median duration of follow-up (range): 16.4 (8.5–24.0) months

	No. of patients	No. of events, n (%)	PFS, median (95% CI), months
Cemiplimab + chemo	312	204 (65.4)	8.2 (6.4–9.3)
Placebo + chemo	154	122 (79.2)	5.0 (4.3–6.2)

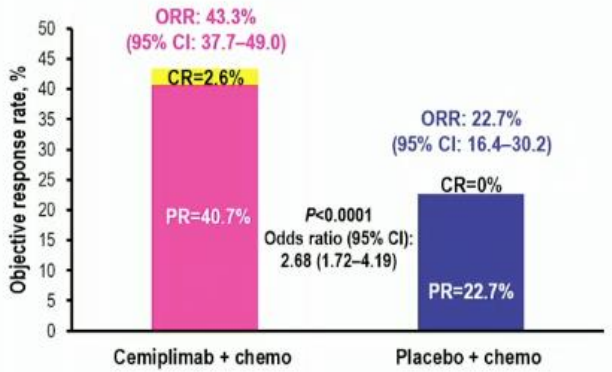
HR (95% CI) = 0.56 (0.44–0.70); *P*<0.0001

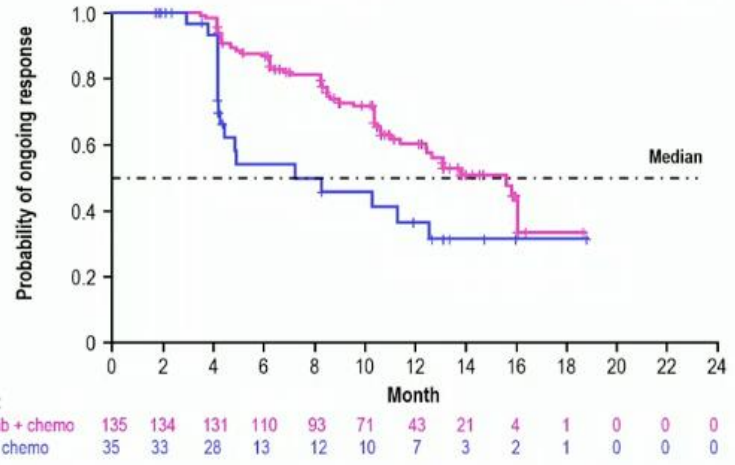


Tumour Response and DOR

Among patients with objective response

	No. of patients	No. of events, n (%)	DOR, median (95% CI), months
Cemiplimab + chemo	135	53 (39.3)	15.6 (12.4–NE)
Placebo + chemo	35	18 (51.4)	7.3 (4.3–12.6)





EMPOWER-Lung 3: cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)

LBA51. Miranda Gogishvili

n (%), unless stated	Cemiplimab + chemo (n=312)		Placebo + chemo (n=153)	
Duration of exposure, median (range), weeks	38.5 (1.4–102.6)		21.3 (0.6–95.0)	
Treatment-emergent AEs, regardless of attribution	**Any grade**	**Grade 3–5**	**Any grade**	**Grade 3–5**
Overall	299 (96)	136 (44)	144 (94)	48 (31)
Led to discontinuation	16 (5)	13 (4)	4 (3)	4 (3)
Led to death	19 (6)	19 (6)	12 (8)	12 (8)
Treatment-related AEs				
Overall	275 (88)	90 (29)	129 (84)	28 (18)
Led to discontinuation	10 (3)	7 (2)	1 (1)	1 (1)
Led to death	4 (1)	4 (1)	1 (1)	1 (1)
Immune-related AEs†				
Overall	59 (19)	9 (3)	–	–
Led to discontinuation	3 (1)	3 (1)	–	–
Led to death	1 (0.3)	1 (0.3)	–	–

PRO Summary

- **Delay** in the time to definitive clinically meaningful deterioration in GHS/QoL [HR, 0.78 (95% CI, 0.51–1.19); *P*=0.248] and pain symptoms [HR, 0.39 (95% CI, 0.26–0.60); *P*<0.0001].
- **Improvement** in overall change from baseline in GHS/QoL [0.61 (95% CI, -2.23, 3.45) *P*=0.673] and pain symptoms [-4.98 (95% CI, -8.36, -1.60); *P*=0.004].

Treatment-emergent AEs in ≥10% of patients in either arm, n (%)	Cemiplimab + chemo (n=312)		Placebo + chemo (n=153)	
	Any grade	**Grade 3–5**	**Any grade**	**Grade 3–5**
Overall	299 (96)	136 (44)	144 (94)	48 (31)
Anaemia	136 (44)	31 (10)	61 (40)	10 (7)
Decreased appetite	53 (17)	3 (1)	18 (12)	0
Fatigue	38 (12)	7 (2)	11 (7)	1 (1)
Constipation	43 (14)	1 (0)	17 (11)	0
Nausea	78 (25)	0	25 (16)	0
Vomiting	38 (12)	0	15 (10)	0
Thrombocytopaenia	41 (13)	8 (3)	19 (12)	2 (1)
Neutropaenia	48 (15)	18 (6)	19 (12)	9 (6)
Alopecia	115 (37)	0	66 (43)	0
Hyperglycaemia	55 (18)	6 (2)	18 (12)	0
Alanine aminotransferase increased	51 (16)	7 (2)	22 (14)	3 (2)
Arthralgia	48 (15)	2 (1)	20 (13)	0
Aspartate aminotransferase increased	46 (15)	1 (0)	18 (12)	3 (2)
Dyspnoea	39 (13)	7 (2)	10 (7)	1 (1)
Asthenia	38 (12)	6 (2)	18 (12)	2 (1)
Decreased weight	35 (11)	4 (1)	13 (8)	0
Insomnia	34 (11)	0	11 (7)	0
Diarrhoea	33 (11)	4 (1)	10 (7)	0
Hypoalbuminaemia	32 (10)	2 (1)	9 (6)	0

EMPOWER-Lung 3: cemiplimab in combination with platinum doublet chemotherapy for first-line (1L) treatment of advanced non-small-cell lung cancer (NSCLC)

LBA51. Miranda Gogishvili

- In patients with advanced NSCLC, 1L cemiplimab in combination with chemotherapy demonstrated clinically meaningful and statistically significant improvement in OS, PFS, ORR, and DOR versus chemotherapy alone
  - OS (primary endpoint): median 21.9 vs 13.0 months; HR 0.71 (95% CI, 0.53-0.93); p=0.014
  - PFS: median 8.2 vs 5.0 months; HR 0.56 (95% CI, 0.44-0.70); p<0.0001
  - ORR: odds ratio, 2.68 (95% CI, 1.72-4.19); p<0.0001

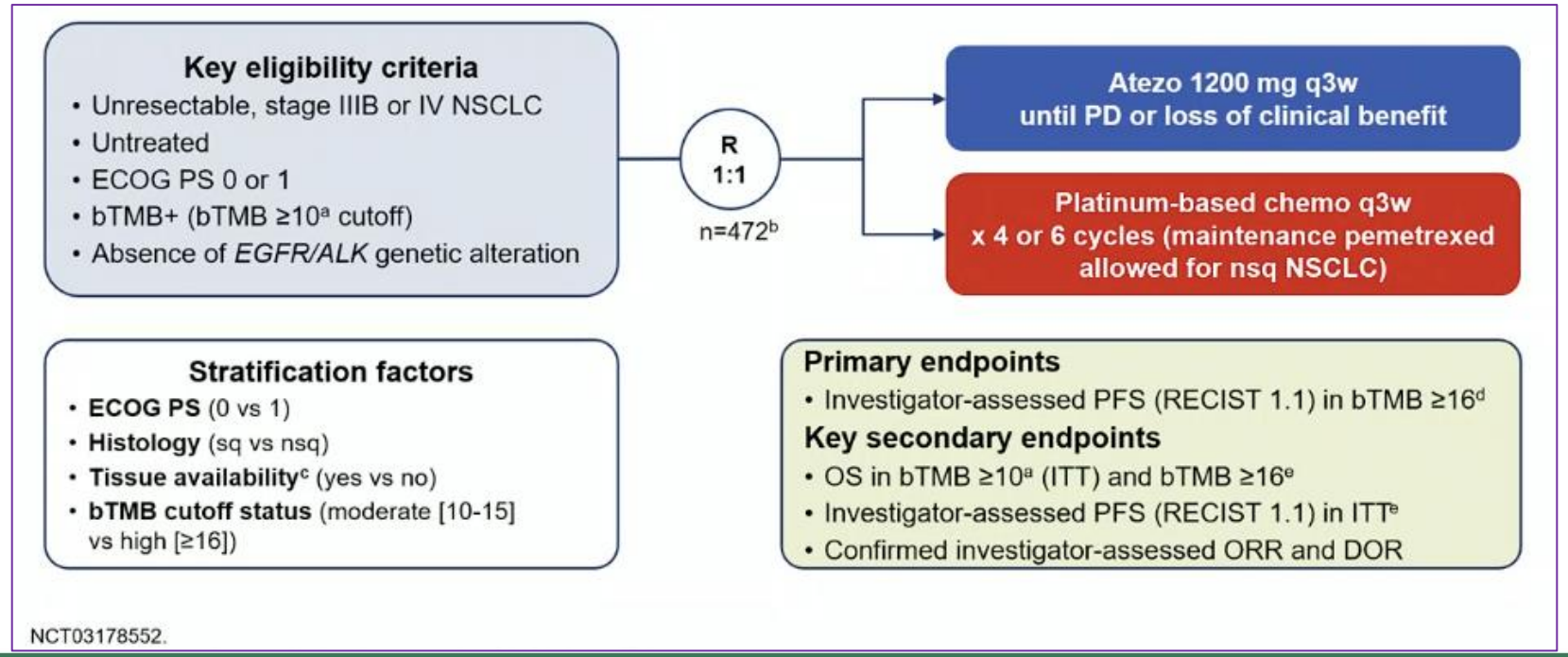
- Cemiplimab in combination with chemotherapy demonstrated an acceptable benefit-risk profile, favourable PROs, low rates of AEs leading to discontinuation, and a safety profile generally consistent with those known for cemiplimab and for platinum-based chemotherapy

- Cemiplimab in combination with platinum-doublet chemotherapy is a new 1L treatment option for patients with advanced NSCLC without targetable mutations irrespective of histology and PD-L1 levels

Atezolizumab (atezo) vs platinum-based chemo in blood-based tumor mutational burden-positive (bTMB+) patients (pts) with first line (1L) advanced/metastatic (m)NSCLC: results of the Blood First Assay Screening Trial (BFAST) Phase 3 Cohort C

12810. Rafal Dziadziuszko, et al.

- BFAST is a global, open-label, multi-cohort trial investigating the safety and efficacy of targeted therapies or immunotherapy in patients with advanced or metastatic (m)NSCLC, identified using a blood-based next-generation sequencing assay
- BFAST Cohort C is the first prospective randomized study to evaluate blood-based (b) TMB as a predictive biomarker for immunotherapy
  - 1L atezolizumab vs platinum-based chemotherapy was investigated in bTMB-positive mNSCLC, as determined by a Foundation Medicine bTMB clinical trial assay (CTA)

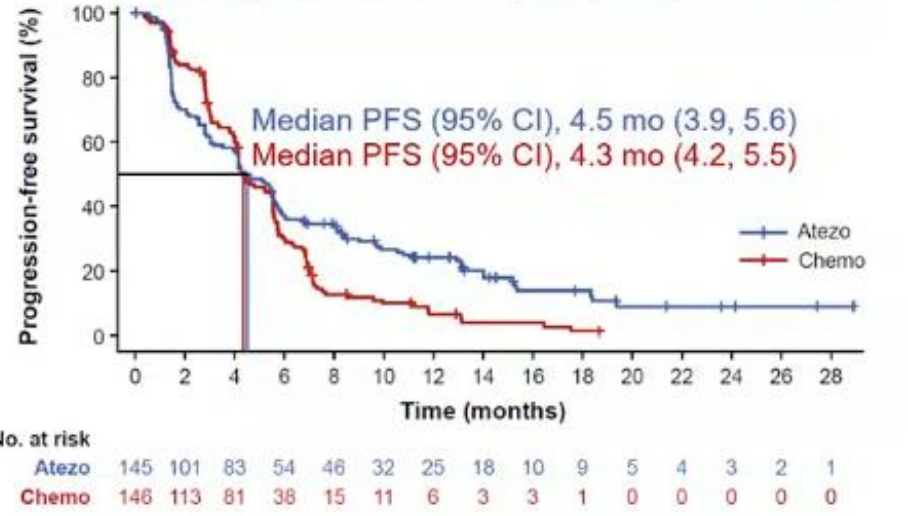


Atezolizumab (atezo) vs platinum-based chemo in blood-based tumor mutational burden-positive (bTMB+) patients (pts) with first line (1L) advanced/metastatic (m) NSCLC: results of the Blood First Assay Screening Trial (BFAST) Phase 3 Cohort C

12810. Rafal Dziadziuszko, et al.

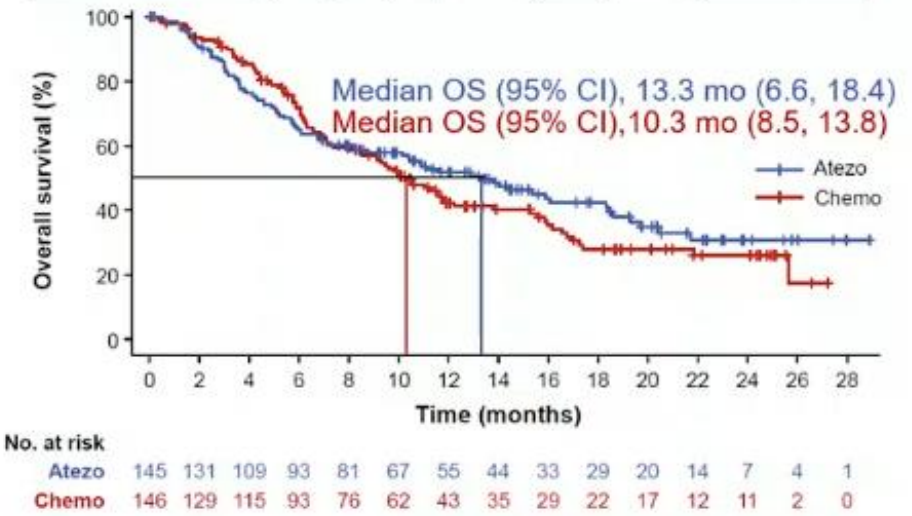
- Median follow-up: 18.2 months
- PFS and OS in the bTMB ≥16 population

	Atezo (n=145)	Chemo (n=146)
PFS events, n (%)	119 (82)	124 (85)
Stratified HR (95% CI)	0.77 (0.59, 1.00); *P*=0.053	



- Although progression rates were initially higher in the atezo vs chemo arm, PFS benefit was seen with atezo after 4 months

	Atezo (n=145)	Chemo (n=146)
OS events, n (%)	82 (57)	88 (60)
Stratified HR (95% CI)	0.87 (0.64, 1.17); *P*=0.35[a]	



Confirmed ORR for bTMB ≥16 was 25.5% (95% CI: 18.7, 33.4) for atezo vs 17.8% (12.0, 25.0) for chemo

Atezolizumab (atezo) vs platinum-based chemo in blood-based tumor mutational burden-positive (bTMB+) patients (pts) with first line (1L) advanced/metastatic (m) NSCLC: results of the Blood First Assay Screening Trial (BFAST) Phase 3 Cohort C

12810. Rafal Dziadziuszko, et al.

n (%)	Atezo (n=234)	Chemo (n=221)
Any grade, all cause	216 (92.3)	216 (97.7)
Grade 3-4	107 (45.7)	127 (57.5)
Grade 5	13 (5.6)	12 (5.4)
Any grade, treatment related	138 (59.0)	194 (87.8)
Grade 3-4	43 (18.4)	102 (46.2)
Grade 5	0	3 (1.4)
Any grade, serious	104 (44.4)	82 (37.1)
Treatment-related serious AEs	27 (11.5)	32 (14.5)
Any grade leading to treatment withdrawal	23 (9.8)	44 (19.9)
Any grade AESI	95 (40.6)	58 (26.2)
Grade 3-4	29 (12.4)	10 (4.5)
AESI requiring corticosteroids	41 (17.5)	20 (9.0)
No. of doses, median	6.0	Gem: 7.0 | Pem: 6.0 Carbo: 4.0 | Cis: 4.0

Atezolizumab (atezo) vs platinum-based chemo in blood-based tumor mutational burden-positive (bTMB+) patients (pts) with first line (1L) advanced/metastatic (m) NSCLC: results of the Blood First Assay Screening Trial (BFAST) Phase 3 Cohort C

12810. Rafal Dziadziuszko, et al.

- BFAST Cohort C did not meet its primary PFS endpoint in the bTMB ≥16 population
- Key secondary endpoints (not formally tested):
  - In the bTMB ≥16 population ORR was improved with atezolizumab vs chemotherapy and a numerical, but not statistically significant, OS improvement was observed
- The safety profile of atezolizumab was favourable compared with that of chemotherapy and consistent with that of atezolizumab monotherapy experience across indications
- The bTMB CTA and F1LCDx assays were highly concordant, showing high PPA, PPV, NPA and NPV
- PFS and OS difference with atezolizumab vs chemotherapy at the F1LCDx bTMB ≥13.6 mut/Mb cutoff were similar to those seen at the clinical trial assay bTMB ≥16 cutoff
- Aditional investigation is needed to refine evaluation of bTMB and define clinically relevant cutoffs for 1L immunotherapy benefit in advanced or metastatic NSCLC
  - Study limitations include lack of PD-L1 expression data (PD-L1 status was not determined because tissue collection was optional) and emergence during the course of the study of a new standard-of care alternative to chemotherapy

- # SEGUNDA LÍNEA Y SUCESIVAS
  - CANOPY-2: Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC
  - ATALANTE-1: Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO)
  - DUBLIN-3 (BPI-2358-103): A Global Phase (Ph) 3 Trial with the Plinabulin/Docetaxel (Plin/Doc) combination vs. Doc in $2^{nd}/3^{rd}$ Line NSCLC Patients (pts) with EGFR-wild type (wt) Progressing on a Prior Platinum-Based Regimen
  - MRTX-500: Phase 2 Trial of Sitravatinib + Nivolumab in Patients With Nonsquamous Non-Small-Cell Lung Cancer Progressing on or After Prior Checkpoint Inhibitor Therapy

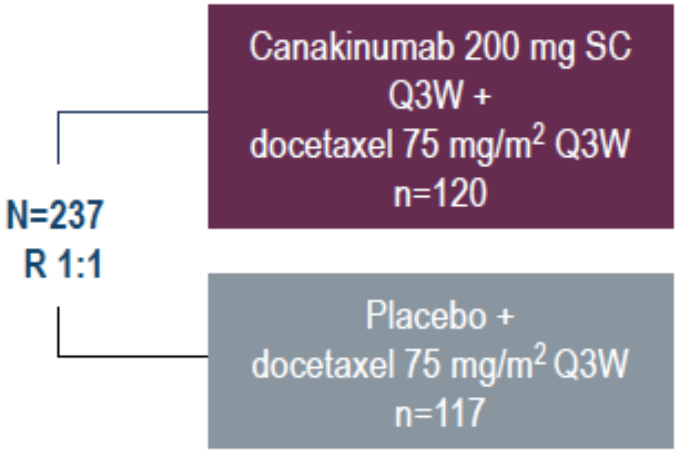
Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC: CANOPY-2

1194MO. Luis Paz-Ares

- Canakinumab is a monoclonal anti-IL-1β antibody, which was associated with reduced lung cancer incidence and mortality in a pre-specified safety monitoring plan for all incident cancers and analysis of the Phase III cardiovascular trial CANTOS

Key eligibility criteria:

- Adults with stage IIIB or IV NSCLC[a]
- SQ or NSQ histology
- No *EGFR* mutation or *ALK* rearrangement
- ECOG PS ≤1
- Previously treated with 1 platinum-based chemotherapy and 1 PD-(L)1 inhibitor either in combination or sequentially



Primary endpoint:

- OS[b]

Secondary endpoints:

- PFS
- ORR
- DCR
- DOR
- PRO
- Safety

2/3L, second/third line; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; NSQ, non-squamous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcomes; Q3W, every 3 weeks; R, randomized; RCT, randomized controlled trial; SQ, squamous.

[a]According to the American Joint Committee on Cancer 8th edition staging system.

[b]90% power to detect a 43% risk reduction in OS (death) at one-sided α=0.025, based on the observation of 137 deaths. An efficacy interim analysis was conducted at 95 (69%) deaths.

Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC: CANOPY-2

1194MO. Luis Paz-Ares

- Baseline characteristics were well balanced between treatment groups (N=237)

	Canakinumab plus docetaxel (n=120)	Placebo plus docetaxel (n=117)
Age, years, median (IQR)	64 (58-70)	63 (56-69)
Male	82 (68%)	85 (73%)
ECOG PS		
0	37 (31%)	37 (32%)
1	83 (69%)	80 (68%)
Tobacco use history		
Never	16 (13%)	19 (16%)
Previous	87 (73%)	80 (68%)
Current	17 (14%)	18 (15%)
Stage at study entry[a]		
IIIB	5 (4%)	4 (3%)
IV	115 (96%)	113 (97%)

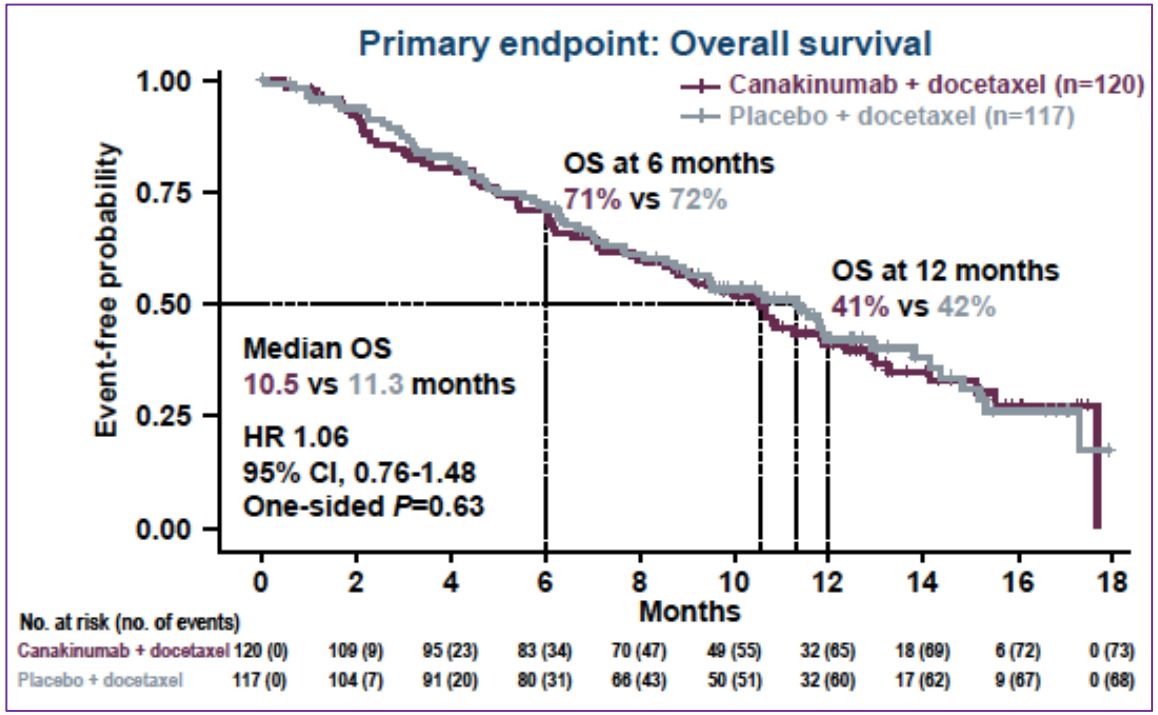
	Canakinumab plus docetaxel (n=120)	Placebo plus docetaxel (n=117)
Histology		
Adenocarcinoma	75 (63%)	75 (64%)
Large cell carcinoma	1 (1%)	0
Squamous cell carcinoma	42 (35%)	39 (33%)
Other	2 (2%)	3 (3%)
Prior lines of therapy[b]		
1	49 (41%)	48 (41%)
2	71 (59%)	69 (59%)
Immunotherapy as last treatment	102 (85%)	96 (82%)

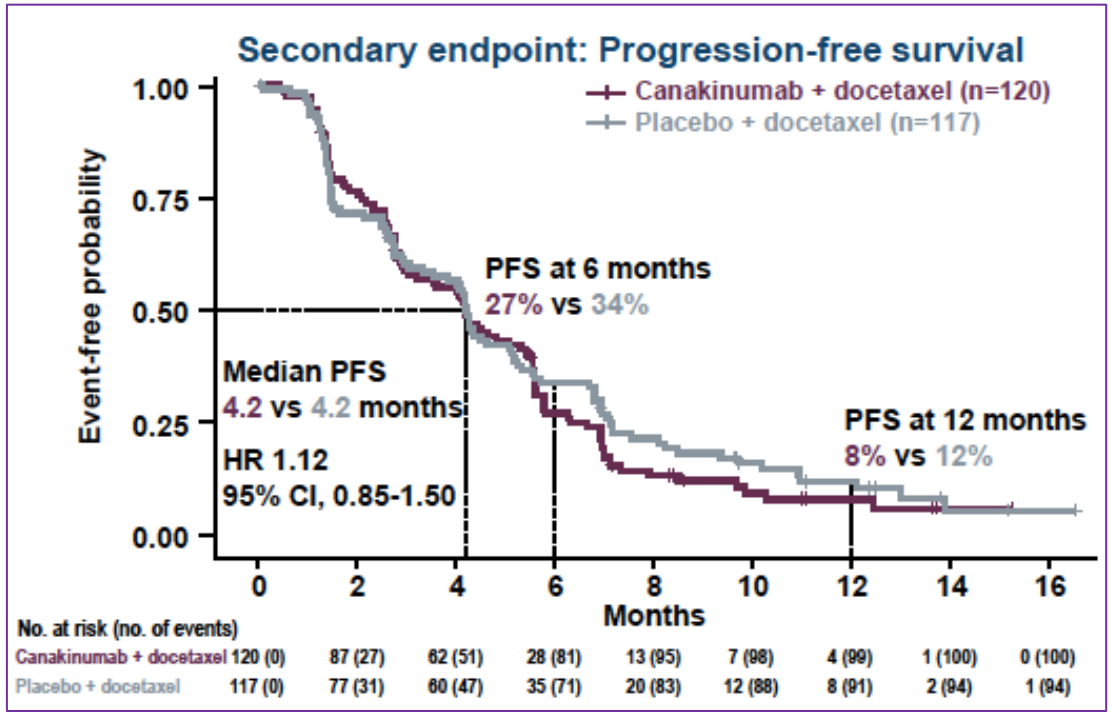
ECOG PS, Eastern Cooperative Oncology Group performance status; IQR, interquartile range.
[a]American Joint Committee on Cancer 8th edition staging system. [b]As per the interactive response technology.

Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC: CANOPY-2

1194MO. Luis Paz-Ares

- Median duration of follow-up: 13.8 months





CI, confidence interval; DCR, disease control rate; HR, hazard ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

- Investigator-assessed ORR was 15% and 14%, and DCR was 66% and 62% in the canakinumab and placebo arms, respectively
- Subgroup analyses did not show statistically significant differences among the subpopulations

Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC: CANOPY-2

1194MO. Luis Paz-Ares

AEs, n (%)	Canakinumab plus docetaxel (n=120)			Placebo plus docetaxel (n=114[a])		
	Any grades	Grade 3/4	Grade 5	Any grades	Grade 3/4	Grade 5
Any AEs	114 (95.0)	74 (61.7)	10 (8.3)	112 (98.2)	73 (64.0)	6 (5.3)
Treatment related	105 (87.5)	61 (50.8)	3 (2.5)	97 (85.1)	48 (42.1)	1 (0.9)
Serious AEs	55 (45.8)	41 (34.2)	10 (8.3)	50 (43.9)	39 (34.2)	6 (5.3)
Treatment related	30 (25.0)	24 (20.0)	3 (2.5)	21 (18.4)	19 (16.7)	1 (0.9)
AEs leading to any drug discontinuation	28 (23.3)	11 (9.2)	7 (5.8)	33 (28.9)	12 (10.5)	3 (2.6)
AEs leading to canakinumab/ placebo discontinuation	16 (13.3)	8 (6.7)	7 (5.8)	12 (10.5)	6 (5.3)	3 (2.6)
AEs of special interest						
Infections[b]	59 (49.2)	18 (15.0)	8 (6.7)	47 (41.2)	18 (15.8)	2 (1.8)
Neutropenia	51 (42.5)	42 (35.0)	0	49 (43.0)	44 (38.6)	0
Thrombocytopenia	27 (22.5)	3 (2.5)	1 (0.8)	26 (22.8)	2 (1.8)	1 (0.9)

- Infections were the most common adverse event observed with canakinumab administration and had been observed to be related to canakinumab treatment.

Canakinumab + docetaxel for the second- or third-line treatment of advanced NSCLC: CANOPY-2

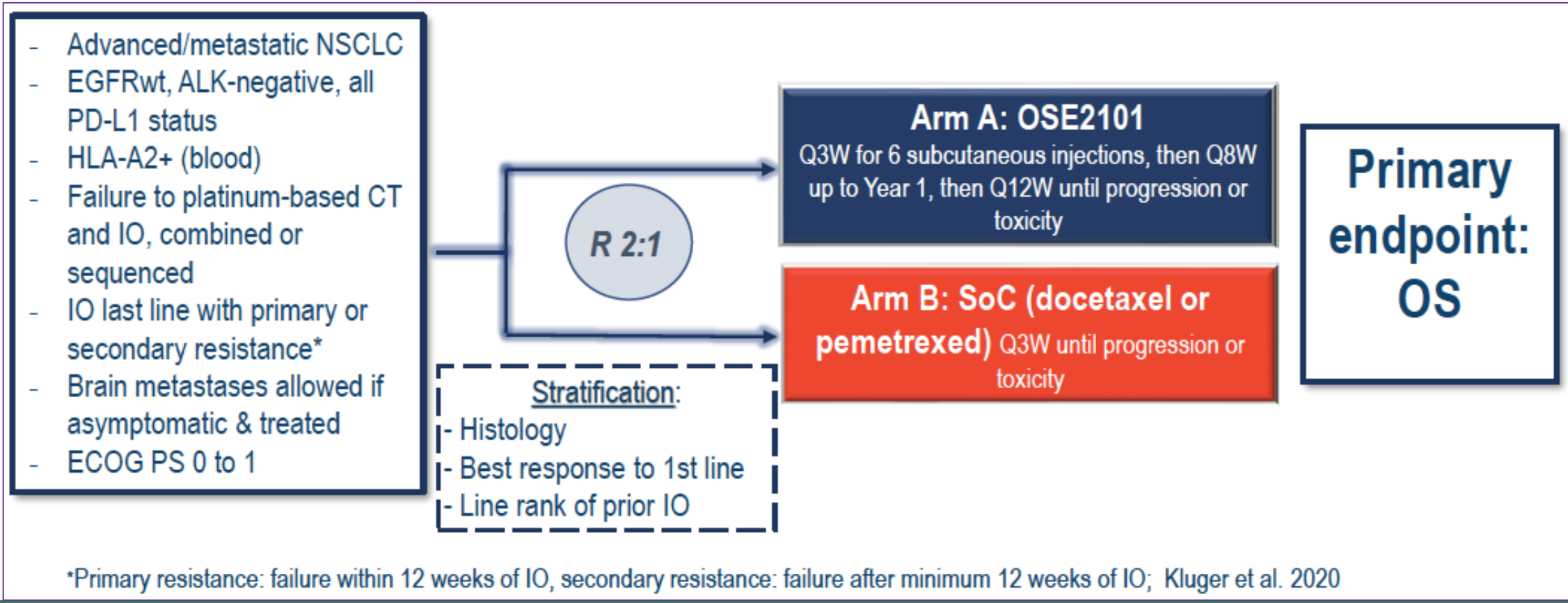
1194MO. Luis Paz-Ares

- The Phase III, randomized CANOPY-2 study did not meet its primary endpoint of OS in patients with NSCLC previously treated with PD-(L)1 inhibitors and platinum-based chemotherapy
- The efficacy results of the canakinumab plus docetaxel group were similar to the placebo plus docetaxel group
- The safety data are consistent with the known, well-characterized safety profiles of canakinumab or docetaxel
  - The most common adverse events of special interest in both treatment arms were as expected for the indication and the safety profiles of the study drugs
    - Infections (49.2% vs 41.2%), fatal infections (6.7% vs 1.8%), neutropenia (42.5% vs 43.0%), and thrombocytopenia (22.5% vs 22.8%) were reported in the canakinumab vs placebo arms, respectively
- Canakinumab is being investigated in other NSCLC treatment settings either as monotherapy or in different treatments combinations

Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final Results of Phase 3 Atalante-1 Randomised Trial

LBA47. Benjamin Besse, et al.

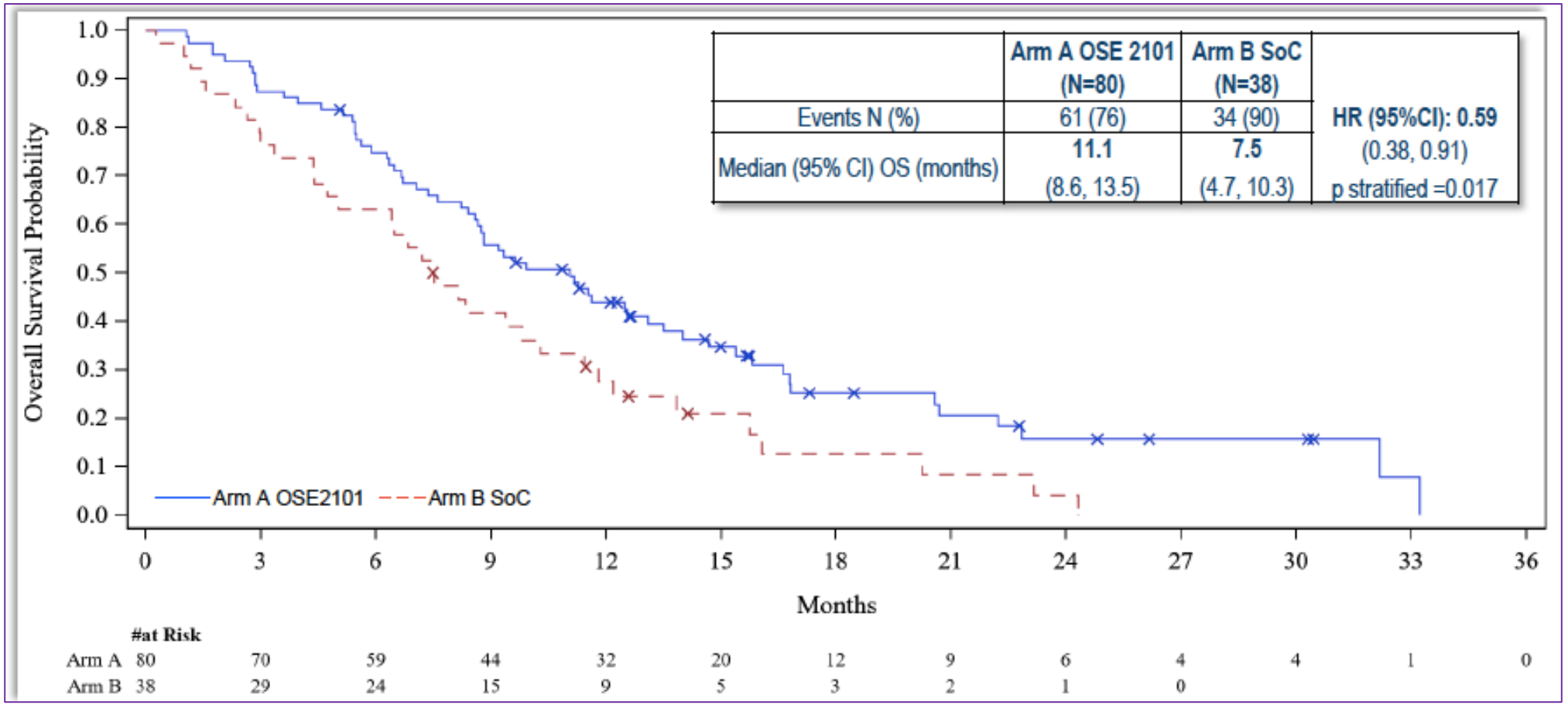
- OSE2101 (Tedopi®) is an anticancer vaccine of 9 neoepitopes restricted to HLA-A2+ targeting 5 TAAs (Tumor-Associated Antigen) frequently expressed in lung cancer: CEA, p53, HER-2, MAGE-2, MAGE-3
- Previous phase 2 study in pretreated NSCLC patients showed promising OS which correlated with T cell immune response



Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final Results of Phase 3 Atalante-1 Randomised Trial

LBA47. Benjamin Besse, et al.

- OS in population of interest (PoI): patients with IO secondary resistance after sequential IO
- Median follow-up 25 months



	Arm A OSE 2101 (N=80)	Arm B SoC (N=38)	
Events N (%)	61 (76)	34 (90)	HR (95%CI): 0.59 (0.38, 0.91) p stratified =0.017
Median (95% CI) OS (months)	11.1 (8.6, 13.5)	7.5 (4.7, 10.3)	

Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final Results of Phase 3 Atalante-1 Randomised Trial

LBA47. Benjamin Besse, et al.

- Disease Control Rate (DCR) at 6 months similar between arms despite a longer PFS and Objective Response (OR) favoring SoC in Pol

Pol	Arm A OSE2101 (N= 80)	Arm B SoC (N=38)	
Patients with measurable lesions at baseline	78	38	
Disease Control Rate at 6 months; N (%)	19 (25)	9 (24)	Odds ratio (95%CI): 1.09 (0.43, 2.75) p=0.87
Objective Response; N (%)	6 (8)	7 (18)	Odds ratio (95%CI): 0.33 (0.10, 1.11) p=0.07
Median (95%CI) PFS (months)	2.7 (1.6; 2.8)	3.2 (2.6; 4.7)	Hazard ratio (95%CI): 1.20 (0.8, 1.8) p=0.40

Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final Results of Phase 3 Atalante-1 Randomised Trial

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- Safety in Pol

	Arm A OSE2101 (N=79)		Arm B SoC (N=37)	
Number of patients with at least one AE	All N (%)	Related N (%)	All N (%)	Related N (%)
All AE	76 (96)	60 (76)	37 (100)	29 (78)
Severe G3-5 AE	**28 (35)***	**9 (11)***	**24 (65)***	**13 (35)***
Fatal G5 AE	4 (5)	0 (0)	5 (14)	0 (0)
Serious AE	26 (33)	9 (11)	18 (49)	3 (8)
AE leading to permanent discontinuation	2 (3)	0 (0)	4 (11)	0 (0)

- Most frequent > 10% Drug related AEs in Pol

	Arm A OSE2101 (N=79)		Arm B SoC (N=37)	
	All grade N (%)	Severe G3-4 N (%)	All grade N (%)	Severe G3-4 N (%)
All Drug-Related AEs	60 (76)	9 (11)*	29 (78)	13 (35)*
Drug-related AEs in > 10% of patients by preferred term				
Administration site reaction**	31 (39)	1 (1)	-	-
Pyrexia	15 (19)	2 (3)	3 (8)	-
Arthralgia	9 (11)	-	1 (3)	-
Asthenia	13 (17)	-	15 (41)	6 (16)
Alopecia	-	-	8 (22)	1 (3)
Diarrhea	3 (4)	-	8 (22)	1 (3)
Neutropenia	-	-	6 (16)	6 (16)
Fatigue	6 (8)	-	5 (14)	-
Anemia	1 (1)	-	5 (14)	-
Nausea	5 (6)	-	5 (14)	-
Vomiting	5 (6)	1 (1)	5 (14)	1 (3)
Decrease appetite	4 (5)	-	4 (11)	-

Cytokine release syndrome was reported in 6 (8%) patients including 1 (1%) severe G3 in OSE2101 arm

Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (IO): Final Results of Phase 3 Atalante-1 Randomised Trial

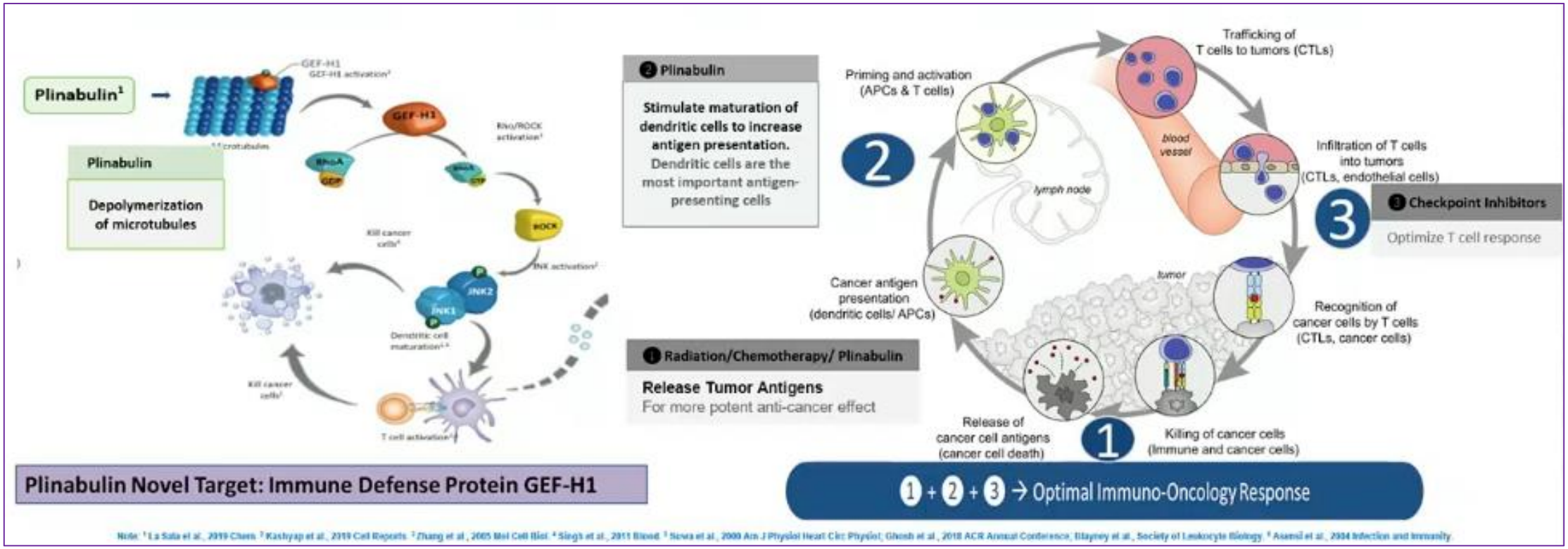
LBA47. Benjamin Besse, et al.

- In the population of patient with secondary resistance to sequential CT-IO, OS was statistically improved in OSE2101 arm with HR of 0.59 and a meaningful gain of median OS of 3.6 months over SoC (docetaxel/pemetrexed). HR for OS in the overall population at final analysis was of 0.86 (ns)
- The cancer vaccine OSE2101 demonstrated efficacy as stand alone compared to an active comparator
- OSE2101 was well tolerated with significantly less severe adverse events (QoL and good ECOG PS 0/1 were better for OSE2102)
- OSE2101 had a favorable benefit/risk versus SoC in advanced HLA-A2+ NSCLC patients with secondary resistance to sequential CT-IO without therapeutic alternatives

DUBLIN-3 (BPI-2358-103): A Global Phase (Ph) 3 Trial with the Plinabulin/Docetaxel (Plin/Doc) combination vs. Doc in 2nd/3rd Line NSCLC Patients (pts) with EGFR-wild type (wt) Progressing on a Prior Platinum-Based Regimen

LBA48. Trevor Feinstein

- Pinabulin: First-in-Class, Selective Immunomodulating Microtubule-Binding Agent (SIMBA)
- Pinabulin induces Dendritic Cell Maduration (the most potent APC), a key step in initiating anti-cancer durable response



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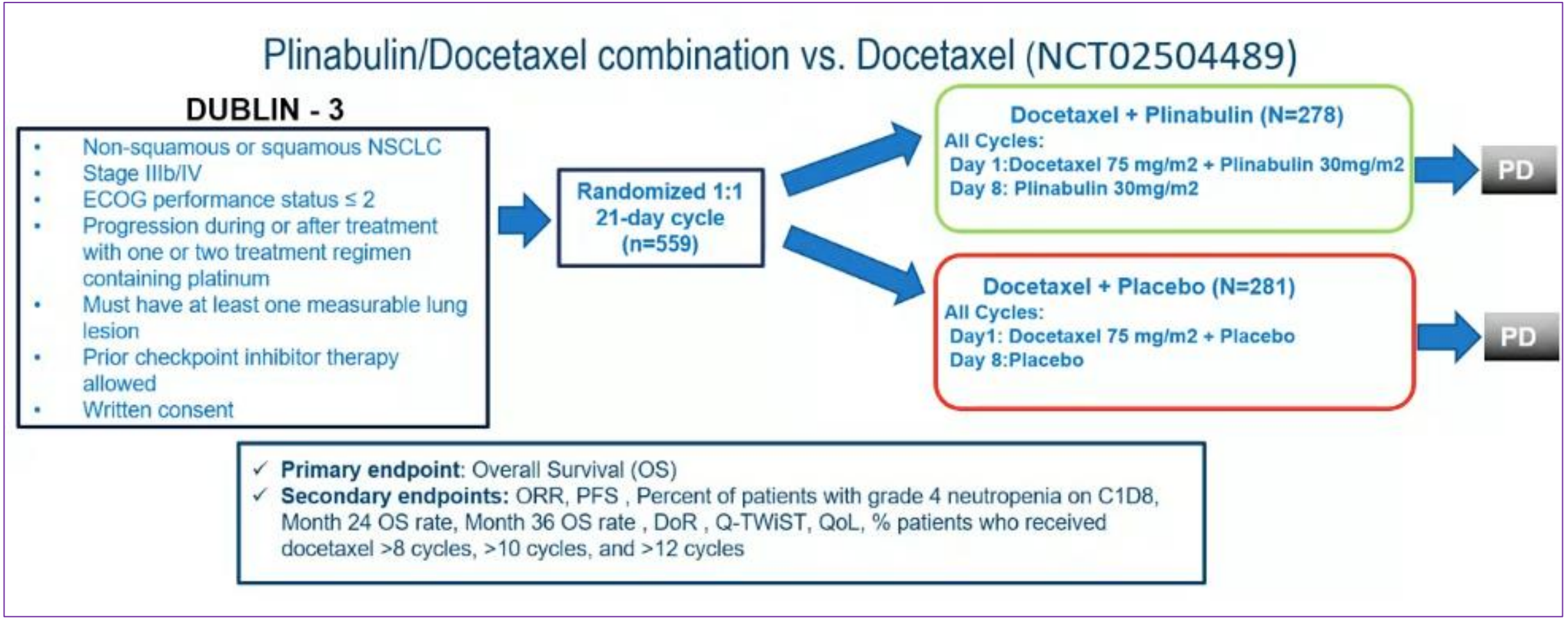

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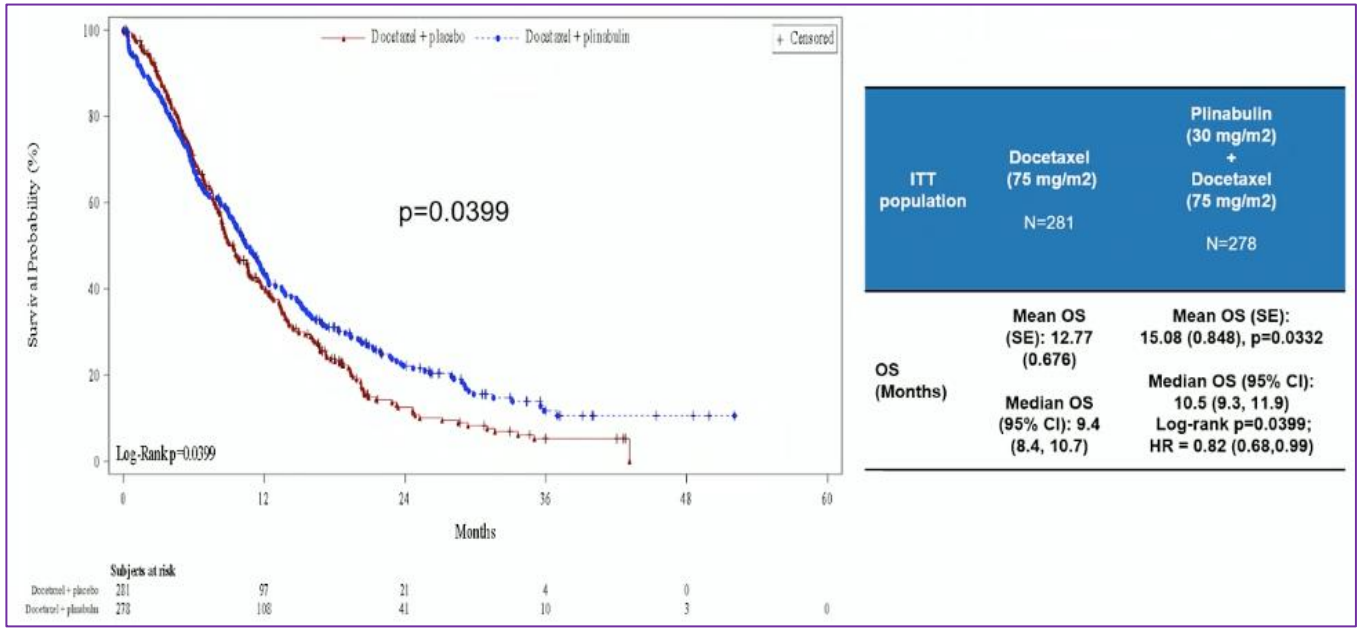
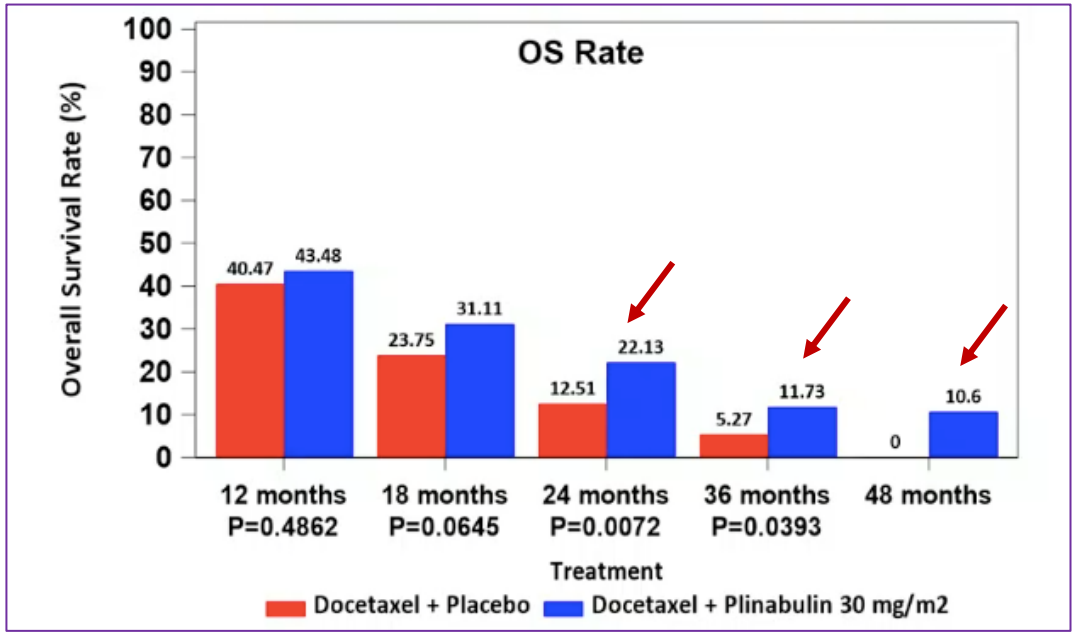


ITT population	Docetaxel (75 mg/m2) N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
OS (Months)	Mean OS (SE): 12.77 (0.676) Median OS (95% CI): 9.4 (8.4, 10.7)	Mean OS (SE): 15.08 (0.848), p=0.0332 Median OS (95% CI): 10.5 (9.3, 11.9) Log-rank p=0.0399; HR = 0.82 (0.68,0.99)



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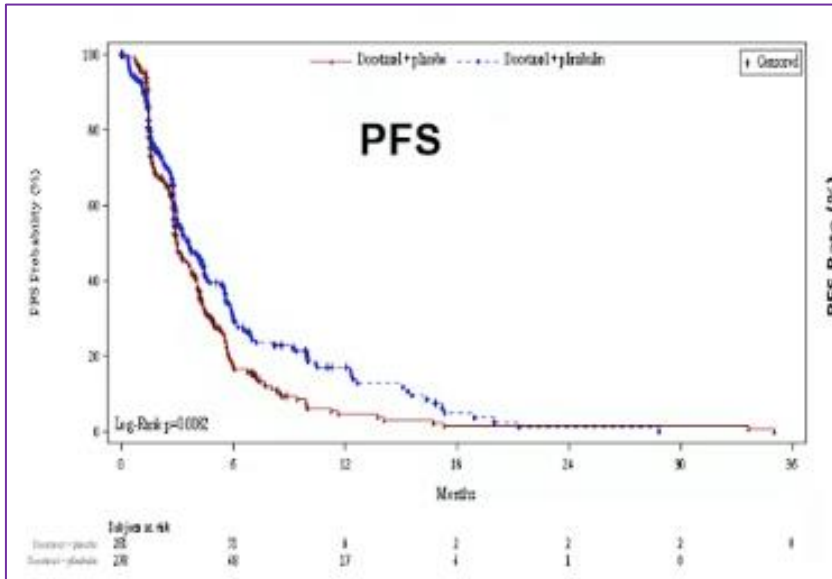
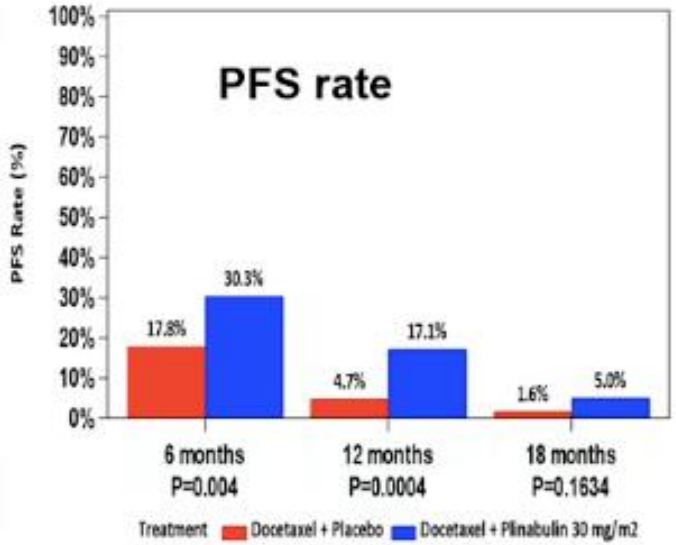
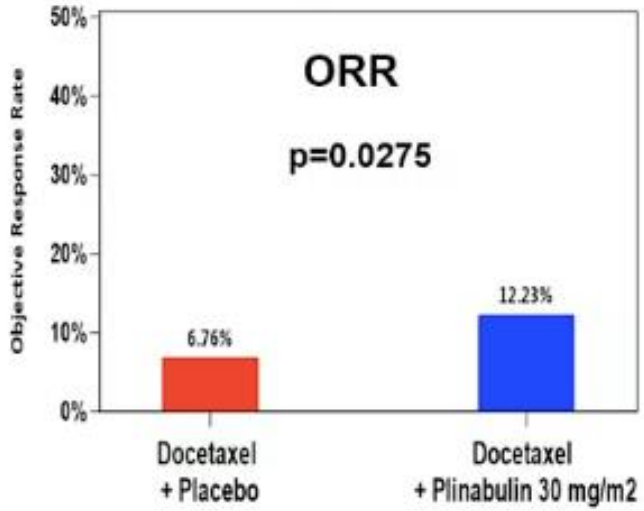






Secondary Endpoint (ITT population)	Docetaxel(75 mg/m2) N=281	Plinabulin (30 mg/m2) + Docetaxel (75 mg/m2) N=278
PFS* (months or M)	Mean PFS (SE): 4.4 Median PFS (95% CI): 3.0 (2.8, 3.7)	Mean PFS (SE): 6.0; p=0.0062 Median PFS (95% CI): 3.6 (3.0, 4.4), Log-rank p=0.0082; HR=0.76 (0.63, 0.93)

*Investigator-Assessed

DUBLIN-3 (BPI-2358-103): A Global Phase (Ph) 3 Trial with the Plinabulin/Docetaxel (Plin/Doc) combination vs. Doc in 2nd/3rd Line NSCLC Patients (pts) with EGFR-wild type (wt) Progressing on a Prior Platinum-Based Regimen

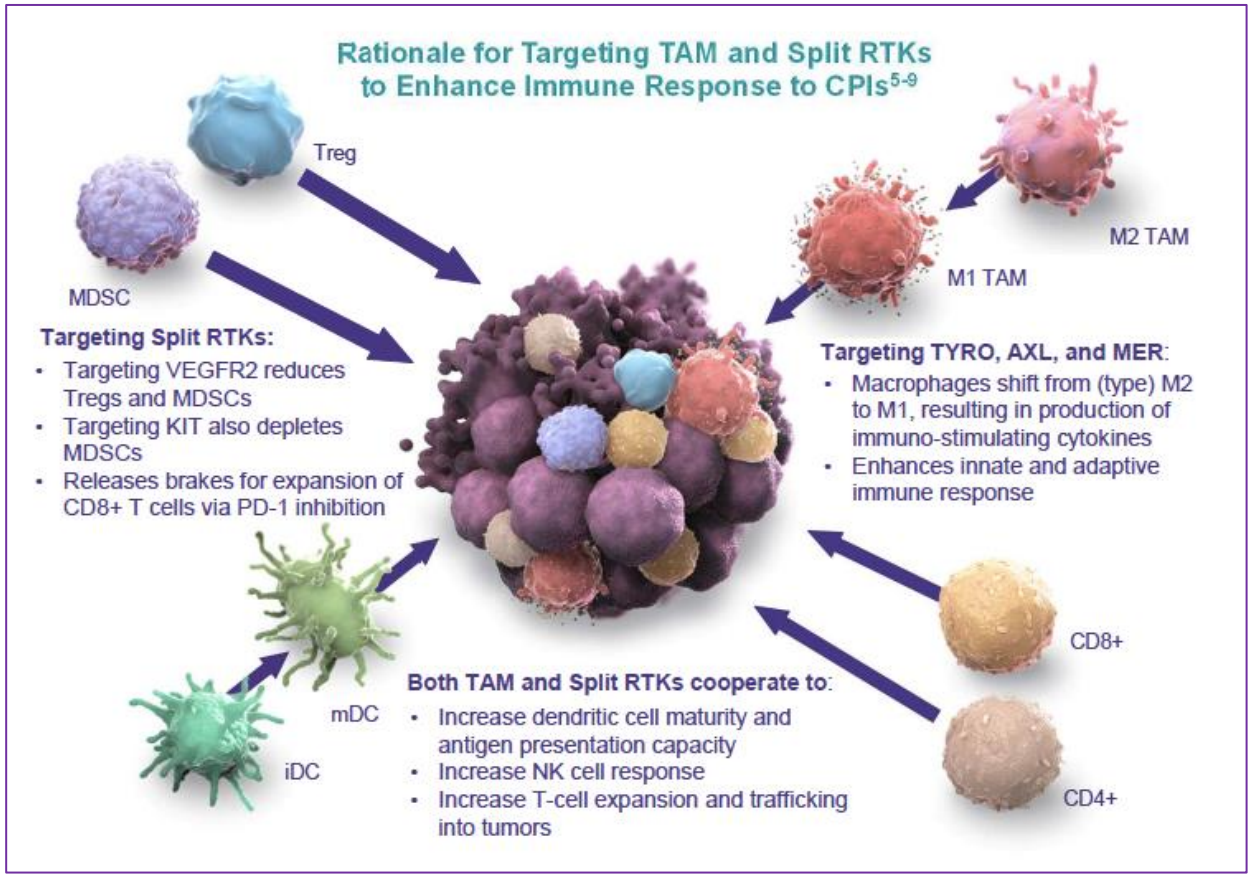
LBA48. Trevor Feinstein

- Dublin-3 study met OS primary endpoint and key secondary endpoints: PFS and ORR
- Plinabulin showed durable anti-cancer benefit in doubling 24 M, 36 M OS rate in Plin/Doc vs Doc. OS rate at 48 M for Plin/Doc was 10.6% vs 0% for Doc
- Plin/Doc was well tolerated, with lower grade 4 and grade 3/4 AE per patient per year in comparison to Doc arm. In addition, plinabulin protected bone marrow by significantly reducing grade 4 neutropenia of Doc (28% to 5%, $p<0.0001$)
- Plin/Doc has a favorable benefit/risk ratio and has the potential of preferred 2nd/3rd line treatment for NSCLC with EGFR wild type.

MRTX-500: Phase 2 Trial of Sitravatinib + Nivolumab in Patients With Nonsquamous Non-Small-Cell Lung Cancer Progressing on or After Prior Checkpoint Inhibitor Therapy

11910. Ticiana A. Leal

- Many patients experience disease progression and developed checkpoint inhibitor therapy (CPI) resistance through various mechanisms, including an immunosuppressive TME
- Sitravatinib is a receptor tyrosine kinase inhibitor (TKI) that targets TAM receptors (TYRO3, AXL, MERTK) and Split-Family Receptors (VEGFR2) which have been shown to modulate the immune TME
- Hypothesis: combination of sitravatinib with nivolumab is a rational approach to augmenting the antitumor immune response and extending long term benefit to patients



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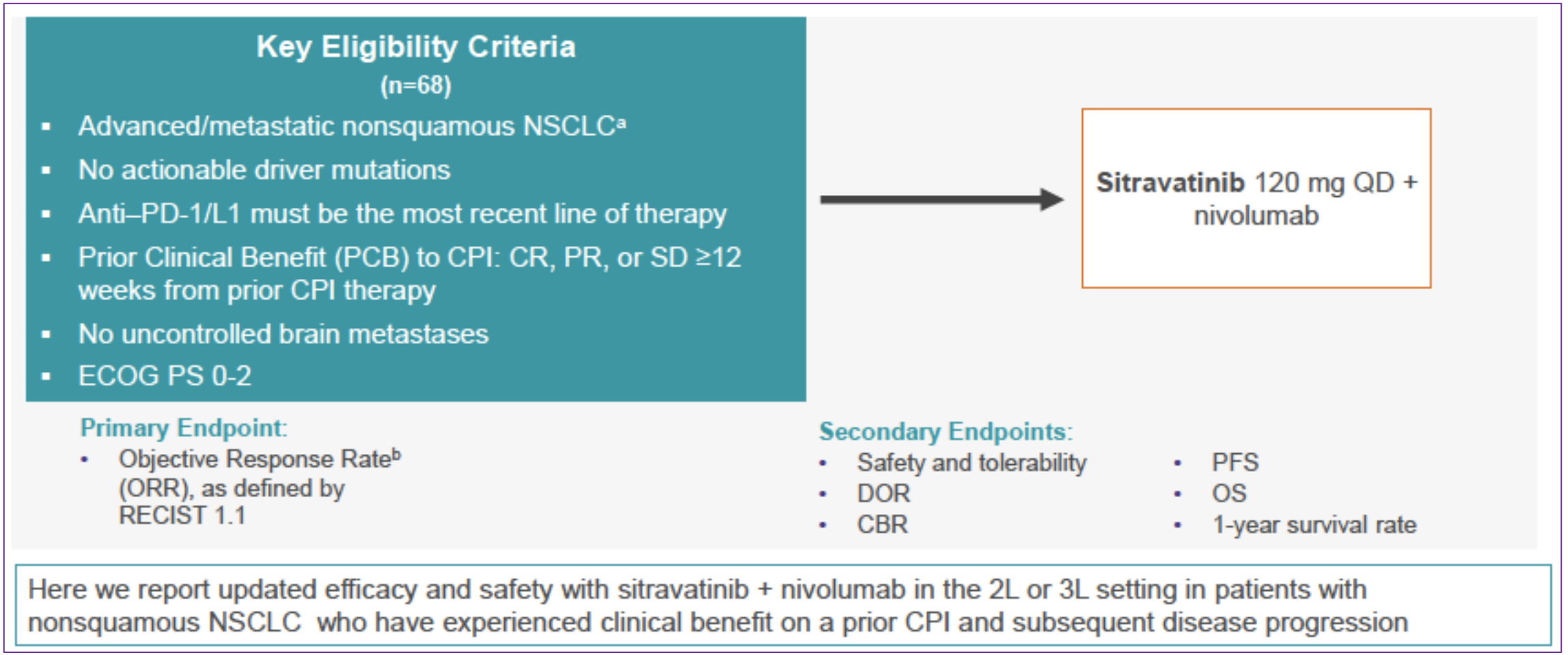

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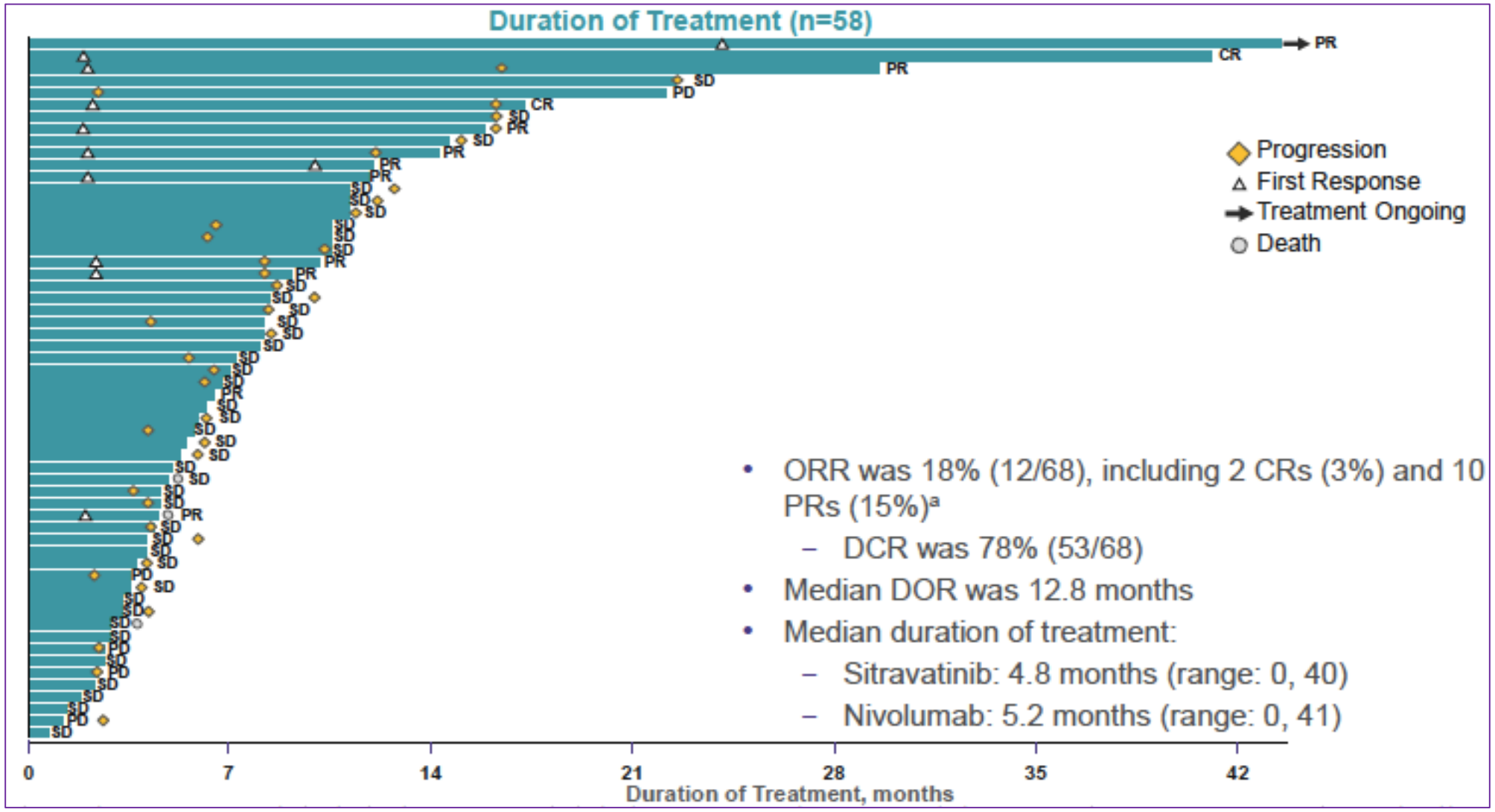

- ORR was 18% (12/68), including 2 CRs (3%) and 10 PRs (15%)[a]
  - DCR was 78% (53/68)
- Median DOR was 12.8 months
- Median duration of treatment:
  - Sitravatinib: 4.8 months (range: 0, 40)
  - Nivolumab: 5.2 months (range: 0, 41)

MRTX-500: Phase 2 Trial of Sitravatinib + Nivolumab in Patients With Nonsquamous Non-Small-Cell Lung Cancer Progressing on or After Prior Checkpoint Inhibitor Therapy

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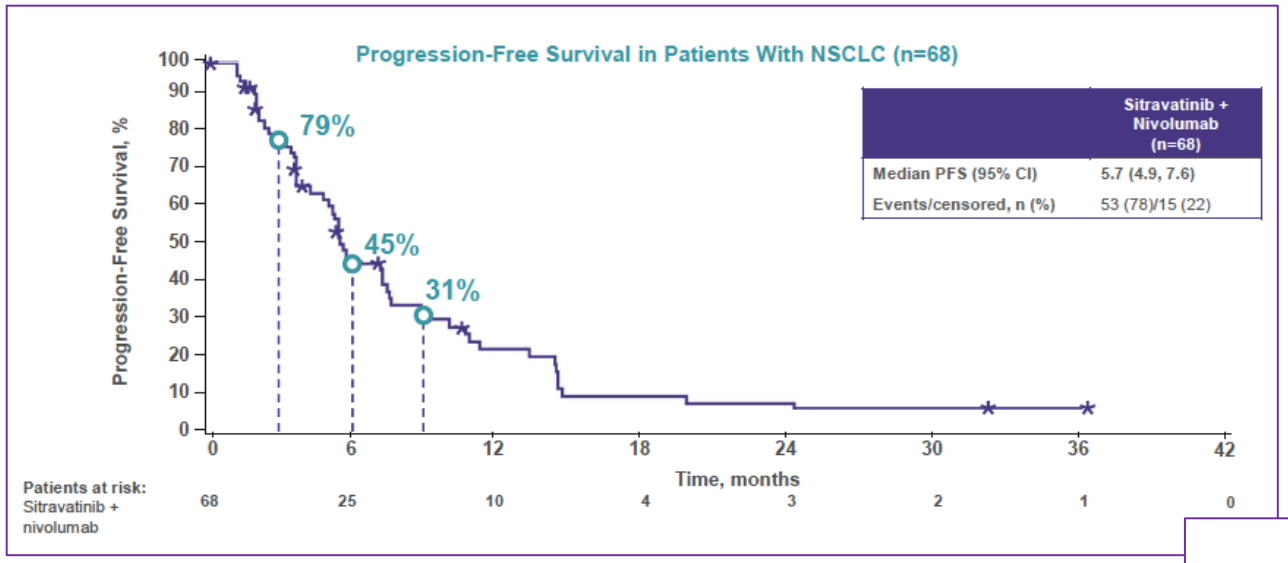

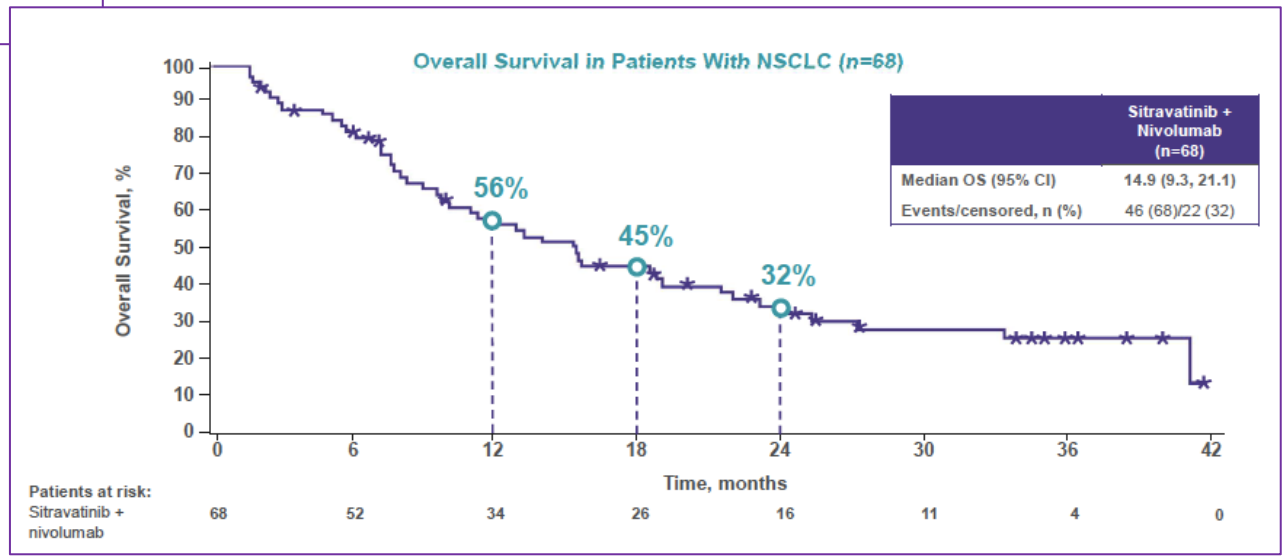

MRTX-500: Phase 2 Trial of Sitravatinib + Nivolumab in Patients With Nonsquamous Non-Small-Cell Lung Cancer Progressing on or After Prior Checkpoint Inhibitor Therapy

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Most Frequent (≥15%) TRAEs (n=68)	2L/3L Sitra + Nivo	
TRAEs	Any Grade	Grade 3-4
Any TRAEs	93%	66%
Most frequent TRAEs, %		
Diarrhea	62%	16%
Fatigue	52%	4%
Nausea	44%	2%
Hypertension	40%	22%
Decreased appetite	35%	0%
Weight decreased	31%	9%
Vomiting	31%	0%
Hypothyroidism	22%	0%
Dysphonia	19%	0%
ALT increase	18%	2%
AST increase	16%	0%
Stomatitis	15%	2%
PPE syndrome	15%	3%
Dehydration	15%	3%

- The most frequent immune-related TRAES included hypothyroidism, diarrhea, ALT increase, AST increase, TSH increase maculopapular rash, and pancreatitis[a]
- No grade 5 events occurred in the CPI-experienced cohort[b]

MRTX-500: Phase 2 Trial of Sitravatinib + Nivolumab in Patients With Nonsquamous Non-Small-Cell Lung Cancer Progressing on or After Prior Checkpoint Inhibitor Therapy

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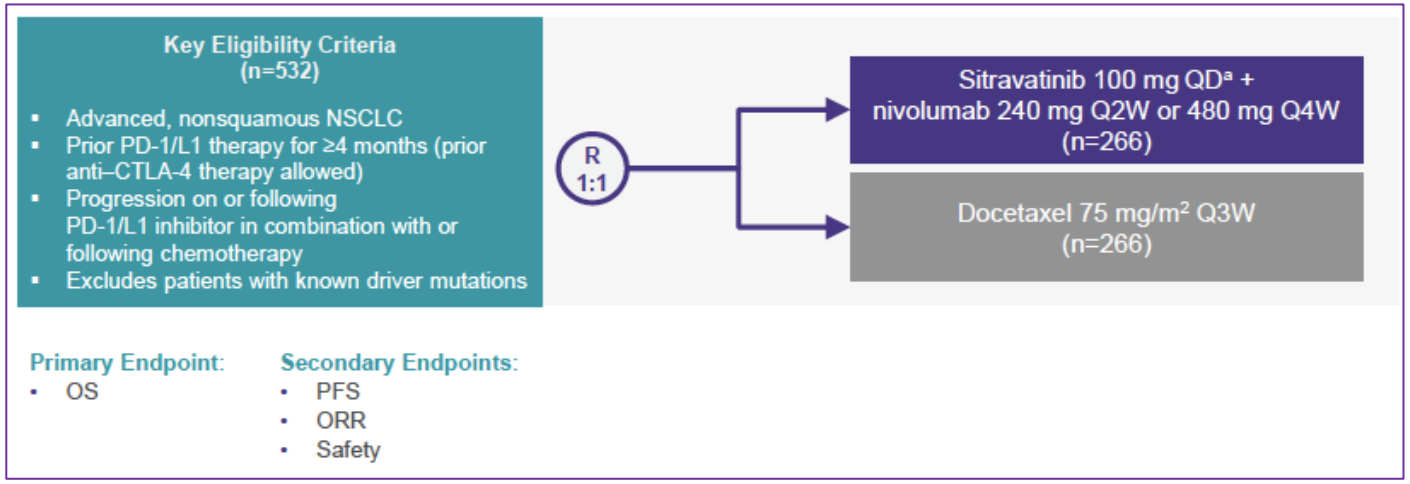
- Sitravatinib + nivolumab demonstrated antitumor activity, encouraging OS, and durable responses in patients with nonsquamous NSCLC with prior clinical benefit from a CPI
  - Median DOR was 12.8 months; ORR was 18% (12/68)
  - 1- and 2-year OS were 56% and 32%, respectively
- No unexpected safety signals with the combination were observed, and AEs were manageable
- These results support the ongoing Phase 3 SAPPHIRE study (NCT03906071), evaluating sitravatinib + nivolumab in patients with nonsquamous NSCLC who received clinical benefit from and subsequently experienced progressive disease on a prior CPI

- SAPPHIRE:

Phase 3, Randomized, Open-Label Trial of 2L/3L Sitravatinib + Nivolumab vs Docetaxel After Progression on or Following CPI in Advanced NSCLC



Lung Cancer UPDATES
ESMO HIGHLIGTHS
17-21 SEPTIEMBRE 2021

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Gracias por su atención