Immunotherapy in Lung Cancer

Hossein Borghaei, MS, DO
Professor and Chief, Thoracic Oncology
The Gloria and Edmund M. Dunn Chair in Thoracic Oncology
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Disclosures

- **Research Support (Clinical Trials):**
  - Millennium, Merck/Celgene, BMS/Lilly
- **Advisory Board/Consultant:**
  - BMS, Lilly, Genentech, Celgene, Pfizer, Merck, EMD-Serono, Boehringer Ingelheim, Astra Zeneca, Novartis, Genmab, Regeneron, BioNTech, Cantargia AB, Amgen, Abbvie, Axiom, PharmaMar, Takeda, Huya Bio, GLG, Daiichi
- **Scientific Advisory Board:**
  - Sonnetbio (Shares), Rgenix (Shares)
- **Data and Safety Monitoring Board:**
  - University of Pennsylvania, CAR T Program, Takeda, Incyte
- **Employment:**
  - Fox Chase Cancer Center

FOX CHASE CANCER CENTER
TEMPLE HEALTH

Long Term Follow UP

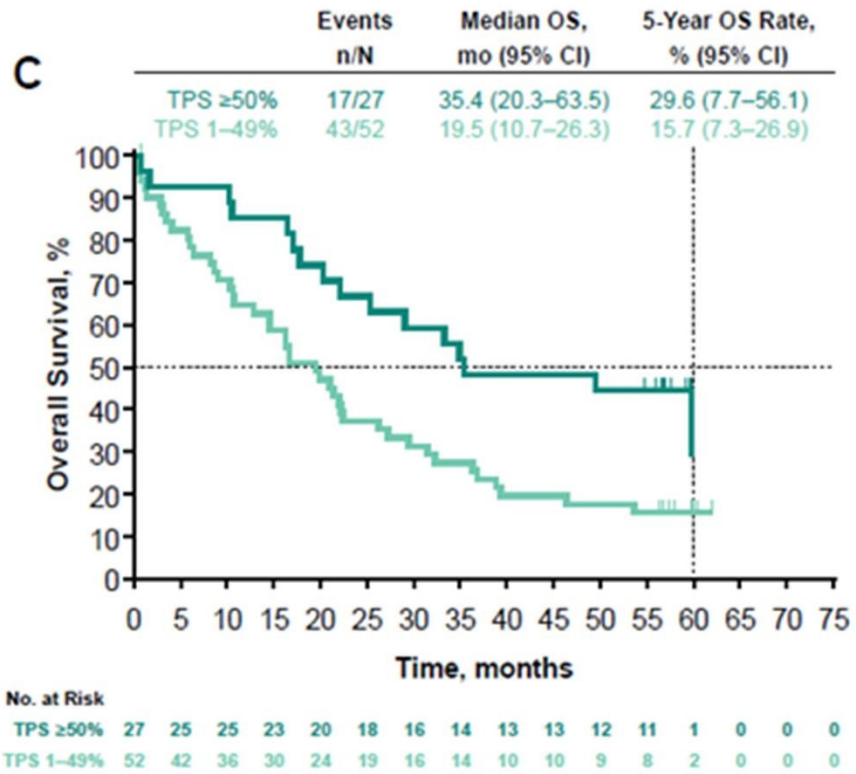
IO Trials

Garon KN001 ASCO 2019

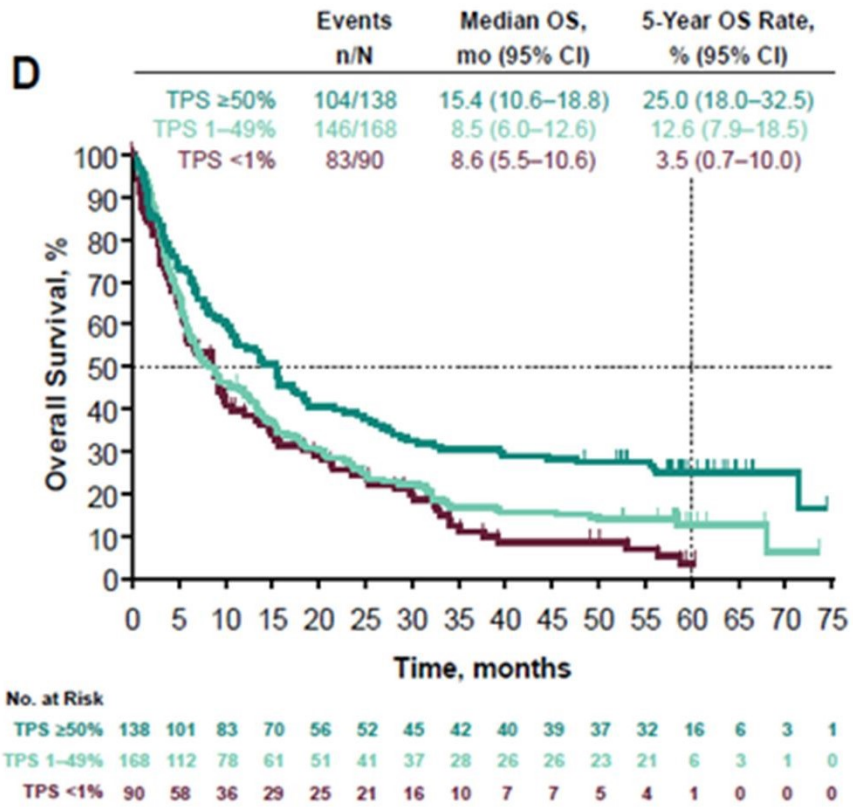
5 year OS: KN-001 Trial

Kaplan-Meier Estimates of OS: (C) Treatment Naive Patients by PD-L1 TPS ≥50% and 1%–49%.[a] (D) Previously Treated Patients by PD-L1 TPS ≥50%, 1%–49%, and <1%.

Treatment-Naive Patients

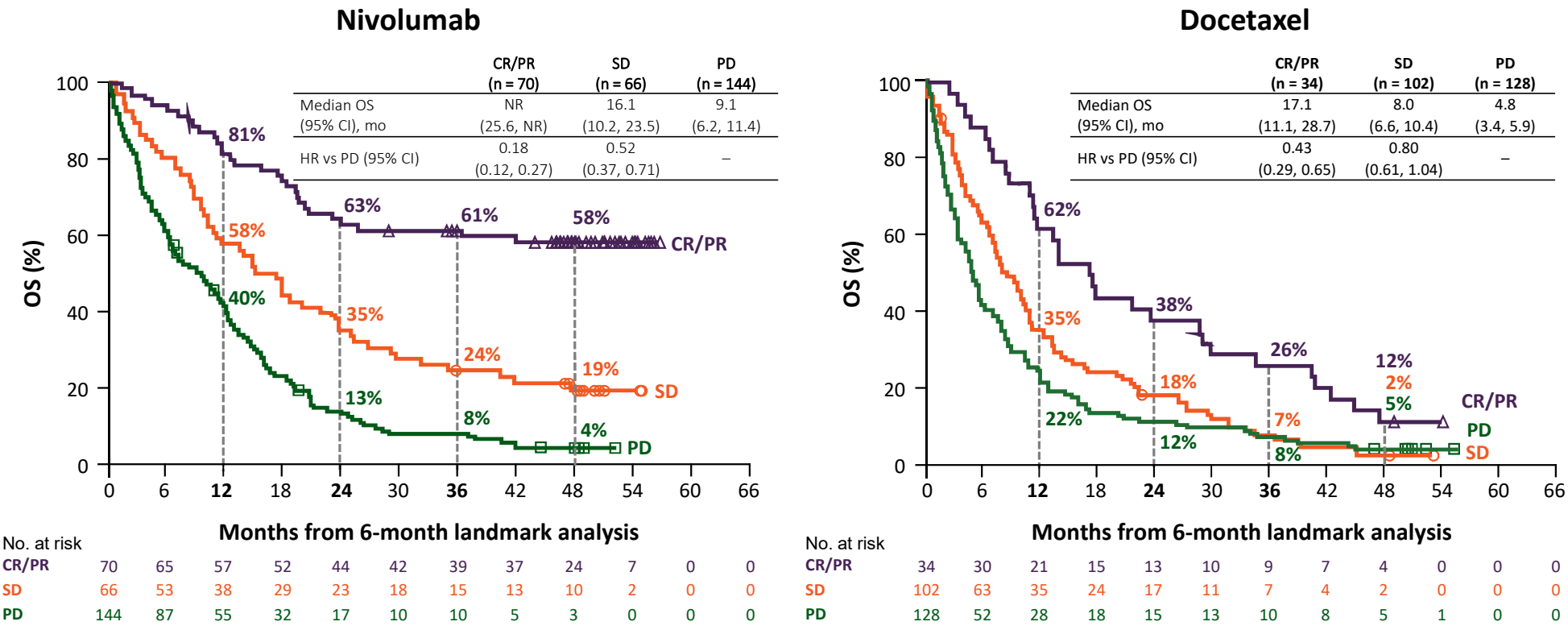


Previously Treated Patients



n, number of patients who died; N, number of patients in the group/subgroup.
[a]PD-L1 TPS <1% group not presented because of small patient numbers (n = 12).

Figure 4. Landmark analysis of OS by response category at 6 months in CheckMate 017/ 057[a]



Brahmer, AACR Poster, 2019

[a]In all randomized patients from CheckMate 017 and 057 studies alive at the 6-month landmark; 65.6% and 61.8% in the nivolumab and docetaxel treatment arms, respectively, were included.
NR, not reached

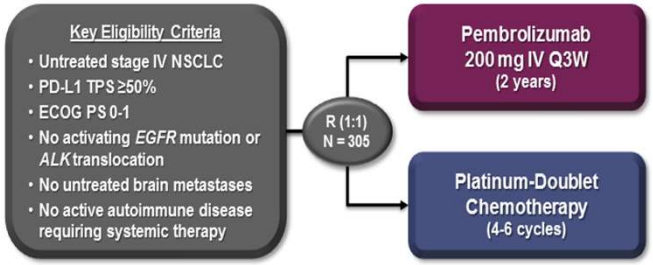
Immunotherapy of NSCLC

Single Agent

Front Line Protocols: IO only

M Reck. ESMO 2016.

KEYNOTE-024 Study Design (NCT02142738)



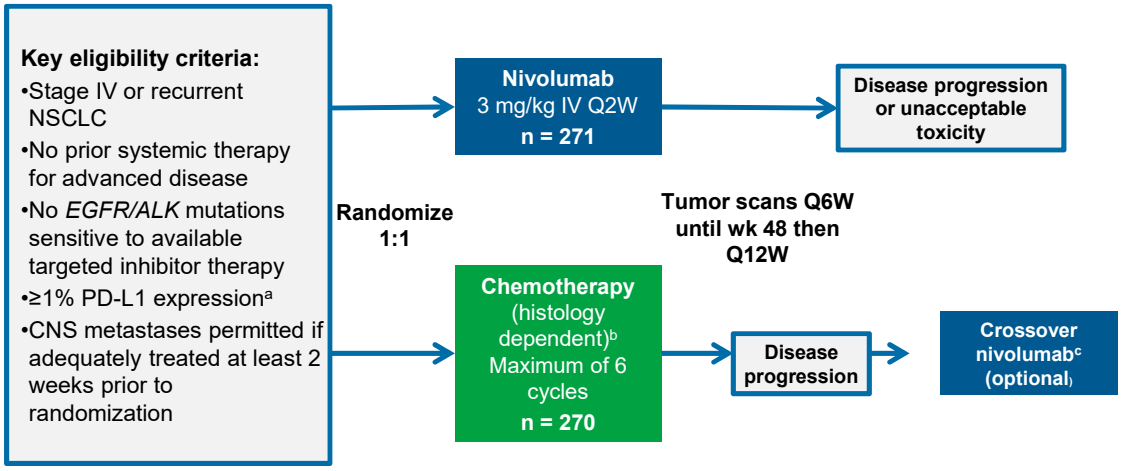
Key End Points

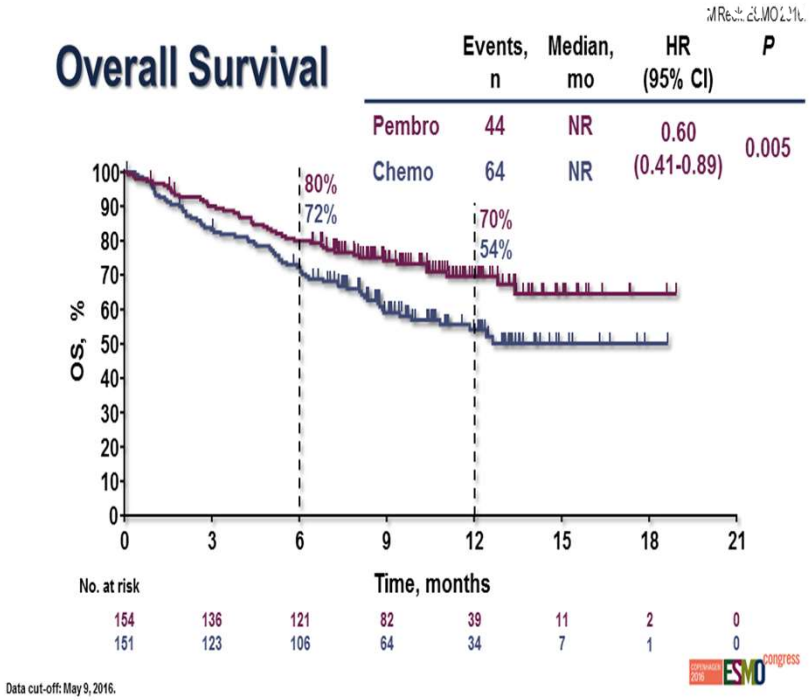
Primary: PFS (RECIST v1.1 per blinded, independent central review)

Secondary: OS, ORR, safety

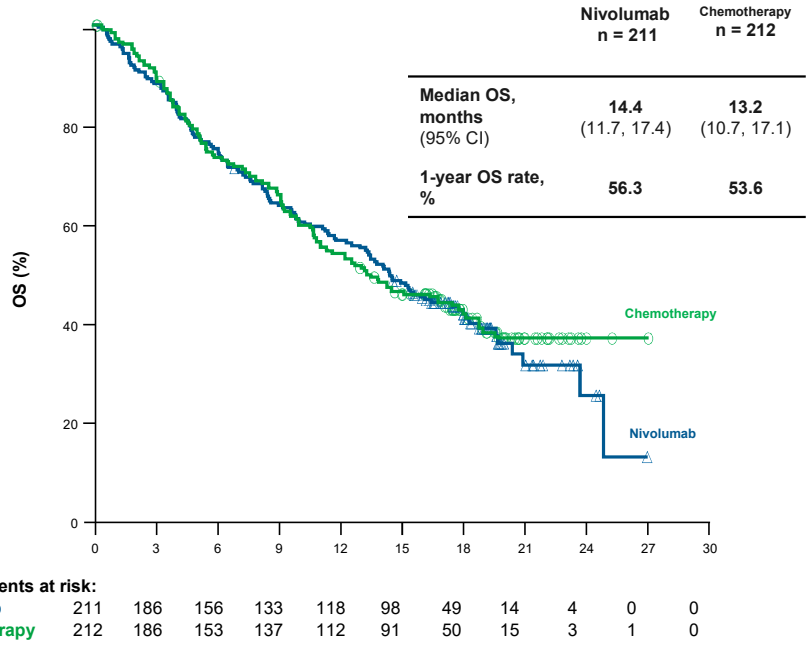
Exploratory: DOR

CheckMate-026





KEYNOTE-024: Reck, NEJM 2016



CheckMate-026: Carbone, NEJM, 2017

KEYNOTE-024 5-Year Survival Update: Pembrolizumab Versus Platinum-Based Chemotherapy for Advanced NSCLC

Key eligibility criteria

- Untreated stage IV NSCLC
- PD-L1 TPS ≥50%
- ECOG PS 0-1
- No activating *EGFR* mutation or *ALK* tranlocation
- No untreated brain metastases
- No active autoimmune disease requiring systemic therapy

R (1:1)
N = 305

Pembrolizumab
200 mg IV Q3W
(2 years)

Platinum-Doublet Chemotherapy
(4-6 cycles)

PD[a]

Pembrolizumab
200 mg Q3W
for 2 years

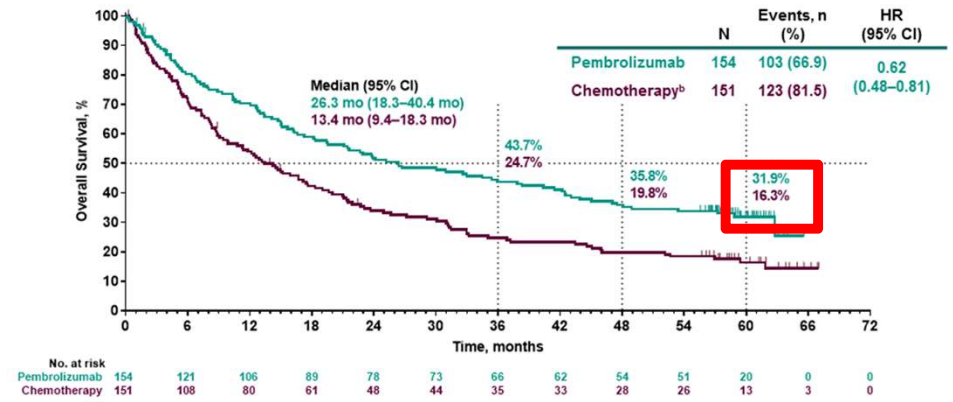
Key endpoints

- Primary: Progression-free survival (PFS) (RECIST v1.1 per blinded, independent central review)
- Secondary: OS, ORR, safety
- Exploratory: Duration of response (DoR)

[a]To be eligible for crossover, progressive disease (PD) had to be confirmed by blinded, independent central radiology review and all safety criteria had to be met.

J Brahmer. ESMO 2020

Overall Survival[a]



[a]ITT population.
[b]Effective crossover rate from chemotherapy to anti–PD-(L)1 therapy, 66.0% (99 patients in total crossed over to anti–PD-[L]1 therapy: 83 patients crossed over to pembrolizumab during the study, and 16 patients received subsequent anti–PD-[L]1 therapy outside of crossover; patients may have received >1 subsequent anti–PD-[L]1 therapy). Data cutoff: June 1, 2020.

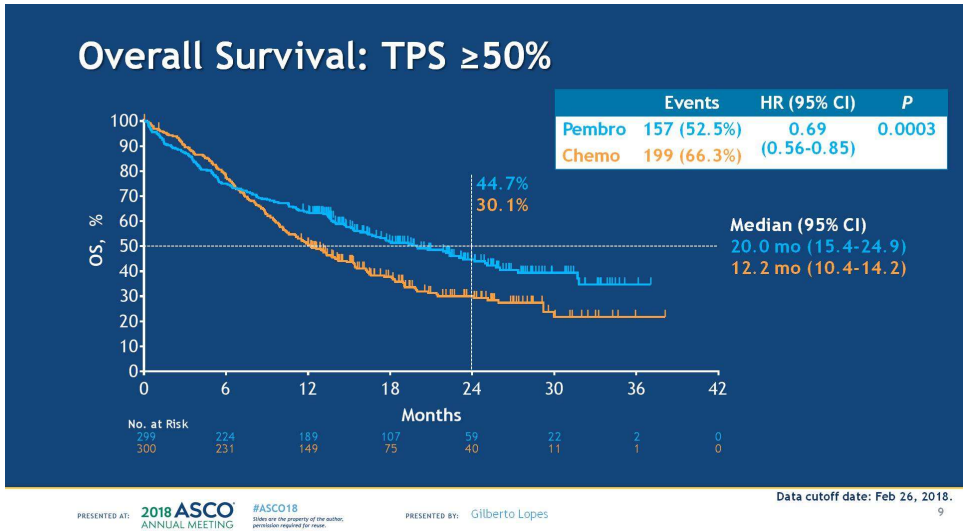
J Brahmer. ESMO 2020

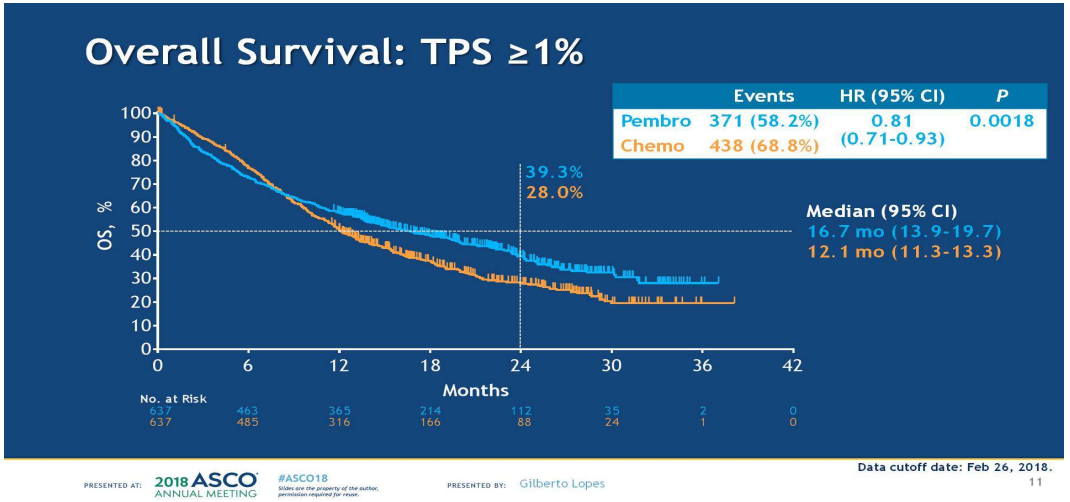
Baseline Characteristics

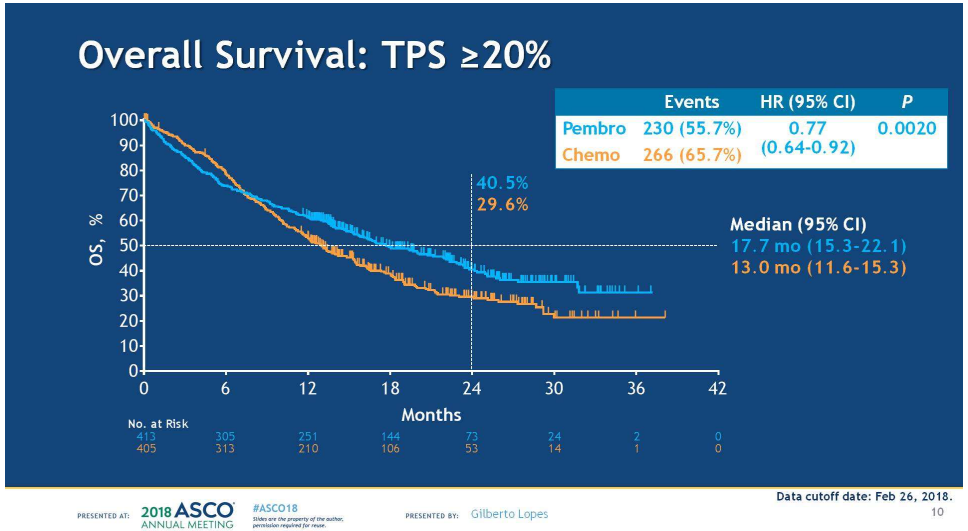
Characteristic	Pembrolizumab N = 154	Chemotherapy N = 151	35 Cycles (2 Years) of Pembrolizumab N = 39[a]	Second Course of Pembrolizumab N = 12[b]
Age, y, median (range)	64.5 (33–90)	66.0 (38–85)	61.0 (43–80)	60.0 (43–77)
Male	92 (59.7)	95 (62.9)	25 (64.1)	8 (66.7)
ECOG PS 1	99 (64.3)	98 (64.9)	23 (59.0)	9 (75.0)
East Asian enrollment site	21 (13.6)	19 (12.6)	8 (20.5)	3 (25.0)
Squamous histology	29 (18.8)	27 (17.9)[c]	2 (5.1)	1 (8.3)
Current/former smoker	149 (96.8)	132 (87.4)	37 (94.9)	12 (100.0)
Treated brain metastases	18 (11.7)	10 (6.6)	9 (23.1)	1 (8.3)
Prior neoadjuvant therapy	3 (1.9)	1 (0.7)	0	0
Prior adjuvant therapy	6 (3.9)	3 (2.0)	0	0

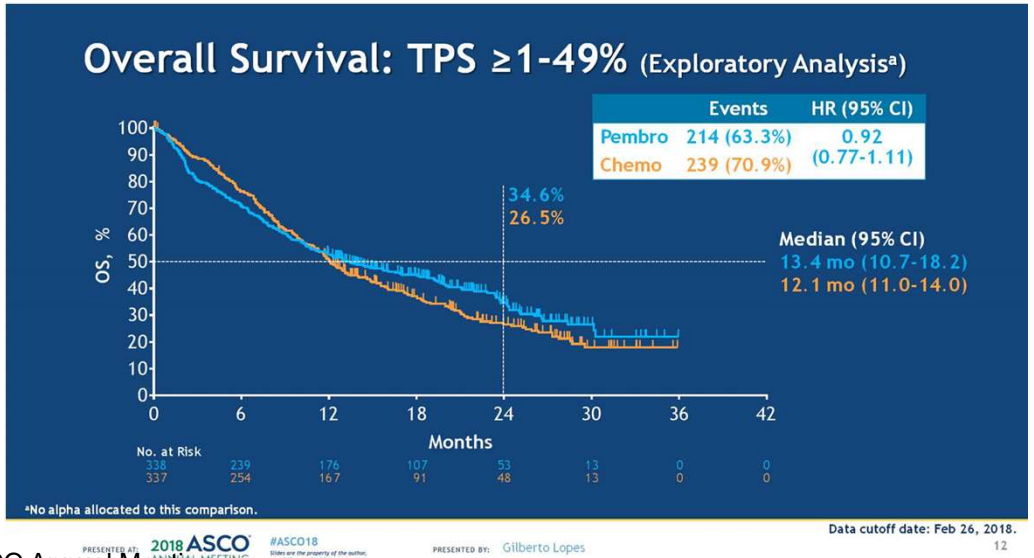
[a]Includes only those patients initially allocated to pembrolizumab who received 35 cycles (2 years) of pembrolizumab according to actual exposure assessment. [b]Includes only those patients initially allocated to pembrolizumab who received a second course of pembrolizumab therapy according to actual exposure assessment. [c]Includes patients with squamous cell carcinoma and poorly differentiated squamous cell carcinoma. Data in table are n (%), unless otherwise noted. Data cutoff: June 1, 2020.

OS in All Sub Groups, KN-042



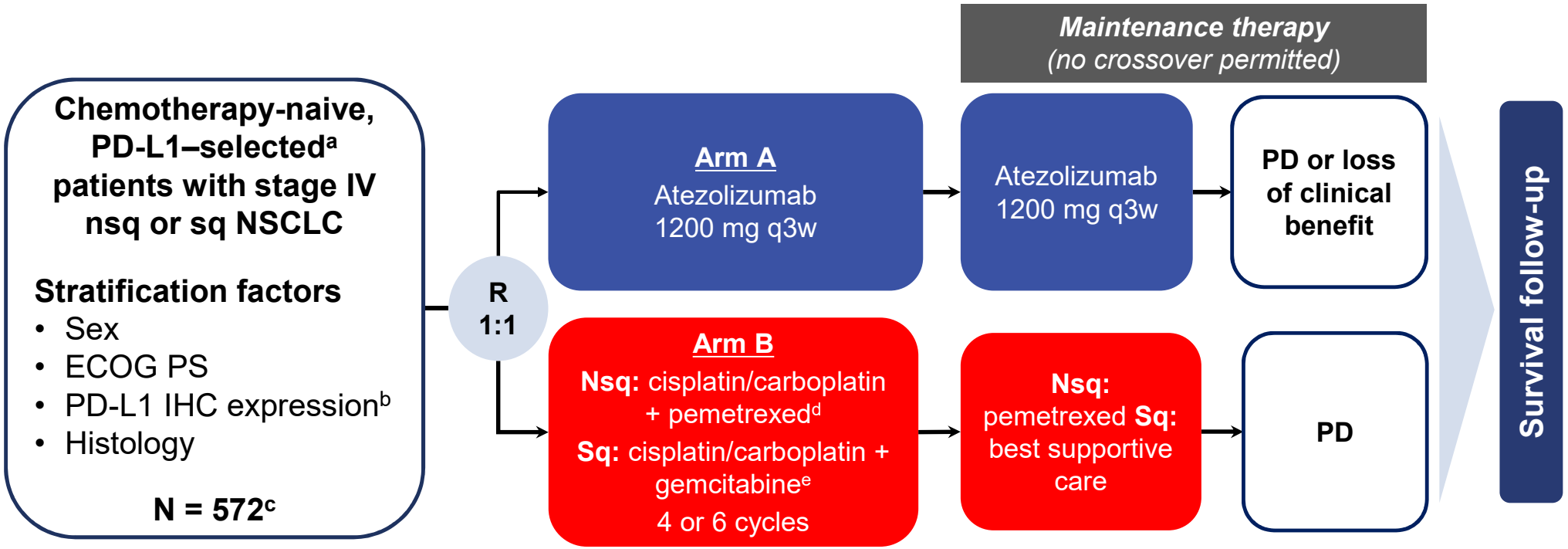






Presented By Gilberto Lopes at 2018 ASCO Annual Meeting

IMpower110 Study Design

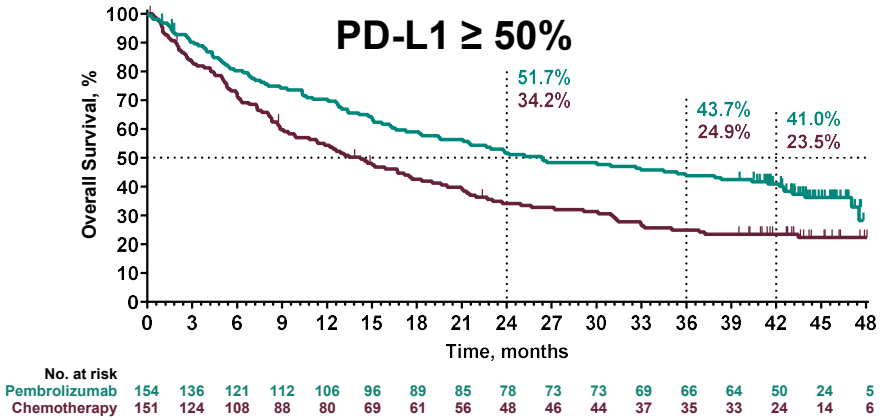


- Primary endpoint: OS in WT population[f]
- Key secondary endpoints: investigator-assessed PFS, ORR and DOR (per RECIST version 1.1)

IC, tumour-infiltrating immune cells; IHC, immunohistochemistry; nsq, non-squamous; PD, progressive disease; q3w, every 3 weeks; R, randomised; sq, squamous; TC, tumour cells; WT, wild-type. [a] PD-L1 expression (VENTANA SP142 IHC assay) ≥ 1% on TC or IC. [b] TC1/2/3 and any IC vs TC0 and IC1/2/3. [c] 554 patients in the WT population. [d] Cisplatin 75 mg/m^2 or carboplatin area under the curve (AUC) 6 + pemetrexed 500 mg/m^2 IV q3w. [e] Cisplatin 75 mg/m^2 + gemcitabine 1250 mg/m^2 or carboplatin AUC 5 + gemcitabine 1000 mg/m^2 IV q3w. [f] WT population excludes patients with *EGFR*+ and/or *ALK*+ NSCLC.

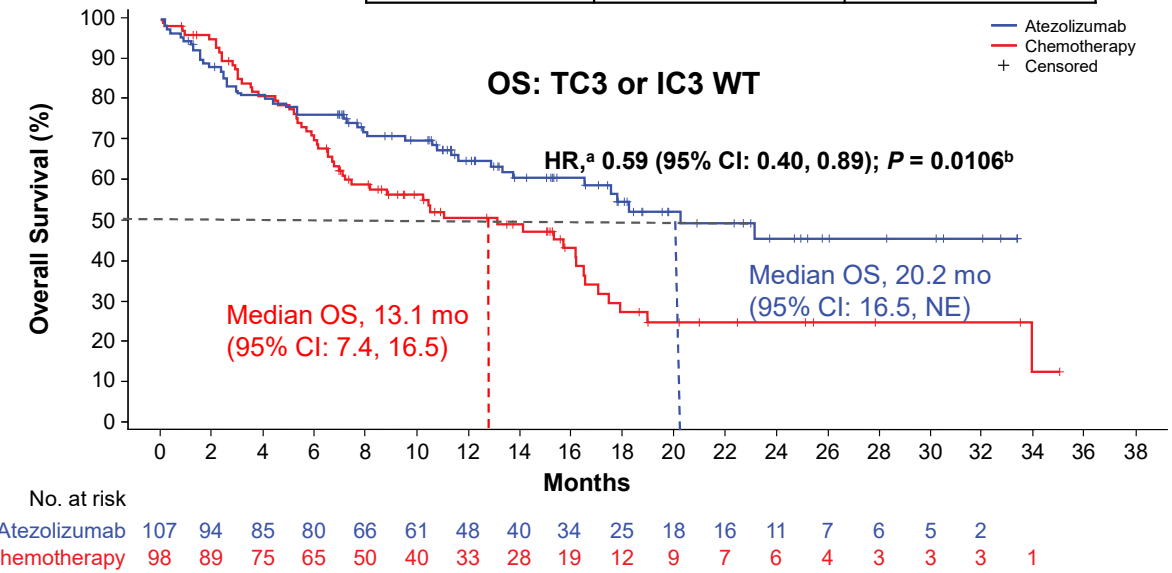
Spigel et al. IMpower110 Interim OS Analysis https://bit.ly/2IxRNHQ

PD-L1 High Groups



	N	Events, n (%)	HR (95% CI)
Pembrolizumab[a]	154	97 (63)	0.65 (0.50–0.86) *P* = 0.001[b]
Chemotherapy	151	113 (75)	

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)



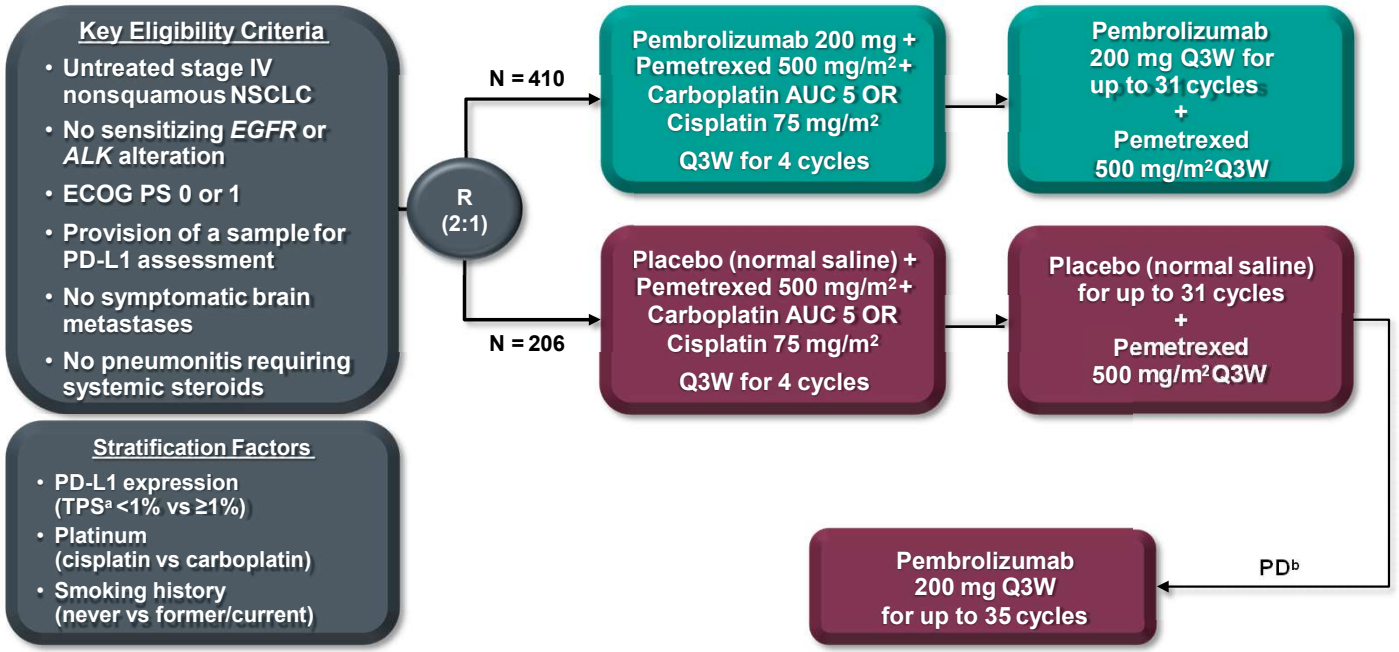
Reck M, et al. 3 year Update, KN-024 Presentation at WCLC 2019, September 7-10, Barcelona (OA14.01)

Spigel, Impower 110, Interim OS, ESMO, 2019

Immunotherapy of NSCLC

IO/Chemo combinations

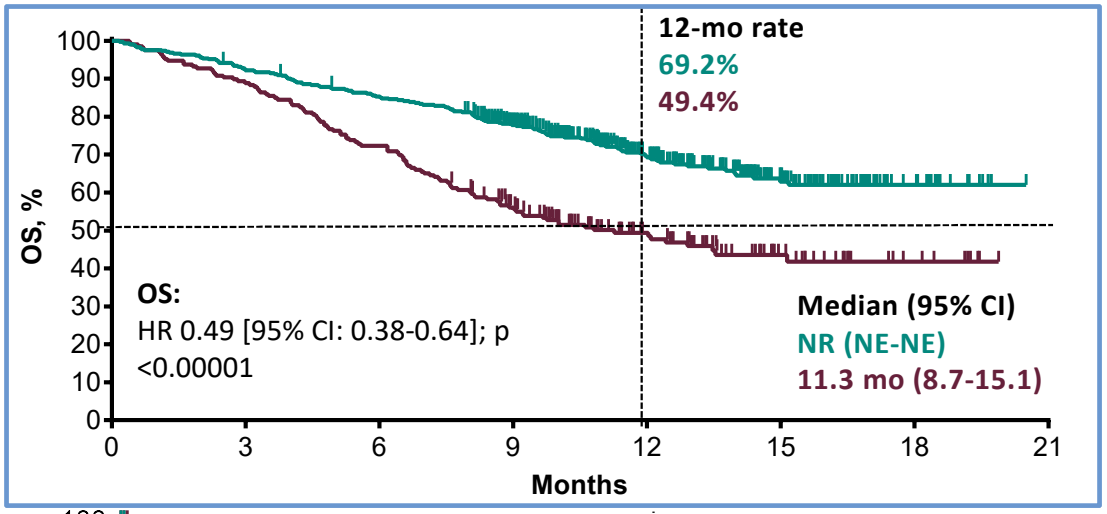
KEYNOTE-189 Study Design (NCT02578680)

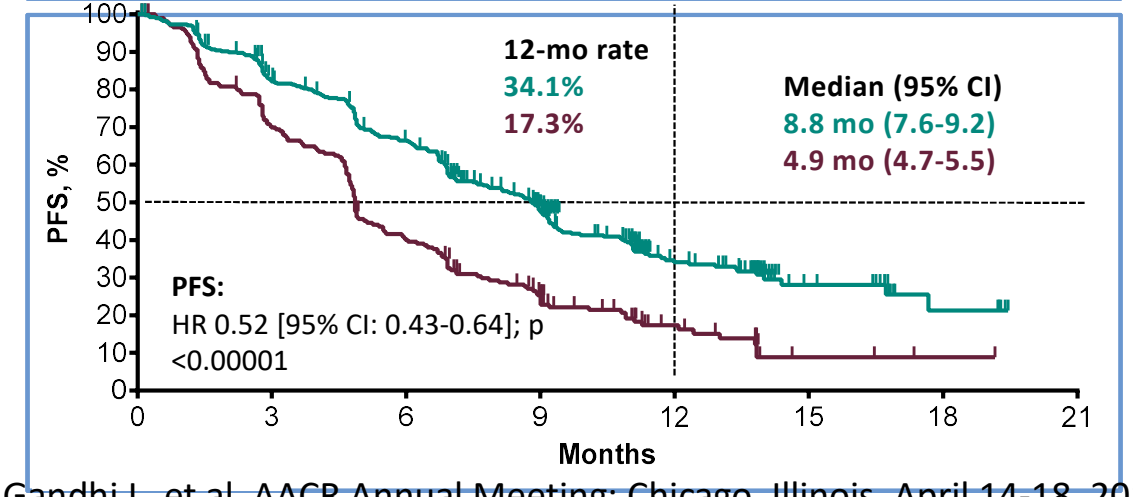


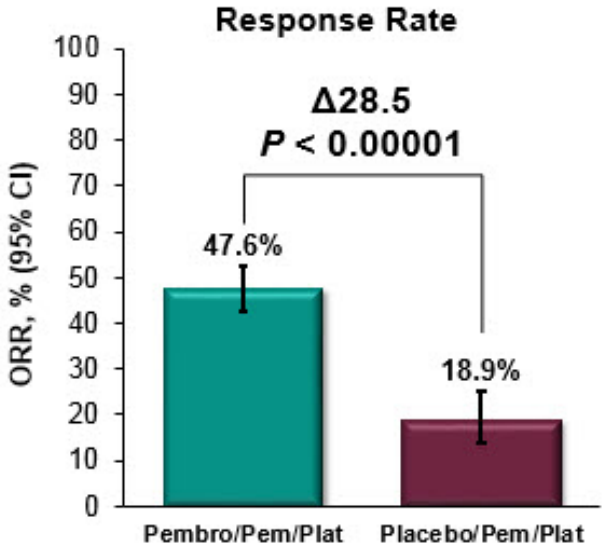
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during the induction or maintenance phases. To be eligible for crossover, PD must have been verified by blinded, independent central radiologic review and all safety criteria had to be met.

Gandhi L, et al. AACR Annual Meeting; Chicago, Illinois, April 14-18, 2018; Abstract CT075

Keynote 189: Met All Primary Endpoints







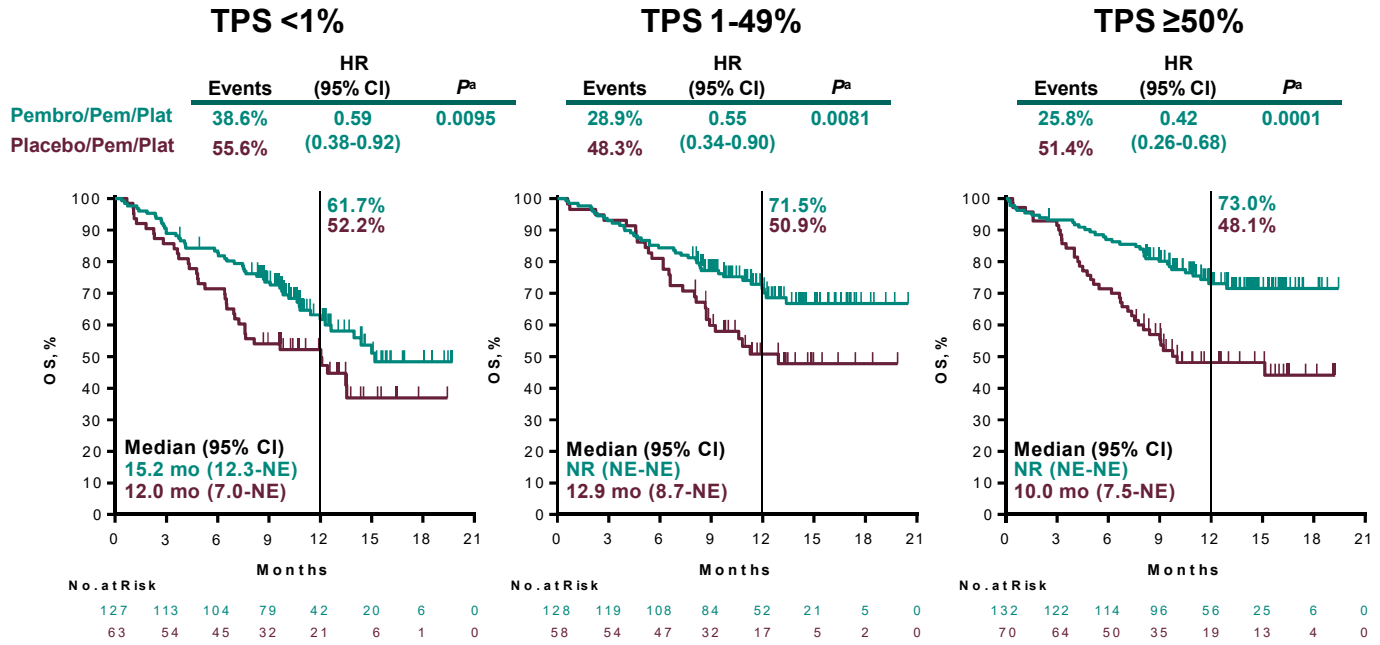
Subgroup Analyses

OS: Positive across all subgroups

PFS: Positive across all subgroups except for PD-L1 TPS <1%

Gandhi L, et al. AACR Annual Meeting; Chicago, Illinois, April 14-18, 2018; Abstract CT075

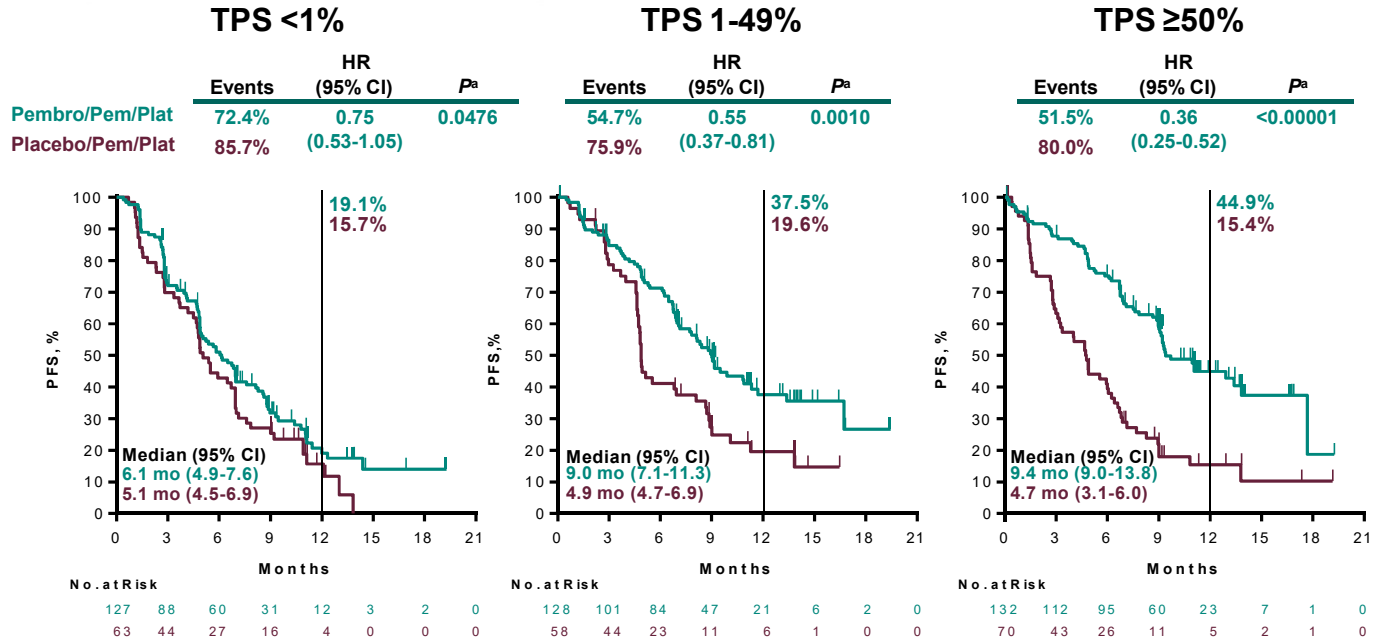
Overall Survival by PD-L1 TPS



[a]Nominal and one-sided. Data cutoff date: Nov 8, 2017.

Gandhi L, et al. AACR Annual Meeting; Chicago, Illinois, April 14-18, 2018; Abstract CT075

Progression-Free Survival by PD-L1 TPS
(RECIST v1.1, BICR)

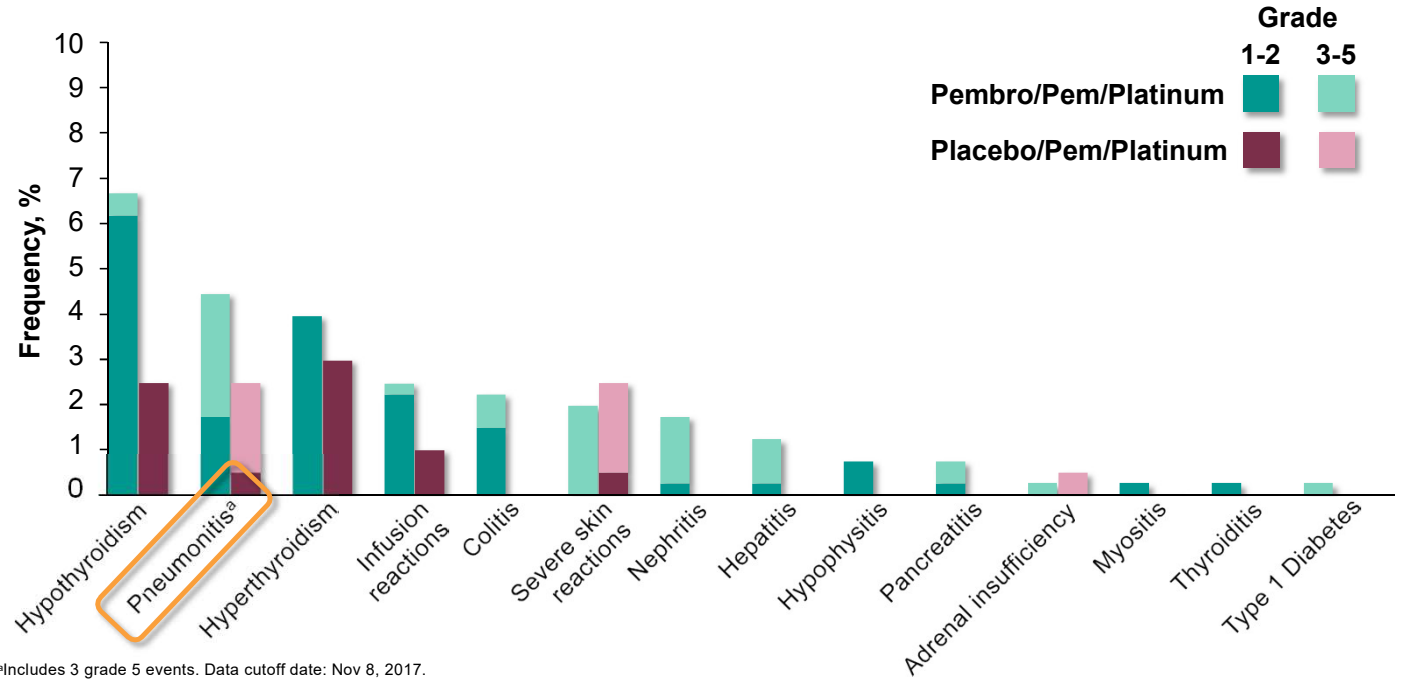


[a]Nominal and one-sided. BICR, blinded, independent central review. Data cutoff date: Nov 8, 2017.

Gandhi L, et al. AACR Annual Meeting; Chicago, Illinois, April 14-18, 2018; Abstract CT075

Acute kidney injury
Incidence: 5.2% in pembrolizumab/pemetrexed/platinum arm vs 0.5% in placebo/pemetrexed/platinum arm
Grade 3-5 incidence: 2.0% vs 0%
Grade 5 events: 2

Immune-Mediated Adverse Events



[a]Includes 3 grade 5 events. Data cutoff date: Nov 8, 2017.

Gandhi L, et al. AACR Annual Meeting; Chicago, Illinois, April 14-18, 2018; Abstract CT075

POOLED ANALYSIS: Background

- Pembrolizumab plus platinum-based chemotherapy improves clinical outcomes over chemotherapy alone as first-line treatment in patients with advanced/metastatic NSCLC (squamous or nonsquamous, without *EGFR/ALK* alterations), irrespective of PD-L1 expression[1-3]
- Better understanding of outcomes with pembrolizumab plus chemotherapy in advanced NSCLC without PD-L1 expression (TPS <1%) is needed
  - These patients are not eligible for pembrolizumab monotherapy
- ***Objective:*** Conduct a pooled analysis of pembrolizumab plus chemotherapy in patients with advanced/metastatic NSCLC without PD-L1 expression (TPS <1%) enrolled in 3 randomized trials

Clinical Study	Trial Design
KEYNOTE-021[1,2] **cohort G** (KN021G) phase 2 OS HR, 0.56 (95% CI, 0.32–0.95)[2]	• Pembrolizumab 200 mg Q3W plus pemetrexed-carboplatin vs pemetrexed-carboplatin • 1:1 randomization ratio • Previously untreated stage IIIB/IV nonsquamous NSCLC; no *EGFR/ALK* alteration
KEYNOTE-189[3,4] (KN189) phase 3 OS HR, 0.56 (95% CI, 0.45–0.70)[4]	• Pembrolizumab 200 mg Q3W plus pemetrexed-platinum vs placebo plus pemetrexed-platinum • 2:1 randomization ratio • Previously untreated stage IV nonsquamous NSCLC; no *EGFR/ALK* alteration
KEYNOTE-407[5,6] (KN407) phase 3 OS HR, 0.64 (95% CI, 0.49–0.85)[6]	• Pembrolizumab 200 mg Q3W plus carboplatin-paclitaxel/nab-paclitaxel vs placebo plus carboplatin-paclitaxel/nab-paclitaxel • 1:1 randomization ratio • Previously untreated stage IV squamous NSCLC

1. Langer CJ, et al. Lancet Oncol. 2016;17(11):1497-1508. 2. Borghaei H, et al. J Thoracic Oncol. 2019;14 (1):124-129. 3. Gandhi L, et al. N Engl J Med. 2018;378(22):2078-2092. 4. Gadgeel S, et al. J Clin Oncol. 2018;37(suppl):abstract 9013. 5. Paz-Ares L, et al. N Engl J Med. 2018;379(21):2040-2051. 6. Paz-Ares L, et al. J Clin Oncol. 2019;36(suppl):abstract 105.

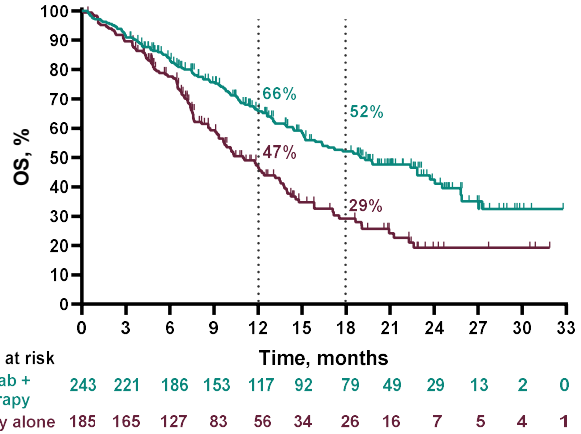
Patients Without Tumor PD-L1 Expression (TPS <1%)

OS

Median (95% CI) OS

19.0 (15.2–24.0) mo

11.0 (9.2–13.5) mo



No. at risk												
Pembrolizumab + chemotherapy	243	221	186	153	117	92	79	49	29	13	2	0
Chemotherapy alone	185	165	127	83	56	34	26	16	7	5	4	1

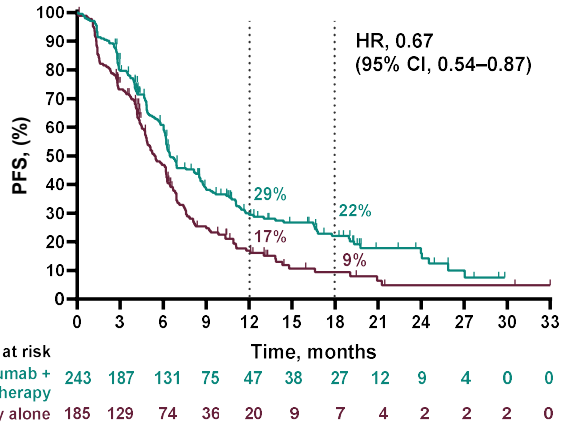
	Events, n	HR (95% CI)
Pembrolizumab + Chemotherapy	112	0.56 (0.43–0.73)
Chemotherapy	110	

PFS

Median (95% CI) PFS

6.5 (6.2–8.5) mo

5.4 (4.7–6.2) mo

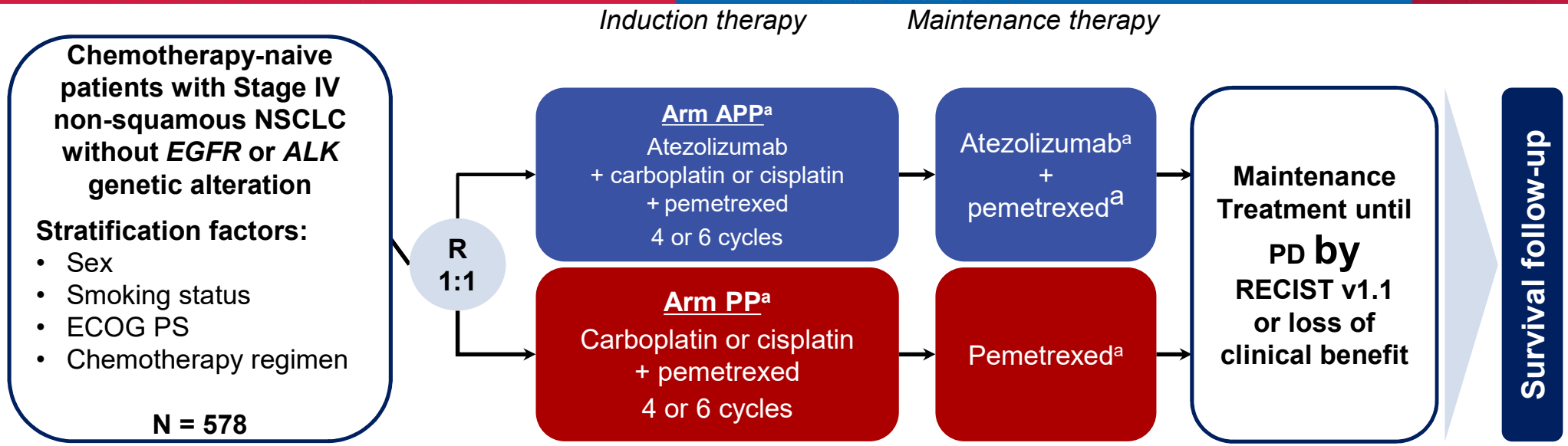


No. at risk												
Pembrolizumab + chemotherapy	243	187	131	75	47	38	27	12	9	4	0	0
Chemotherapy alone	185	129	74	36	20	9	7	4	2	2	2	0

	Events, n	HR (95% CI)
Pembrolizumab + Chemotherapy	172	0.67 (0.54–0.84)
Chemotherapy	145	

- Borghaei, WCLC Barcelona, 2019

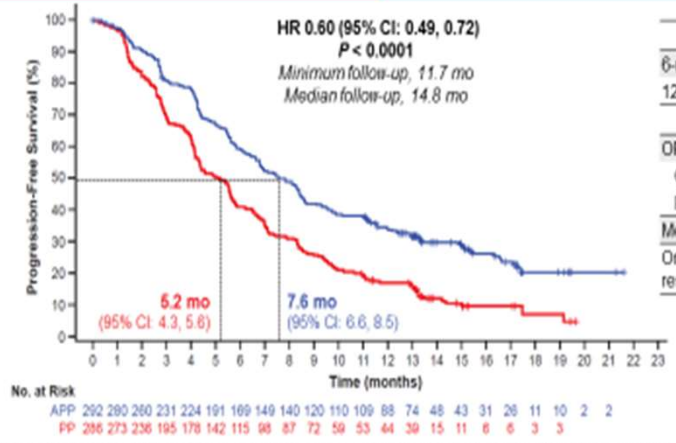
IMpower132: PFS and Safety Results with 1L Atezolizumab + Carboplatin/Cisplatin + Pemetrexed in Stage IV Non-Squamous NSCLC



- Co-primary endpoints: INV-assessed PFS and OS
- Secondary endpoints: INV-assessed ORR and DOR, PRO and safety measures
- Exploratory analyses: clinical and biomarker subgroup analyses
  - Biomarker-evaluable tissue not mandatory for enrolment (was available from 60% of patients)

DOR, duration of response; INV, investigator; R, randomization; ORR, objective response rate; OS, overall survival; PD, progressive disease, PFS, progression-free survival; PRO, patient-reported outcomes. [a] Atezolizumab: 1200 mg IV q3w; Carboplatin: AUC 6 mg/mL/min IV q3w; Cisplatin: 75 mg/m^2 IV q3w; Pemetrexed: 500 mg/m^2 IV q3w. NCT02657434. Data cutoff: May 22, 2018

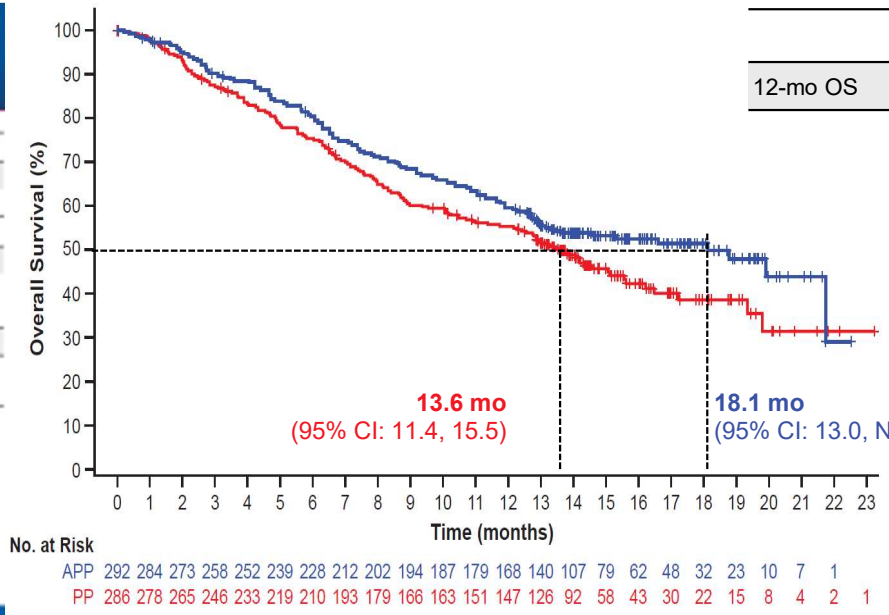
Final Investigator-Assessed PFS, ORR and DOR



	APP	PP
6-mo PFS	59.1%	40.9%
12-mo PFS	33.7%	17.0%
	APP	PP
ORR, %	47%	32%
CR	2%	1%
PR	45%	32%
Median DOR, mo	10.1	7.2
Ongoing response, %	42%	30%

CR, complete response; DOR, duration of response; HR, hazard ratio; IRF, independent review facility; ORR, objective response rate; PR, partial response.
IRF-assessed median PFS was 7.2 mo with APP and 6.6 mo with PP (stratified HR: 0.758 [95% CI: 0.623, 0.923]; $P = 0.055$)
Data cutoff: May 22, 2018.

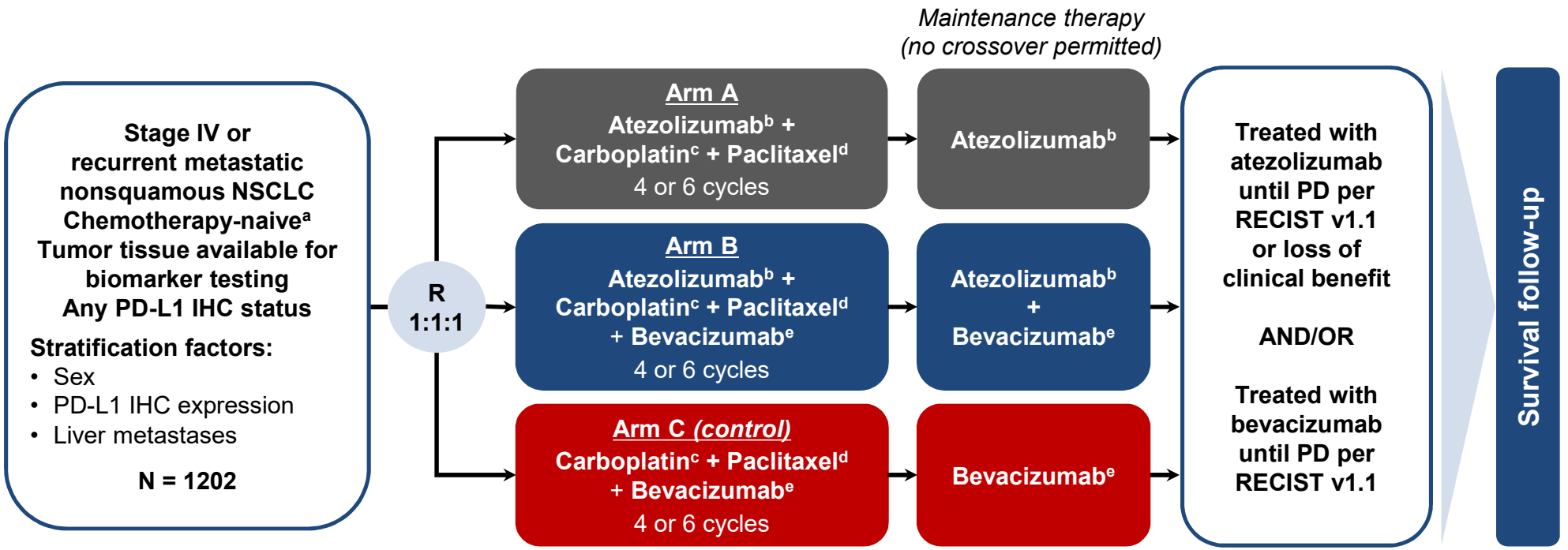
Presented by: Dr Vassiliki A. Papadimitrakopoulou IMpower132: Efficacy & Safety 6



	APP	PP
12-mo OS	59.6%	55.4%

HR: 0.81 (95% CI: 0.64, 1.03)
***P* = 0.0797**
Minimum follow-up: 11.7 mo
Median follow-up: 14.8 mo

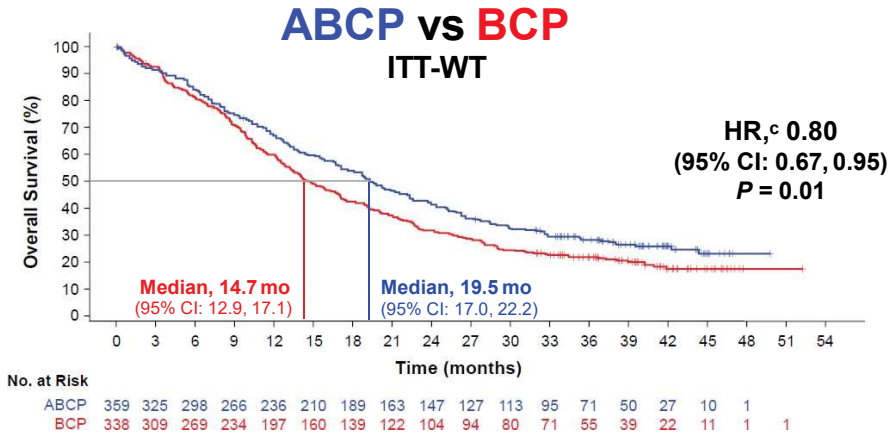
IMpower150 Study Design

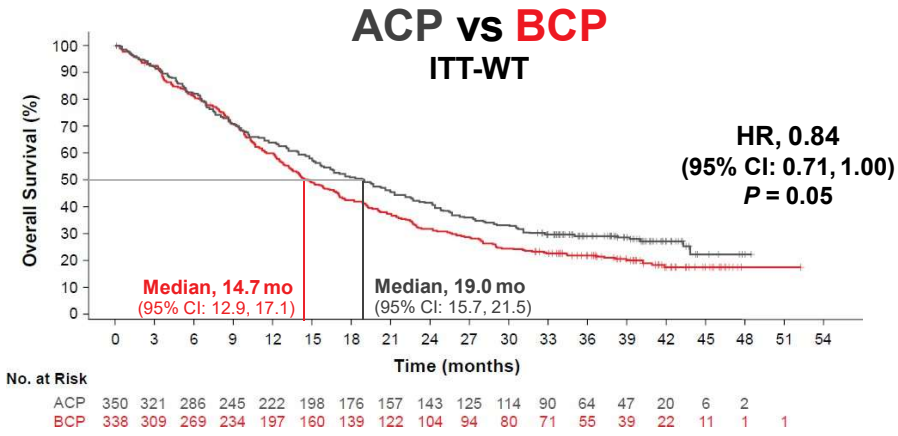


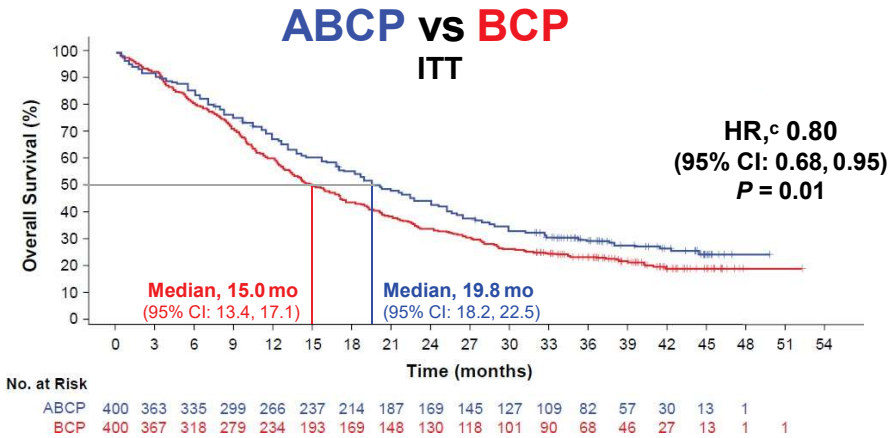
[a] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.
[b] Atezolizumab: 1200 mg IV q3w. [c] Carboplatin: AUC 6 IV q3w. [d] Paclitaxel: 200 mg/m^2 IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w.

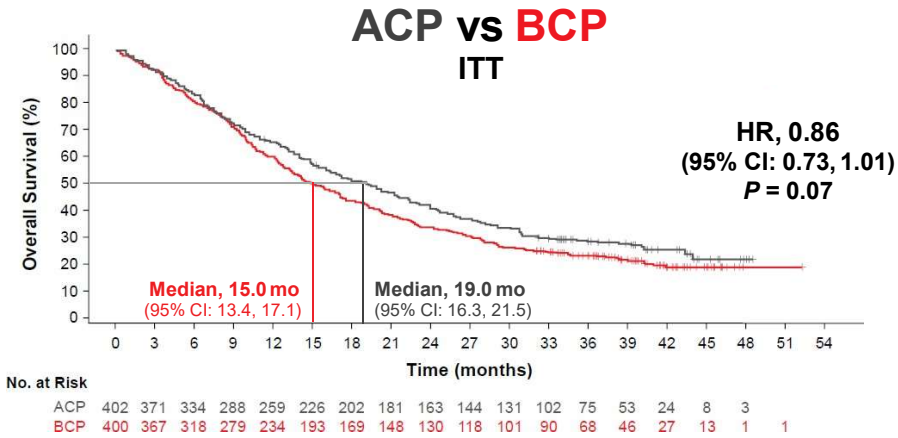
Socinski M, et al. Presented at ASCO Annual Meeting Chicago, Illinois, June 1-5, 2018; Abstract 9002

OS in ITT-WT and ITT Populations[a,b]





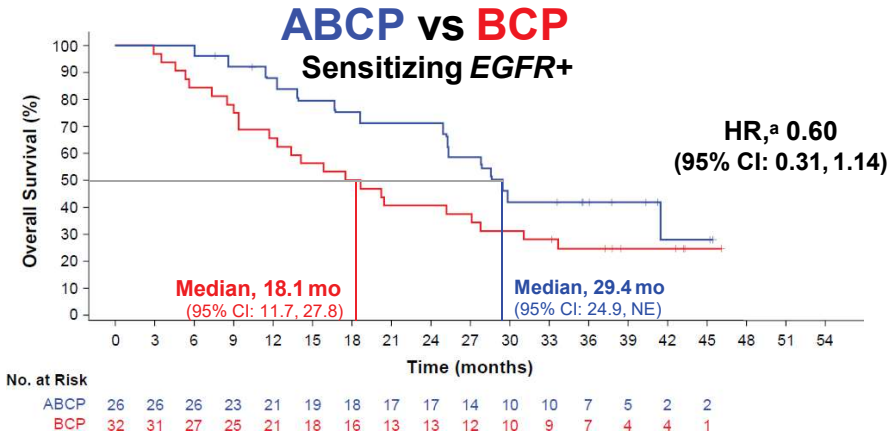


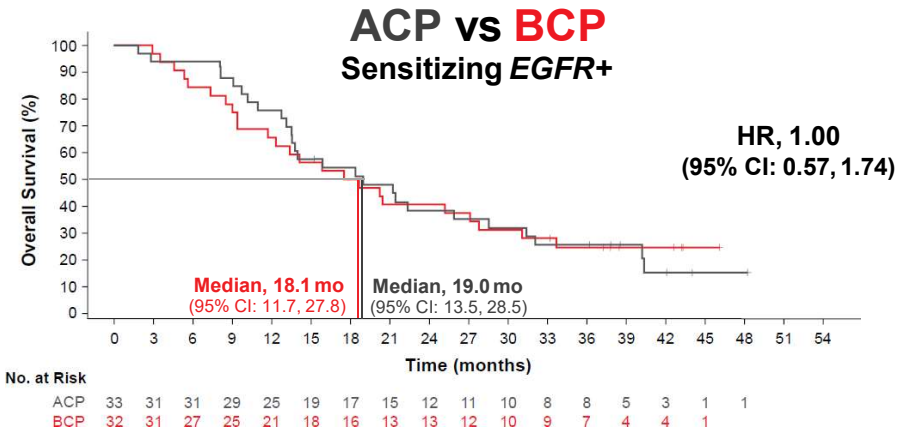


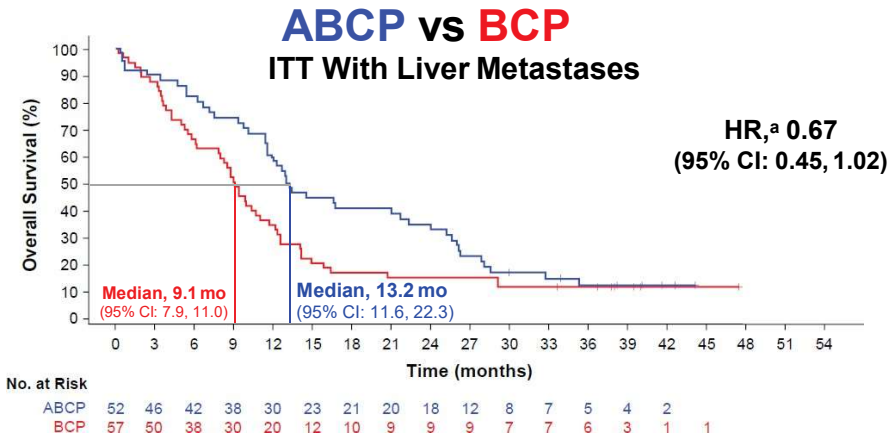
Median follow-up (ITT-WT): Arm B vs Arm C, 39.8 mo; Arm A vs Arm C, 39.3 mo. Median follow-up (ITT): Arm B vs Arm C, 39.8 mo; Arm A vs Arm C, 39.3 mo; minimum follow-up (ITT; all arms), 32.4 mo. [a] ITT-WT population excluded patients with *EGFR* or *ALK* genetic alterations. [b] Stratified analyses. [c] OS analysis for Arm B vs Arm C was considered final at the second interim OS analysis; data are shown for descriptive purposes only. Data cutoff: September 13, 2019.

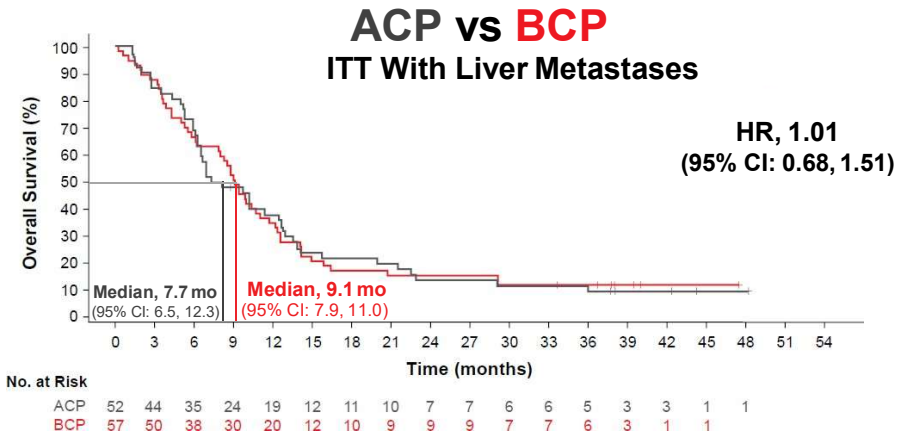
Socinski et al. IMpower150 final analysis. https://bit.ly/3aPgILP

OS in Populations With Sensitizing *EGFR* Mutation or Baseline Liver Metastases







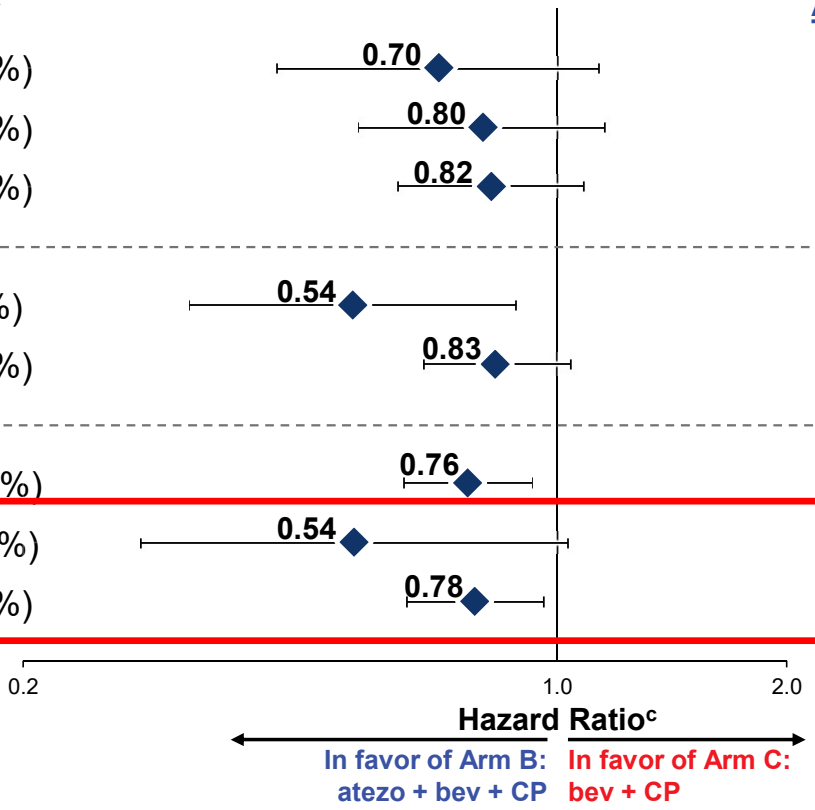


NE, not estimable. Sensitizing *EGFR* mutations = exon 19 deletion and Leu858Arg mutations. [a] OS analysis for Arm B vs Arm C was considered final at the second interim OS analysis; data are shown for descriptive purposes only. Minimum follow-up (ITT; all arms), 32.4 mo. Data cutoff: September 13, 2019.

Socinski et al. IMpower150 final analysis. https://bit.ly/3aPgILP

OS in Key Subgroups (Arm B vs Arm C)

Subgroup	n (%)[a]	Median OS, mo: Arm B	Median OS, mo: Arm C
PD-L1–High (TC3 or IC3) WT	136 (20%)	25.2	15.0
PD-L1–Low (TC1/2 or IC1/2) WT	226 (32%)	20.3	16.4
PD-L1–Negative (TC0 and IC0) WT	339 (49%)	17.1	14.1
Liver Metastases WT	94 (14%)	13.2	9.1
No Liver Metastases WT	602 (86%)	19.8	16.7
ITT (including *EGFR/ALK*+)	800 (100%)	19.8	14.9
EGFR/ALK+ only	104[b] (13%)	NE	17.5
ITT-WT	696 (87%)	19.2	14.7



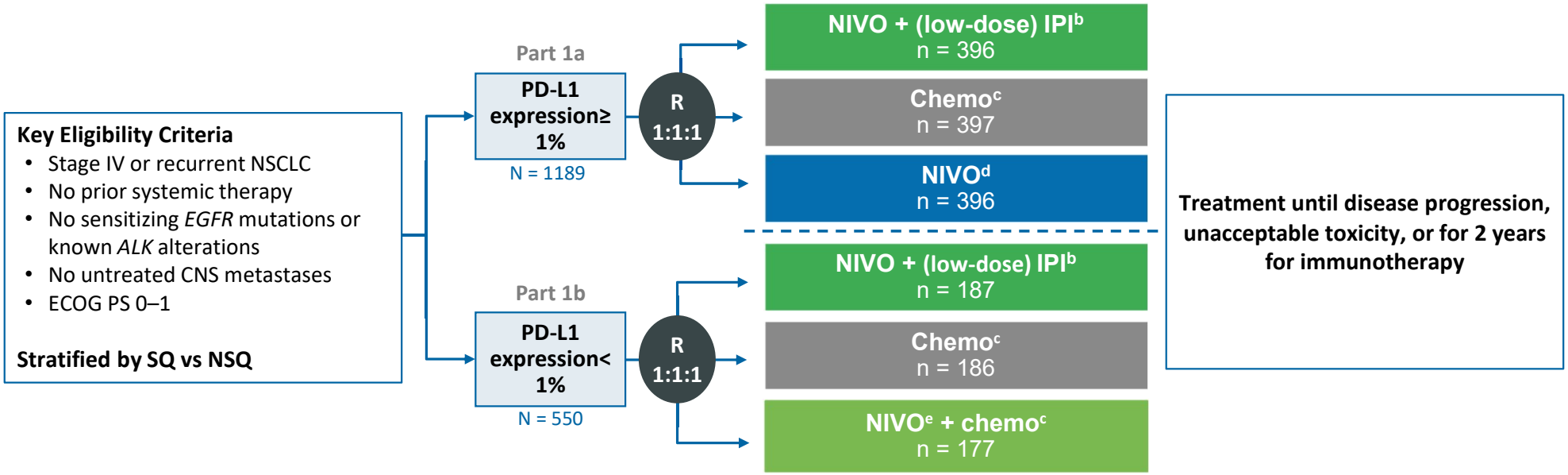
NE, not estimable.
[a] Prevalence % for PD-L1 IHC and liver metastases subgroups out of ITT-WT (n=696); prevalence of ITT, *EGFR/ALK*+, and ITT-WT out of ITT (n=800).
[b] One patient had *EGFR* exon 19 deletion and also tested *ALK* positive per central lab.
[c] Stratified HR for ITT and ITT-WT; unstratified HR for all other subgroups. Data cutoff: January 22, 2018

Socinski M, et al. Presented at ASCO Annual Meeting Chicago, Illinois, June 1-5, 2018; Abstract 9002

IO/IO COMBINATION

IPI/ Nivo Concentration

CheckMate 227 Part 1 Study Design[a]

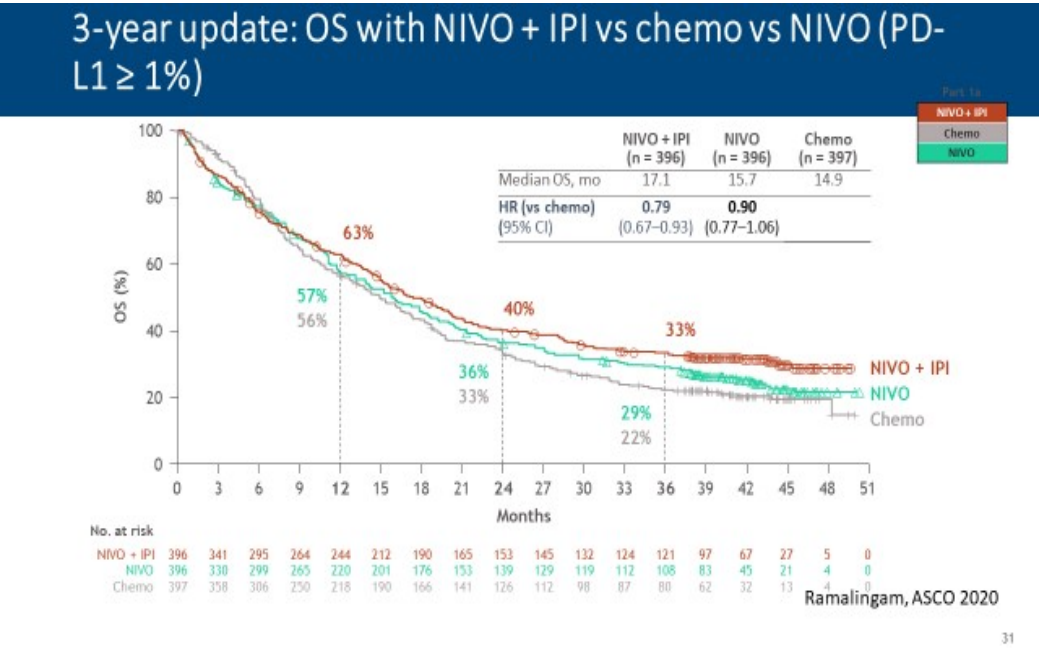


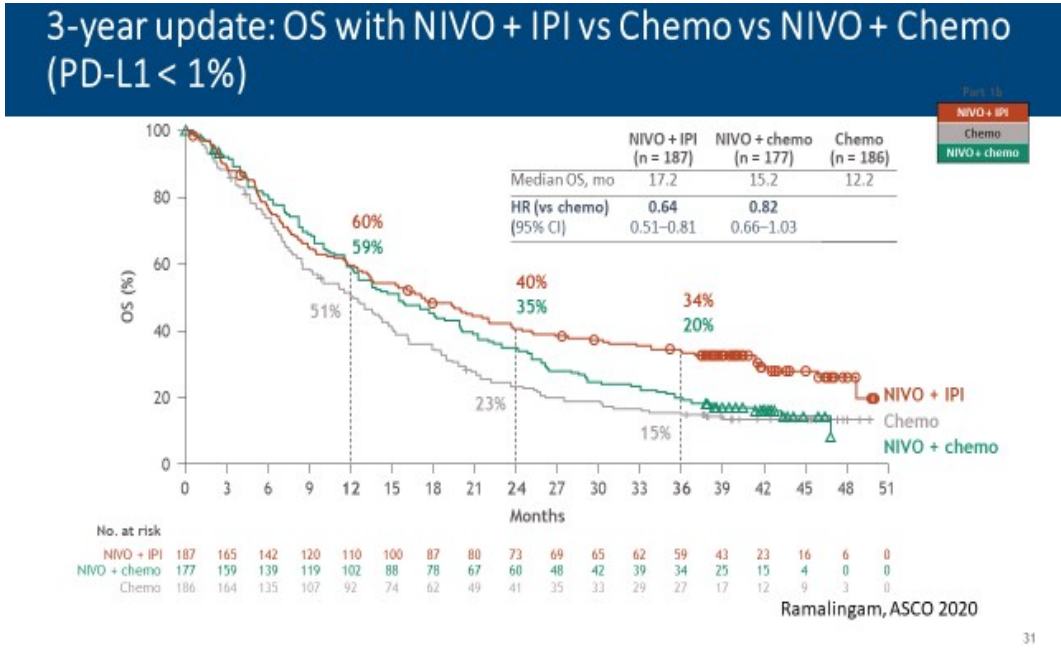
Independent co-primary endpoints: NIVO + IPI vs chemo
- PFS in high TMB (≥10 mut/Mb) population[f]
- OS in PD-L1 ≥ 1% population[g]

Secondary endpoints (PD-L1 hierarchy):
- PFS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO vs chemo** in PD-L1 ≥ 50%

S. Peters, ESMO 2019; Database lock: July 2, 2019; **minimum follow-up for primary endpoint: 29.3 months**

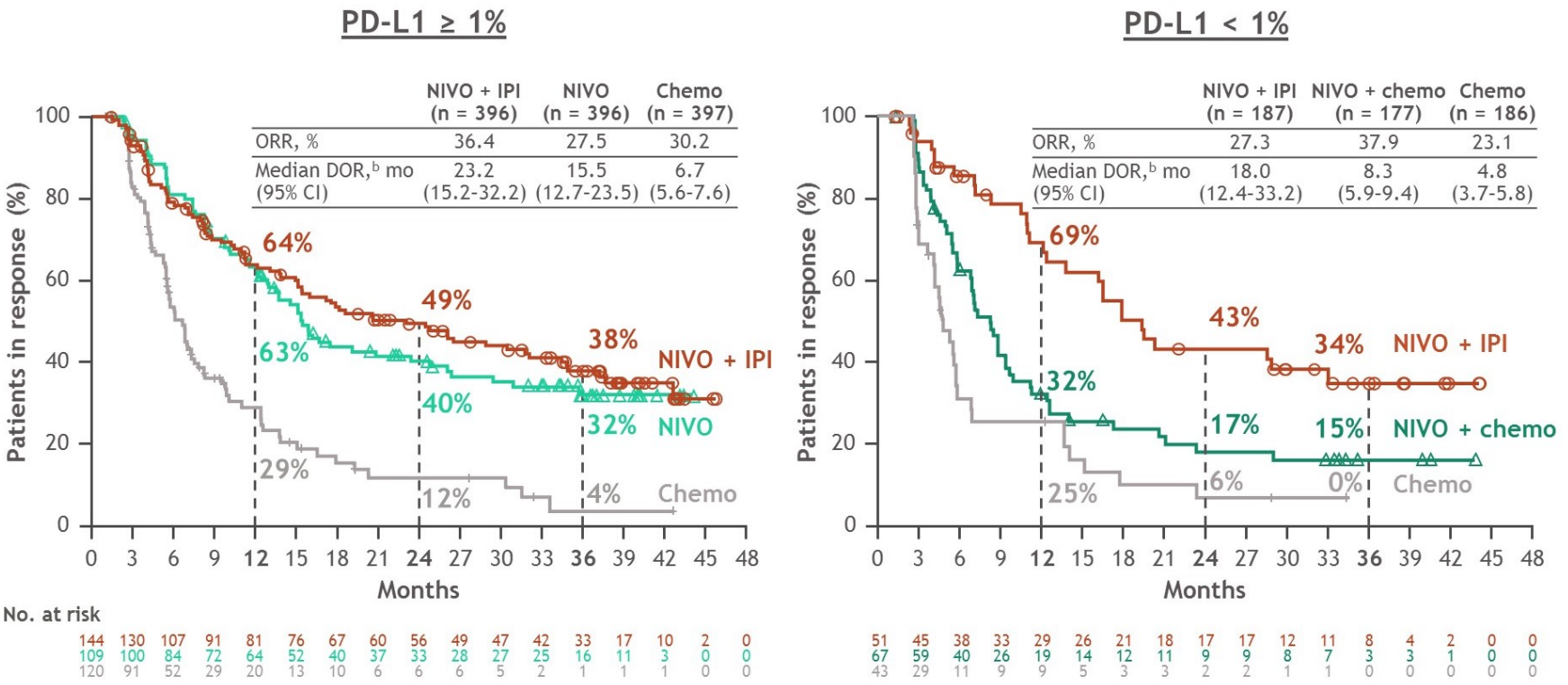
3-Year OS CheckMate-227





TMB NOT predictive of OS benefit!

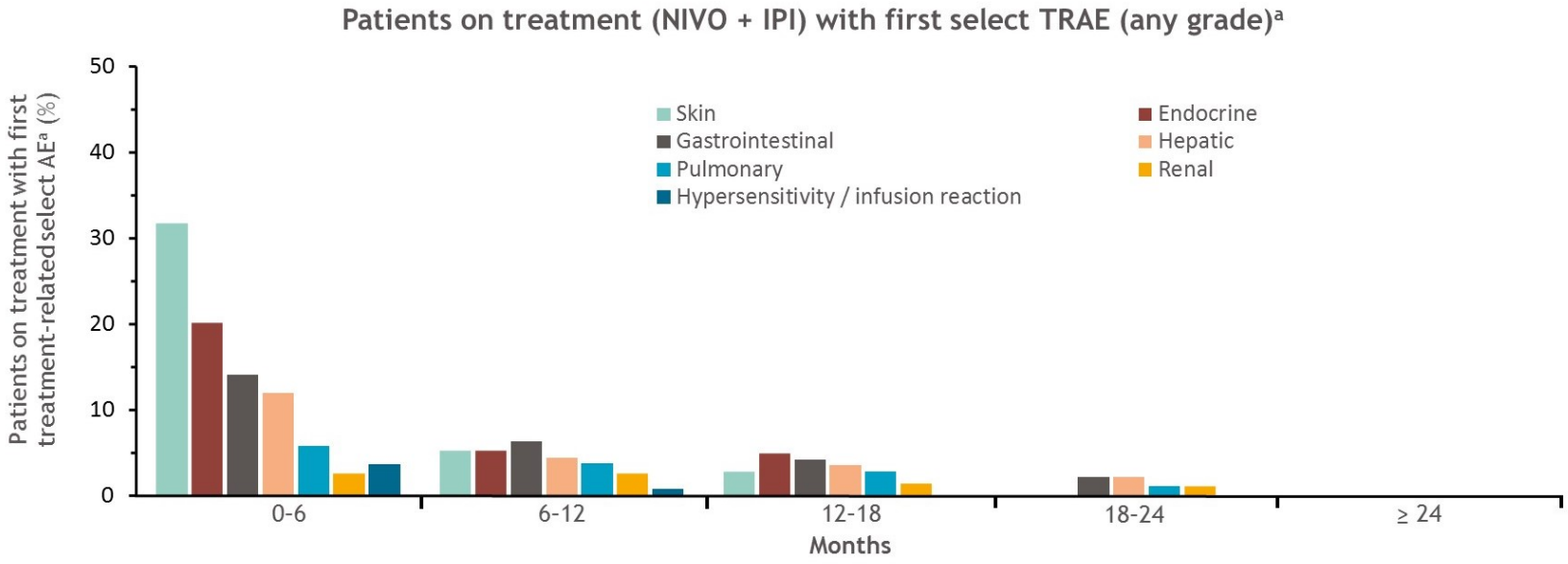
CheckMate-227: 3-Year ORR and DOR



Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), NIVO (240 mg Q2W), and NIVO (360 mg Q3W) + chemo. [a]ORR and DOR were assessed by blinded independent central review; [b]DOR was reported for responders only in each treatment arm.

9

CheckMate-227: Treatment-Related AEs: Nivo + Ipi



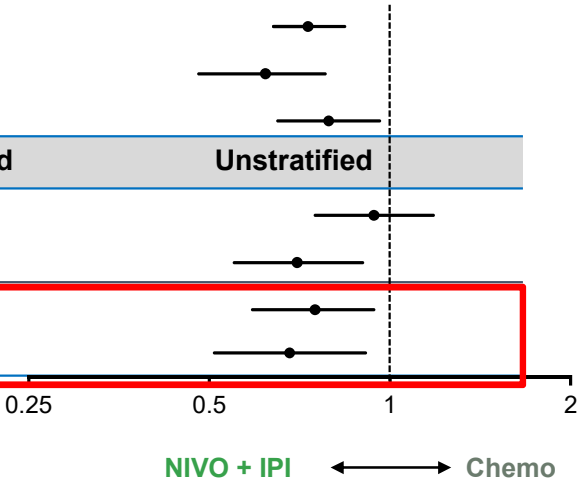
No. on study	576	433	352	275	225
No. on treatment	576	270	143	92	69
No. with a first event	342	17	9	1	0

Database lock: February 28, 2020. Dosage was NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W). Maximum treatment duration for NIVO + IPI was 2 years.
[a]Select AEs were events with a potential immunological cause that required frequent monitoring/intervention; percentages were for patients who had events of any grade reported between first dose and 30 days after last dose of study treatment.

Ramalingam S, et al. Presented at 2020 ASCO Annual Meeting. Abstract #9500.

OS for NIVO + IPI vs Chemo by Tumor PD-L1 Expression, TMB Status, and Combined Subgroups in All Randomized Patients

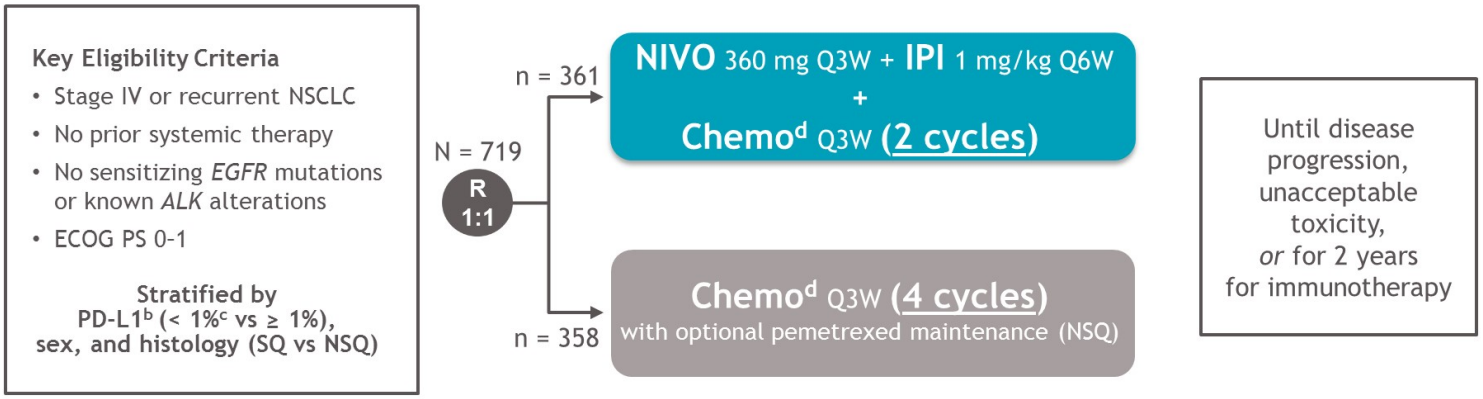
		Median OS, months NIVO + IPI n = 583	Chemo n = 583	HR	HR (95% CI)
Randomized groups				**Stratified**	**Stratified**
PD-L1	All randomized (N = 1166)	17.1	13.9	0.73	
	PD-L1 < 1% (n = 373)	17.2	12.2	0.62	
	PD-L1 ≥ 1% (n = 793)	17.1	14.9	0.79[a]	
Additional exploratory subgroups analyses[b,c]				**Unstratified**	**Unstratified**
PD-L1	1–49% (n = 396)	15.1	15.1	0.94	
	≥ 50% (n = 397)	21.2	14.0	0.70	
TMB[d] (mut/Mb)	low, < 10 (n = 380)	16.2	12.6	0.75	
	high, ≥ 10 (n = 299)	23.0	16.4	0.68	



- No consistent correlation was observed between survival outcomes with NIVO + IPI vs chemo and PD-L1 or TMB alone or in combination[1]

S. Peters, ESMO 2019; Database lock: July 2, 2019; **minimum follow-up for primary endpoint: 29.3 months**

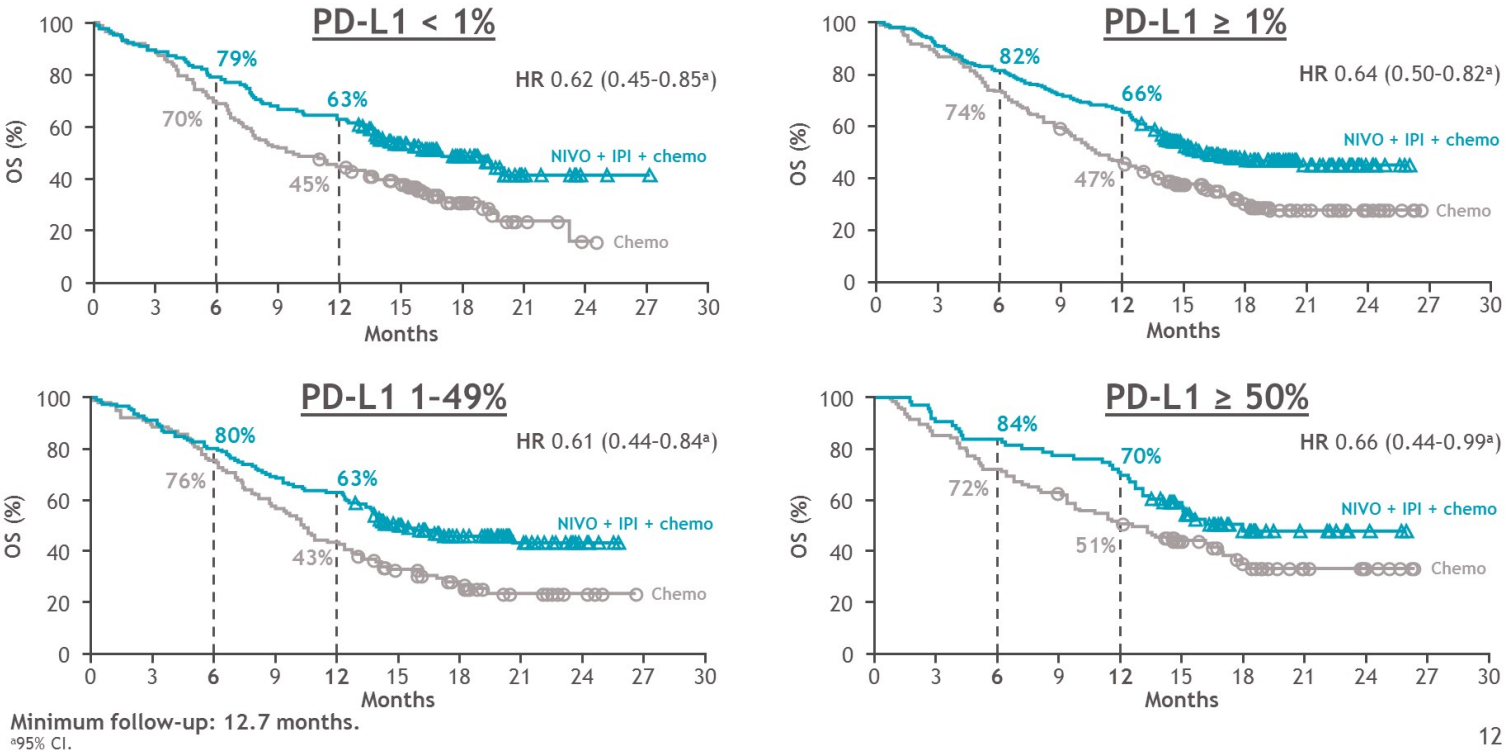
CheckMate 9LA study design[a]



Interim database lock: October 3, 2019; minimum follow-up: 8.1 months for OS and 6.5 months for all other endpoints.
Updated database lock: March 9, 2020; minimum follow-up: 12.7 months for OS and 12.2 months for all other endpoints.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]**NSQ**: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

Overall survival by PD-L1 expression level



Minimum follow-up: 12.7 months.

[a]95% CI.

Is PD-L1 status needed?

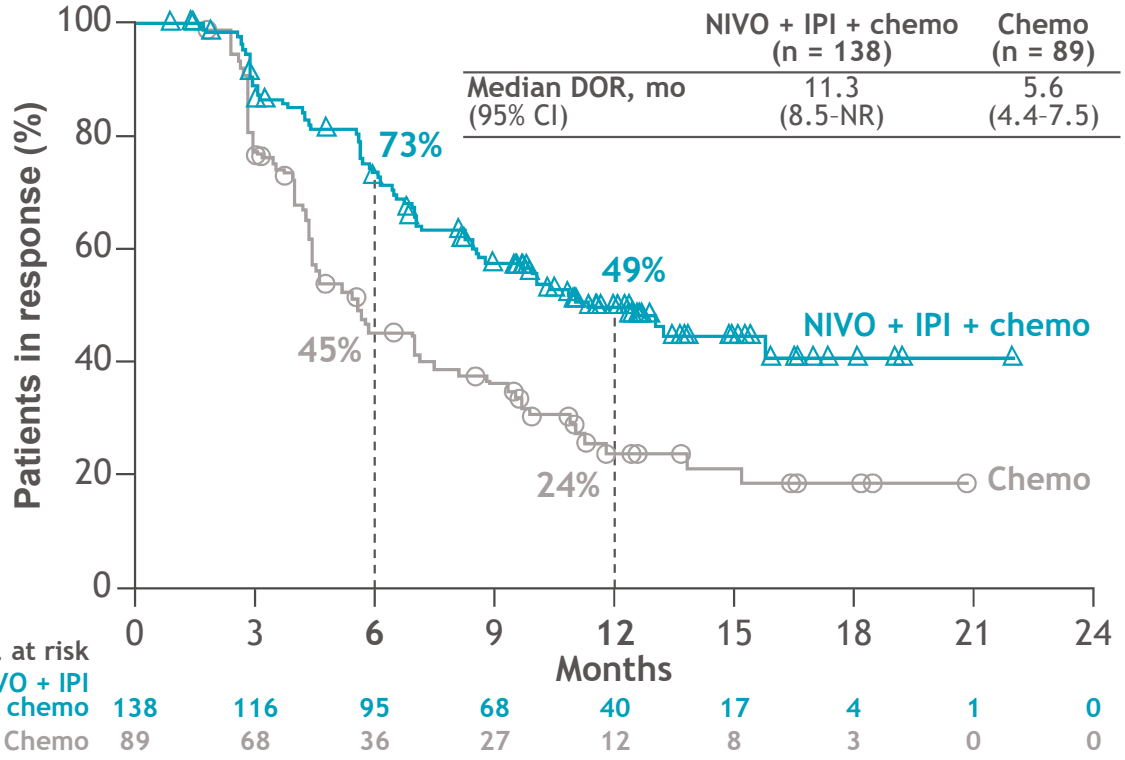
Presented By Martin Reck at ASCO 2020

Overall response rate per BICR and duration of response

Response rates

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
ORR, n (%)	138 (38)	89 (25)
Odds ratio (95% CI)	1.9 (1.4–2.6)	
BOR, n (%)		
CR	8 (2)	4 (1)
PR	130 (36)	85 (24)
SD	164 (45)	185 (52)
PD	32 (9)	45 (13)
DCR, n (%)	302 (84)	274 (76)

Duration of response

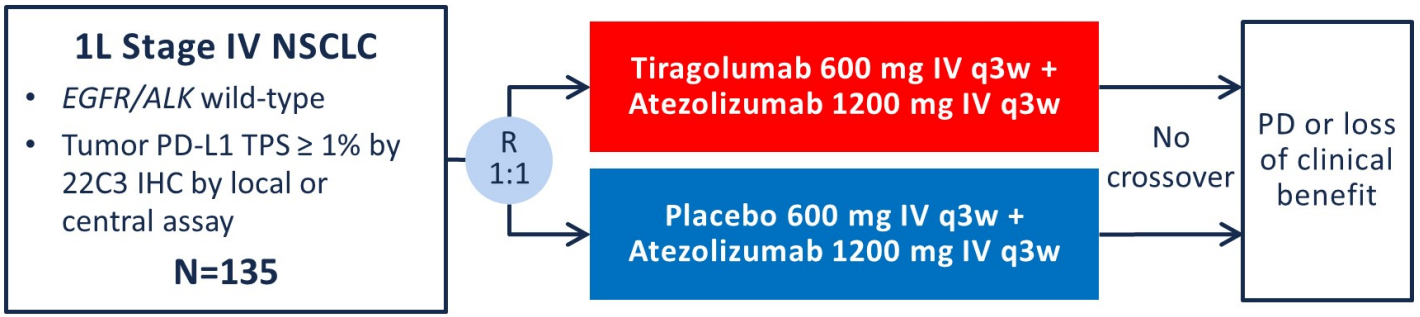


- At interim analysis, ORR was significantly improved with NIVO + IPI + chemo vs chemo[a]

Minimum follow-up: 6.5 months at interim analysis; 12.2 months for updated analysis

[a]ORR was 38% versus 25%, respectively, *P* = 0.0003.

CITYSCAPE Study Design



Stratification Factors:

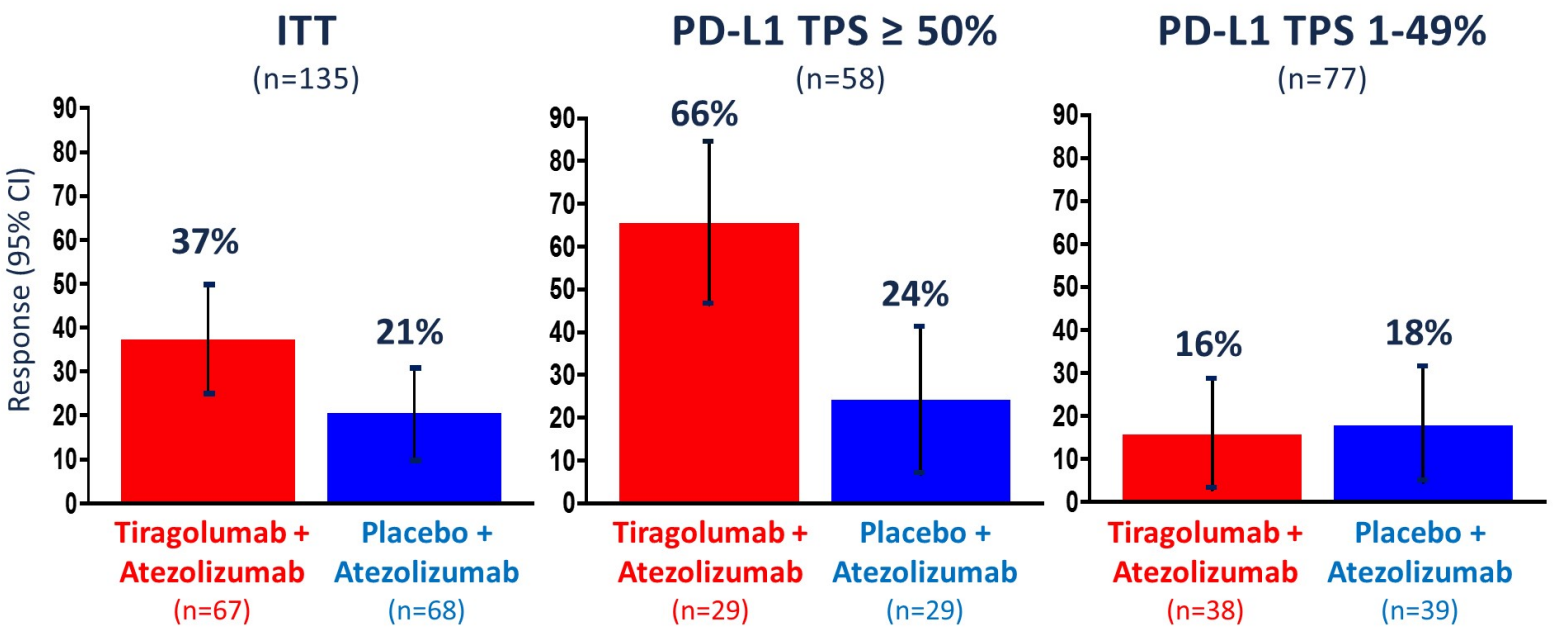
- PD-L1 TPS (1-49% vs ≥ 50%)
- Histology (Non-Squamous vs Squamous)
- Tobacco use (yes vs no)

- **Co-Primary Endpoints: ORR** and **PFS**
- **Key Secondary Endpoints: Safety**, DOR, OS, Patient-reported outcomes (PROs)
- **Exploratory Endpoints:** Efficacy analysis by PD-L1 status

DOR = duration of response; IHC = immunohistochemistry; ORR = confirmed overall response rate; OS = overall survival; PD = progressive disease; PFS = progression free survival ; q3w = every 3 weeks; R = randomized; TPS = tumor proportion score

Presented By Melissa Johnson at TBD

Updated Confirmed Overall Response Rate (ORR)

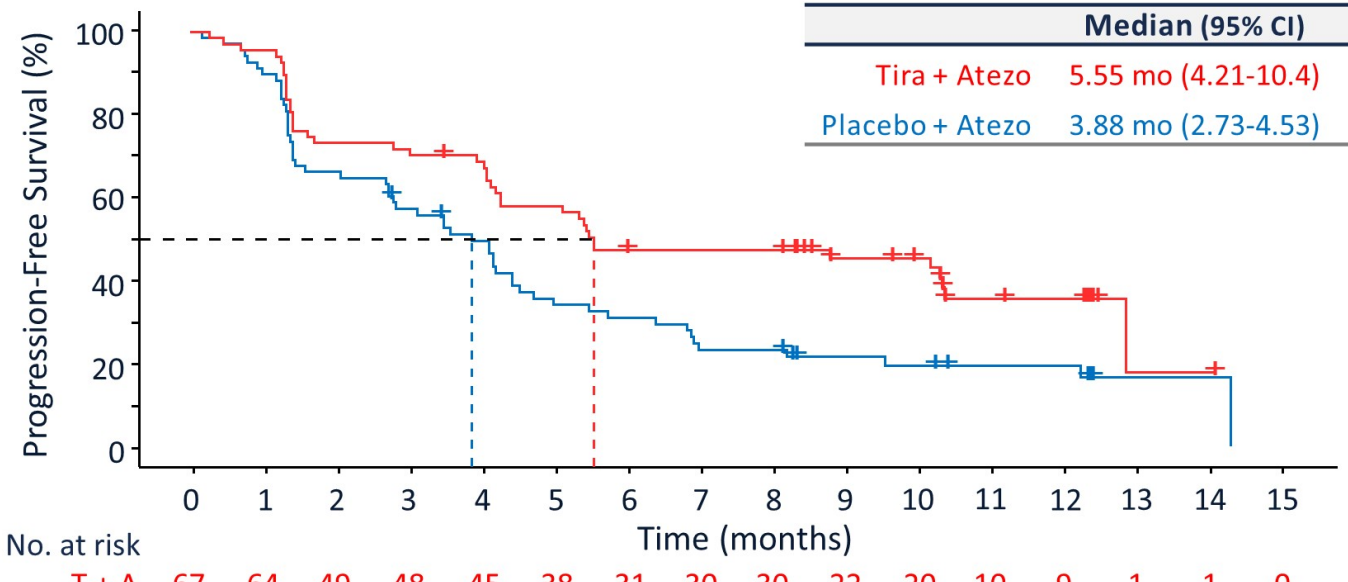


ITT = intention-to-treat; TPS = tumor proportion score

Updated data cutoff: 02 Dec 2019

Presented By Melissa Johnson at TBD

Updated Investigator-Assessed PFS: ITT



	Median (95% CI)	HR (95% CI)
Tira + Atezo	5.55 mo (4.21-10.4)	0.58* (0.38-0.89)
Placebo + Atezo	3.88 mo (2.73-4.53)	

*stratified HR

No. at risk																Events
T + A	67	64	49	48	45	38	31	30	30	22	20	10	9	1	1	0	41 (61%)
P + A	68	61	45	38	32	22	20	15	15	10	9	7	7	1	1	0	55 (81%)

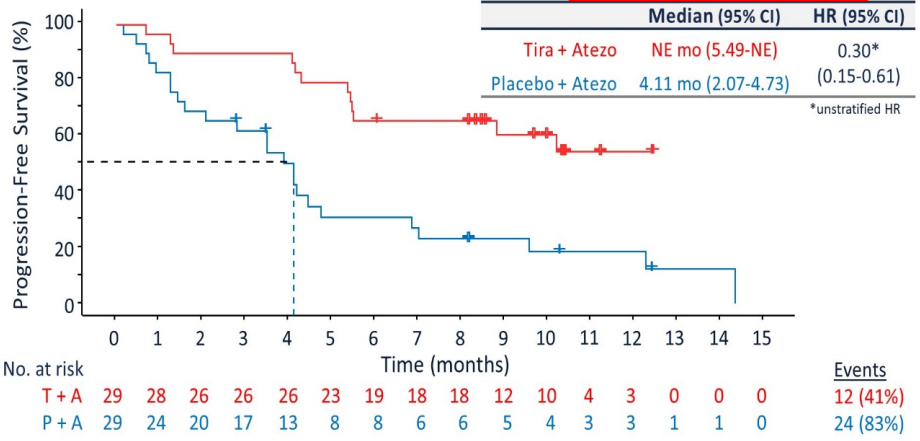
ITT= intention-to-treat; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab

Follow data cutoff: 02 December 2019

Presented By Melissa Johnson at TBD

CITYSCAPE TRIAL

Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%



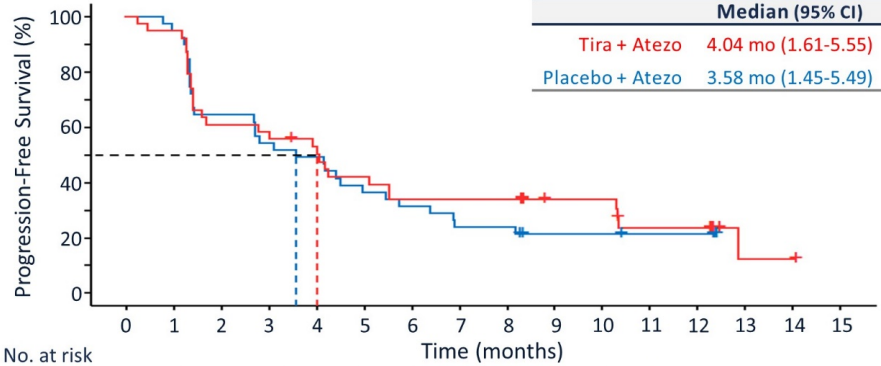
	Median (95% CI)	HR (95% CI)
Tira + Atezo	NE mo (5.49-NE)	0.30* (0.15-0.61)
Placebo + Atezo	4.11 mo (2.07-4.73)	

*unstratified HR

No. at risk																Events
T + A	29	28	26	26	26	23	19	18	18	12	10	4	3	0	0	0	12 (41%)
P + A	29	24	20	17	13	8	8	6	6	5	4	3	3	1	1	0	24 (83%)

NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score Follow data cutoff: 02 December 2019

Updated Investigator-Assessed PFS: PD-L1 TPS 1-49%



	Median (95% CI)	HR (95% CI)
Tira + Atezo	4.04 mo (1.61-5.55)	0.89* (0.53-1.49)
Placebo + Atezo	3.58 mo (1.45-5.49)	

*unstratified HR

No. at risk																Events
T + A	38	36	23	22	19	15	12	12	12	10	10	6	6	1	1	0	29 (76%)
P + A	39	37	25	21	19	14	12	9	9	5	5	4	4	0	0	0	31 (80%)

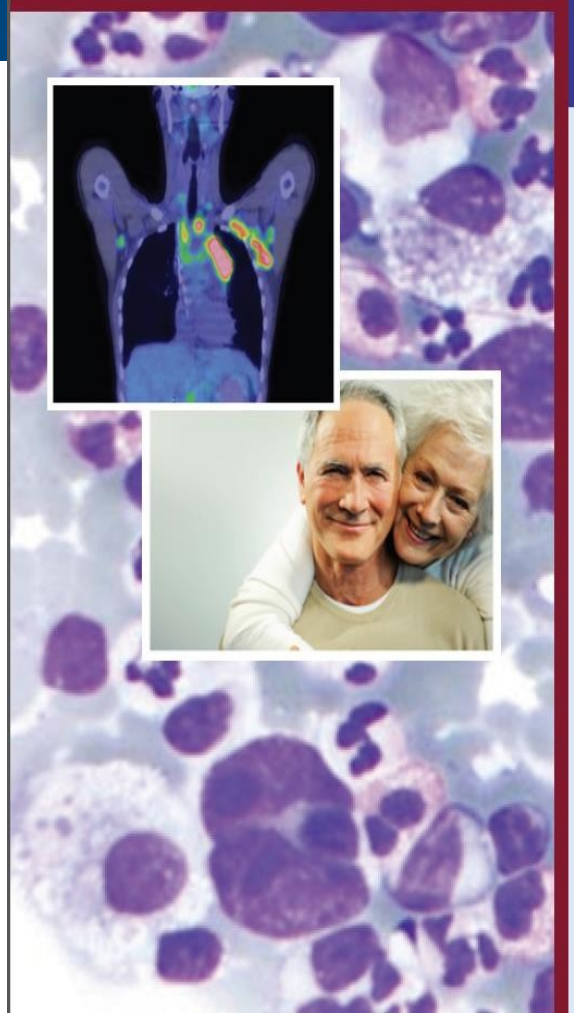
NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score Follow data cutoff: 02 December 2019

Presented By Melissa Johnson at TBD

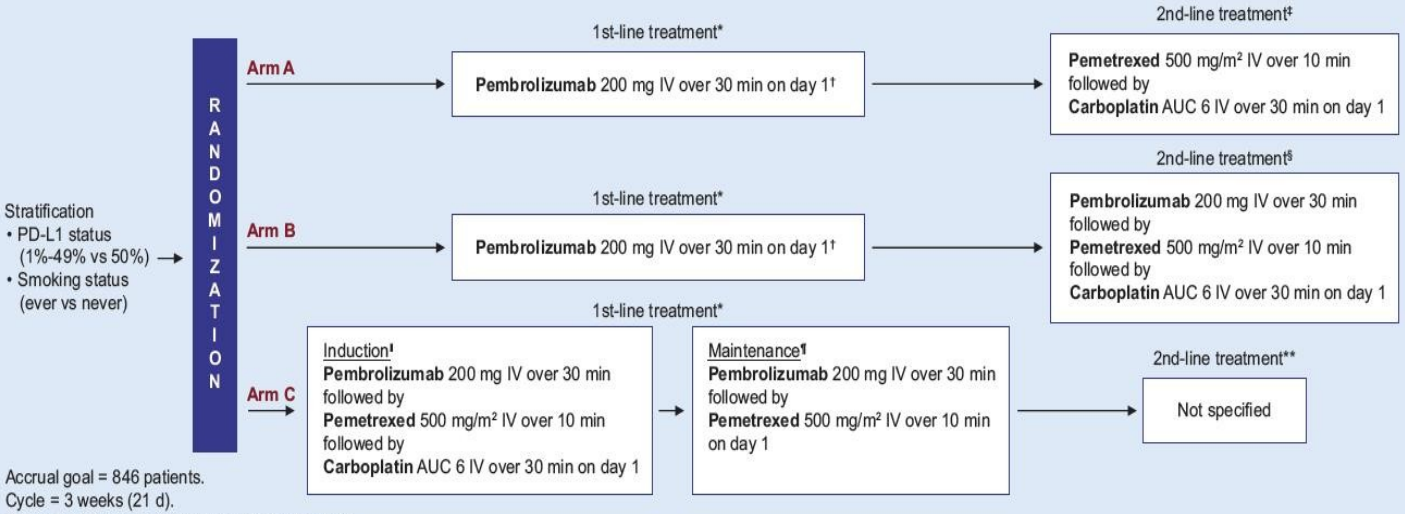
Is there a Role for Sequential Therapy?

EA5163/S1709/INSIGNA

A Randomized, Phase III Study of Firstline Immunotherapy Alone or in Combination With Chemotherapy in Induction/Maintenance or Postprogression in Advanced Nonsquamous Non-Small Cell Lung Cancer (NSCLC) With Immunobiomarker SIGNature-driven Analysis



Study Schema



Accrual goal = 846 patients.
Cycle = 3 weeks (21 d).
*Repeat until progression or maximum of 2 years.
†If no progression by 2 years of pembrolizumab (MK-3475), patient continues on observation until progression, then proceeds to 2nd-line therapy.
‡Repeat for 4 cycles or until disease progression. Pemetrexed can then be given as maintenance until disease progression per standard of care.
§Repeat for 4 cycles or until disease progression. Pembrolizumab and pemetrexed can then be given as maintenance until disease progression or 2 years of pembrolizumab treatment in total. Pemetrexed alone may continue per standard of care.
‖Repeat for 4 cycles, then proceed to maintenance. If disease progression occurs prior to the completion of 4 cycles, patient should instead enter long-term follow-up and continue to the 2nd-line treatment off study, per standard of care.
¶Repeat for 2 years of total treatment across induction and maintenance, or until disease progression. Pemetrexed alone may continue per standard of care.
**Patient enters long-term follow-up and receives 2nd-line treatment off study, per standard of care.
PD-L1 = programmed death-ligand 1.

Conclusions

- Chemotherapy plus Immunotherapy is A standard of care for the treatment of NSCLC
- Chemotherapy plus immunotherapy has at least additive efficacy
- Efficacy of combination therapy is shown across many sub groups
- We should work towards personalized care by investing more in biomarkers that would either select or de-select patients for specific treatments
- IO/IO combination +/- a short course of chemotherapy is now FDA approved
- The role of sequential therapy will be addressed by EA5163/S1709