Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

Iniciativa científica de:
GECP lung cancer research

Cáncer de Pulmón metastásico sin dianas terapéuticas

Rafael López Castro

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Abstracts destacados

Proffered paper non-metastatic NSCLC and other thoracic malignancies

- #**LBA51**: Keynote 024 5-year OS update. Ph.III
- #**LBA52**: EMPOWER-Lung 1: Cemiplimab vs chemo 1st line NSCLC PD-L1 ≥50% Ph.III
- #**LBA53**: Precision Immuno-Oncology: 1st analysis of PIONeeR Study
- #**LBA54**: ONO-4538-52/Tasuki-52: Paclitaxel/carbo/beva +- Nivolumab en 1st line Ph.III
- #**LBA55**: WJOG @Be Study. Ph. II Atezo + beva in neNSCLC with high PD-L1 expression

Mini oral NSCLC

- #**LBA56**: ORIENT-12: Sintilimab + gemcitabine and platinum (GP) 1st line sqNSCLC
- #**1260MO**: ATALANTE-1 phase III. OSE-2101 in HLA-A2+ NSCLC after failure to immune checkpoint inhibitors
- #**LBA58**: FORCE trial. Nivo + RT in advanced NSCLC
- #**LBA59**: Checkmate 9LA PROs

#LBA51

KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab (pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS)≥50%. *Brahmer JR et al.*

Julie R. Brahmer,[1] Delvys Rodríguez-Abreu,[2] Andrew G. Robinson,[3] Rina Hui,[4] Tibor Csőszi,[5] Andrea Fülöp,[6] Maya Gottfried,[7] Nir Peled,[8] Ali Tafreshi,[9] Sinead Cuffe,[10] Mary O'Brien,[11] Suman Rao,[12] Katsuyuki Hotta,[13] Ticiana A. Leal,[14] Jonathan W. Riess,[15] Erin Jensen,[16] Bin Zhao,[16] M. Catherine Pietanza,[16] Martin Reck[17]

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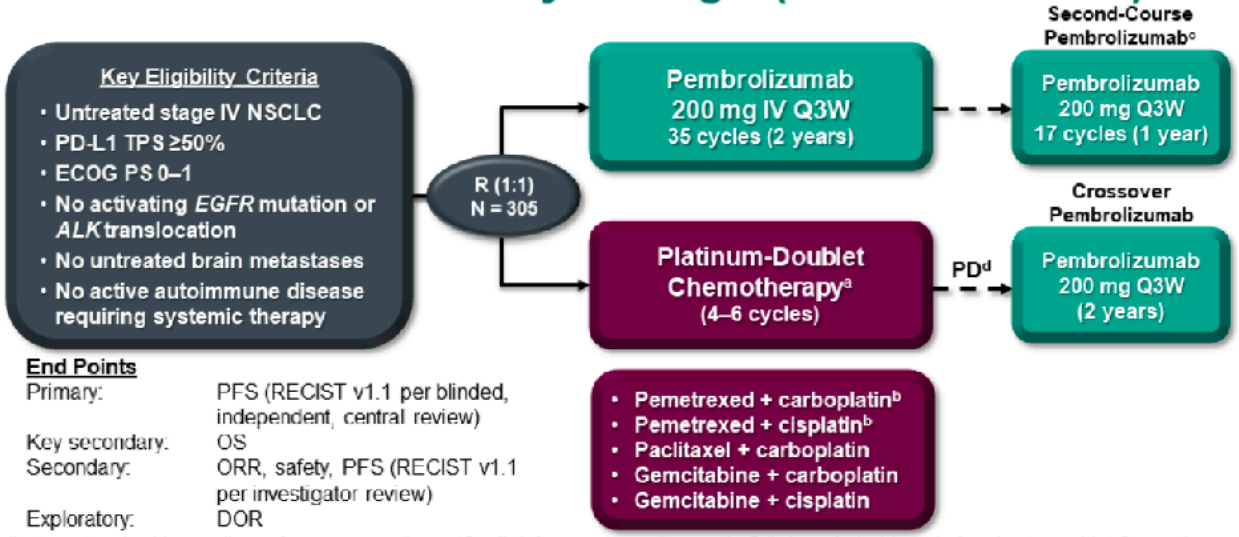
#LBA51

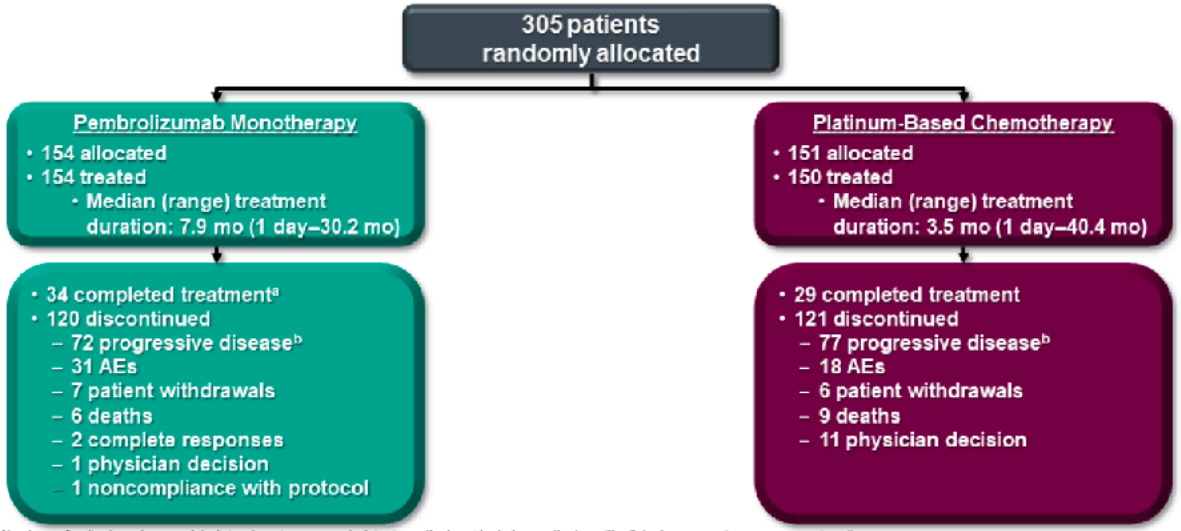
KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab (pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS)≥50%

KEYNOTE-024 Study Design (NCT02142738)



[a]Optional pemetrexed maintenance therapy for nonsquamous disease. [b]Permitted for nonsquamous disease only. [c]Patients randomized to pembrolizumab who completed 2 years of therapy or who stopped pembrolizumab after achieving CR and then had PD were eligible for a second course of pembrolizumab monotherapy. [d]Before the DMC recommendation and amendment 8, which permitted those in the chemotherapy arm to be offered pembrolizumab (based on interim analysis 2 data), patients were eligible for crossover when PD was confirmed by blinded, independent, central radiology review.

Disposition of Study Treatment



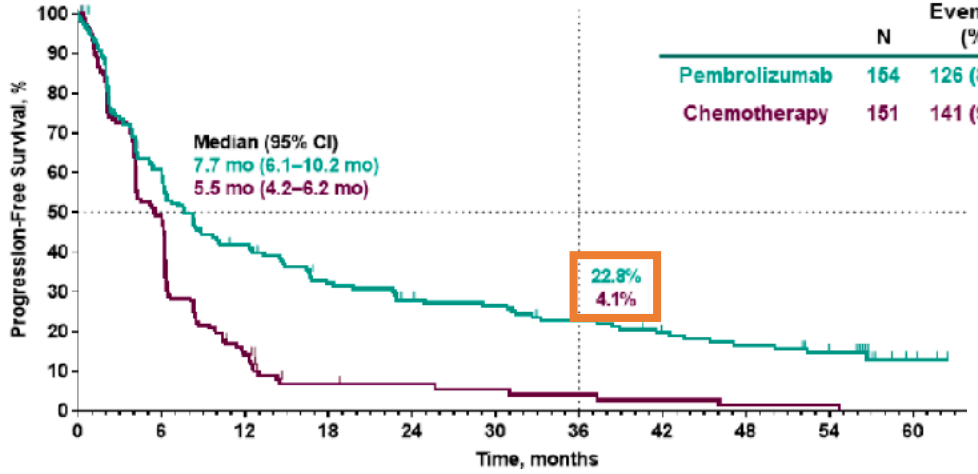
[a]Number of patients who completed treatment, as reported by investigator. [b]Includes patients with clinical progression or progressive disease.
Data cutoff: June 1, 2020.

- 66% effective crossover rate: 83 patients crossed over to pembro + 16 to other anti PD-(L)1 therapy
- 51.9% patients on pembro received 2nd line (including 12 pts pembro rechallenge)
- Median time from random to data cut-off: 59.9m

#LBA51 KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab (pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS)≥50%

Progression-Free Survival[a]

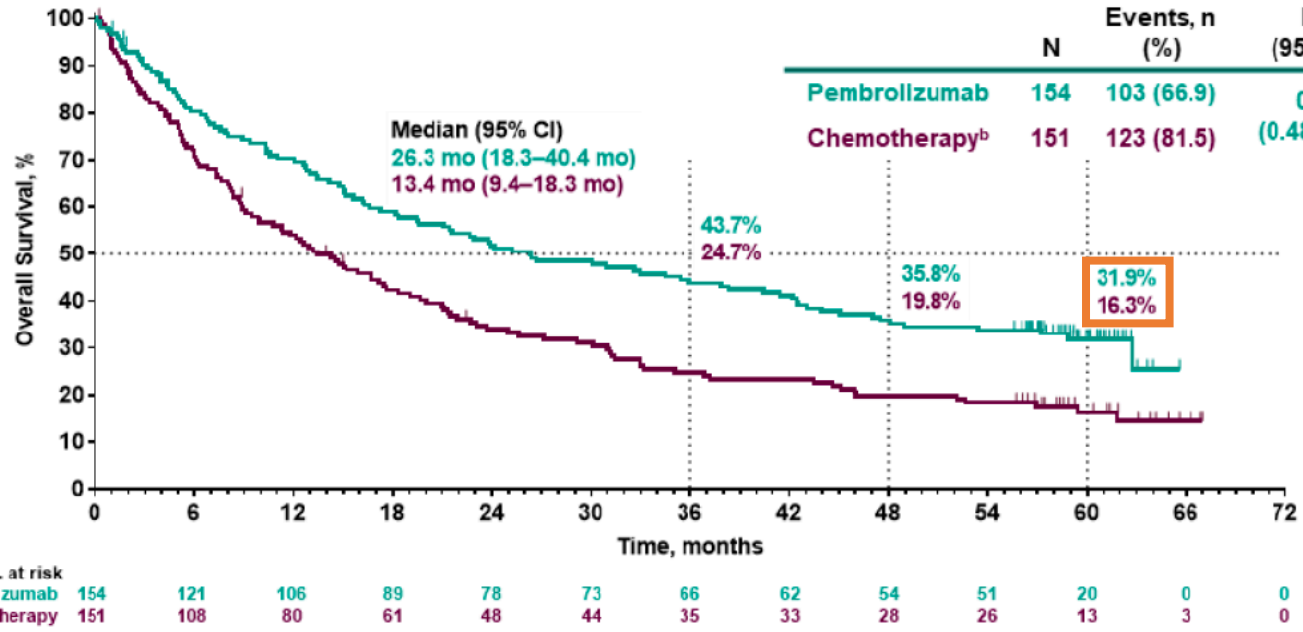
By RECIST v1.1 per Investigator Review[b]



	N	Events, n (%)	HR (95% CI)
Pembrolizumab	154	126 (81.8)	0.50 (0.39–0.65)
Chemotherapy	151	141 (93.4)	

not reached.
T population. [b]Secondary endpoint; primary endpoint was PFS assessed per blinded, independent, central radiology review.
ta cutoff: June 1, 2020.

Overall Survival[a]



	N	Events, n (%)	HR (95% CI)
Pembrolizumab	154	103 (66.9)	0.62 (0.48–0.81)
Chemotherapy[b]	151	123 (81.5)	

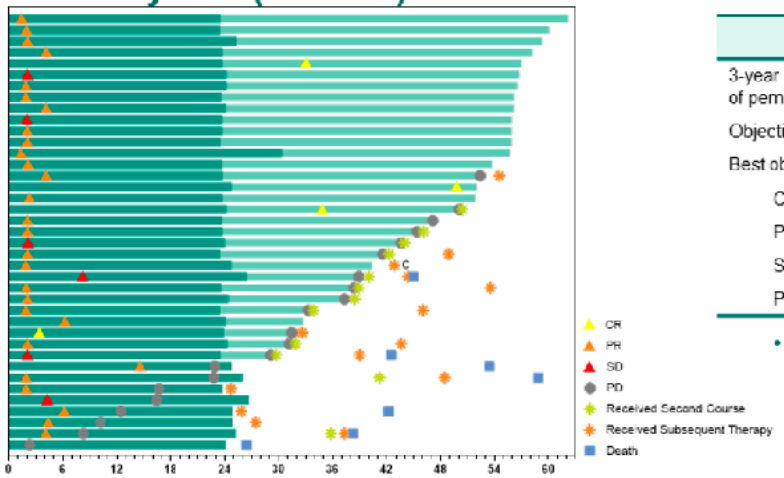
- ORR: 46.1% vs 31.1%
- Partial response: 41.6% vs 31.1%
- Complete response: 4.5% vs 0

#LBA51

KEYNOTE-024 5-year OS update: first-line (1L) pembrolizumab (pembro) vs platinum-based chemotherapy (chemo) in patients (pts) with metastatic NSCLC and PD-L1 tumor proportion score (TPS)≥50%

Treatment Duration and Time to Response[a]

35 Cycles (2 Years) of Pembrolizumab Completed



	N = 39[b]
3-year OS rate from completion of pembrolizumab, %	81
Objective response, n (%)	32 (82)
Best objective response, n (%)	
Complete response	4 (10)
Partial response	28 (72)
Stable disease	6 (15)
Progressive disease	1 (3)

- At data cutoff, 18/39 patients (46%) were alive without PD or subsequent therapy for NSCLC per investigator assessment
  - 1 patient developed a secondary malignancy and was treated accordingly

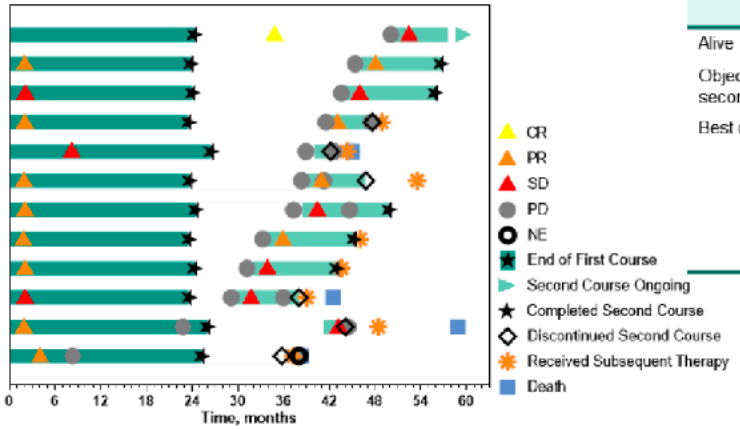
Adverse Events

	Pembrolizumab[a] N = 154	Chemotherapy[a] N = 150	35 Cycles (2 Years) of Pembrolizumab[a] N = 39
Treatment-related AEs, n (%)	118 (76.6)	135 (90.0)	34 (87.2)
Grade 3–5[b]	48 (31.2)	80 (53.3)	6 (15.4)
Serious	35 (22.7)	31 (20.7)	4 (10.3)
Led to discontinuation	21 (13.6)	16 (10.7)	0
Led to death	2 (1.3)	3 (2.0)	0
Immune-mediated AEs and infusion reactions, n (%)[c]	53 (34.4)	8 (5.3)	12 (30.8)
Grade 3–5	21 (13.6)	1 (0.7)	3 (7.7)
Led to death	1 (0.6)	0	0

Exposure-adjusted AE rates in the ITT population decreased over time in both treatment groups

Treatment Duration and Time to Response[a]

Second Course of Pembrolizumab[b]



	N = 12[c]
Alive at data cutoff, n (%)	8 (67)
Objective response during second course, n (%)	4 (33)
Best objective response, n (%)	
Complete response	0
Partial response	4 (33)
Stable disease	6 (50)
Progressive disease	1 (8)

- At data cutoff, 5/12 patients (42%) were alive without PD per investigator assessment
  - 3 (25%) did not receive subsequent therapy

- With 5y FU pembro improves meaningfully OS an responses vs chemo
- Pts who completed 2y pembro had long term OS. Feasible 2nd course with same tx
- Lower G3-5 AEs with pembro
- 1st Ph.III trial demonstrating 5y efficacy with 1st line IO in PD-L1 ≥50%

#LBA52

- EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%. *Sezer A. et al*

Ahmet Sezer,[1] Saadettin Kilickap,[2] Mahmut Gümüş,[3] Igor Bondarenko,[4] Mustafa Özgüroğlu,[5] Miranda Gogishvili,[6] Haci M Turk,[7] Irfan Cicin,[8] Dmitry Bentsion,[9] Oleg Gladkov,[10] Philip Clingan,[11] Virote Sriuranpong,[12] Naiyer Rizvi,[13] Bo Gao,[14] Siyu Li,[14] Sue Lee,[14] Chieh-I Chen,[14] Tamta Makharadze,[15] Semra Paydas,[16] Marina Nechaeva,[17] Frank Seebach,[18] David M Weinreich,[18] George D Yancopoulos,[18] Giuseppe Gullo,[18] Israel Lowy,[18] Petra Rietschel[18]

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#LBA52 EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

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EMPOWER

EMPOWER-Lung 1 Study Design (NCT03088540)

Key Eligibility Criteria
- Treatment-naïve advanced NSCLC
- PD-L1 ≥50%
- No *EGFR*, *ALK* or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases and controlled hepatitis B or C or HIV were allowed

Stratification Factors:
- Histology (squamous vs non-squamous)
- Region (Europe, Asia or ROW)

R 1:1

Arm A
Cemiplimab monotherapy IV
350 mg Q3W
Treat until PD or 108 weeks

PD → Optional continuation of cemiplimab + 4 cycles of chemotherapy

Arm B
4–6 cycles of investigator's choice chemotherapy

PD → Optional crossover to cemiplimab monotherapy

Follow-up

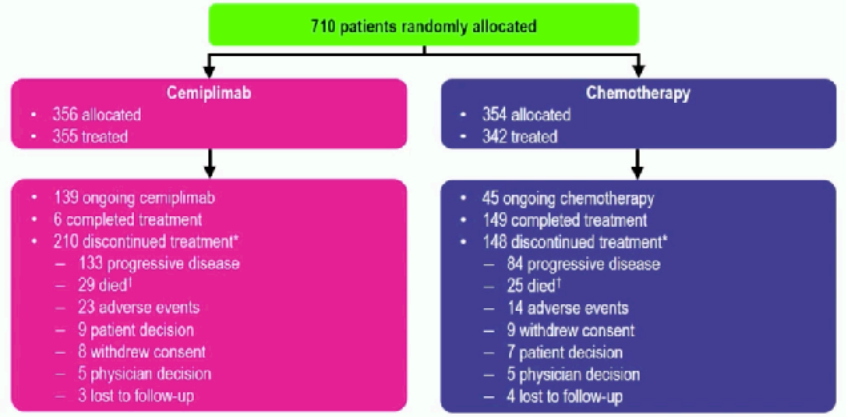
Endpoints:
- Primary: OS and PFS
- Secondary: ORR (key), DOR, HRQoL and safety

N=710

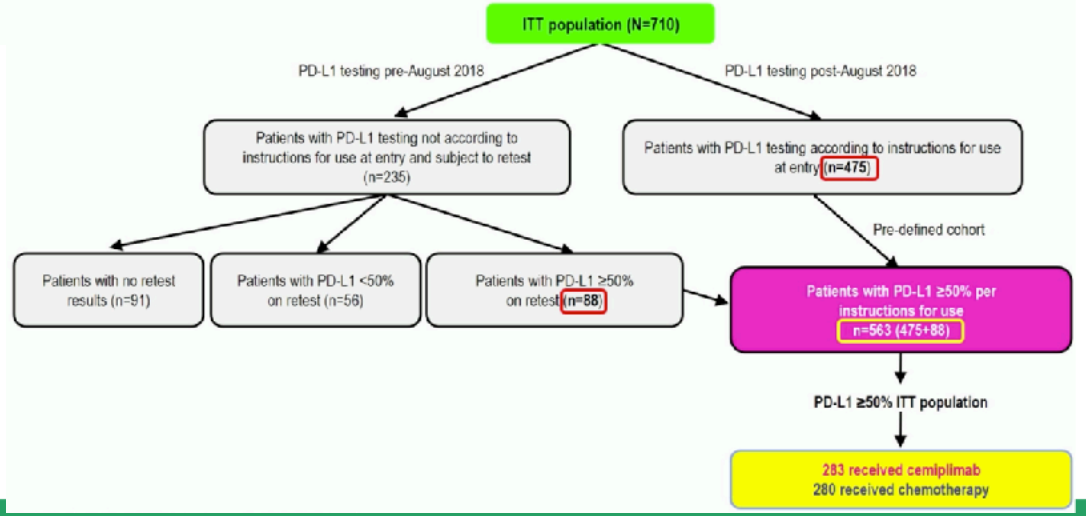
Five interim analyses were prespecified per protocol

Second interim analysis (1 March 2020) presented here

Disposition

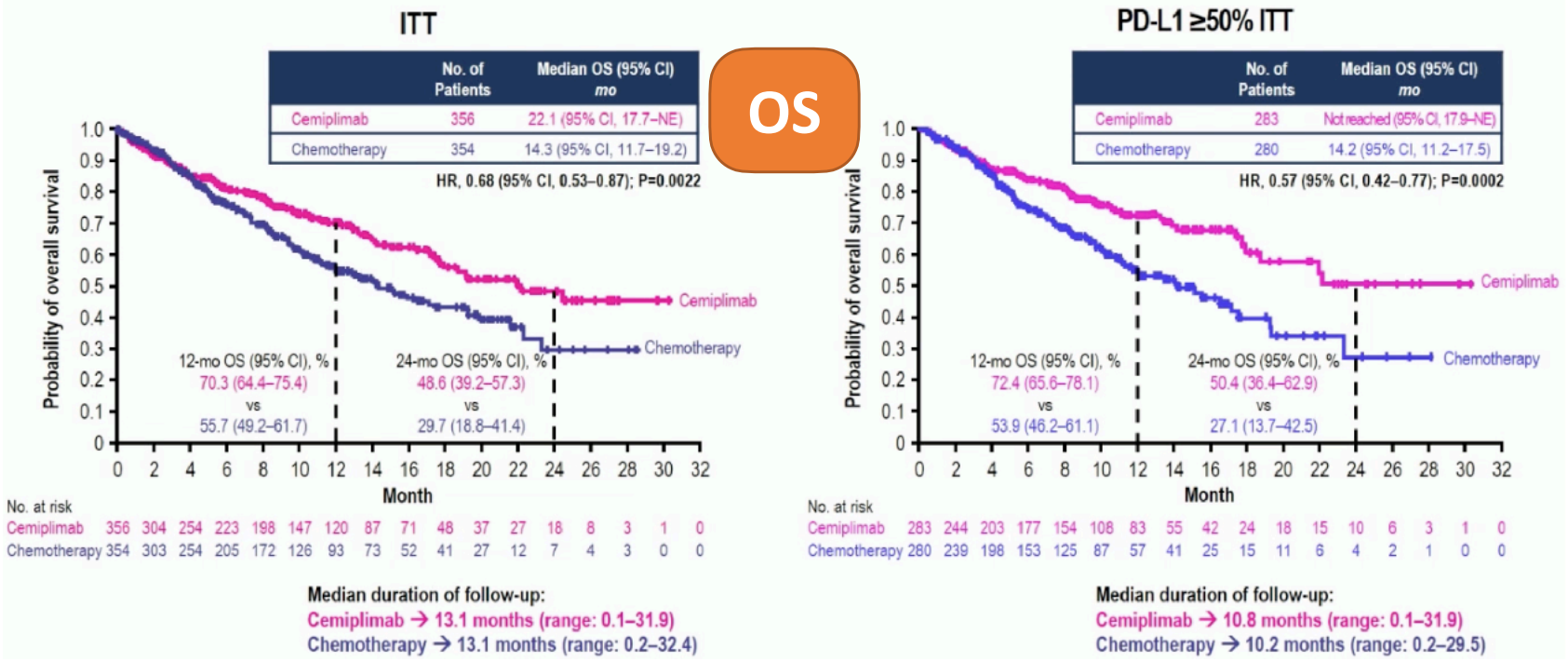


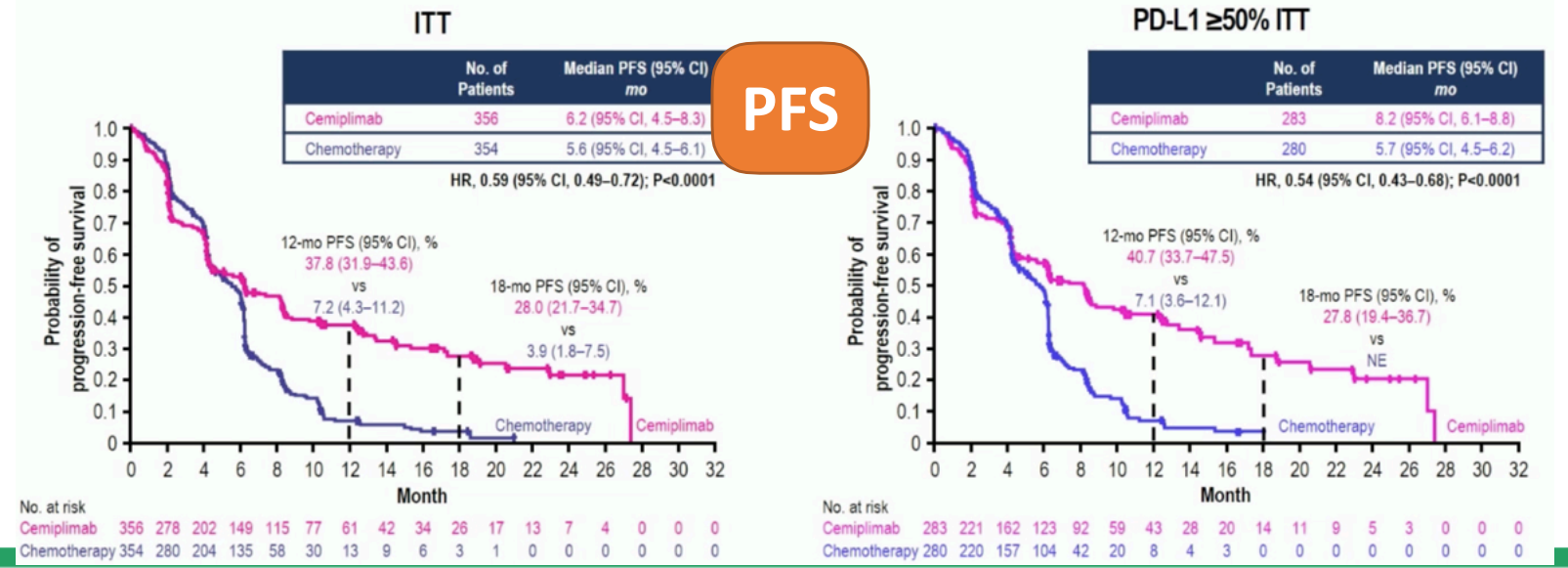
- 150 of 203 patients (73.9%) who progressed on chemotherapy received cemiplimab as a **crossover** treatment
- 50 of 158 patients (31.6%) who progressed on cemiplimab received **extended cemiplimab treatment with the addition of chemotherapy**



#LBA52

EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

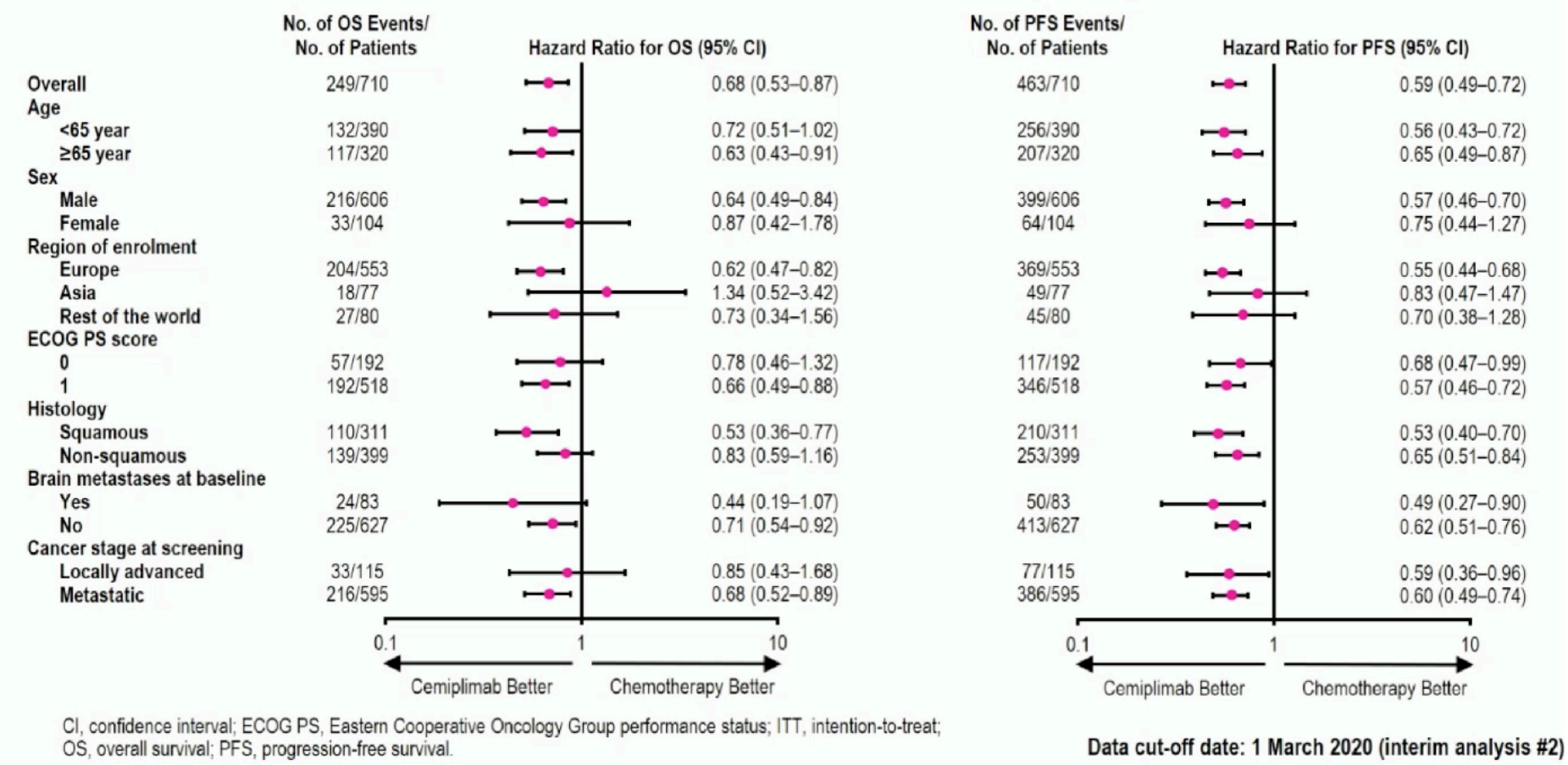




#LBA52

EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

OS & PFS - ITT



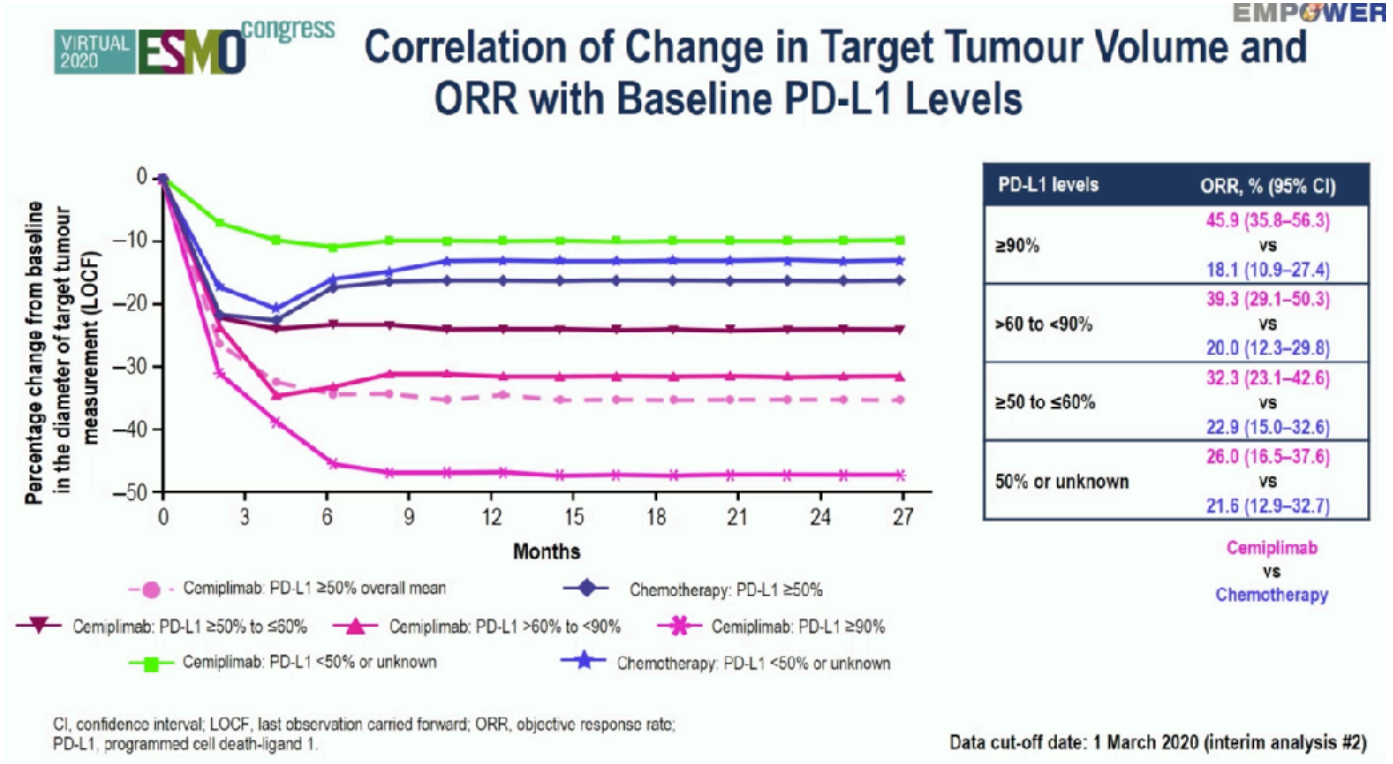
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.

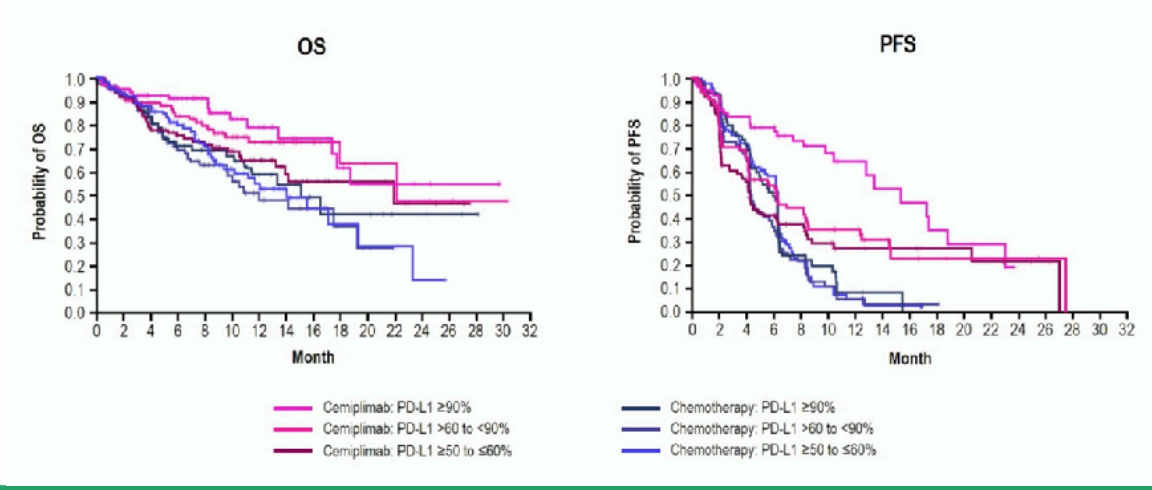
Data cut-off date: 1 March 2020 (interim analysis #2)

#LBA52

EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

	ITT		PD-L1 ≥50%	
	Cemiplimab (n=356)	Chemo (n=354)	Cemiplimab (n=283)	Chemo (n=280)
ORR	36.5%	20.6%	39.2%	20.4%
Median DOR (m)	21.0	6.0	16.7	6.0
Time to response (m)	2.1	2.1	2.1	2.1





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EMPOWER-Lung 1: Phase 3 first-line (1L) cemiplimab monotherapy vs platinum-doublet chemotherapy (chemo) in advanced non-small cell lung cancer (NSCLC) with programmed cell death-ligand 1 (PD-L1) ≥50%

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n (%), unless stated	Cemiplimab (n=355)		Chemotherapy (n=342)	
Median duration of exposure (range), weeks	27.3 (0.3–115.0)		17.7 (0.6–86.7)	
Treatment-emergent AEs, regardless of attribution	Any grade	Grade 3–5	Any grade	Grade 3–5
Overall	313 (88.2)	132 (37.2)	322 (94.2)	166 (48.5)
Led to discontinuation	23 (6.5)	15 (4.2)	14 (4.1)	8 (2.3)
Led to death	34 (9.6)	34 (9.6)	31 (9.1)	31 (9.1)
Treatment-related AEs				
Overall	204 (57.5)	50 (14.1)	303 (88.6)	134 (39.2)
Led to discontinuation	18 (5.1)	9 (2.5)	12 (3.5)	8 (2.3)
Led to death	9 (2.5)	9 (2.5)	7 (2.0)	7 (2.0)
Sponsor-identified immune-related AEs				
Overall	62 (17.5)	13 (3.7)	8 (2.3)	1 (0.3)
Led to discontinuation	9 (2.5)	5 (1.4)	0	0
Led to death	1 (0.3)	1 (0.3)	0	0

Safety Summary

Treatment-emergent AEs in ≥10% of patients in either arm, n (%)	Cemiplimab (n=355)		Chemotherapy (n=342)	
	Any grade	Grade 3–5	Any grade	Grade 3–5
Overall	313 (88.2)	132 (37.2)	322 (94.2)	166 (48.5)
Anaemia	52 (14.6)	12 (3.4)	171 (50.0)	56 (16.4)
Decreased appetite	42 (11.8)	2 (0.6)	63 (18.4)	1 (0.3)
Fatigue	36 (10.1)	4 (1.1)	58 (17.0)	5 (1.5)
Pneumonia	33 (9.3)	17 (4.8)	37 (10.8)	19 (5.6)
Constipation	27 (7.6)	0	52 (15.2)	0
Nausea	22 (6.2)	0	97 (28.4)	4 (1.2)
Vomiting	15 (4.2)	0	49 (14.3)	4 (1.2)
Thrombocytopaenia*	7 (2.0)	0	52 (15.2)	28 (8.2)
Neutropaenia*	6 (1.7)	2 (0.6)	63 (18.4)	35 (10.2)
Decreased platelet count*	5 (1.4)	0	36 (10.5)	12 (3.5)
Alopaecia	4 (1.1)	0	82 (24.0)	2 (0.6)
Peripheral neuropathy	3 (0.8)	1 (0.3)	37 (10.8)	1 (0.3)
Decreased neutrophil count*	2 (0.6)	1 (0.3)	42 (12.3)	18 (5.3)

- PFS & OS benefit
- Higher ORR & DoRHigh crossover rate (74%)
- The higher PD-L1 expression, the higher the benefit on Cemiplimab
- Longer exposure to Cemiplimab but better safety results

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Precision Immuno-Oncology for advanced NSCLC patients treated with PD(L)1 immune checkpoint inhibitors (ICIs)

An analysis of the first 100 pts from the **PIONeeR Project**

Fabrice Barlesi, MD, PhD

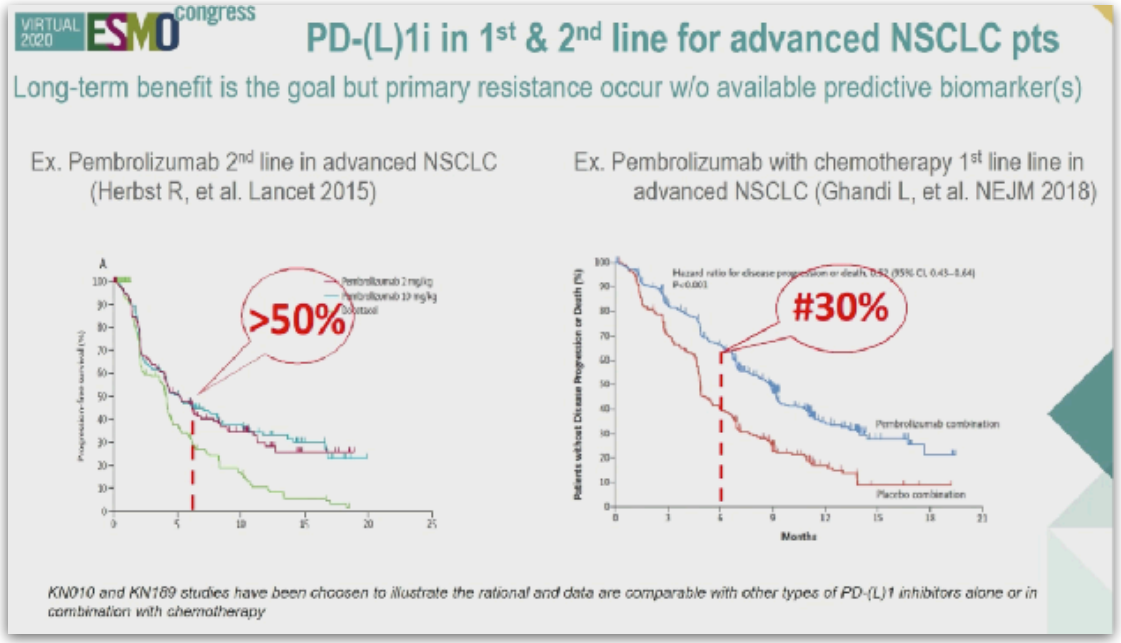
On behalf of the PIONeeR consortium

Aix Marseille University, CNRS, INSERM, CRCM, Marseille, France

Gustave Roussy Cancer Campus, Villejuif, France

#LBA53

Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study



#LBA53 Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study

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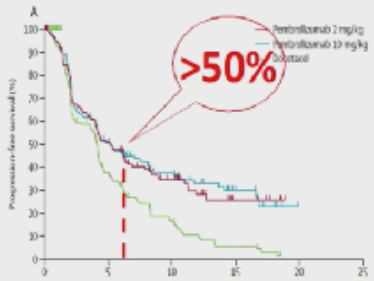
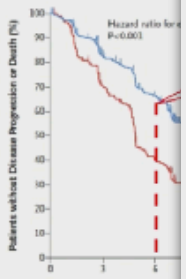
PD-(L)1i in 1st & 2nd line for advanced NSCLC pts

Long-term benefit is the goal but primary resistance occur w/o available predictive biomarker(s)

Ex. Pembrolizumab 2nd line in advanced NSCLC (Herbst R, et al. Lancet 2015)



Ex. Pembrolizumab with chemotherapy 1st line line in advanced N



KN010 and KN189 studies have been choosen to illustrate the rational and data are comparable with c combination with chemotherapy

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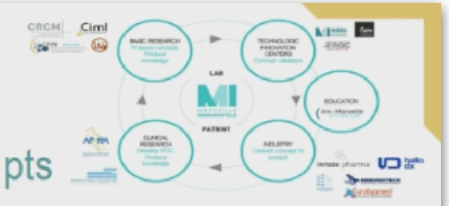
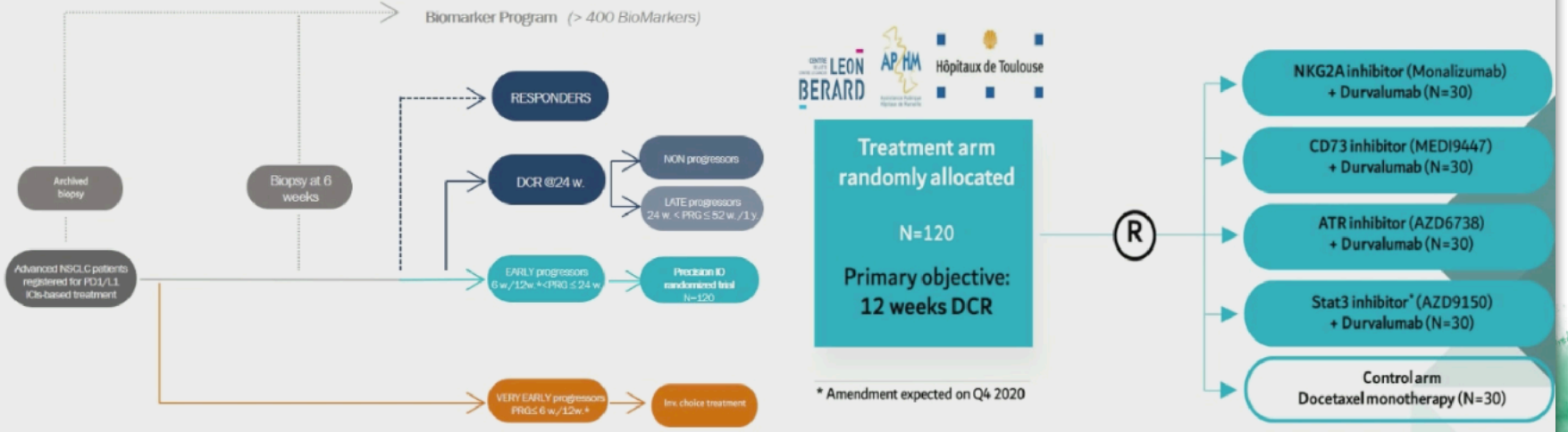
The PIONeeR project

Understand, Predict and Overcome resistances to PD-(L)1i in adv. NCSLC pts



Understand and Predict: PIONeeR biomarkers trial

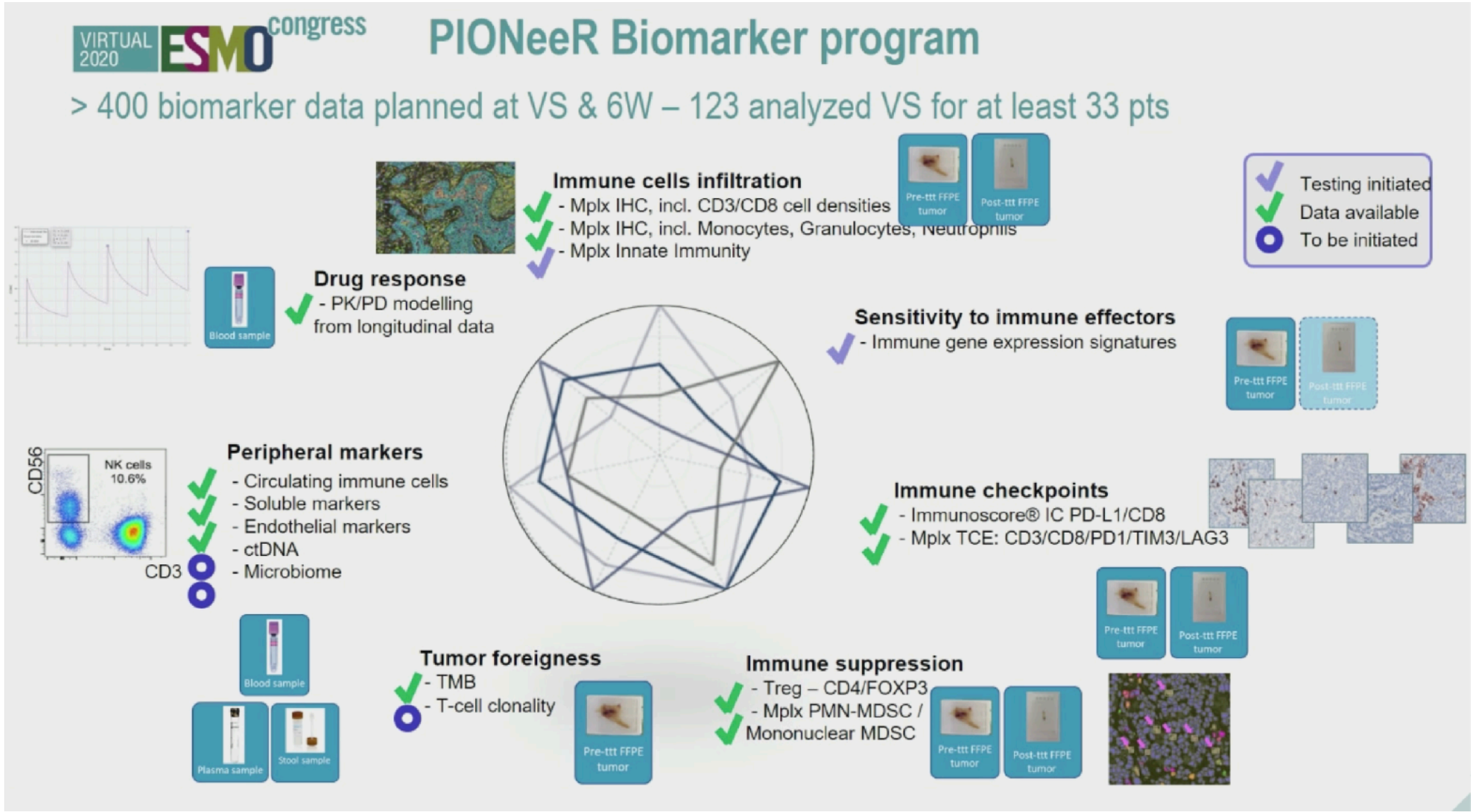
Overcome: PIONeeR umbrella trial



* Amendment expected on Q4 2020

#LBA53

Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study



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Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study

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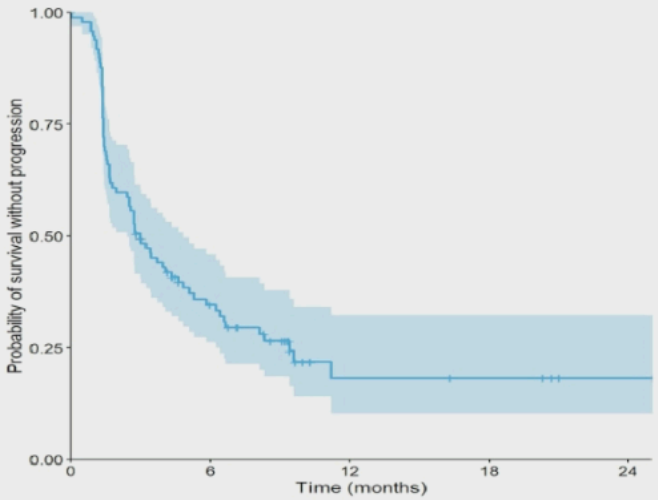
PIONeeR Biomarkers: First 100 patients analysis

Outcomes (ITT population)

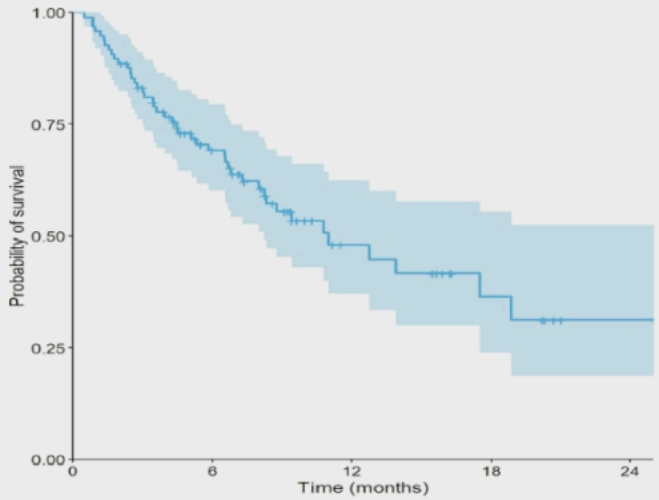
Median length of follow-up: **6.55 months** (range 0.01 – 26.15)

Overall Response Rate: **13%** (95%CI 7.1% – 21.2%)

Median PFS (71 events): **3.0 m** (95%CI 2.4 – 4.8)



Median **OS** (44 events): **11.0 m** (95%CI 8.2 – NR)



#LBA53 Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study

Clinical Characteristics & biomarkers associated with Objective Response

Timepoint	Biomarker	Non-Responders		Responders		P-value
		N valid	Mean	N valid	Mean	
Pre-treatment	PD-L1+ tumor cell percentage*	70	14%	11	33%	*0,045*
	Cytotoxic T cells CD3+/CD8+ density in the Tumor	43	298 cells/mm²	7	383 cells/mm²	*0,041*
	Cytotoxic T cells at TSI (Tumor-Stroma Interface)	26	178 cells/mm²	4	511 cells/mm²	*0,041***
	Effective T cell density in the Tumor	43	116 cells/mm²	7	172 cells/mm²	*0,008*
	Regulatory T-cell density in the Stroma	49	18 cells/mm²	7	70 cells/mm²	*0,010*
	Tissue factor blood concentration (endothelial activation)	28	21,6 fM	6	8,8 fM	*0,046*
6 weeks	Neutrophils in the Stroma	9	16 cells/mm²	2	73 cells/mm²	*0,036*

Clinical Characteristics associated with PFS & OS

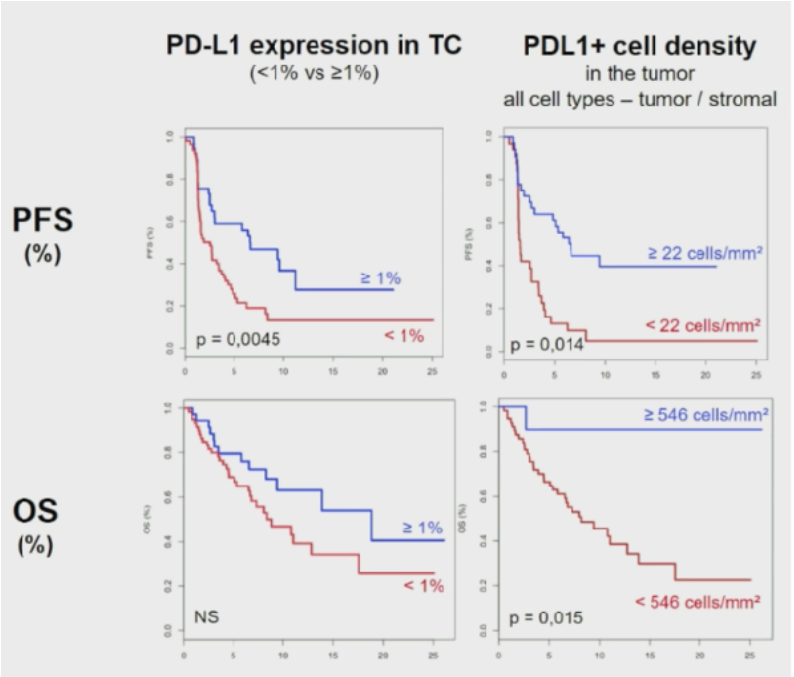
	Median PFS (months)	HR (95%CI), *p-value*
ECOG PS (2/3 vs 0/1)*	**1,22** [0,49;NA] vs **3,22** [2,53;5,32]	**10.8** [2.9 – 30.4], *p=0.002*
Histological Subtype (Others *vs* ADC)	**1,51** [1,35;3,45] vs **4,63** [2,53;11,20]	**2.24** [1.3 – 3.9], *p=0.007*
Type of PD-(L)1i (Pembro. vs Nivo.)	**3,22** [1,77;NA] vs **2,56** [1,54;4,07]	**0.58** [0.34 – 1.0], *p=0.049*
PD-L1 TC expression (<1% vs ≥1%)*	**2,25** [1,58;3,71] vs **6,60** [2,99;NA]	**2.0** [1.2 – 3.5], p=0.004

	Median OS (months)	HR (95%CI), *p-value*
ECOG PS (2/3 vs 0/1)*	**3,09** [0,49;NA] vs **12,78** [8,31;NA]	**3.9** [1.1 – 10.3], *p=0.041*

#LBA53 Precision Immuno-Oncology for advanced Non-Small Cell Lung Cancer (NSCLC) patients (pts) treated with PD1/L1 immune checkpoint inhibitors (ICIs): a first analysis of the PIONeeR Study

Biomarkers associated with PFS & OS

	Hazard Ratio PFS [95% IC]	*p-value*
PD-L1 expression in TC (%) *	0,98 [0,96;0,99]	*0,0209*
Circulating Activated T cells * **	1,06 [1,02;1,10]	*0,0008*
Serum IL6 *	1,00 [1,00;1,01]	*0,047*
Cytotoxic T cells in the tumor **	1,00 [1,00;1,01]	*0,047*
	Hazard Ratio OS [95% IC]	***p-value***
Circulating T cells *	0,99 [0,99;0,99]	*0,039*
Circulating Activated T cells *	1,07 [1,03;1,12]	*0,001*
Serum IL6 *	1,00 [1,00;1,01]	*0,037*
Serum TNFα *	1,04 [1,01;1,09]	*0,031*



- FIrst and largest study of biomarkers in NSCLC treated with PD-(L)1 inhibitors
- ECOG PS, main predictor for OS
- Biomarkers analysis suggest predictive value for PD-L1 tummor expression (PDL1 + cell density); density of Cytotoxic T cells in tumor, density of immunosuppressive cells (Treg)
- Still ongoing… objective to design an “immunogram” helping drive management of mNSCLC

#LBA54

TASUKI NIVOLUMAB CLINICAL TRIALS

VIRTUAL 2020 ESMO congress

ONO-4538-52 / TASUKI-52

Randomized phase III trial of nivolumab in combination with carboplatin, paclitaxel, and bevacizumab as first-line treatment for patients with advanced or recurrent non-squamous NSCLC

Jong-Seok Lee (presenting author), Shunichi Sugawara, Jin-Hyoung Kang, Hye Ryun Kim, Naoki Inui, Toyoaki Hida, Ki Hyeong Lee, Tatsuya Yoshida, Hiroshi Tanaka, Cheng-Ta Yang, Makoto Nishio, Yuichiro Ohe, Tomohide Tamura, Nobuyuki Yamamoto, Chong-Jen Yu, Hiroaki Akamatsu, Yoshinobu Namba, Naoki Sumiyoshi, and Kazuhiko Nakagawa

#LBA54

Randomized phase III trial of nivolumab in combination with carboplatin, paclitaxel, and bevacizumab as first-line treatment for patients with advanced or recurrent non-squamous NSCLC

Study Design

Key Eligibility Criteria

- Treatment-naïve stage IIIB / IV non-squamous NSCLC patients
- No sensitizing *EGFR* or *ALK* alterations
- PD-L1 all comer
- ECOG PS 0–1

N = 550

R 1:1

Nivolumab / Carboplatin / Paclitaxel / Bevacizumab[a)]
NIVO : 360 mg IV q3w

SD, PR, CR

Nivolumab / Bevacizumab

Treatment was continued until PD, unacceptable toxicity

Placebo / Carboplatin / Paclitaxel / Bevacizumab[a)]

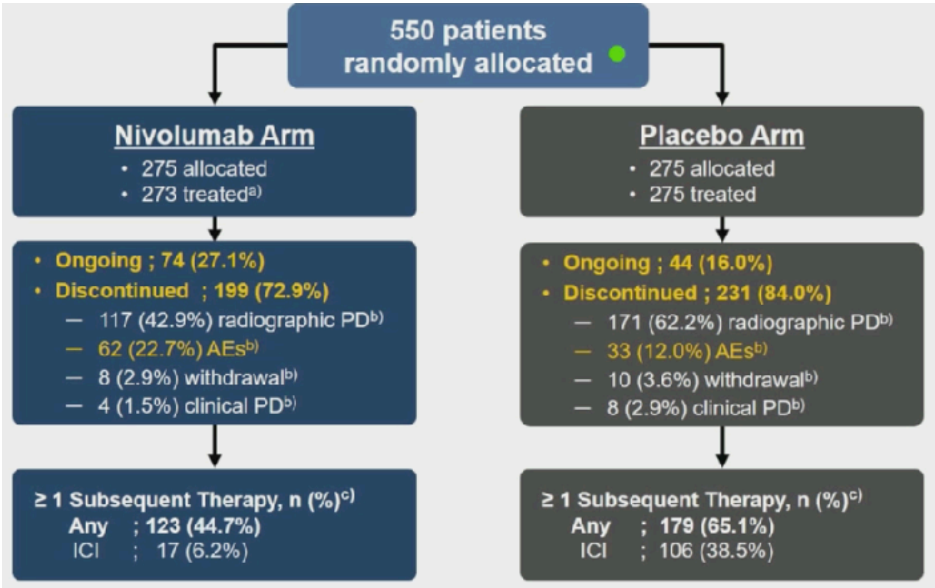
SD, PR, CR

Placebo / Bevacizumab

- **Primary Endpoint:**
  - PFS assessed by IRRC[b)]
- **Secondary Endpoint:**
  - OS, ORR, Safety

Stratification Factors

- PD-L1 (IHC 28-8) : ≥ 50%, 1%–49%, < 1% or indeterminate
- ECOG PS : 0, 1
- Sex : Male, Female



Interim Analysis

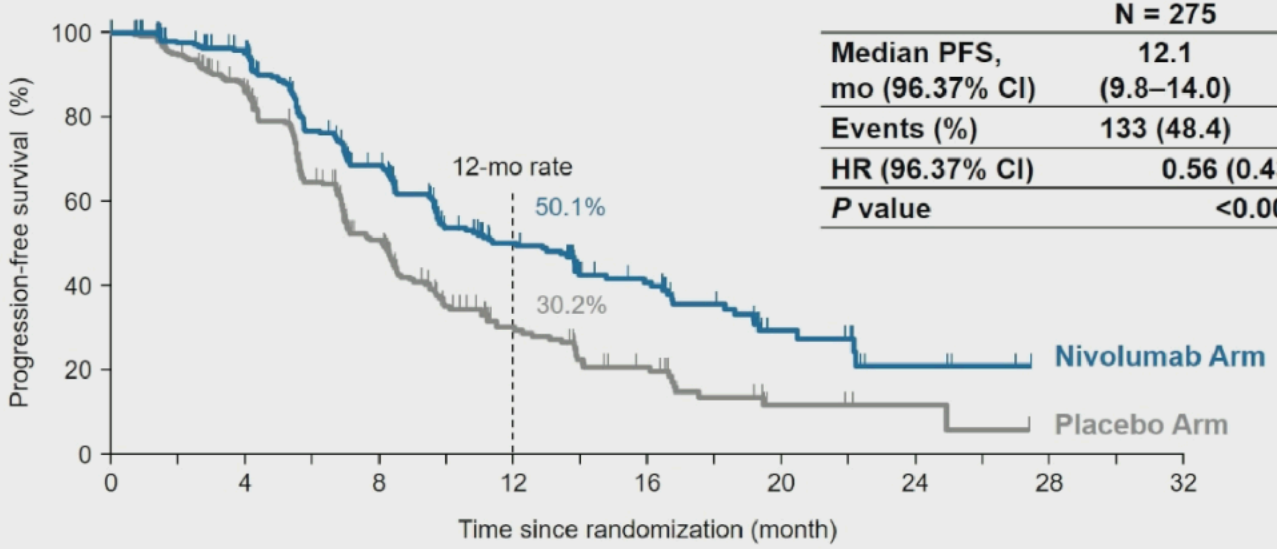
- Data cutoff: 10th feb 2020
- 306 events
- Minimum FU 7.4m
- α boundary: <0.0363

Baseline characteristics

		Nivolumab Arm N = 275	Placebo Arm N = 275
Age	median (range) < 65 years, n (%) ≥ 65 years, n (%)	66.0 (27–85) 131 (47.6) 144 (52.4)	66.0 (33–83) 111 (40.4) 164 (59.6)
Female, n (%)*		70 (25.5)	69 (25.1)
ECOG PS, n (%)*	0 1	129 (46.9) 146 (53.1)	128 (46.5) 147 (53.5)
Smoking status, n (%)	Current / Former Never	214 (77.8) 61 (22.2)	221 (80.4) 54 (19.6)
Country, n (%)	Japan Korea Taiwan	188 (68.4) 62 (22.5) 25 (9.1)	183 (66.5) 63 (22.9) 29 (10.5)
Metastases, n (%)	Bone Liver Brain	56 (20.4) 19 (6.9) 36 (13.1)	83 (30.2) 20 (7.3) 41 (14.9)
Tumor PD-L1 expression, n (%)*	< 1% or indeterminate 1%–49% ≥ 50%	120 (43.6) 82 (29.8) 73 (26.5)	120 (43.6) 81 (29.5) 74 (26.9)

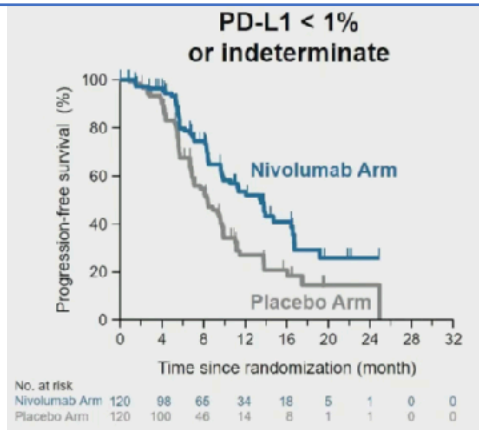
#LBA54 Randomized phase III trial of nivolumab in combination with carboplatin, paclitaxel, and bevacizumab as first-line treatment for patients with advanced or recurrent non-squamous NSCLC

Primary endpoint: PFS at interim analysis

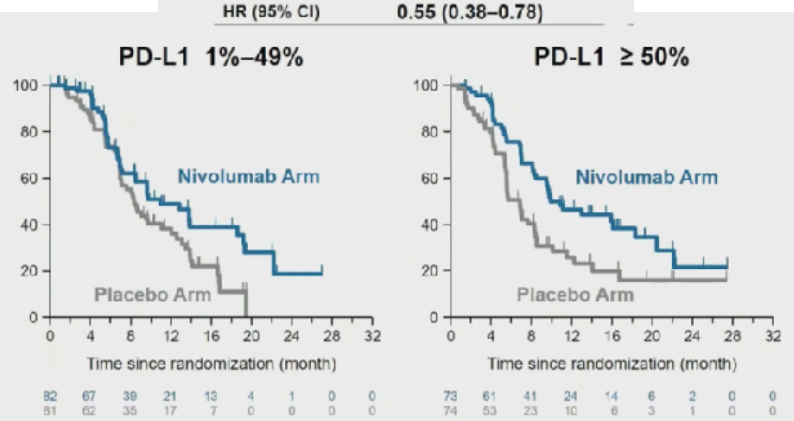


	Nivolumab Arm N = 275	Placebo Arm N = 275
Median PFS, mo (96.37% CI)	12.1 (9.8–14.0)	8.1 (7.0–8.5)
Events (%)	133 (48.4)	173 (62.9)
HR (96.37% CI)	0.56 (0.43–0.71)	
P value	<0.0001	

PFS by PD-L1 expression



	Nivolumab Arm N = 120	Placebo Arm N = 120
Median PFS, mo (95% CI)	13.6 (9.8–16.6)	8.4 (7.0–9.8)
HR (95% CI)	0.55 (0.38–0.78)	



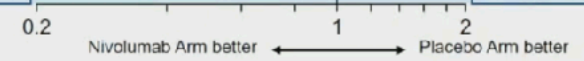
	Nivolumab Arm N = 82	Placebo Arm N = 81
Median PFS, mo (95% CI)	11.0 (7.2–18.6)	8.4 (7.0–11.1)
HR (95% CI)	0.63 (0.42–0.96)	

	Nivolumab Arm N = 73	Placebo Arm N = 74
Median PFS, mo (95% CI)	9.9 (8.3–18.3)	6.9 (5.6–8.3)
HR (95% CI)	0.55 (0.36–0.83)	

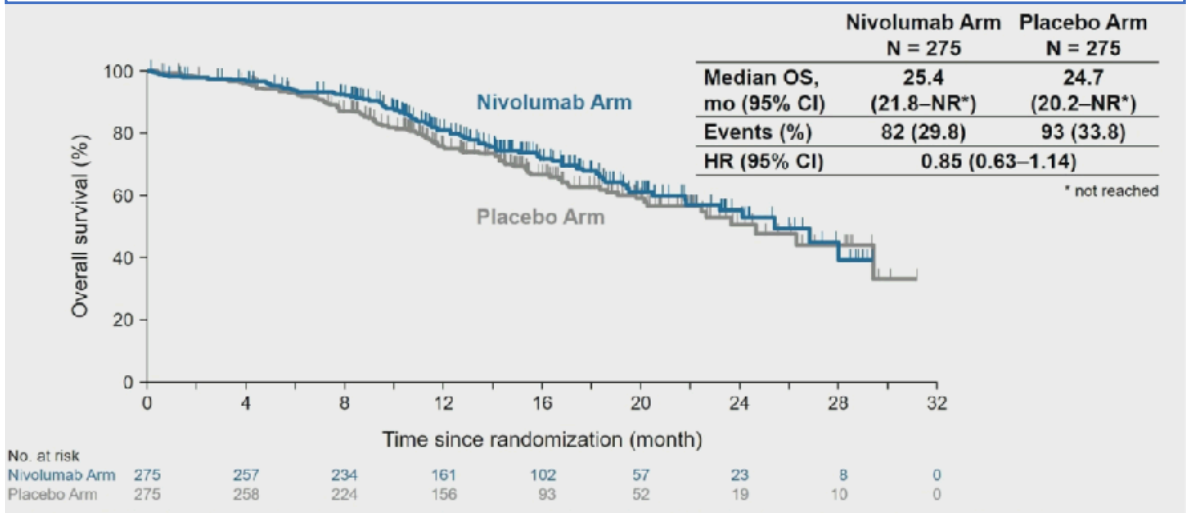
#LBA54 Randomized phase III trial of nivolumab in combination with carboplatin, paclitaxel, and bevacizumab as first-line treatment for patients with advanced or recurrent non-squamous NSCLC

Primary by subgroups

Subgroup	Median PFS, mo		Unstratified HR (95% CI)
	Nivolumab Arm N = 275	Placebo Arm N = 275	
All randomized (n = 550)	12.1	8.1	0.57 (0.46–0.72)
< 65 years (n = 242)	11.4	7.0	0.50 (0.35–0.69)
≥ 65 years (n = 308)	12.9	8.3	0.65 (0.47–0.88)
Japan (n = 371)	13.4	8.2	0.57 (0.43–0.75)
Korea (n = 125)	10.6	7.1	0.56 (0.34–0.93)
Taiwan (n = 54)	9.7	8.5	0.64 (0.31–1.32)
Male (n = 411)	12.9	7.7	0.53 (0.41–0.69)
Female (n = 139)	10.0	8.7	0.72 (0.45–1.15)
ECOG PS 0 (n = 257)	13.8	8.4	0.56 (0.39–0.78)
ECOG PS 1 (n = 293)	9.9	7.6	0.58 (0.43–0.79)
Current / Former smoker (n = 435)	13.0	7.7	0.56 (0.43–0.71)
Never smoker (n = 115)	9.7	8.7	0.69 (0.40–1.18)
Liver metastases (n = 39)	5.8	5.5	0.55 (0.25–1.23)
Bone metastases (n = 139)	8.3	7.1	0.87 (0.56–1.37)
Brain metastases (n = 77)	10.6	7.1	0.65 (0.36–1.18)
PD-L1 < 1% or indeterminate (n = 240)	13.6	8.4	0.55 (0.38–0.78)
PD-L1 1%–49% (n = 163)	11.0	8.4	0.63 (0.42–0.96)
PD-L1 ≥ 50% (n = 147)	9.9	6.9	0.55 (0.36–0.83)



OS (Secondary objective)



	Nivolumab Arm N = 275	Placebo Arm N = 275
Median OS, mo (95% CI)	25.4 (21.8–NR*)	24.7 (20.2–NR*)
Events (%)	82 (29.8)	93 (33.8)
HR (95% CI)	0.85 (0.63–1.14)	

* not reached

ORR

	Nivolumab Arm N = 275	Placebo Arm N = 275
ORR, n (%)	169 (61.5)	139 (50.5)
Odds ratio (95% CI)	1.55 (1.11–2.17)	
BOR, n (%)		
CR	14 (5.1)	8 (2.9)
PR	155 (56.4)	131 (47.6)
SD	71 (25.8)	108 (39.3)
PD	5 (1.8)	11 (4.0)
NE	30 (10.9)	17 (6.2)
DOR, median (range), mo	11.0 (1.1+–25.8+)	7.0 (1.2+–26.0+)
Patients with ongoing response at the data cutoff date, n (%)	61/169 (36.1)	21/139 (15.1)

+ : censored

#LBA54 Randomized phase III trial of nivolumab in combination with carboplatin, paclitaxel, and bevacizumab as first-line treatment for patients with advanced or recurrent non-squamous NSCLC

TRAEs summary

Patients, n (%)	Nivolumab Arm N = 273	Placebo Arm N = 275
Any TRAEs	269 (98.5)	274 (99.6)
Any TRAEs Grade 3 / 4	201 (73.6)	198 (72.0)
Serious TRAEs	114 (41.8)	74 (26.9)
TRAEs leading to discontinuation	45 (16.5)	12 (4.4)
TRAEs leading to dose delay	132 (48.4)	123 (44.7)
TRAEs leading to death	5 (1.8)[a)]	4 (1.5)[b)]

- PFS benefit HR 0.56 in nivo arm regardless PD-L1 expression
- OS HR ns, trend benefit in nivo arm
- No new safety signals

AESIs

Patients, n (%)	Nivolumab Arm N = 273		Placebo Arm N = 275	
	Any Grade	Grade 3 / 4	Any Grade	Grade 3 / 4
Rash	139 (50.9)	34 (12.5)	72 (26.2)	4 (1.5)
Diarrhea / Colitis	61 (22.3)	15 (5.5)	35 (12.7)	4 (1.5)
Hepatitis	30 (11.0)	9 (3.3)	29 (10.5)	4 (1.5)
Hypothyroidism / Thyroiditis	28 (10.3)	1 (0.4)	7 (2.5)	0 (0)
Pneumonitis	23 (8.4)	7 (2.6)	5 (1.8)	2 (0.7)
Nephritis and renal dysfunction	20 (7.3)	2 (0.7)	13 (4.7)	1 (0.4)
Adrenal insufficiency	15 (5.5)	4 (1.5)	6 (2.2)	1 (0.4)
Hyperthyroidism	15 (5.5)	0 (0)	4 (1.5)	0 (0)
Hypersensitivity	13 (4.8)	3 (1.1)	8 (2.9)	1 (0.4)
Hypophysitis	5 (1.8)	3 (1.1)	1 (0.4)	0 (0)
Diabetes mellitus	4 (1.5)	3 (1.1)	1 (0.4)	0 (0)

TRAEs ≥20%

	Nivolumab Arm N = 273		Placebo Arm N = 275	
	Any Grade	Grade 3 / 4	Any Grade	Grade 3 / 4
Alopecia	143 (52.4)	0 (0.0)	150 (54.5)	0 (0.0)
Peripheral sensory neuropathy	120 (44.0)	3 (1.1)	118 (42.9)	7 (2.5)
Neutrophil count decreased	116 (42.5)	87 (31.9)	139 (50.5)	98 (35.6)
White blood cell count decreased	93 (34.1)	40 (14.7)	98 (35.6)	41 (14.9)
Constipation	85 (31.1)	3 (1.1)	81 (29.5)	1 (0.4)
Decreased appetite	81 (29.7)	8 (2.9)	96 (34.9)	13 (4.7)
Rash	81 (29.7)	13 (4.8)	40 (14.5)	1 (0.4)
Anaemia	78 (28.6)	15 (5.5)	92 (33.5)	17 (6.2)
Arthralgia	69 (25.3)	0 (0.0)	75 (27.3)	2 (0.7)
Nausea	68 (24.9)	3 (1.1)	83 (30.2)	5 (1.8)
Malaise	68 (24.9)	1 (0.4)	71 (25.8)	0 (0.0)
Myalgia	66 (24.2)	0 (0.0)	78 (28.4)	0 (0.0)
Hypertension	65 (23.8)	37 (13.6)	79 (28.7)	42 (15.3)
Proteinuria	65 (23.8)	13 (4.8)	69 (25.1)	10 (3.6)
Neuropathy peripheral	59 (21.6)	1 (0.4)	62 (22.5)	2 (0.7)
Platelet count decreased	59 (21.6)	16 (5.9)	61 (22.2)	6 (2.2)

#LBA55

- WJOG @Be Study: A Phase II Study of Atezolizumab (Atez) With Bevacizumab (Bev) for Non-Squamous (Sq) Non-Small-Cell Lung Cancer (NSCLC) with High PD-L1 Expression

Takashi Seto, Kaname Nosaki, Mototsugu Shimokawa, Ryo Toyozawa, Shunichi Sugawara, Hidetoshi Hayashi, Haruyasu Murakami, Terufumi Kato, Seiji Niho, Hideo Saka, Masahide Oki, Hiroshige Yoshioka, Isamu Okamoto, Haruko Daga, Koichi Azuma, Hiroshi Tanaka, Kazumi Nishino, Miyako Satouchi, Nobuyuki Yamamoto, Kazuhiko Nakagawa
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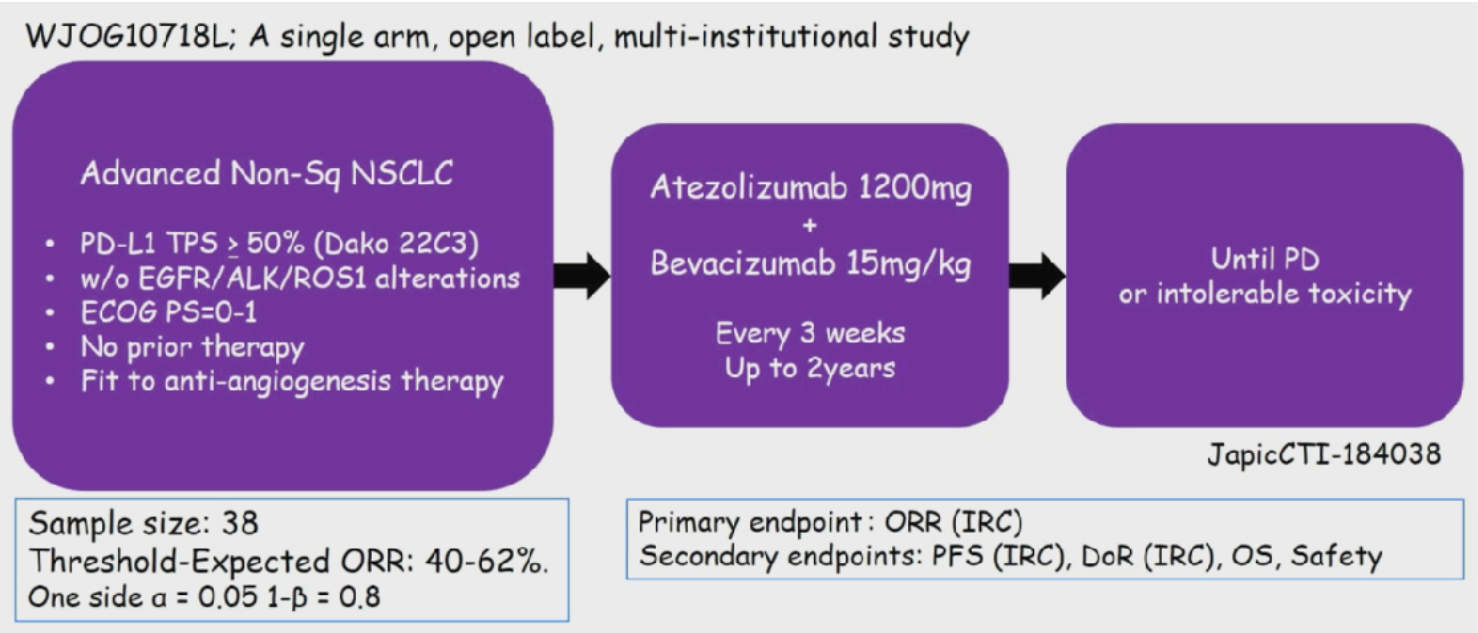
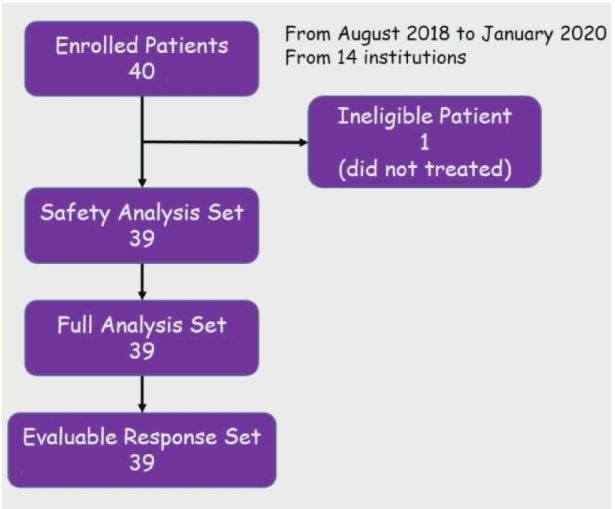
#LBA55 WJOG @Be Study: A Phase II Study of Atezolizumab (Atez) With Bevacizumab (Bev) for Non-Squamous (Sq) Non-Small-Cell Lung Cancer (NSCLC) with High PD-L1 Expression.



		Total n=39	% or range
Gender	Man	33	84.6
	Woman	6	15.4
Age	median	67	41-75
Body weight	median	56.1	41-73.2
Smoking History	Yes	36	92.3
	No	3	7.7
Histological type	Adeno	37	94.9
	Other	2	5.1
Stage	IIIB/C	2/2	5.1/5.1
	IVA/B	18/15	46.2/38.5
	Recurrence	2	5.1
PD-L1 TPS	50-74%	13	33.3
	75-100%	26	66.7
PS	0/1	25/14	64.1/35.9
Treatment history	Ope/RT	6/8	15.4/20.5

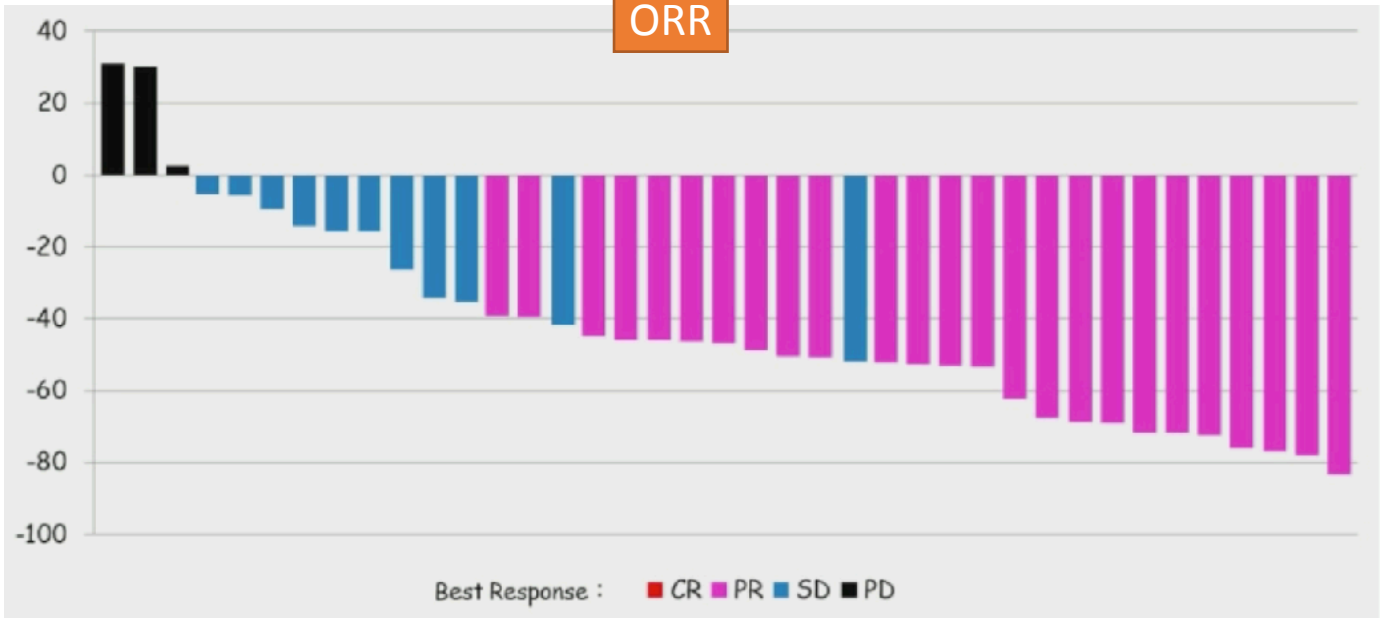


#LBA55 WJOG @Be Study: A Phase II Study of Atezolizumab (Atez) With Bevacizumab (Bev) for Non-Squamous (Sq) Non-Small-Cell Lung Cancer (NSCLC) with High PD-L1 Expression.

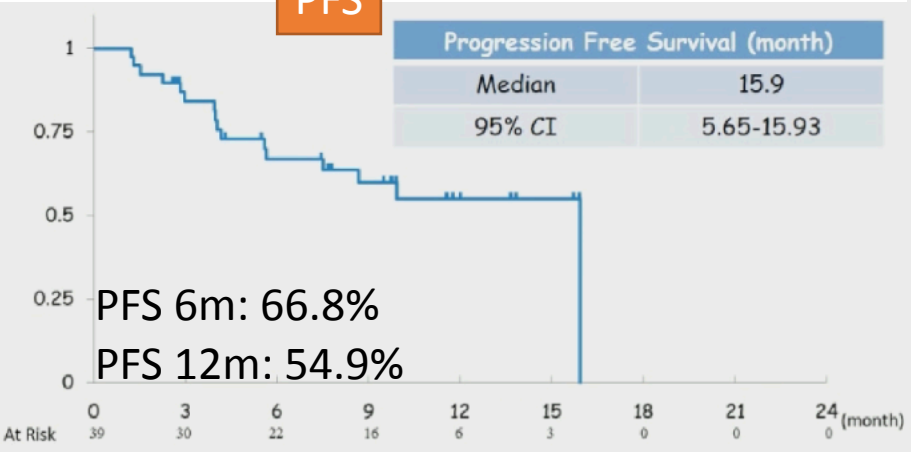
n = 38		
Best response	**n**	**%**
CR	0	0
PR	25	64.1
SD	11	28.2
PD	3	7.7
NE	0	0
ORR (CR + PR)	25	64.1
90% CI	49.69-76.83	
95% CI	47.18-78.80	

Threshold expected ORR 40-62%

ORR



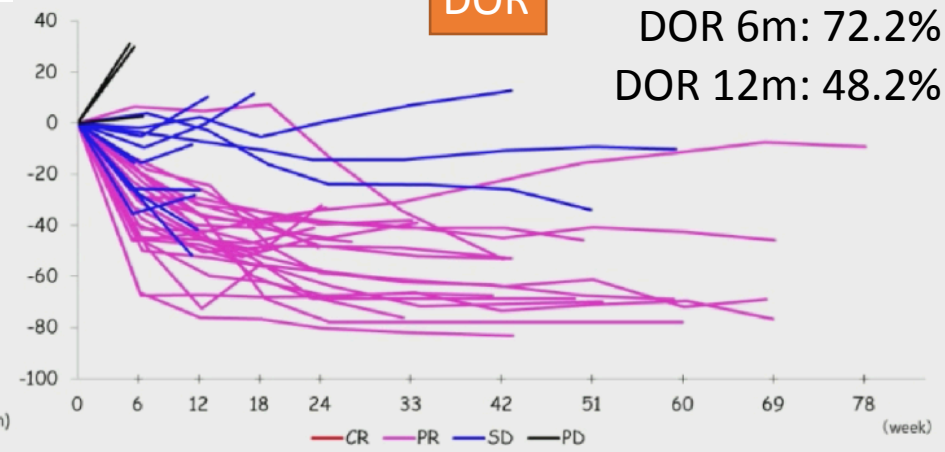
PFS



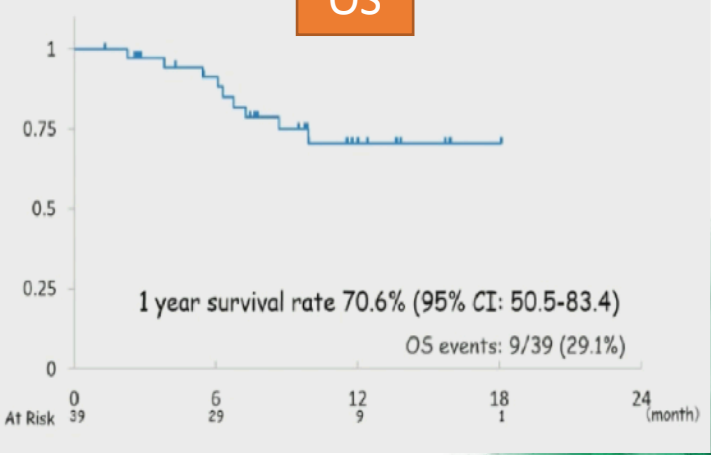
DOR

DOR 6m: 72.2%

DOR 12m: 48.2%



OS



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G 3-4 AEs CTCAE v.4.0

CTCAE v 4.0 Term	Grade 3	Grade 4	ALL Grade
	Case (%)	Case	Case (%)
All	15 (38.5)	0	38 (97.4)
Pericarditis	1 (2.6)	0	1 (2.6)
Infection	1 (2.6)	0	1 (2.6)
Lung infection	2 (5.1)	0	2 (5.1)
Hyponatremia	1 (2.6)	0	4 (10.3)
Encephalopathy	1 (2.6)	0	1 (2.6)
Hypertension	6 (15.4)	0	18 (46.2)
Colitis	2 (5.1)	0	2 (5.1)
Diarrhea	1 (2.6)	0	4 (10.3)
Ileus	1 (2.6)	0	1 (2.6)
Anorexia	1 (2.6)	0	7 (17.9)
Vomiting	1 (2.6)	0	3 (7.7)
Cholecystitis	1 (2.6)	0	1 (2.6)
Dermatitis	1 (2.6)	0	2 (5.1)
Proteinuria	1 (2.6)	0	13 (33.3)
Fever	1 (2.6)	0	11 (28.2)
ALT increased	3 (7.7)	0	8 (20.5)
AST increased	2 (5.1)	0	9 (23.1)
GGTP increased	1 (2.6)	0	3 (7.7)
ALP increased	1 (2.6)	0	2 (5.1)
White blood cell decreased	1 (2.6)	0	1 (2.6)
Neutrophil count decreased	1 (2.6)	0	2 (5.1)
Weight gain	1 (2.6)	0	2 (5.1)

Discontinuation of treatment (n=19)

Total	n=40	%
Compete treatment	0	0
Continue treatment	20	50
Discontinue treatment	20	50
Main reason of discontinuation		
1) Progression or clinically uncontrollable	17	42.5
2) Due to adverse events	2	5
3) Patients offers	0	0
4) Death	0	0
5) Ineligible	1	2.5
6) Some other reasons	0	0
Details of discontinuation due to AEs		
1) Grade4 adverse events	0	0
2) Interstitial pneumonia greater than grade 2	0	0
3) Uncontrollable toxicities	0	0
4) judgement from investigators in consideration of safety	2*	5

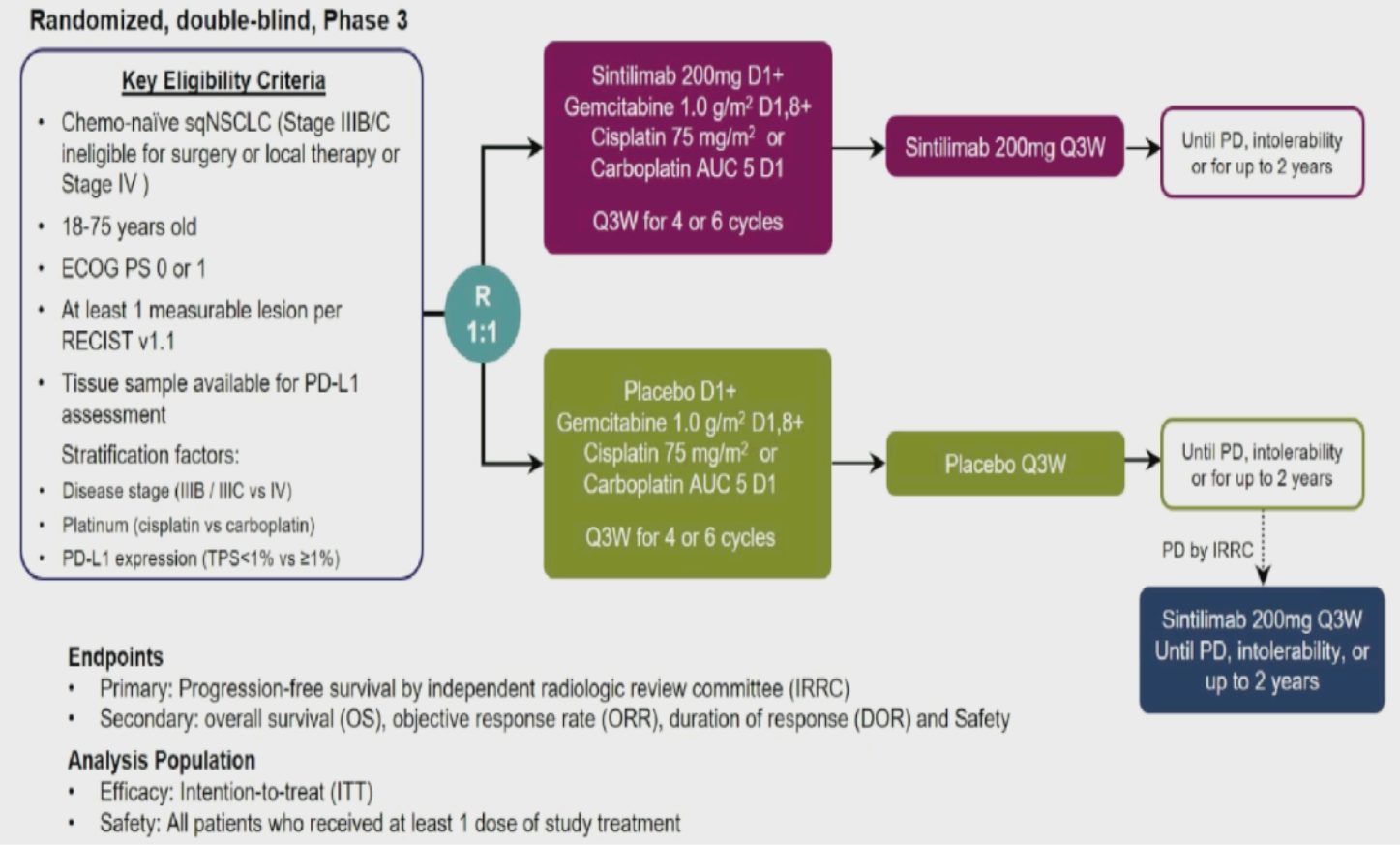
SAE related to treatment

CTCAE v 4.0 Term	Atezolizumab related	Bevacizumab related	Both related
	Case (%)	Case (%)	Case (%)
All	9 (23.1)	6 (15.4)	9 (23.1)
Lung infection	1 (2.6)	1 (2.6)	1 (2.6)
Anorexia	1 (2.6)	1 (2.6)	1 (2.6)
Encephalopathy	1 (2.6)	0	1 (2.6)
Bronchopulmonary hemorrhage	1 (2.6)	1 (2.6)	1 (2.6)
Colitis	2 (5.1)	1 (2.6)	2 (5.1)
Diarrhea	1 (2.6)	0	1 (2.6)
Vomiting	1 (2.6)	0	1 (2.6)
Cholecystitis	1 (2.6)	1 (2.6)	1 (2.6)
Fever	2 (5.1)	1 (2.6)	2 (5.1)
Infusion related reaction	1 (2.6)	1 (2.6)	1 (2.6)

- ORR 64.1%
- mPFS 15.9m
- mDoR 10.4m
- 1y OS 70.6%
- No G.4 SAEs

#LBA56

ORIENT-12: sintilimab plus gemcitabine and platinum (GP) as first-line (1L) treatment for locally advanced or metastatic squamous non-small-cell lung cancer (sqNSCLC). *Zhou C et al*

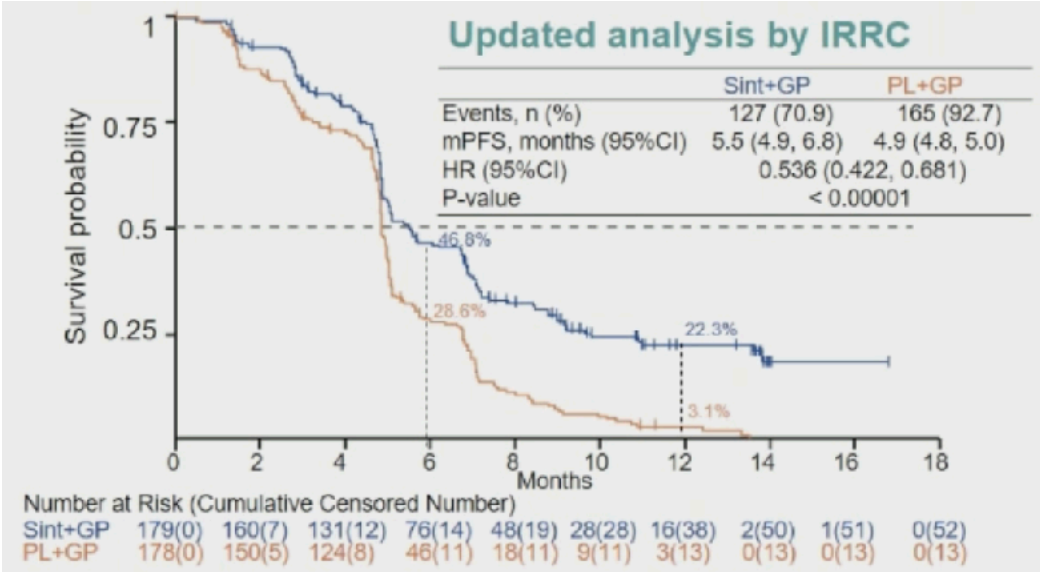


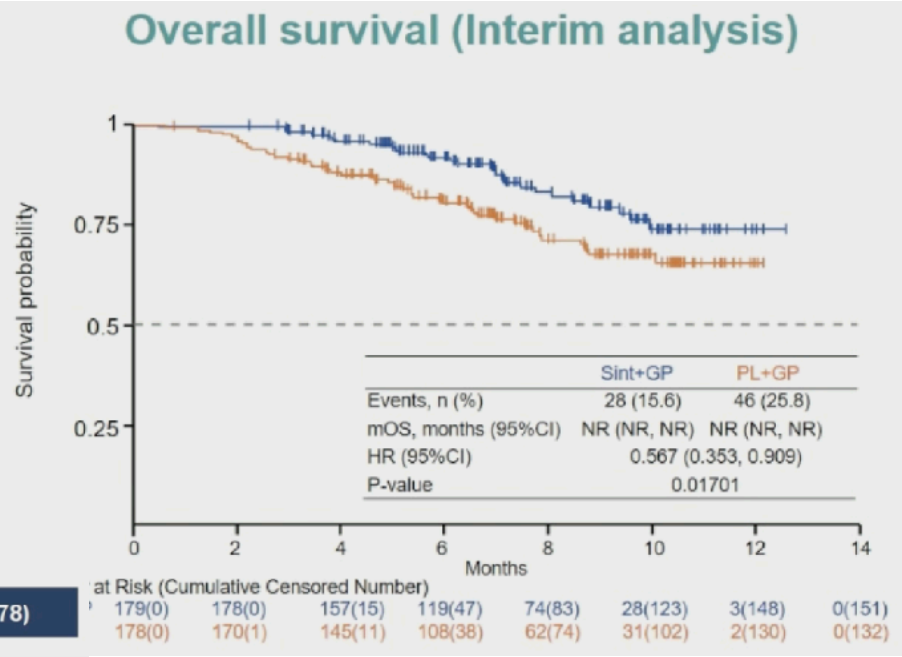
Characteristics	Sint + GP (N=179)	PL + GP (N=178)
Median age (range) – yr	64 (39, 75)	62 (33, 75)
>60 – no. (%)	111 (62.0)	102 (57.3)
Sex, male– no. (%)	163 (91.1)	164 (92.1)
ECOG PS score – no. (%)		
0	30 (16.8)	22 (12.4)
1	149 (83.2)	156 (87.6)
Smoking status – no. (%)		
Never	24 (13.4)	31 (17.4)
Current/Former	155 (86.6)	147 (82.6)
Disease stage – no. (%)		
IIIB / IIIC	39 (21.8)	44 (24.7)
IV	140 (78.2)	134 (75.3)
PD-L1 TPS – no. (%)¶		
<1%§	59 (33.0)	63 (35.4)
≥1%	120 (67.0)	115 (64.6)
Platinum choice – no. (%)		
Cisplatin	69 (38.5)	66 (37.1)
Carboplatin	110 (61.5)	112 (62.9)

¶ Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay
§ Patients not evaluable for PD-L1 expression status were included in PD-L1 TPS<1%

#LBA56

ORIENT-12: sintilimab plus gemcitabine and platinum (GP) as first-line (1L) treatment for locally advanced or metastatic squamous non-small-cell lung cancer (sqNSCLC)





Best response %	Sintilimab + CT	Placebo + CT
CR	0.6	0
PR	44.1	35.4
SD	41.3	44.9
PD	10.1	14.0
ORR (95%CI)	44.7 (37.3-52.3)	35.4 (28.4-42.9)
DCR (95%CI)	86.0 (80.1-90.8)	80.3 (73.7-85.9)

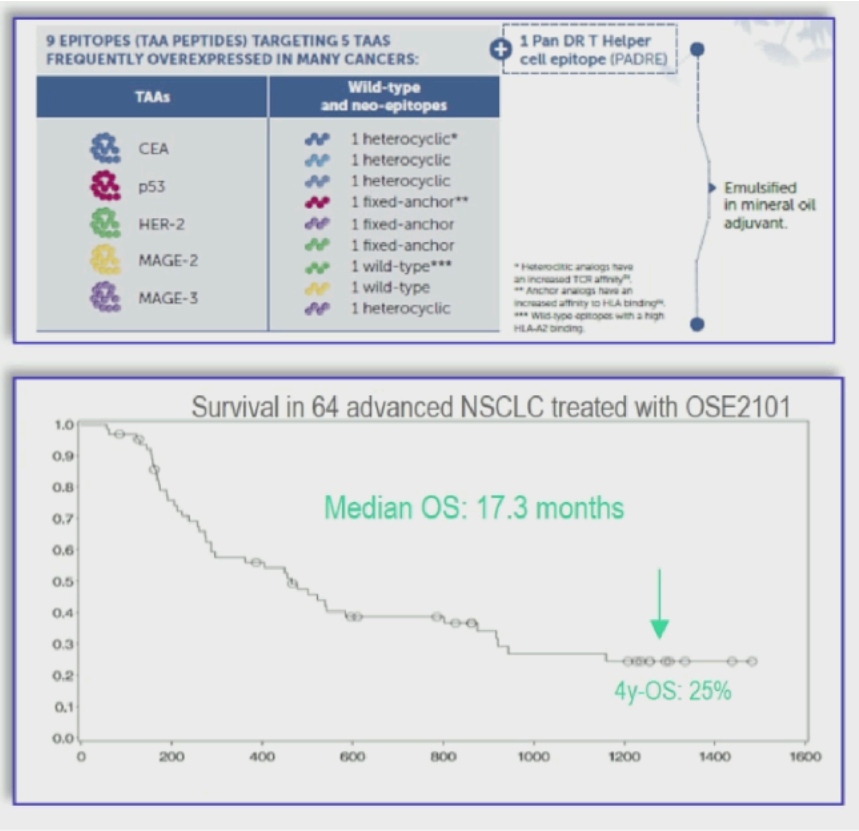
	Sint + GP (N=179)	PL + GP (N=178)
Treatment duration (sintilimab / placebo)		
Mean (SD) – months	7.4 (4.11)	5.8 (3.12)
Median (range) – cycles	9.0 (1, 25)	8.0 (1, 21)
TEAE, n (%)	179 (100)	178 (100)
Grade 3-5	155 (86.6)	148 (83.1)
TEAE leading to death	8 (4.5)	12 (6.7)
Serious AE	90 (50.3)	80 (44.9)
AE leading to any treatment component interruption	123 (68.7)	114 (64.0)
AE leading to sintilimab / placebo withdrawal	18 (10.1)	15 (8.4)
irAE§	74 (41.3)	47 (26.4)
Grade 3-5	11 (6.1)	8 (4.5)
irAE leading to death	2 (1.1)	4 (2.2)

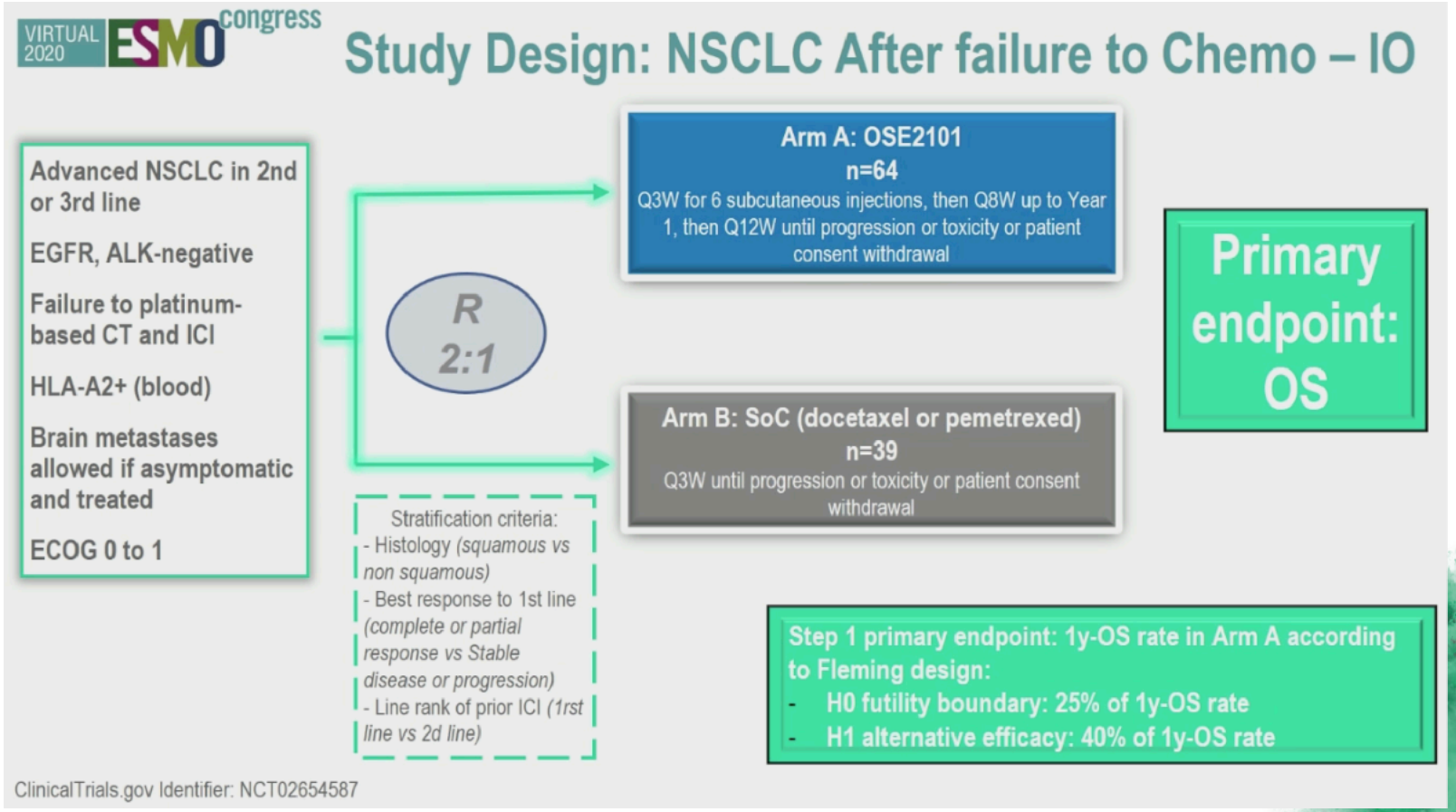
¶ Data cutoff date: Mar. 25, 2020. Data during crossover phase were not included
§ Evaluated by investigator

- Significant improvement in PFS in chemo/IO arm
- OS tendency favourable to experimental arm
- Manageable safety profile

#1260MO

Activity of OSE-2101 in HLA-A2+ non-small cell lung cancer (NSCLC) patients after failure to immune checkpoint inhibitors (ICI): Step 1 results of phase III ATALANTE-1 randomised trial. *Giaccone G et al*





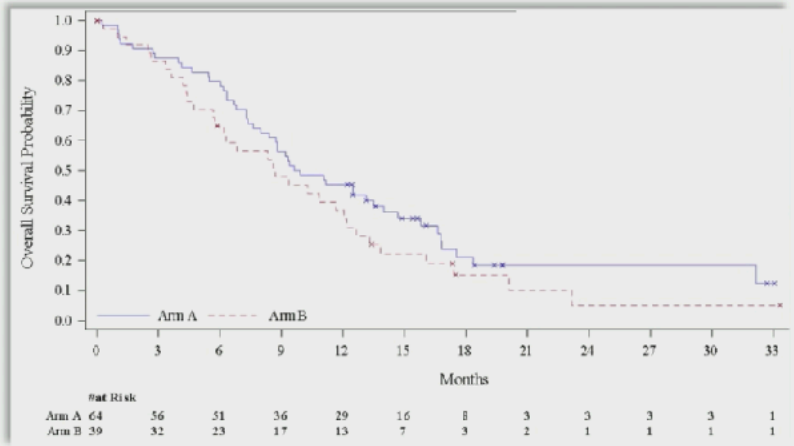
#1260MO

ORIENT-12: sintilimab plus gemcitabine and platinum (GP) as first-line (1L) treatment for locally advanced or metastatic squamous non-small-cell lung cancer (sqNSCLC)

		Arm A OSE2101 (N=64)	Arm B SoC (N=39)
Age (years)	Median (range)	65.5 (44, 82)	62.0 (43, 71)
Gender (N, %)	Male	44 (69)	25 (64)
	Female	20 (31)	14 (36)
ECOG PS at study entry (N,%)	Grade 0	20 (31)	8 (21)
	Grade 1	44 (69)	31 (79)
Histology (N, %)	Squamous	19 (30)	12 (31)
	Non-squamous	45 (70)	27 (69)
Line of previous ICI (N,%)	1st line ICI	7 (11)	8 (20)
	2nd line ICI	56 (87)	31 (80)
	3rd line ICI	1 (2)	-
Best response to ICI (N, %)	CR / PR / SD	28 (44)	17 (44)
	Progression	36 (56)	22 (56)
TNM Stage at study entry (N,%)	III	4 (7)	5 (13)
	IV	54 (93)	33 (87)
Metastases at study entry (N,%)	Brain	11 (17%)	3 (8%)
	Liver	15 (23%)	9 (23%)
	Pleural	20 (31%)	11 (28%)

Cut-off 26FEB2020 before COVID-19 impact : 103 patients with a follow-up of 1 year (210 randomised patients)

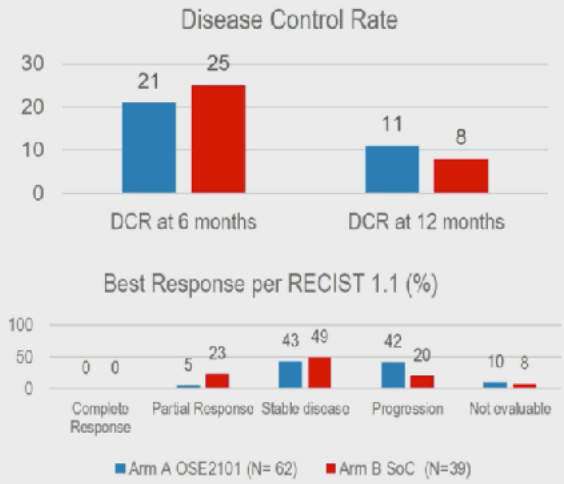
Step-1 primary endpoint achieved with a 1y-OS rate of 46%



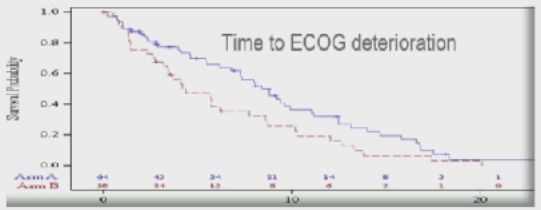
	Arm A OSE2101 (N= 63)	Arm B SoC (N=36)
1y-OS rate (95%CI)	46% (33, 59)	36% (21, 54)
Median OS (mo.) (95%CI)	9.8 (8.0, 13.5)	8.7 (5.8, 12.1)
HR stratified (95%CI); p value	0.71 (0.44, 1.16); p=0.17	

Cut-off 26FEB2020 before COVID-19 impact: 103 patients with 1year of Follow Up; Step 1 primary endpoint 1y-OS rate in mITT (99 patients); Kaplan-Meier OS in ITT (103 patients)

Good ECOG PS status maintained longer with OSE2101



	Arm A OSE2101 (N= 63)	Arm B SoC (N=36)	HR stratified (95%CI)
PFS (median in mo.)	1.7	4.3	1.5 (0.9, 2.5)
Time to ECOG deterioration* (median in mo.)	8.4	4.4	0.44 (0.26, 0.75)



* p = 0.002: Time from randomization to earliest time when ECOG becomes >1; patients who died without ECOG>1 were assigned ECOG=5

Less severe adverse effects in OSE2101 (14%) vs SoC (43%)*

	Arm A OSE2101 (N=63)		Arm B SoC (N=37)	
	All grade N (%)	Severe G3-4 N (%)	All grade N (%)	Severe G3-4 N (%)
All Drug-Related AEs	**50 (79)**	**9 (14)**	**28 (76)**	**16 (43)**
Drug-Related AEs > 10% of patients				
Injection site reaction*	35 (56)	1 (2)	1 (3)	-
Pyrexia	10 (16)	-	2 (5)	-
Asthenia	9 (14)	-	13 (35)	4 (11)
Cytokine release syndrome	7 (11)	1 (2)	-	-
Alopecia	-	-	14 (38)	2 (5)
Neutropenia	-	-	8 (22)	7 (19)
Decrease appetite	2 (3)	-	6 (16)	-
Diarrhea	2 (3)	1 (2)	5 (14)	2 (5)
Anemia	-	-	5 (14)	-
Nausea	2 (3)	-	4 (11)	-
Fatigue	5 (8)	-	4 (11)	1 (3)
Pain in extremity	1 (2)	-	4 (11)	-

Cut-off 26FEB2020 before COVID-19 impact; Safety set 100 patients (3 patients not treated);
*Injection site reaction as high-level term for injection site pain, nodular erythema, induration, inflammation, pain, pruritus... * p<0.05

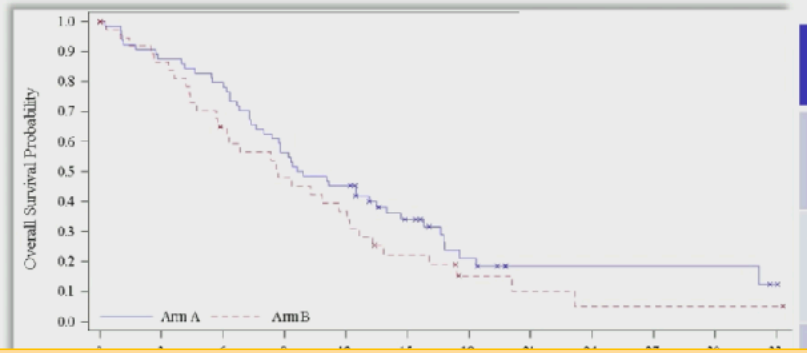
#1260MO

ORIENT-12: sintilimab plus gemcitabine and platinum (GP) as first-line (1L) treatment for locally advanced or metastatic squamous non-small-cell lung cancer (sqNSCLC)

		Arm A OSE2101 (N=64)	Arm B SoC (N=39)
Age (years)	Median (range)	65.5 (44, 82)	62.0 (43, 71)
Gender (N, %)	Male	44 (69)	25 (64)
	Female	20 (31)	14 (36)
ECOG PS at study entry (N,%)	Grade 0	20 (31)	8 (21)
	Grade 1	44 (69)	31 (79)
Histology (N, %)	Squamous	19 (30)	12 (31)
	Non-squamous	45 (70)	27 (69)
Line of previous ICI (N,%)	1st line ICI	7 (11)	8 (20)
	2nd line ICI	56 (87)	31 (80)
	3rd line ICI	1 (2)	-
Best response to ICI (N, %)	CR / PR / SD	28 (44)	17 (44)
	Progression	36 (56)	22 (56)
TNM Stage at study entry (N,%)			
Metastases at study entry (N,%)			

Cut-off 26FEB2020 before COVID-19 im

Step-1 primary endpoint achieved with a 1y-OS rate of 46%



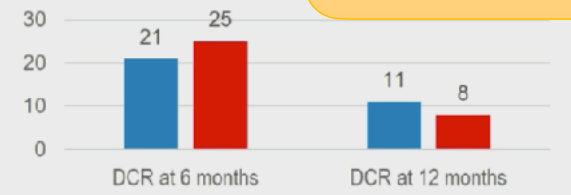
	Arm A OSE2101 (N= 63)	Arm B SoC (N=36)
1y-OS rate (95%CI)	46% (33, 59)	36% (21, 54)
Median OS (mo.) (95%CI)	9.8 (8.0, 13.5)	8.7 (5.8, 12.1)
HR		(0.44, 1.16); p=0.17

TT (99 patients); Kaplan-

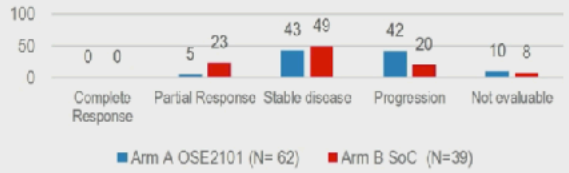
- Step-1 primary endpoint 1y-OS rate 46% with OSE2101
- OSE2101 better tolerated than SoC and with less deterioration of ECOG PS
- Prematurely closed on Feb'20 due tu COVID-19 pandemic emergence and safety risks
- Favorable benefit of OSE2101 over SoC in mNSCLC in HLA-A2+ patients.
- FU for OS; combination studies

Good ECOG PS status ma

Disease Co



Best Response per RECIST 1.1 (%)



PFS (median in mo.)	1.7	4.3	1.5 (0.9, 2.5)
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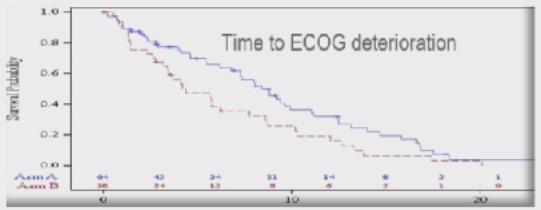


* p = 0.002: Time from randomization to earliest time when ECOG becomes >1; patients who died without ECOG>1 were assigned ECOG=5

	Arm B SoC (N=37)	
	All grade N (%)	Severe G3-4 N (%)
All Drug-Related AEs	28 (76)	16 (43)
Drug-Related AEs > 10% of patients		
Injection site reaction*	1 (3)	-
Pyrexia	2 (5)	-
Asthenia	13 (35)	4 (11)
Cytokine release syndrome	-	-
Alopecia	14 (38)	2 (5)
Neutropenia	8 (22)	7 (19)
Decrease appetite	6 (16)	-
Diarrhea	5 (14)	2 (5)
Anemia	5 (14)	-
Nausea	4 (11)	-
Fatigue	4 (11)	1 (3)
Pain in extremity	4 (11)	-

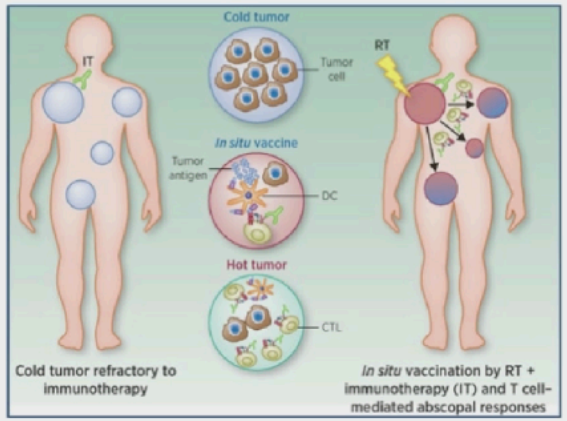
Cut-off 26FEB2020 before COVID-19 impact; Safety set 100 patients (3 patients not treated);
*Injection site reaction as high-level term for injection site pain, nodular erythema, induration, inflammation, pain, pruritus... * p<0.05

#LBA58

ORR in patients receiving Nivolumab plus radiotherapy in advanced Non-Small Cell Lung Cancer - first results from the FORCE trial. *Bozorgmehr F et al*

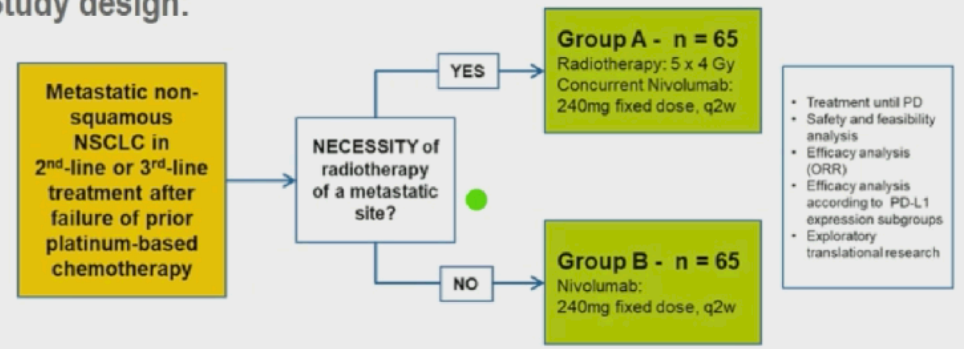
Hypothesis:

Ionizing radiation enhances an anti-tumor immunity, which is boosted/unleashed by immune checkpoint blockade.



Baker et al., Radiation Oncology 2016

Study design:



Sample size justification:

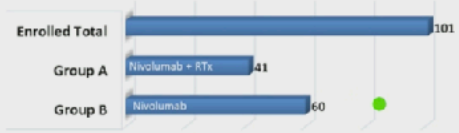
- ORR in nivolumab-treated group is assumed to be 19% (CM-057) [Borghaei et al, NEJM 2015].
- Based on the reported ORR of 37% in a PD-L1>10% expressing population [Borghaei et al, NEJM 2015], an ORR of 35% is expected for nivolumab-RT combination treatment.
- N=50 subjects per group are required to detect **whether the ORR is >19%** by applying a binomial test at a one-sided significance level of 0.05 with a probability of 1-b=0.8, assuming an actual response rate of 35% [Borghaei et al, NEJM 2015].
- N=65 patients per group will be enrolled to take potential dropouts and patients with a lacking PD-L1 assessment into account.

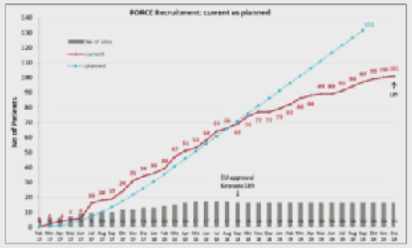
#LBA58

ORR in patients receiving Nivolumab plus radiotherapy in advanced Non-Small Cell Lung Cancer - first results from the FORCE trial

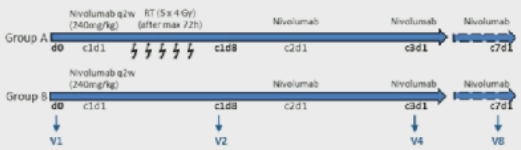
Recruitment, biomarker acquisition and sites of irradiation

Recruitment: 101 patients / 16 centers





Biomarker sample aquisition:
at 4 time points per patient



Preliminary forecast: 85% sample return rate

Site of irradiation (Group A)	n (%)
Bone	21 (51%)
Lymph node	7 (17%)
Skin	2 (5%)
Other	11 (27%)

VIRTUAL ESMO 2020 congress

Baseline characteristics

unfavorable characteristics more prevalent in patients receiving nivolumab plus radiotherapy (group A)

		Group A (Nivolumab+RTx) n = 41 (100%)	Group B (Nivolumab only) n= 60 (100%)	p-value (Chi²)	
Gender	Male	24 (58.5%)	35 (58%)	0.984	
Mean age		64.7 ± 7.2	67.7 ± 8.7	0.069	
Smoking history		40 (97.5%)	52 (87%)	0.059	
Line of Nivolumab treatment	2nd-line	33 (80.5%)	53 (88%)	0.276	
	3rd-line	8 (19.5%)	7 (12%)		
PDL1-Status	≥ 1	18 (47% of 38)	36 (64% of 56)	0.104	
ECOG performance status	1	33 (80.5%)	35 (58%)	0.02	In group A:
CCI	≥ 2	9 (22%)	13 (22%)	0.973	
SCS	> 9	7 (17%)	8 (13%)	0.604	
M-Status (UICC8)	M1a	7 (17%)	27 (46%)	0.006	← less M1a
	M1b	10 (24%)	14 (24%)		
	M1c	24 (58.5%)	18 (30.5%)		← more M1c
Metastatic type	Single/oligo	10 (25%)	17 (29%)	0.639	
	Diffuse/multiple	30 (75%)	41 (71%)		
Intrathoracic metastases		26 (63%)	42 (71%)	0.413	
Extrathoracic mets		38 (93%)	37 (63%)	< 0.001	← more extrathoracic mets
- Skin		7 (18% of 38)	1 (1% of 37)	0.027	
- Bone		25 (66% of 38)	13 (35% of 37)	0.008	← more bone mets
- Liver / kidney / brain / adrenal gland / LN / other sites of metastatic disease				not significant	

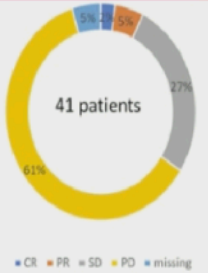
Response rate: primary objective of achieving an ORR > 19% in group A could not be met. Treatment related AEs: no difference in frequency or severity observed.

Response rate:

The primary objective was to achieve an ORR > 19 % in group A

→ This objective could not be met (p=0.991 for one-sided binomial test).

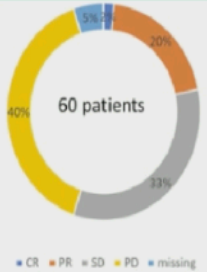
Group A Nivolumab + RTx



imputed RR 8%

imputed DCR 35%

Group B Nivolumab only



imputed RR 24%

imputed DCR 57%

Treatment related AEs:

		Group A	Group B	p-value
Patients with treatment related AEs grade 3-4		7 (17%)	9 (15%)	0.779 (Chi²-test)
Number of treatment related AEs grade 3-4	1	6 (86%)	5 (56%)	0.176 (Mann-Whitney-U-test)
	2	1 (14%)	1 (11%)	
	3	0	2 (22%)	
	9	0	1 (11%)	
	total	8	22	

#LBA58

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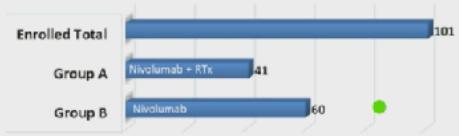
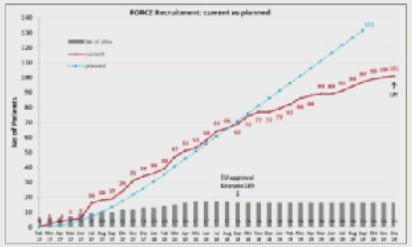
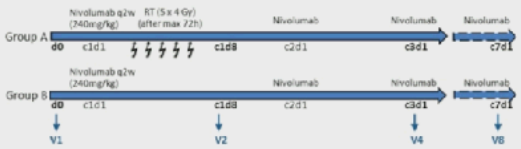




Biomarker sample aquisition:
at 4 time points per patient



Preliminary forecast: 85% sample return rate

Site of irradiation (Group A)	n (%)
Bone	21 (51%)
Lymph node	7 (17%)
Skin	2 (5%)
Other	11 (27%)

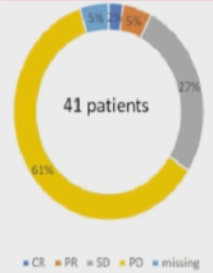
Response rate: primary objective of achieving an ORR > 19% in group A could not be met. Treatment related AEs: no difference in frequency or severity observed.

Response rate:

The primary objective was to achieve an ORR > 19 % in group A

→ This objective could not be met (p=0.991 for one-sided binomial test).

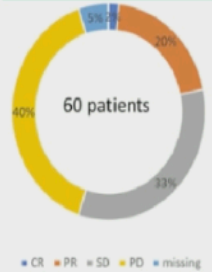
Group A
Nivolumab + RTx



imputed RR 8%

imputed DCR 35%

Group B
Nivolumab only



imputed RR 24%

imputed DCR 57%

Treatment related AEs:

		Group A	Group B	p-value
Patients with treatment related AEs grade 3-4		7 (17%)	9 (15%)	0.779 (Chi^2-test)
Number of treatment related AEs grade 3-4	1	6 (86%)	5 (56%)	0.176 (Mann-Whitney-U-test)
	2	1 (14%)	1 (11%)	
	3	0	2 (22%)	
	9	0	1 (11%)	
	total	8	22	

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Baseline characteristics

unfavorable characteristics more prevalent in patients receiving nivolumab plus radiotherapy (group A)

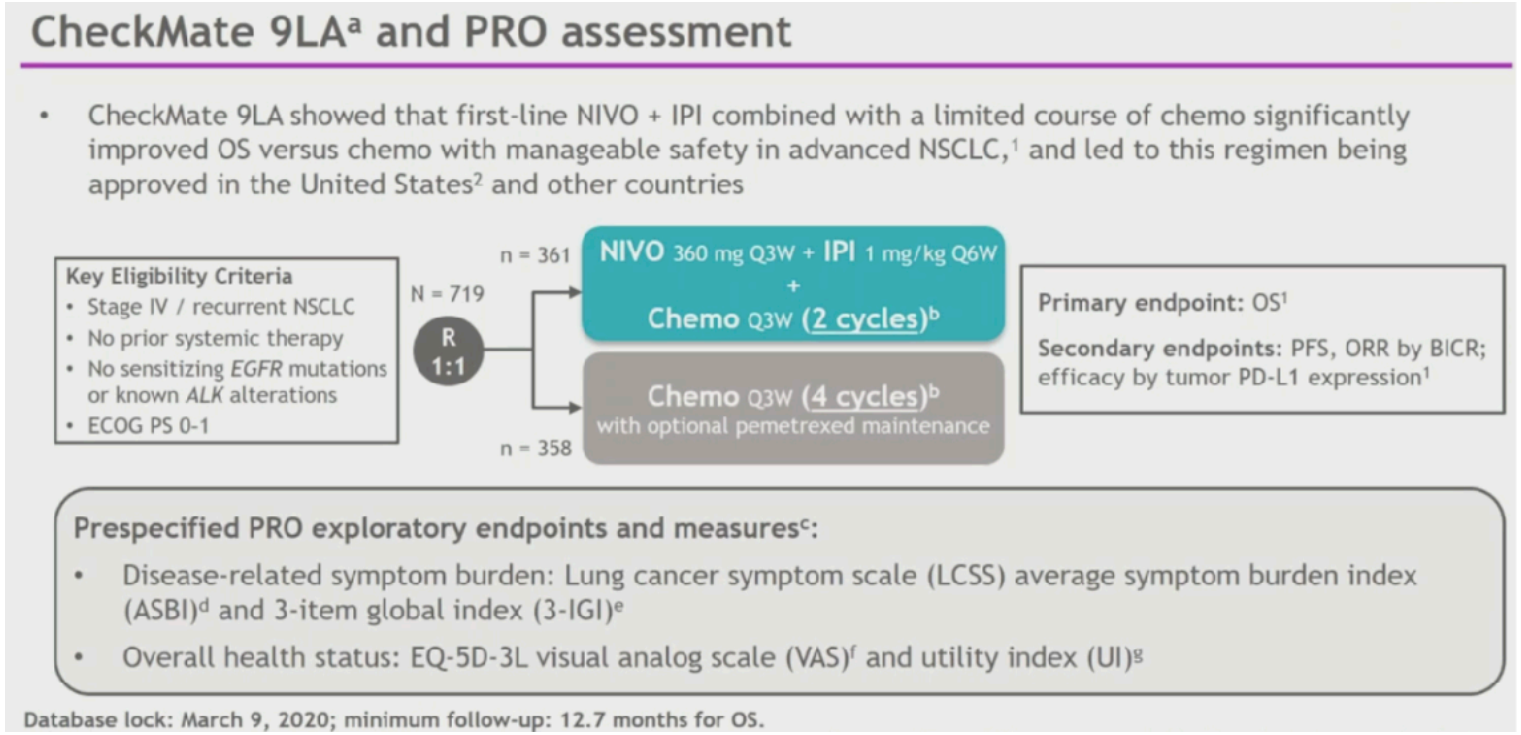
		Group A (Nivolumab+RTx) n = 41 (100%)	Group B (Nivolumab only) n= 60 (100%)	p-value (Chi^2)
Gender	Male	24 (58.5%)	35 (58%)	0.984
Mean age		64.7 ± 7.2	67.7 ± 8.7	0.069
Smoking history		40 (97.5%)	52 (87%)	0.059
Line of Nivolumab treatment	2nd-line	33 (80.5%)	53 (88%)	0.276
	3rd-line	8 (19.5%)	7 (12%)	
PDL1-Status	≥ 1	18 (47% of 38)	36 (64% of 56)	0.104
ECOG performance status	1	33 (80.5%)	35 (58%)	0.02
CCI	≥ 2	9 (22%)	13 (22%)	0.973
SCS	> 9	7 (17%)	8 (13%)	0.604
M-Status (UICC8)	M1a	7 (17%)	27 (46%)	0.006
	M1b	10 (24%)	14 (24%)	
	M1c	24 (58.5%)	18 (30.5%)	
Metastatic type	Single/oligo	10 (25%)	17 (29%)	0.639
	Diffuse/multiple	30 (75%)	41 (71%)	
Intrathoracic metastases		26 (63%)	42 (71%)	0.413
Extrathoracic mets		38 (93%)	37 (63%)	< 0.001
- Skin		7 (18% of 38)	1 (1% of 37)	0.027
- Bone		25 (66% of 38)	13 (35% of 37)	0.008
- Liver / kidney / brain / adrenal gland / LN / other sites of metastatic disease				not significant

In group A:
- ← more ECOG 1
- ← less M1a
- ← more M1c
- ← more extrathoracic mets
- ← more bone mets

- Combination of Nivo + RT safe and feasible
- Premature close. Disbalance in experimental arm (more ECOG 1, higher tumor load and bone mts)
- 8% ORR below expected. No strong abscopal effect observed

#LBA59

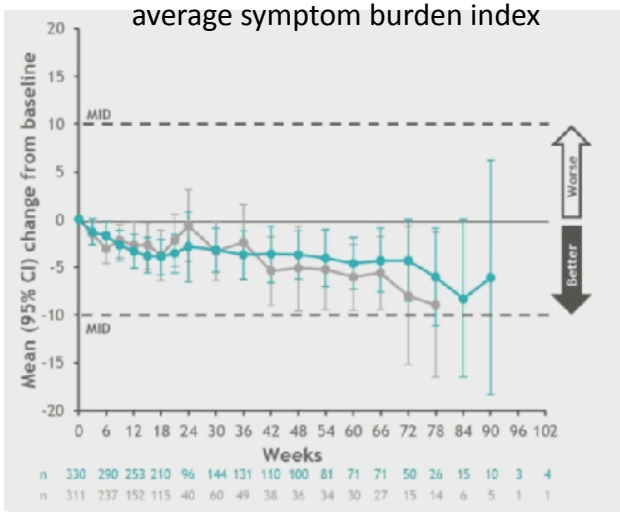
First-line nivolumab (NIVO) + ipilimumab (IPI) combined with 2 cycles of platinum-based chemotherapy (chemo) vs 4 cycles of chemo in advanced non-small cell lung cancer (NSCLC): Patient-reported outcomes (PROs) from CheckMate 9LA. *Reck M et al.*



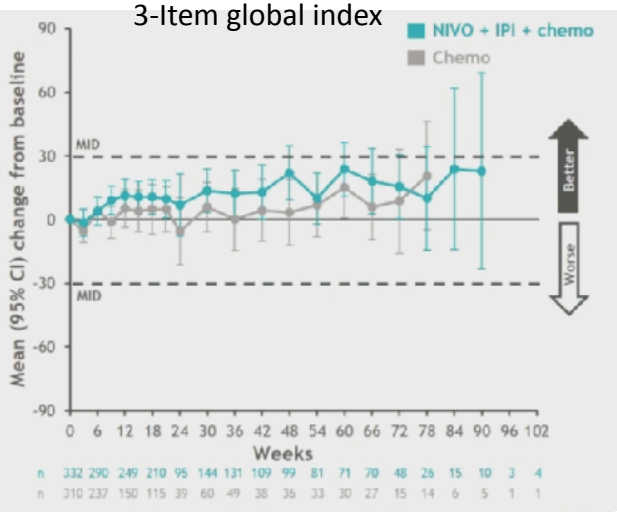
#LBA59

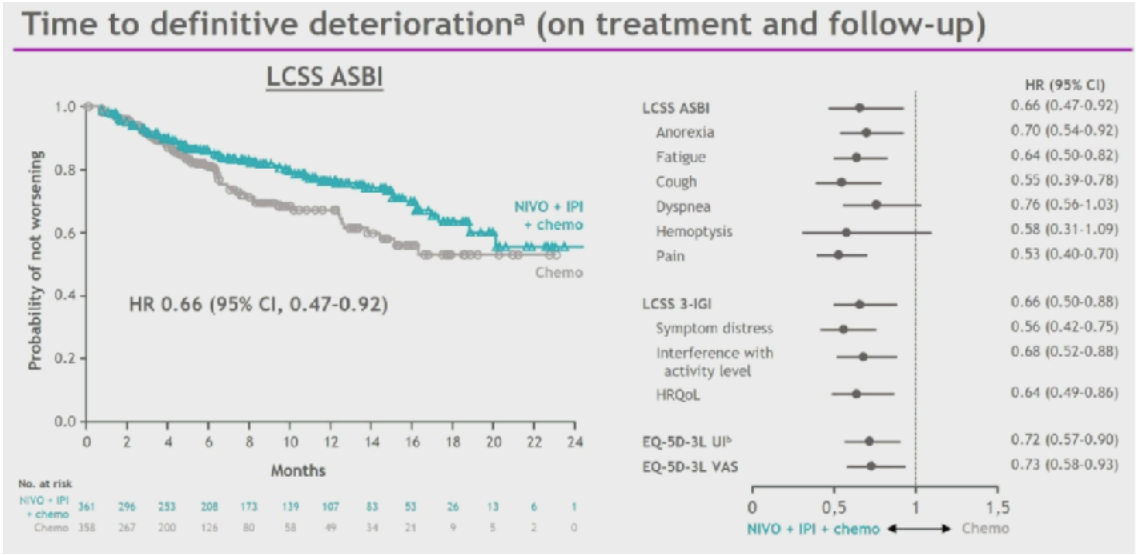
ORR in patients receiving Nivolumab plus radiotherapy in advanced Non-Small Cell Lung Cancer - first results from the FORCE trial

Lung cancer symptom scale
average symptom burden index

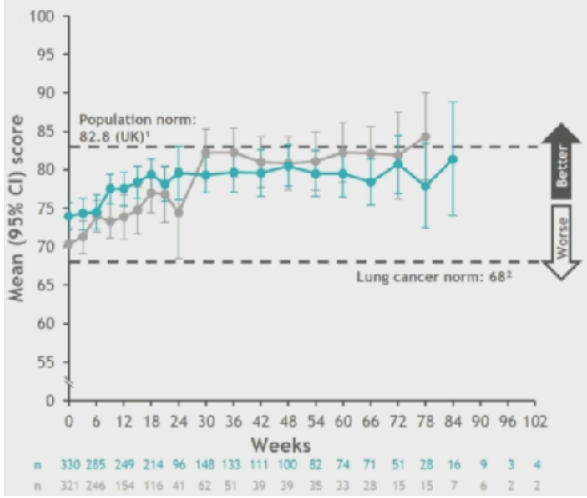


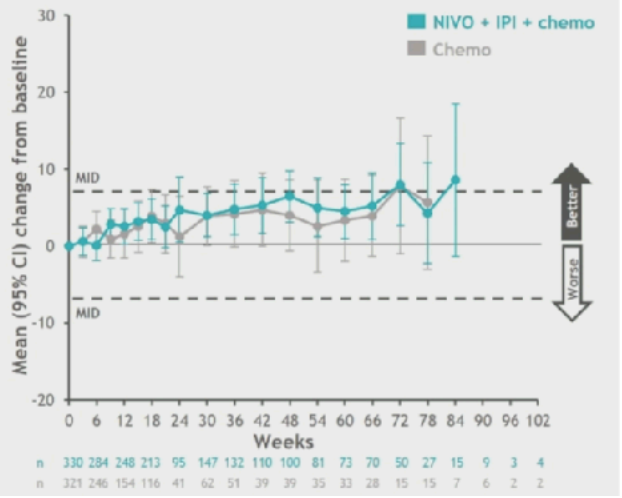
Lung cancer symptom scale
3-Item global index





EQ-5D-3L VAS





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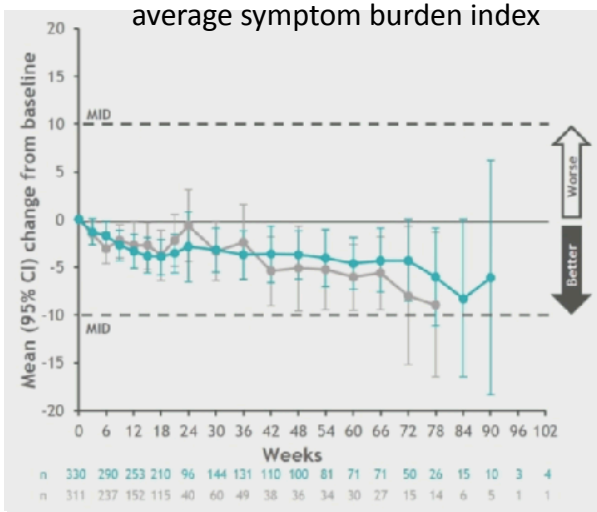
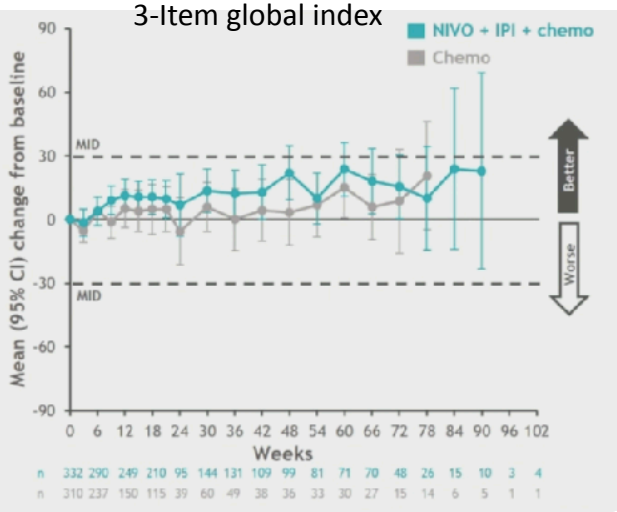


Lung cancer symptom scale
3-Item global index



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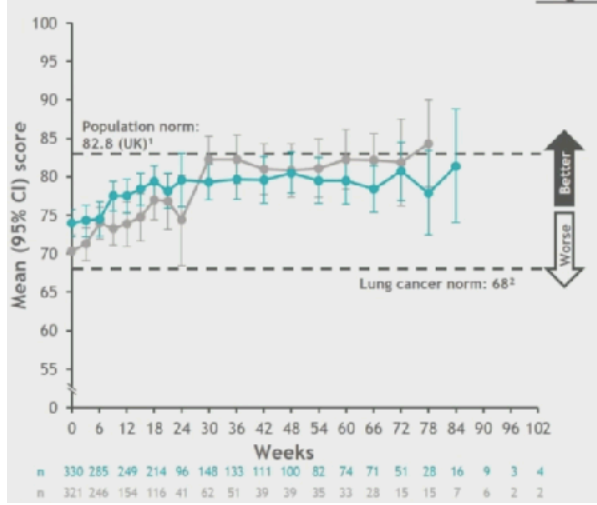

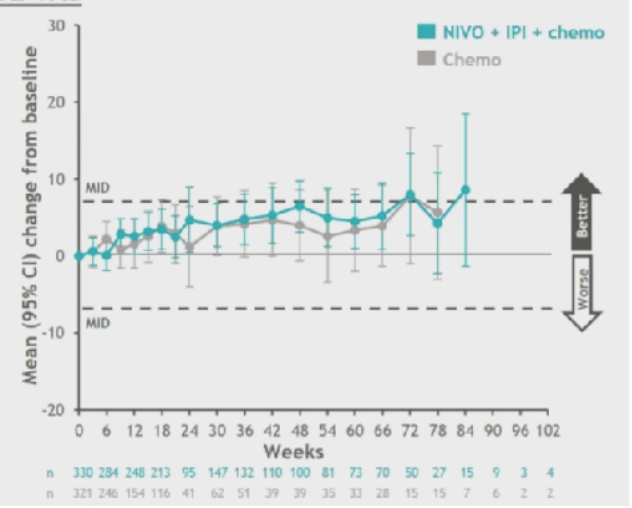

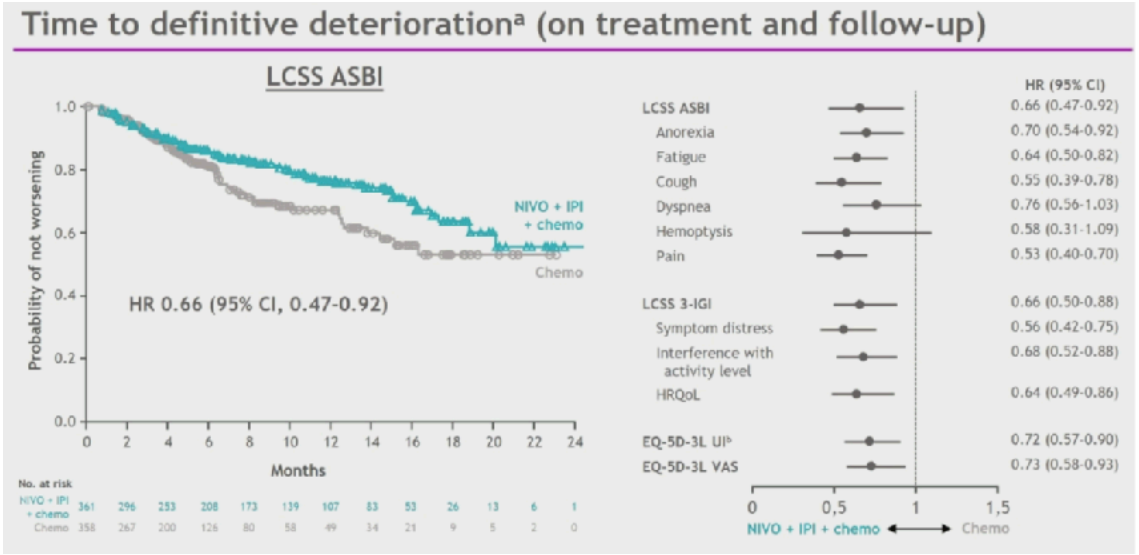

- Nivo+Ipi + chemo 2 cycles maintained or improved symptom burden and overall health status from baseline similar to chemo
- Decreased risk and delayed time to definitive deterioration in health-related QoL with combo

Lung Cancer UPDATES
ESMO HIGHLIGTHS
19-21 SEPTIEMBRE 2020

Iniciativa científica de:
GECP lung cancer research

Cáncer de Pulmón metastásico sin dianas terapéuticas

Rafael López Castro

Hospital Clínico Universitario de Valladolid