Memorial Cancer Institute
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Lung Cancer Immunotherapy

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NOSCM
NEW ORLEANS SUMMER CANCER MEETING

Research Support:

BMS

Genentech/Roche

Pfizer

Biodesix

MSD

Merck Serono

Lilly Oncology

Boheringer Ingelheim

Novartis

Astra-Zeneca

Liquid Genomics

Speakers Bureau/Stocks: *None*

Origins of cancer immunology

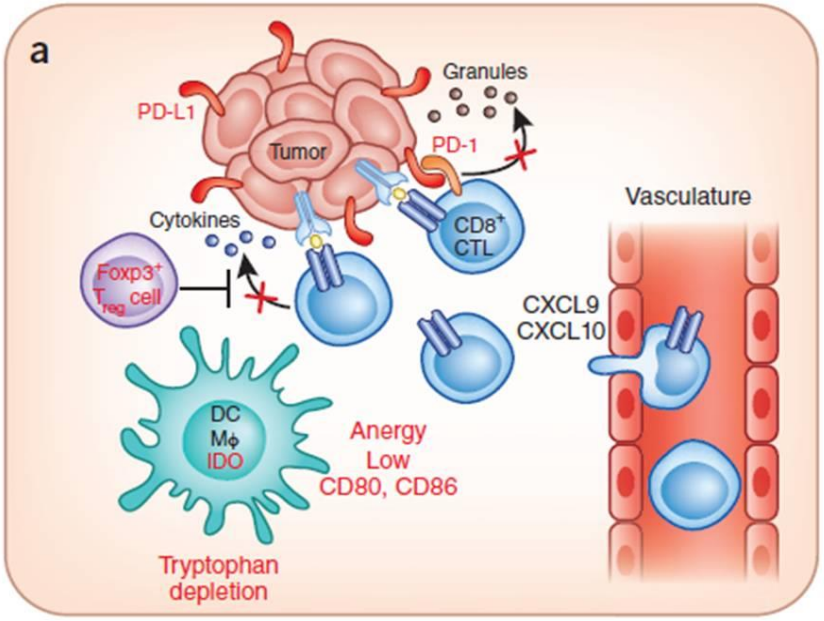
William Coley
1862-1936

- Anecdotal reports of erysipelas (*S. pyogenes*) infection coinciding with cancer regression (1800s)
- Coley's Toxins: heat-killed *Serratia marcescens* and *Streptococcus pyogenes*
- Coley WB. The treatment of malignant tumors by repeated inoculations of Erysipelas, with a report of ten original cases. Am J Med Sci 1893;105:487–511.
- Coley regarded by some as the father of cancer immunotherapy

T cell inflamed vs. non-inflamed tumors and responses to checkpoint inhibitors

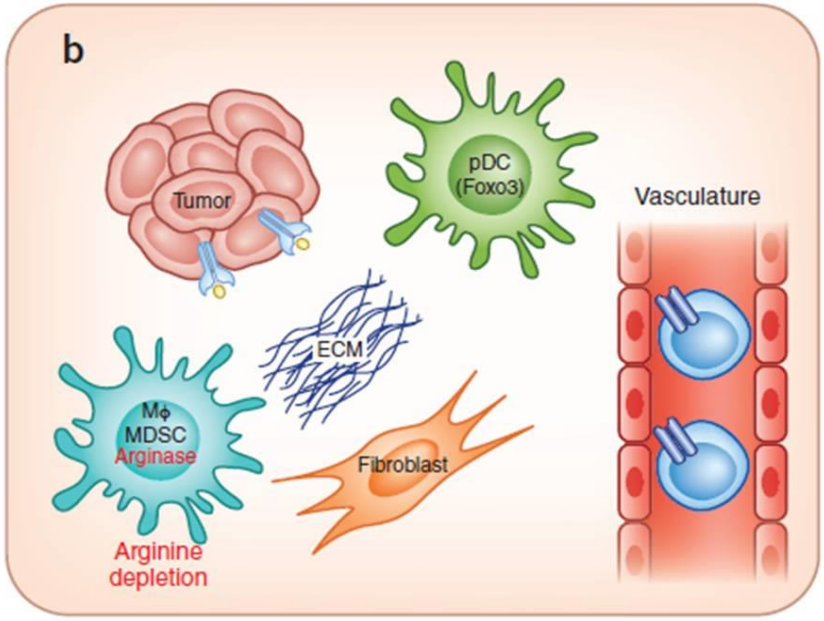
Working model: immunobiology of T cell-inflamed and non-inflamed tumor microenvironment

T cell-inflamed



- Chemokines
- CD8⁺ T cells
- Type I IFN signature
- Immune escape: Inhibitory pathways
- ***Most immunotherapy responders have this phenotype***

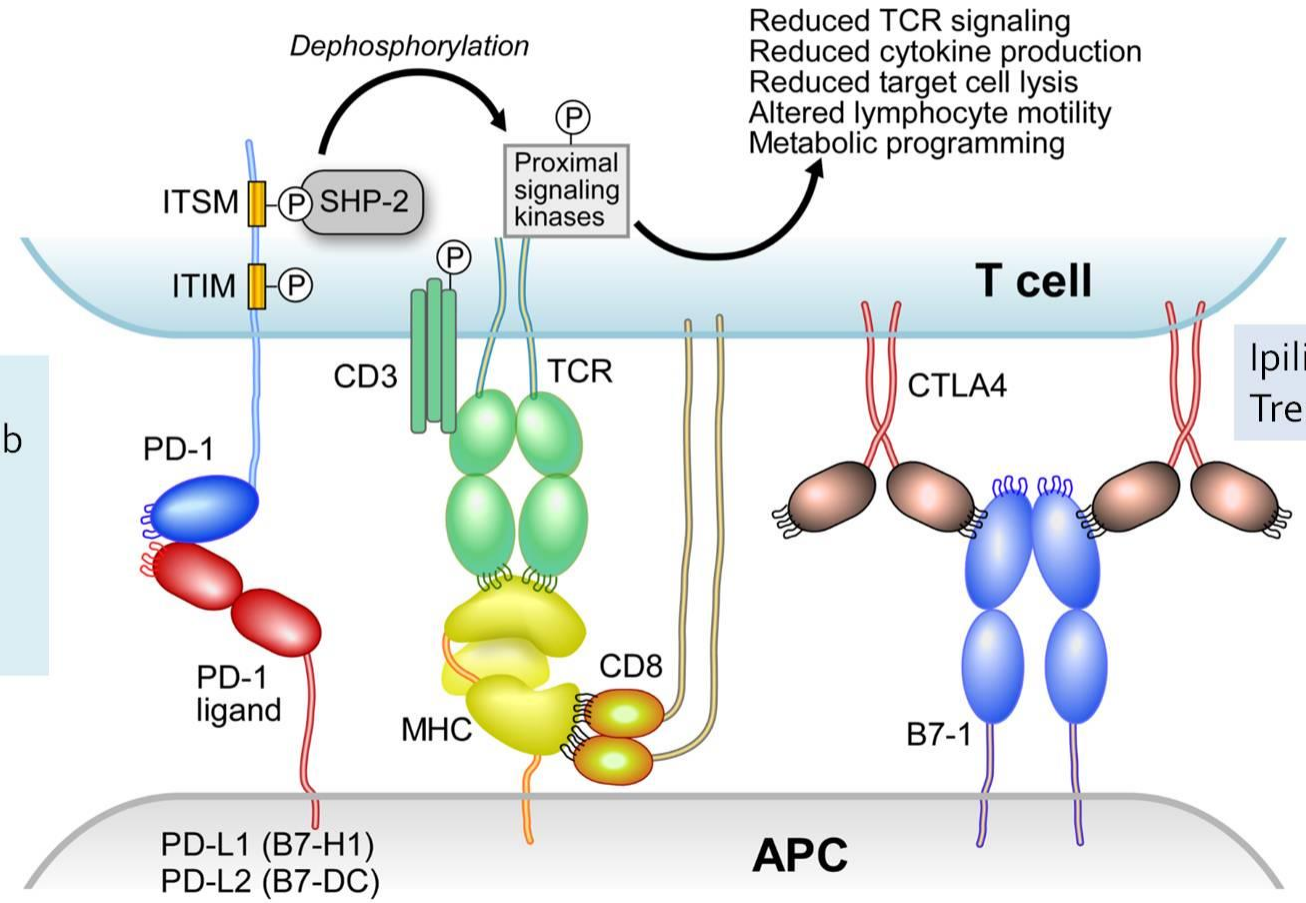
Non-T cell-inflamed



- Low inflammatory signature
- Absent intratumoral CD8⁺ T cells
- Immune escape: T cell exclusion

Nature Immunol. 2013

The PD-1 pathway inhibits T cell activation



Nivolumab
Pembrolizumab

Atezolizumab
Avelumab
Durvalumab

Ipilimumab
Tremelimumab

Freeman, ESMO IO 2015

Checkpoint Blockade

Anti-CTLA-4	Anti-PD-L1	Anti-PD-1
Ipilimumab (Fully human IgG1) FDA approved 2011	**MDX-1105** (Fully human IgG4) Phase I	**MDX-1106, Nivolumab** (Fully human IgG4) FDA approved for melanoma, NSCLC, urothelial carcinoma, RCC, HL, SCCHN
Tremelimumab (Fully human IgG2) Phase III	**MPDL3280A, RG7446, Atezolizumab** Phase II-III FDA approved 2016 NSCLC	**CT-011 Pidilizumab** (Humanized IgG1) Phase II
	MEDI4736, Durvalumab; Phase III	**MK3475 Pembrolizumab** (formerly Lambrolizumab) (Humanized IgG4) FDA approved for melanoma, NSCLC, SCCHN
	MSB0010718C, Avelumab Phase I-II	**AMP-224** (B7-DC/IgG1fusion protein) Phase I-II
		MEDI0680, AMP514 Phase I

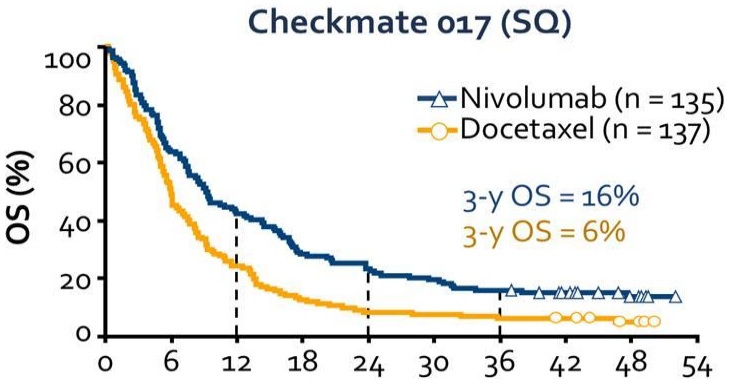
NSCLC Second line Immunotherapy

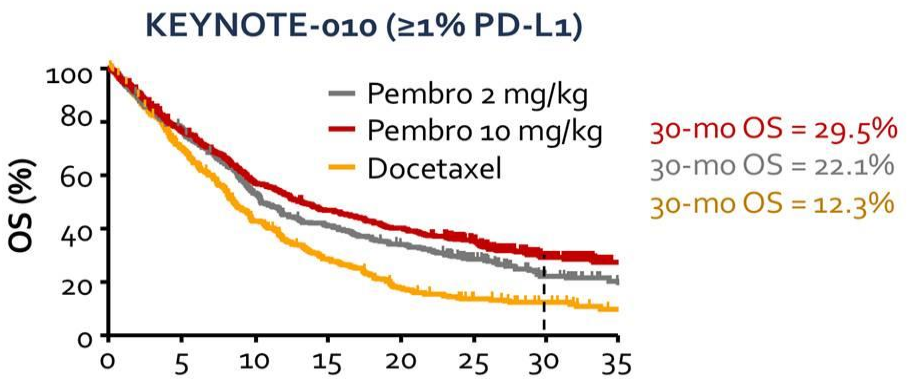
Nivolumab [Checkmate 057 and 017]

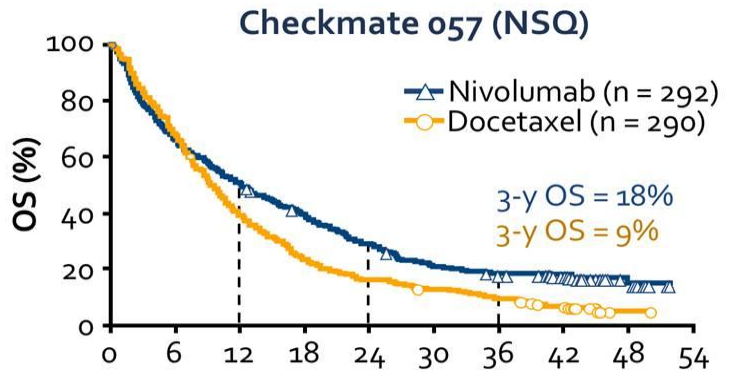
Pembrolizumab [Keynote 010]

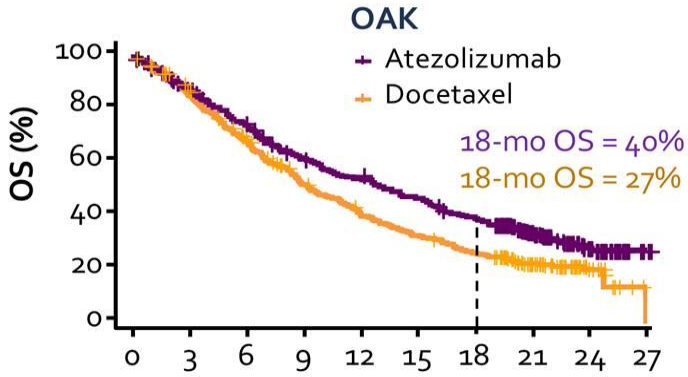
Atezolizumab [Oak]

A consistent but limited OS benefit in 2nd line







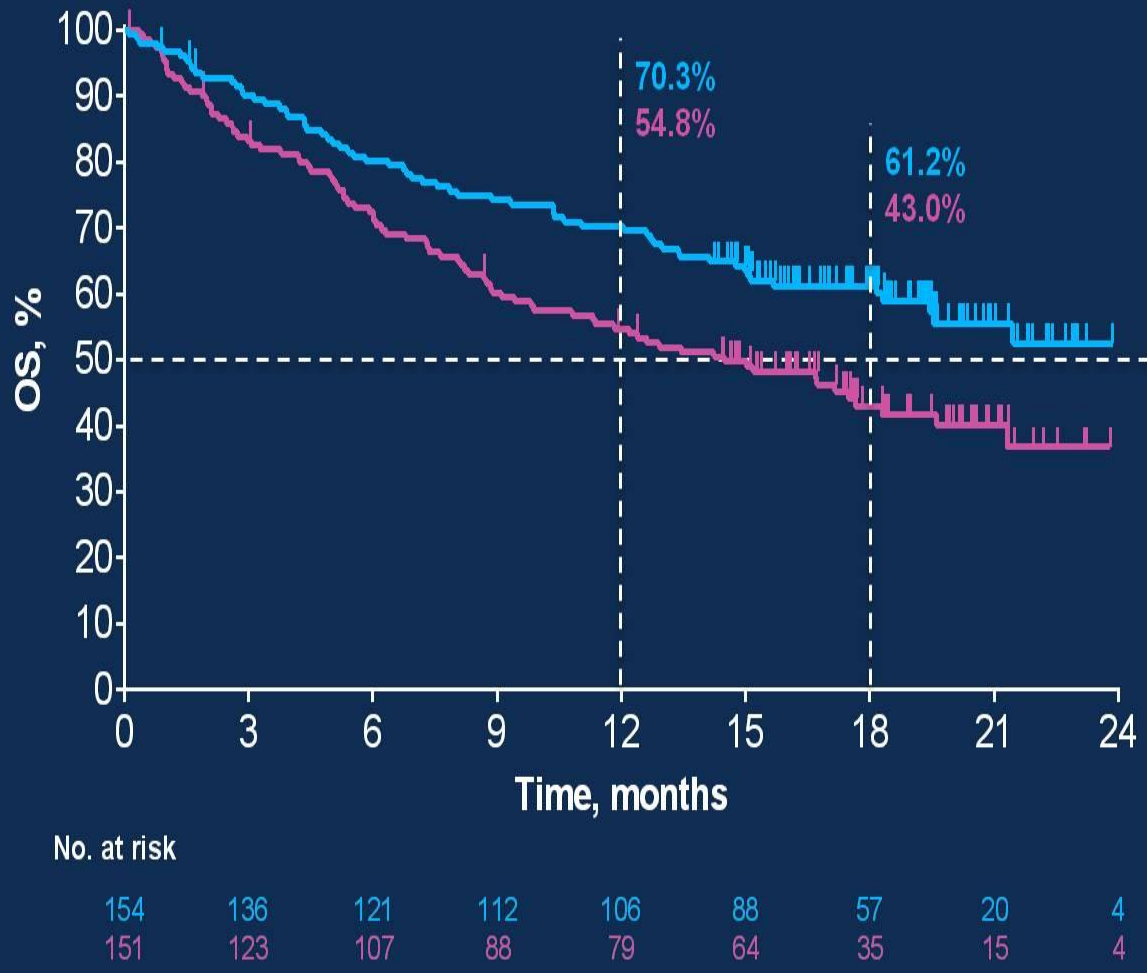


Felip, ESMO 2017; Herbst, ASCO 2017; Rittmeyer, Lancet 2017

NSCLC First line Immunotherapy

Pembrolizumab [Keynote 024]

Kaplan-Meier Estimate of OS: Updated Analysis



	Events, n	HR (95% CI)
Pembrolizumab	63	0.63 (0.46-0.88)
Chemotherapy	84	$P = 0.003$[a]

Median (95% CI)
NR (19.4 mo-NE)
14.5 mo (9.8-19.6)

[a]Nominal *P* value.
Data cutoff: Jan 5, 2017.

Combining Immunotherapy

1) Chemotherapy: (NSQCC)

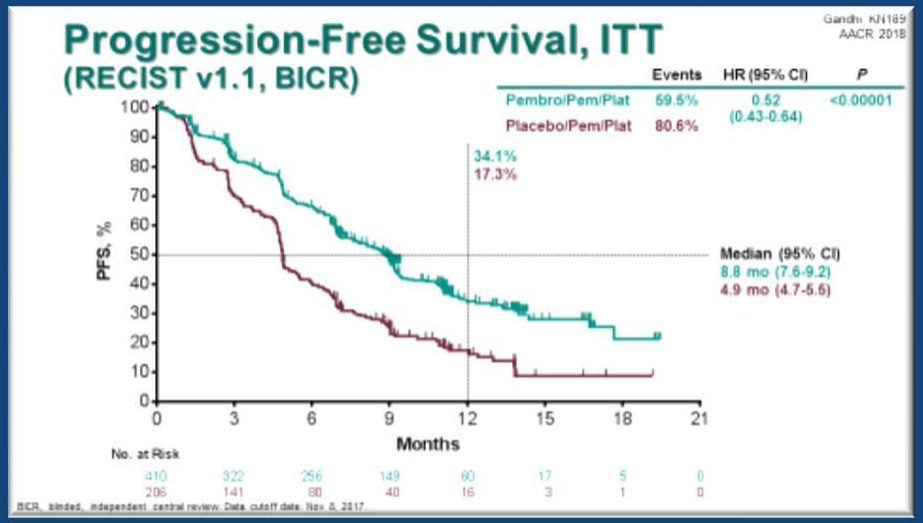
   Carboplatin/Pemetrexed/Pembrolizumab
   [Keynote 021 (9/2017) and Keynote 189 (1/2018)]

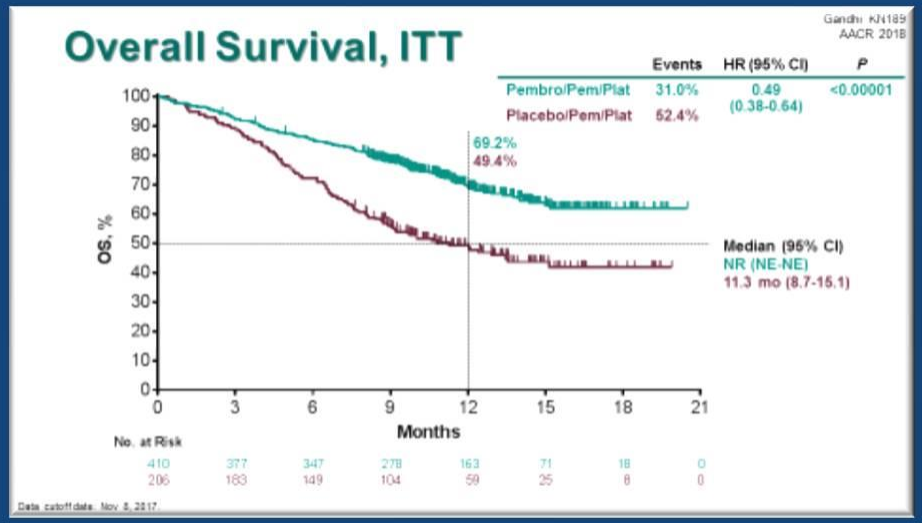
2) Immunotherapy (NSQCC and SQCC)

   Ipilimumab and nivolumab

   [Checkmate 227 (2/2018)]

KEYNOTE 189 Co-primary endpoints: mPFS and mOS

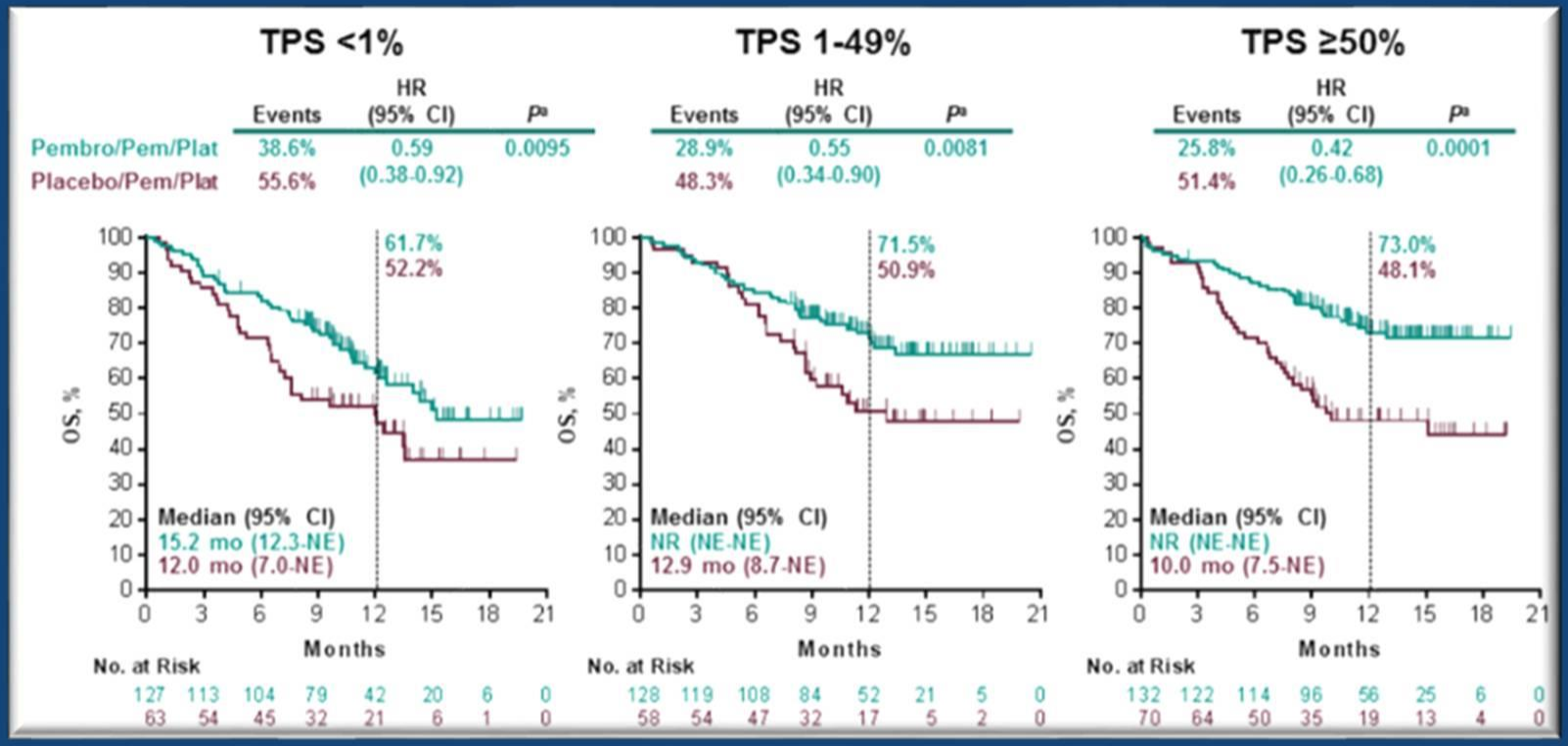




	CPP	Control
mPFS (mo)	8.8 (7.6-9.2)	4.9 (4.7-5.5)
HR, 95% CI, *p* value	0.52 (0.43-0.64) *P = <0.00001*	

	CPP	Control
mOS (mo)	NR	11.3 (8.7-15.1)
HR, 95% CI, *p* value	0.49 (0.38-0.64) *P = <0.00001*	

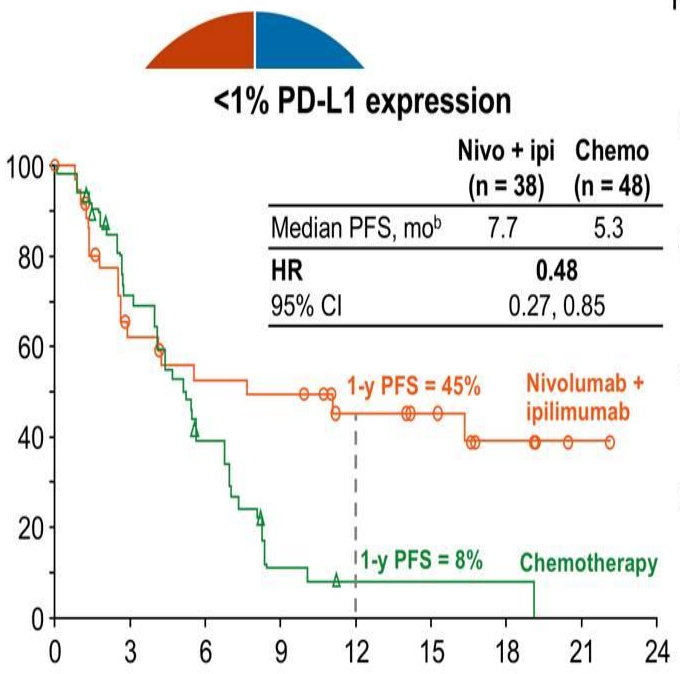
KEYNOTE 189: OS by PDL1 Expression

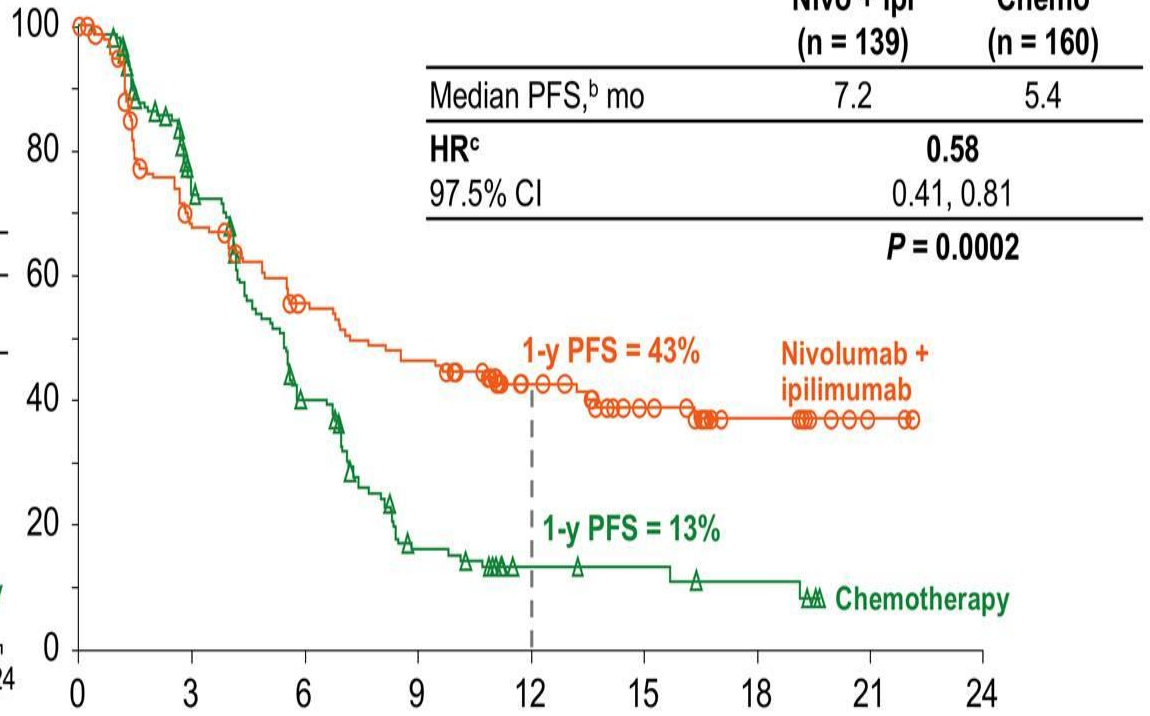


Gandhi, L. NEJM 2018
@MLJohnsonMD2

Presented By Melissa Johnson at 2018 ASCO Annual Meeting

Ipilimumab/nivolumab is better than platinum chemotherapy in TMB ≥ 10Mb irrespective of PD-L1 CheckMate 227





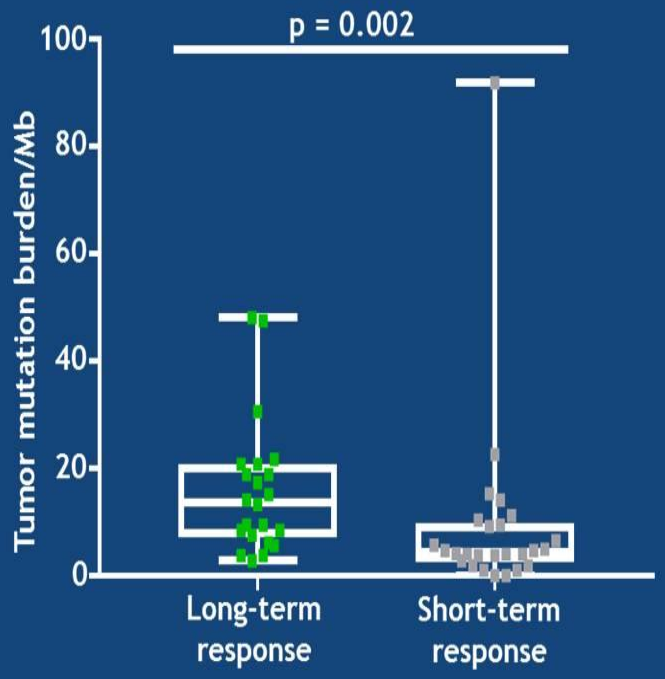
Primary endpoint PFS in high TMB (≥10Mut/Mb)

HR 1.07 in <10Mut/Mb

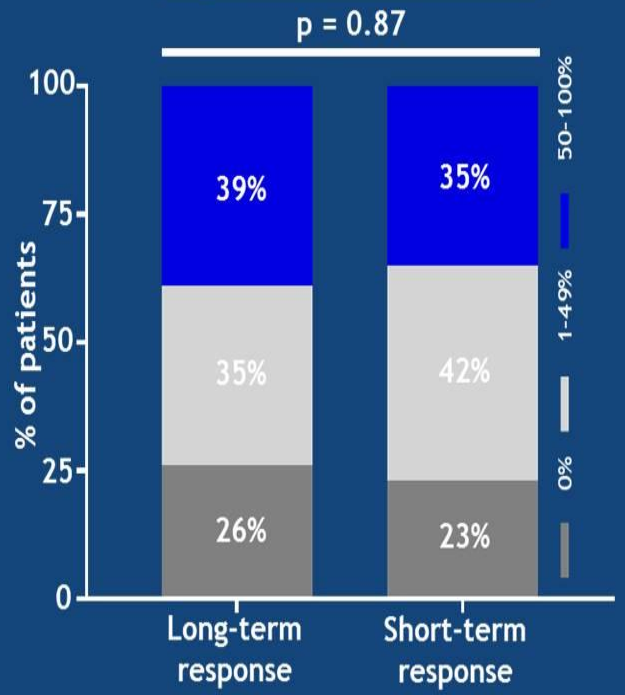
Hellmann, NEJM 2018

TMB and PD-L1 expression among responders with long- vs short-term response

TMB is higher in those with LTR



Proportion of high PD-L1 expression is similar



Rizvi H, et al. ASCO 2018.

ASCO 2018

- Keynote 042: First Line (NSQCC)

  Carbo/Pem vs Pembro [PD-L1 >1%]

- IMPOWER 150: First Line (NSQCC)

  Carbo/Paclit/Bev/Atezo vs SOC

- IMPOWER 131: First Line (SQCC)

  Carbo/Nab-Pac/Atezo vs SOC

- KEYNOTE 407: First Line (SQCC)

  Carbo/Paclit or Nab/Pembro vs SOC

Pembrolizumab vs Platinum-Based Chemotherapy as First-Line Therapy for Advanced/Metastatic NSCLC With a PD-L1 TPS ≥1%: Open-Label, Phase 3 KEYNOTE-042 Study

Gilberto Lopes,[1] Yi-Long Wu,[2] Iveta Kudaba,[3] Dariusz M Kowalski,[4] Byoung Chul Cho,[5] Hande Z Turna,[6] Gilberto Castro, Jr,[7] Vichien Srimuninnimit,[8] Konstantin K. Laktionov,[9] Igor Bondarenko,[10] Karou Kubota,[11] Gregory M Lubiniecki,[12] Jin Zhang,[12] Debra Kush,[12] Tony Mok[13]

[1]Sylvester Comprehensive Cancer Center at the University of Miami, Miami, FL, USA; [2]Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guandong, China; [3]Riga East Clinical University - Latvian Oncology Center, Riga, Latvia; [4]The Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; [5]Yonsei Cancer Center, Seoul, South Korea; [6]Instanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey; [7]Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil; [8]Siriraj Hospital, Bangkok, Thailand; [9]NN Blokhin Russian Cancer Research Center, Moscow, Russia; [10]Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [11]Nippon Medical School Hospital, Tokyo, Japan; [12]Merck & Co., Inc., Kenilworth, NJ, USA; [13]The Chinese University of Hong Kong, Shatin, Hong Kong PRC

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Gilberto Lopes

Presented By Gilberto Lopes at 2018 ASCO Annual Meeting

KEYNOTE-042 Study Design

Key Eligibility Criteria

- Untreated locally advanced or metastatic NSCLC of any histology
- PD-L1 TPS ≥1%
- No sensitizing *EGFR* or *ALK* alterations
- ECOG PS 0 or 1
- No untreated or unstable CNS metastases
- No history of pneumonitis that required systemic corticosteroids

Stratification Factors

- Region (east Asia vs rest of the world)
- ECOG PS (0 vs 1)
- Histology (squamous vs nonsquamous)
- PD-L1 TPS (≥50% vs 1-49%)

Randomize 1:1

N = 637 → Pembrolizumab 200 mg Q3W for up to 35 cycles

N = 637 → Carboplatin AUC 5 or 6 Q3W + Paclitaxel 200 mg/m^2 Q3W[a] OR Carboplatin AUC 5 or 6 Q3W + Pemetrexed 500 mg/m^2 Q3W[a] for up to 6 cycles

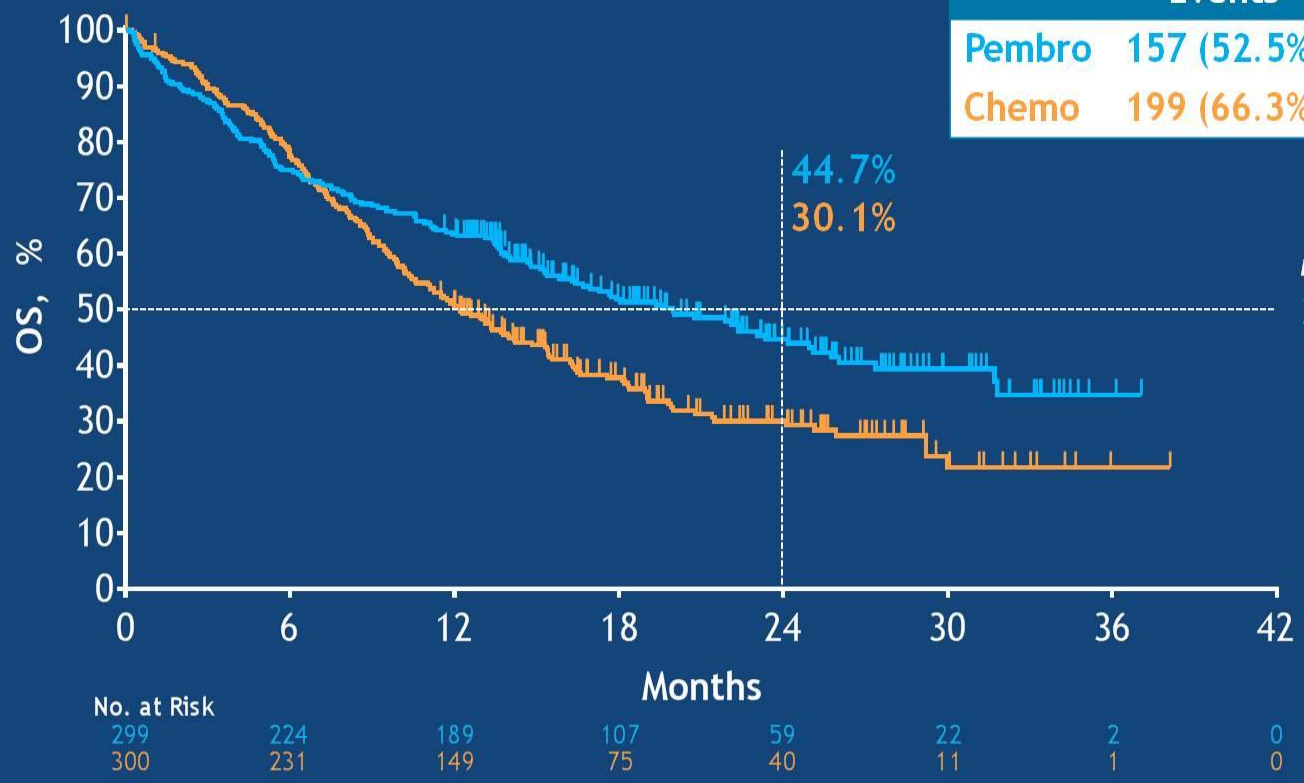
End points

- Primary: OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%
- Secondary: PFS and ORR in TPS ≥50%, ≥20%, and ≥1%; safety in TPS ≥1%

[a]Pemetrexed maintenance therapy was optional but strongly encouraged for patients with nonsquamous histology.

Overall Survival: TPS ≥50%

	Events	HR (95% CI)	*P*
Pembro	157 (52.5%)	0.69 (0.56-0.85)	0.0003
Chemo	199 (66.3%)		

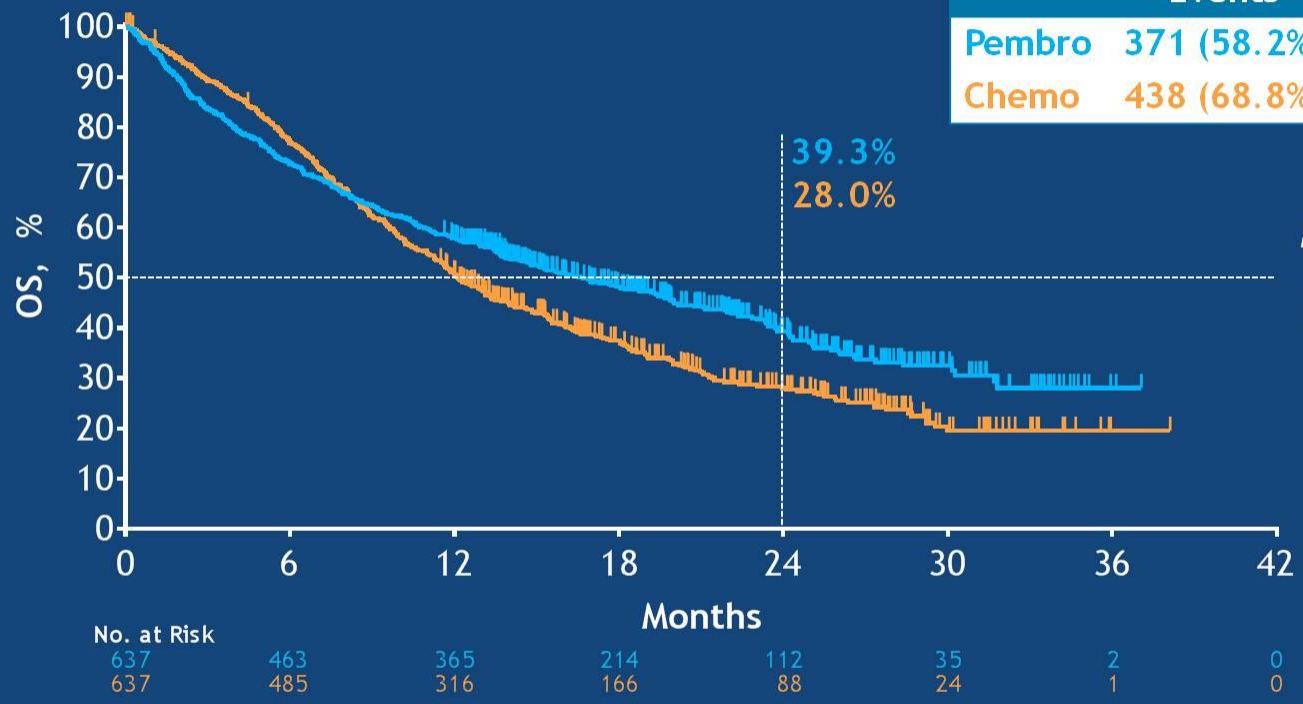


Median (95% CI)
20.0 mo (15.4-24.9)
12.2 mo (10.4-14.2)

Presented By Gilberto Lopes at 2018 ASCO Annual Meeting

Overall Survival: TPS ≥1%

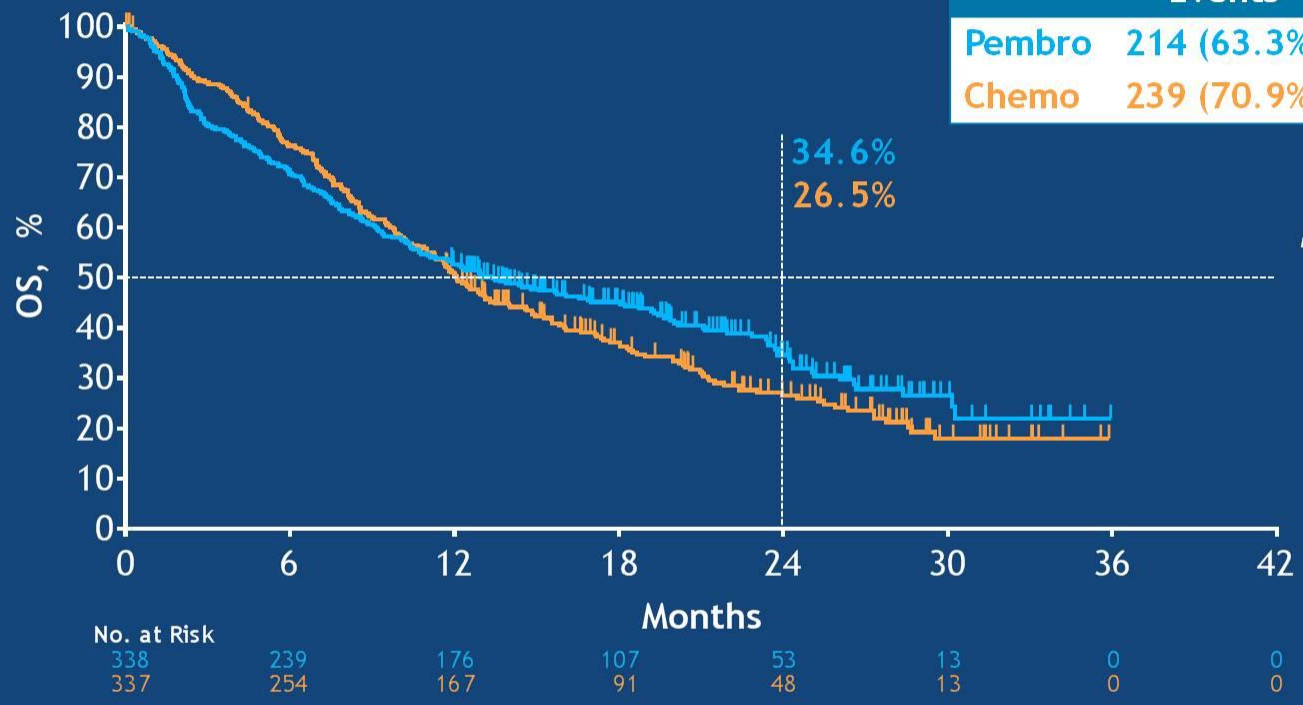
	Events	HR (95% CI)	*P*
Pembro	371 (58.2%)	0.81 (0.71-0.93)	0.0018
Chemo	438 (68.8%)		



Median (95% CI)
16.7 mo (13.9-19.7)
12.1 mo (11.3-13.3)

Overall Survival: TPS ≥1-49% (Exploratory Analysis[a])

	Events	HR (95% CI)
Pembro	214 (63.3%)	0.92 (0.77-1.11)
Chemo	239 (70.9%)	



Median (95% CI)
13.4 mo (10.7-18.2)
12.1 mo (11.0-14.0)

[a]No alpha allocated to this comparison.

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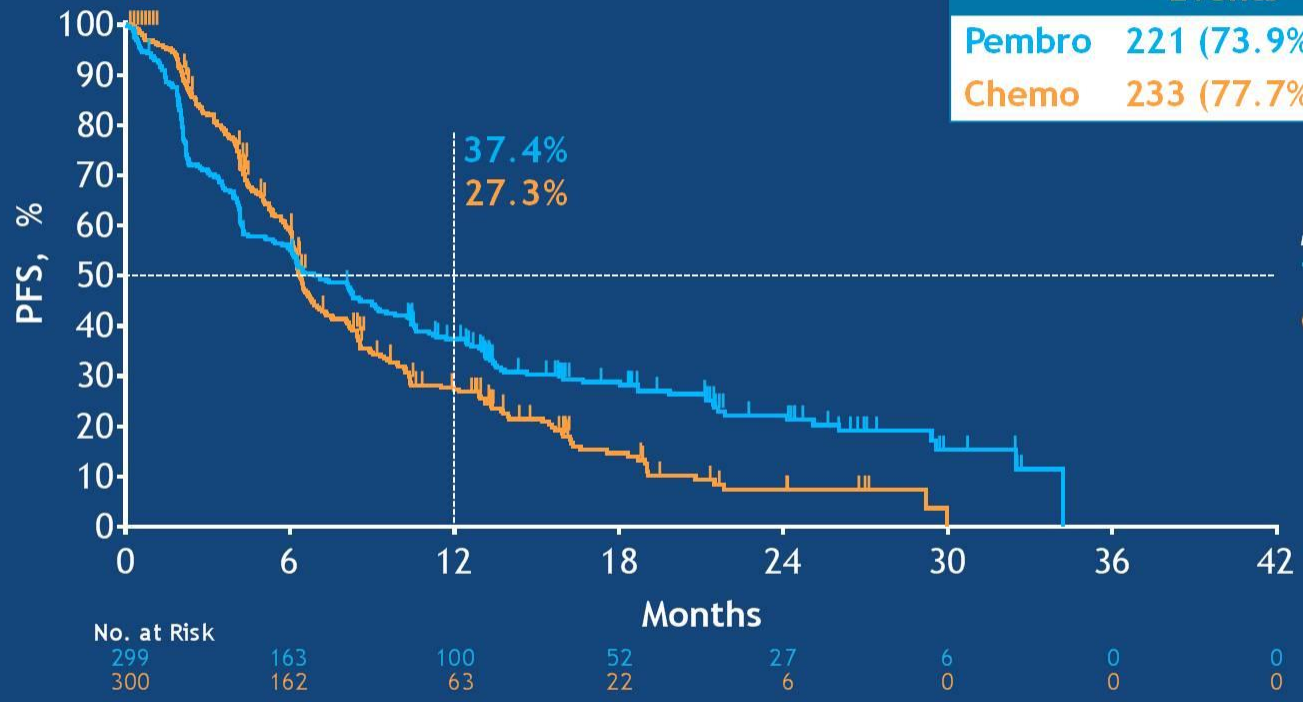
Progression-Free Survival: TPS ≥50%
(RECIST v1.1, BICR)

	Events	HR (95% CI)	*P*
Pembro	221 (73.9%)	0.81 (0.67-0.99)	0.0170[a]
Chemo	233 (77.7%)		

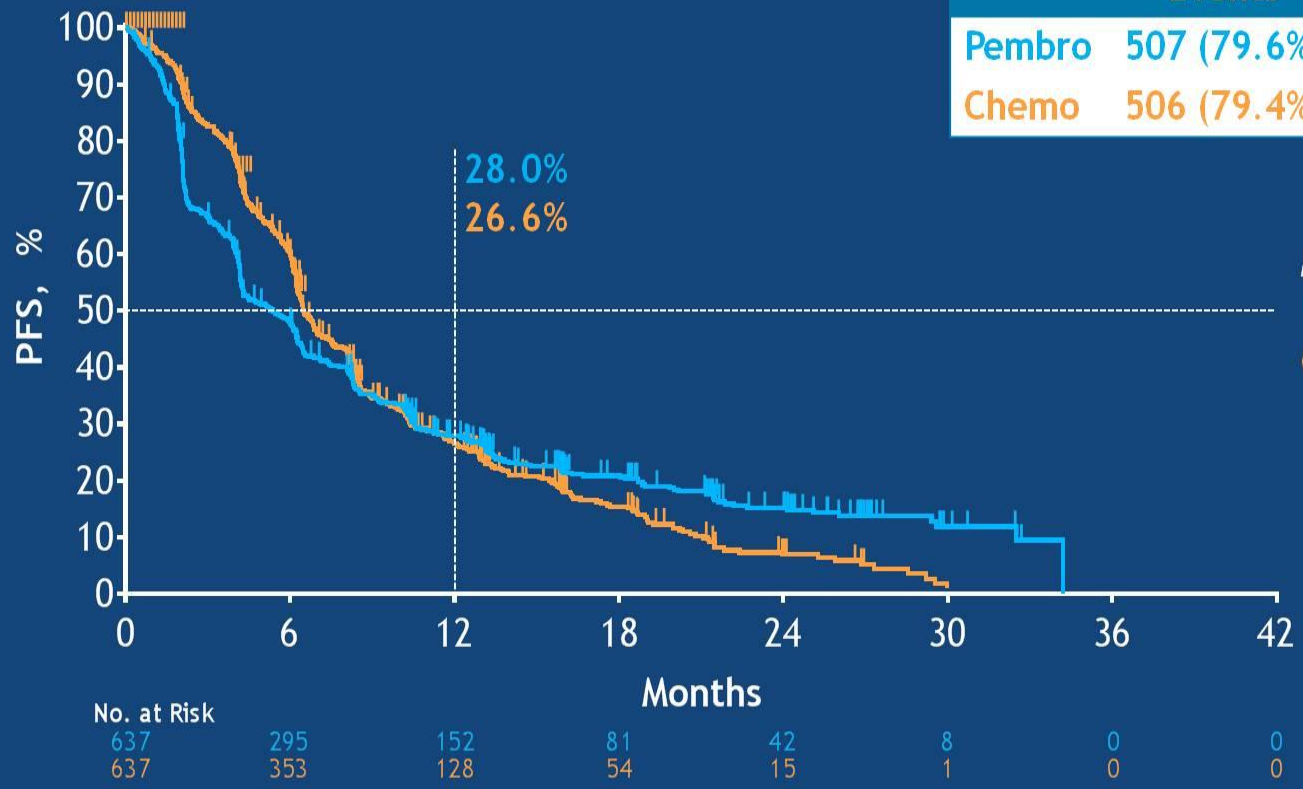


Median (95% CI)
7.1 mo (5.9-9.0)
6.4 mo (6.1-6.9)

[a]Protocol-specified significance boundary not met. BICR, blinded independent central review.

Progression-Free Survival: TPS ≥1%
(RECIST v1.1, BICR)

	Events	HR (95% CI)
Pembro	507 (79.6%)	1.07 (0.94-1.21)
Chemo	506 (79.4%)	



Median (95% CI)
5.4 mo (4.3-6.2)
6.5 mo (6.3-7.0)

Formal comparison of pembrolizumab vs chemotherapy not performed based on hierarchical testing strategy.

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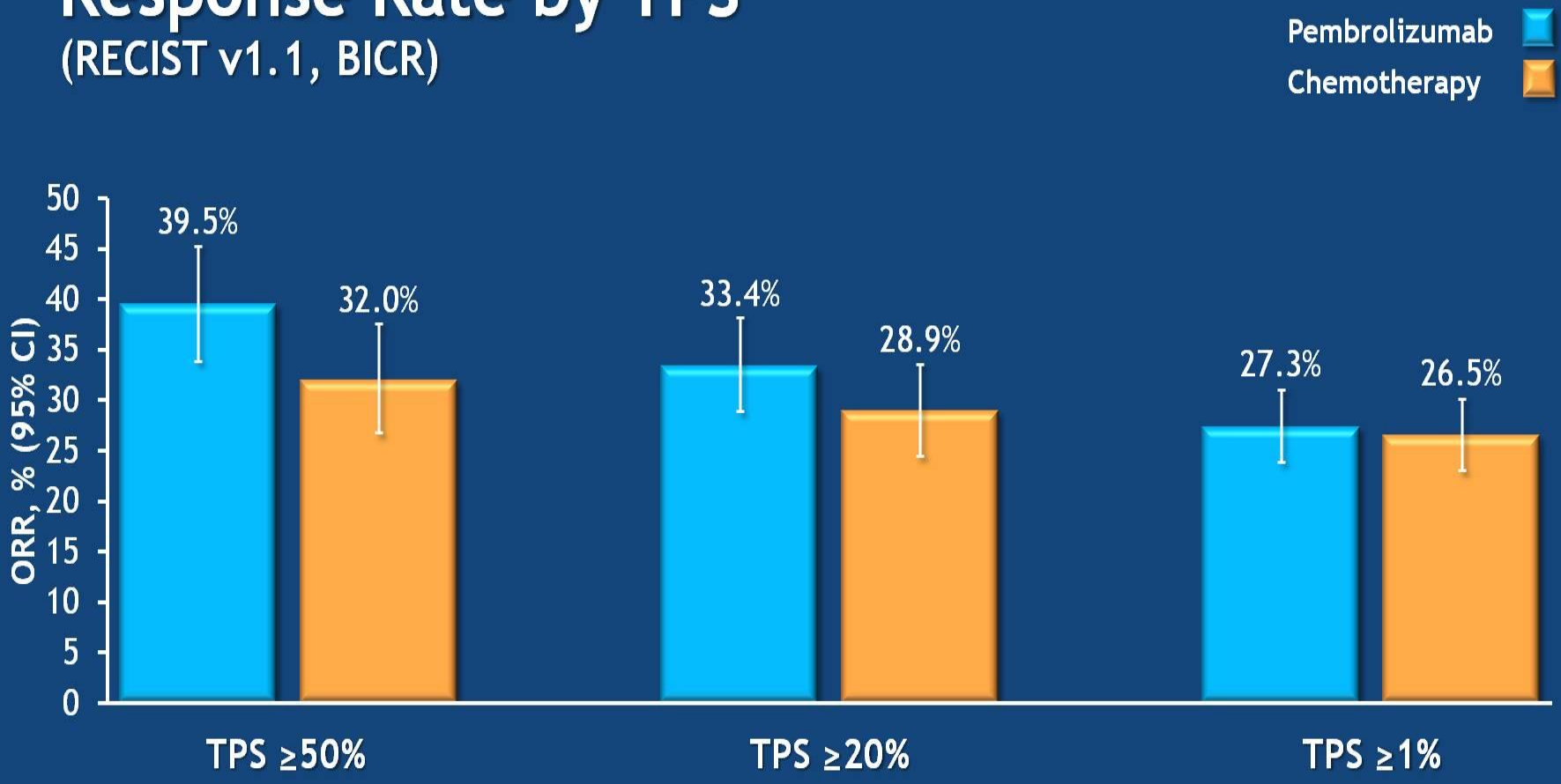
Response Rate by TPS
(RECIST v1.1, BICR)



ORR for TPS 1-49%: 16.6% (95% CI 12.8-21.0) for pembro vs 21.7% (95% CI 17.4-26.4).
CR in pembro arm: 0 with TPS ≥50%, 2 with TPS ≥20%, 3 with TPS ≥1%; CR in chemo arm: 0 with TPS ≥50%, 1 with TPS ≥20%, 3 with TPS ≥1%.

Data cutoff date: Feb 26, 2018.

Summary and Conclusions

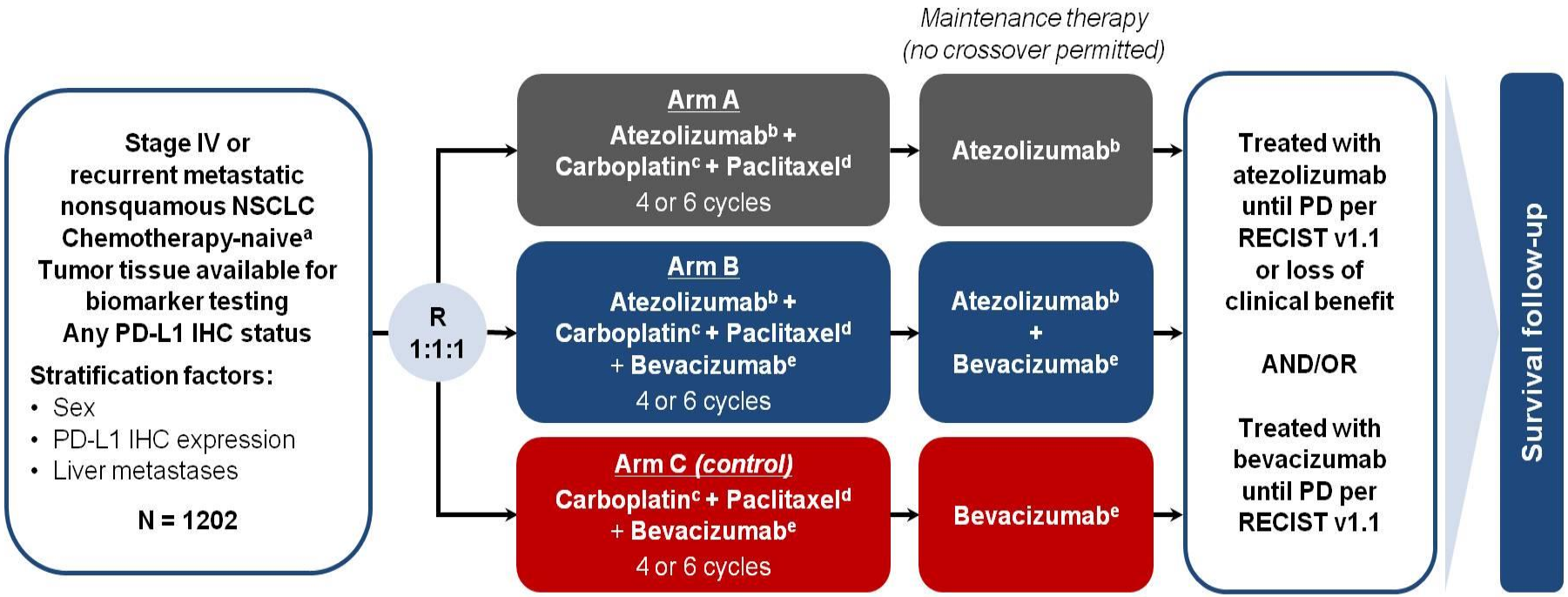
- Pembrolizumab significantly improved OS over platinum-based chemotherapy as first-line therapy for advanced/metastatic NSCLC with PD-L1 TPS ≥50%, ≥20%, and ≥1%
  - HR (95% CI) of 0.69 (0.56-0.85), 0.77 (0.64-0.92), and 0.81 (0.71-0.93), respectively
  - Greater magnitude of benefit for pembrolizumab at higher levels of PD-L1 expression is consistent with previous studies of pembrolizumab monotherapy in metastatic NSCLC
  - In an exploratory analysis of TPS 1-49% population, HR (95% CI) was 0.92 (0.77-1.11)
- No significant PFS benefit for pembrolizumab at this analysis
  - Based on recommendation of external data monitoring committee, study is continuing to evaluate PFS based on additional follow-up
- Duration of response longer in patients treated with pembrolizumab than chemotherapy at all levels of PD-L1 expression

IMpower150: Overall Survival Analysis of a Randomized Phase III Study of Atezolizumab + Chemotherapy ± Bevacizumab vs Chemotherapy + Bevacizumab in 1L Nonsquamous NSCLC

Mark A. Socinski,[1] Robert Jotte,[2] Federico Cappuzzo,[3] Francisco Orlandi,[4] Daniil Stroyakovskiy,[5] Naoyuki Nogami,[6] Delvys Rodríguez-Abreu,[7] Denis Moro-Sibilot,[8] Christian A. Thomas,[9] Fabrice Barlesi,[10] Gene Finley,[11] Claudia Kelsch,[12] Anthony Lee,[12] Shelley Coleman,[12] Yijing Shen,[12] Marcin Kowanetz,[12] Ariel Lopez-Chavez,[12] Alan Sandler,[12] Martin Reck[13]

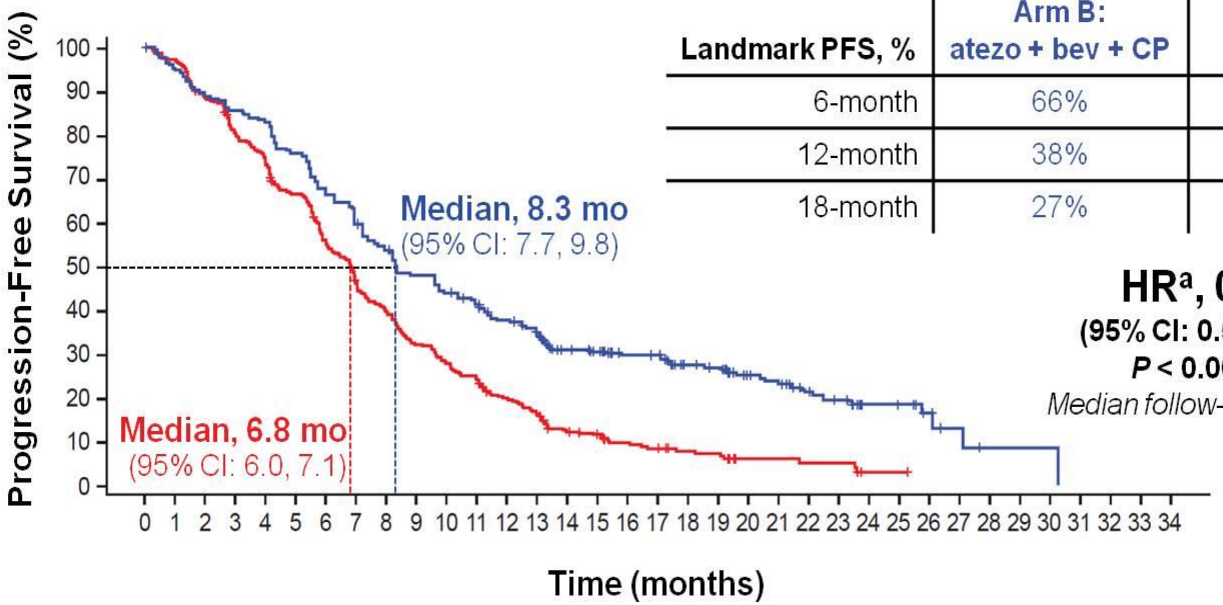
[1]Florida Hospital Cancer Institute, Orlando, FL; [2]Rocky Mountain Cancer Centers, Denver, CO and US Oncology, Houston, TX; [3]Azienda Unità Sanitaria Locale della Romagna, Ravenna, Italy; [4]Instituto Nacional del Torax, Santiago, Chile; [5]Moscow City Oncology Hospital, Moscow, Russia; [6]National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; [7]Complejo Hospitalario Univesitario Insular Materno-Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [8]Centre Hospitalier Universitaire de Grenoble Alpes, Grenoble, France; [9]New England Cancer Specialists, Scarborough, ME; [10]Aix Marseille University, Assistance Publique Hôpitaux de Marseille, Marseille, France; [11]Allegheny Health Network Cancer Institute, Pittsburgh, PA; [12]Genentech, Inc., South San Francisco, CA; [13]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany

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.

Updated PFS Analysis in the ITT-WT (Arm B vs Arm C)



Landmark PFS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
6-month	66%	56%
12-month	38%	20%
18-month	27%	8%

HR[a], 0.59
(95% CI: 0.50, 0.70)
***P* < 0.0001[b]**
Median follow-up: ~20 mo

No. at Risk

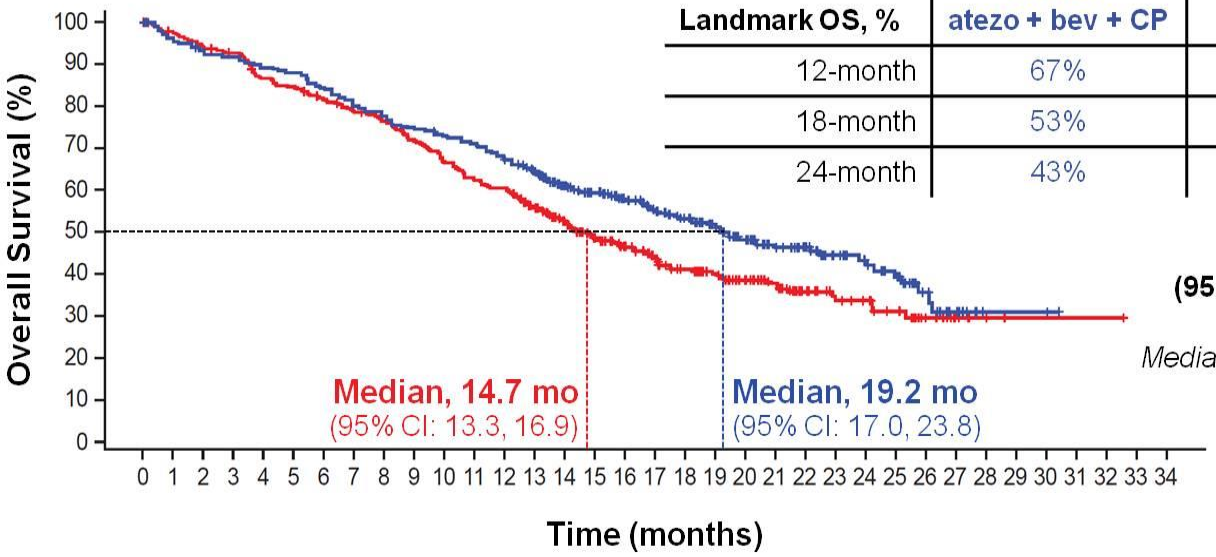
Atezo+Bev+CP	359	336	315	301	293	267	234	213	190	168	154	146	125	112	85	80	69	68	53	50	37	33	24	20	12	11	6	3	1	1	1
Bev+CP	337	323	294	263	244	215	180	148	127	103	89	78	61	50	35	29	21	18	14	13	6	6	5	5	1	1					

- Statistically significant and clinically meaningful PFS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was previously observed[1] and continued to improve with additional follow-up

[a] Stratified HR. [b] For descriptive purposes only. Data cutoff: January 22, 2018

1. Reck M, et al. ESMO IO 2017 [abstract LBA1_PR].

OS in the ITT-WT (Arm B vs Arm C)



Landmark OS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
12-month	67%	61%
18-month	53%	41%
24-month	43%	34%

HR[a], 0.78
(95% CI: 0.64, 0.96)
***P* = 0.0164**
Median follow-up: ~20 mo

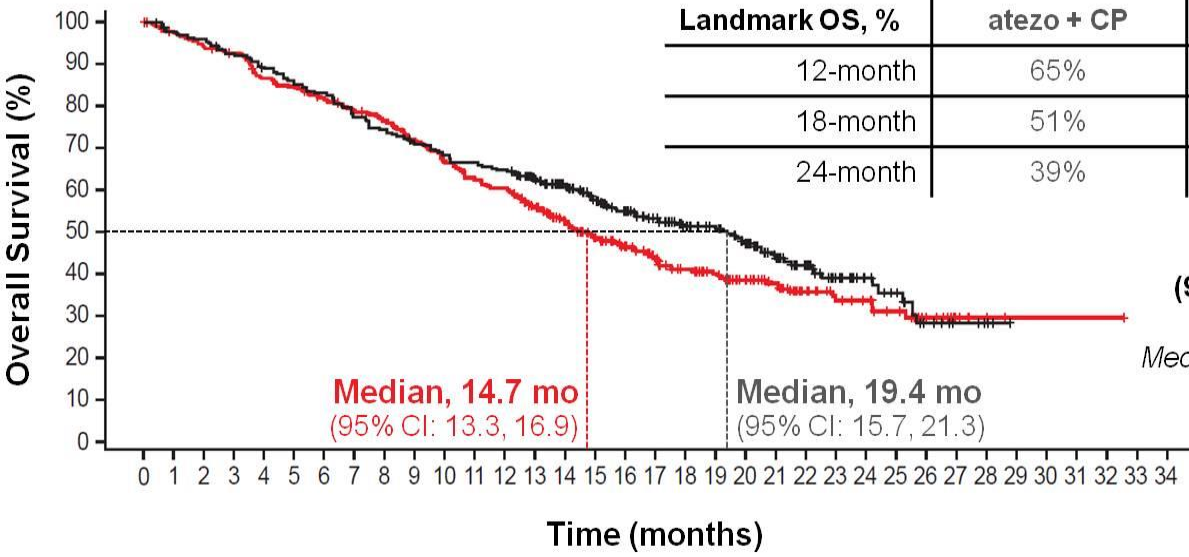
No. at Risk

Atezo+Bev+CP	359	339	328	323	314	310	296	284	273	264	256	250	235	218	188	167	147	133	119	103	84	66	57	41	34	28	16	9	2	2	2
Bev+CP	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1

- Statistically significant and clinically meaningful OS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was observed

[a] Stratified HR.
Data cutoff: January 22, 2018

OS in the ITT-WT (Arm A vs Arm C)



Landmark OS, %	Arm A: atezo + CP	Arm C: bev + CP
12-month	65%	61%
18-month	51%	41%
24-month	39%	34%

HR[a], 0.88
(95% CI: 0.72, 1.08)
***P* = 0.2041**
Median follow-up: ~20 mo

No. at Risk

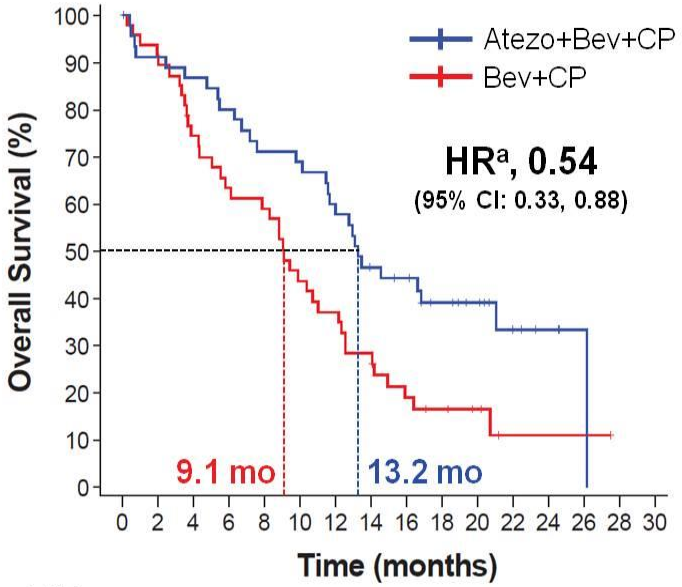
Atezo+CP	349	339	331	319	307	294	284	266	255	244	234	227	221	203	180	153	131	115	100	91	77	60	46	33	23	18	9	5	3
Bev+CP	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1

- A trend toward OS benefit was observed with atezolizumab + chemotherapy vs bevacizumab + chemotherapy, but the efficacy boundary has not yet been crossed and will be tested again at the time of the final analysis

[a] Stratified HR.
Data cutoff: January 22, 2018

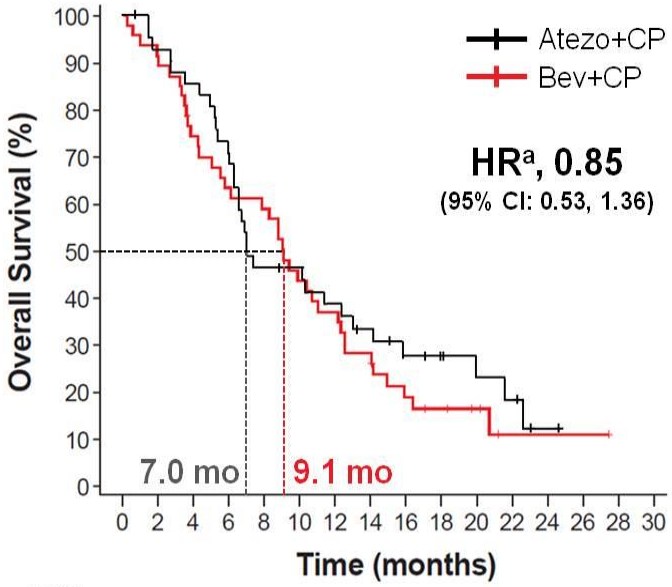
Addition of Bevacizumab to Atezolizumab and Chemotherapy Prolongs Survival of Patients With Liver Metastases in the ITT-WT

Arm B vs Arm C



No. at Risk														
Atezo+Bev+CP	47	41	39	36	32	31	26	20	18	13	10	5	3	1
Bev+CP	47	42	34	29	27	20	17	13	8	6	4	1	1	1

Arm A vs Arm C

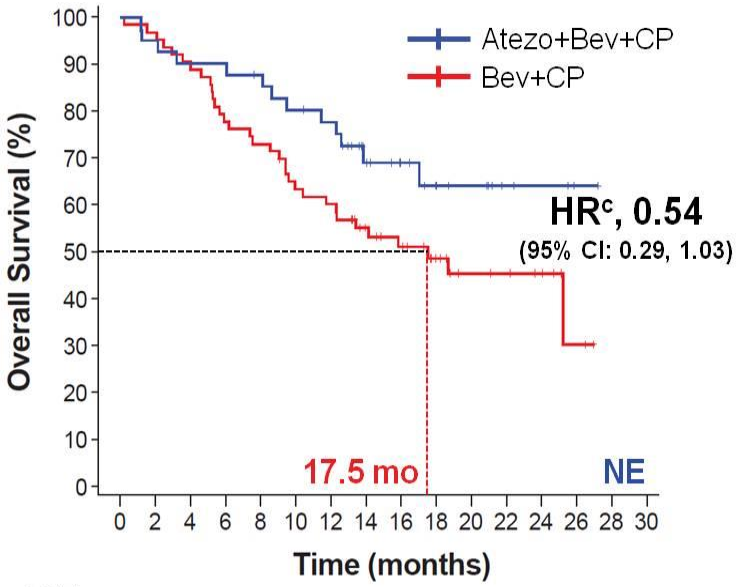


No. at Risk													
Atezo+CP	42	38	35	28	19	18	15	12	9	7	5	4	1
Bev+CP	47	42	34	29	27	20	17	13	8	6	4	1	1	1

[a] Unstratified HR.
Data cutoff: January 22, 2018

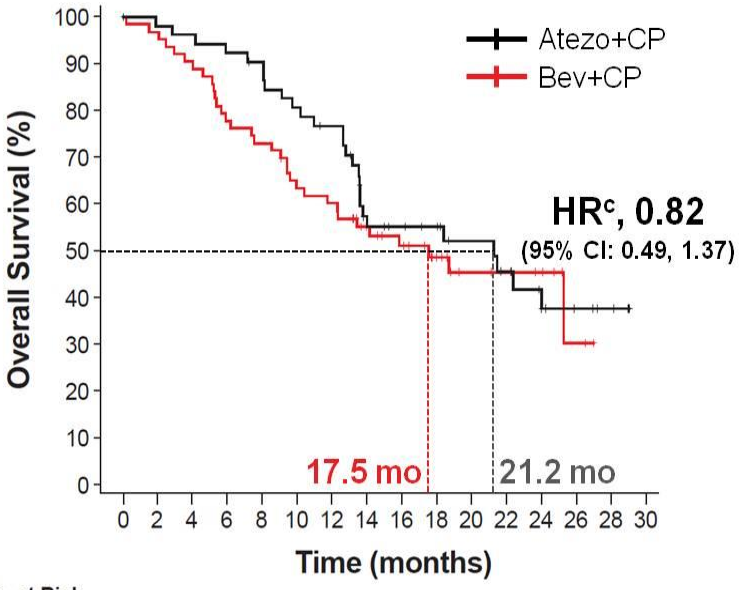
Addition of Bevacizumab to Atezolizumab and Chemotherapy Prolongs Survival of *EGFR/ALK*+ Patients[a]

Arm B[b] *vs Arm C*



No. at Risk														
Atezo+Bev+CP	41	39	37	37	35	32	30	20	15	11	9	5	4	2
Bev+CP	63	61	57	49	46	39	37	28	24	17	12	11	7	2

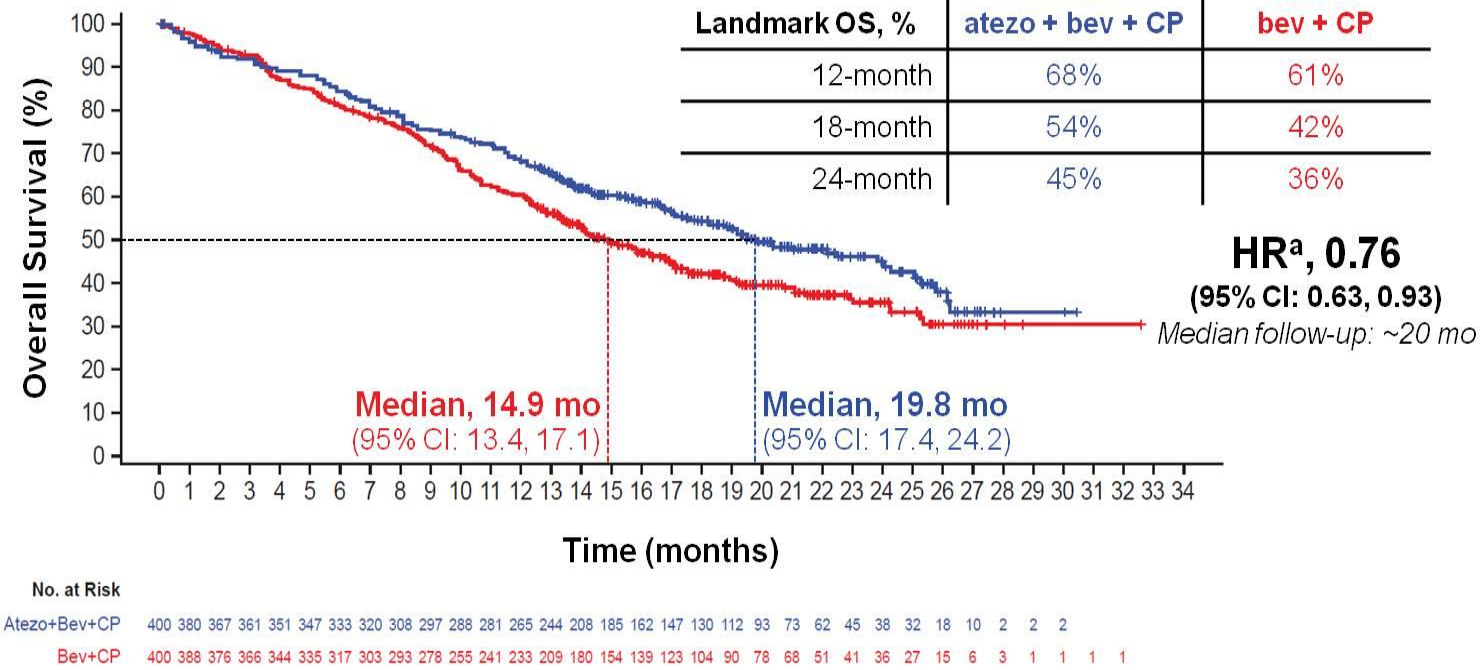
Arm A vs Arm C



No. at Risk														
Atezo+CP	53	51	50	48	46	41	37	24	22	20	16	13	8	6	4
Bev+CP	63	61	57	49	46	39	37	28	24	17	12	11	7	2

[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] One patient had *EGFR* exon 19 deletion and also tested *ALK* positive per central lab. [c] Unstratified HR.
Data cutoff: January 22, 2018

OS in the ITT (Arm B vs Arm C)



Landmark OS, %	Arm B: atezo + bev + CP	Arm C: bev + CP
12-month	68%	61%
18-month	54%	42%
24-month	45%	36%

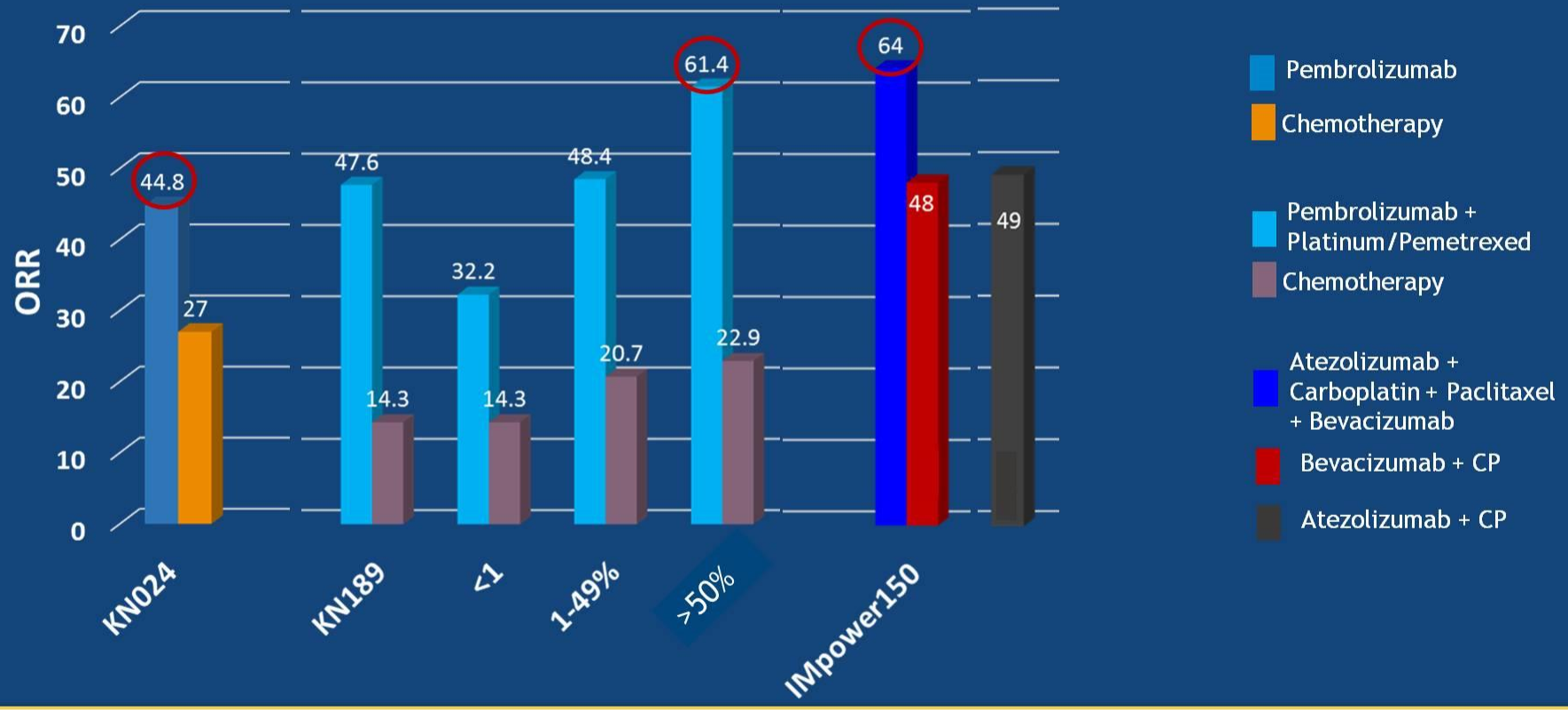
- Clinically meaningful OS benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy was observed in all patients

[a] Stratified HR.
Data cutoff: January 22, 2018

Summary

- IMpower150 met its co-primary PFS and OS endpoints and demonstrated a statistically significant and clinically meaningful benefit with atezolizumab + bevacizumab + chemotherapy vs bevacizumab + chemotherapy in 1L nonsquamous NSCLC, across all PD-L1 subgroups
- Clinical benefit was observed in key subgroups of patients with *EGFR/ALK* genomic alterations and liver metastases at baseline, with the addition of bevacizumab to atezolizumab + chemotherapy
- The efficacy boundary has not yet been crossed for atezolizumab + chemotherapy vs bevacizumab + chemotherapy and will be tested again at the time of the final analysis
- These data demonstrate that atezolizumab + bevacizumab + chemotherapy provide a new standard of care, particularly for key patient populations studied in this trial

Chemotherapy does improve ORR



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When might we still consider chemotherapy + IO?

- Symptomatic patients
- Poor prognosis with monotherapy
- Patients receiving steroids

IMpower131: Primary PFS and Safety Analysis of a Randomized Phase III Study of Atezolizumab + Carboplatin + Paclitaxel or Nab-Paclitaxel vs Carboplatin + Nab-Paclitaxel as 1L Therapy in Advanced Squamous NSCLC

Robert Jotte,[1,2] Federico Cappuzzo,[3] Ihor Vynnychenko, [4] Daniil Stroyakovskiy,[5] Delvys Rodriguez Abreu,[6] Maen Hussein,[7] Ross Soo,[8] Henry J. Conter,[9] Toshiyuki Kozuki,[10] Carlos da Silva,[11] Vilma Graupner,[12] Shawn W. Sun,[13] Ray Lin,[13] Helen Jessop,[12] Marcin Kowanetz,[13] Tien Hoang,[13] Alan Sandler,[13] Mark A. Socinski[14]

[1]Rocky Mountain Cancer Centers, Denver, CO; [2]US Oncology, Houston, TX; [3]Azienda Unità Sanitaria Locale della Romagna, Ravenna, Italy; [4]Sumy State University, Sumy, Ukraine; [5]Moscow City Oncology Hospital, Moscow Healthcare Department, Moscow Oblast, Russia; [6]Complejo Hospitalario Universitario Insular-Materno Infantil de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Spain; [7]Sarah Cannon Research Institute/Florida Cancer Specialists, Lady Lake, FL; [8]Department of Haematology-Oncology, National University Hospital, Singapore; [9]William Osler Health System, Brampton, ON, Canada; [10]Department of Thoracic Oncology and Medicine, National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; [11]Fundação Pio XII Institution – Cancer Hospital of Barretos, Barretos, São Paulo, Brazil; [12]F. Hoffmann-La Roche, Ltd, Basel, Switzerland; [13]Genentech, Inc., South San Francisco, CA; [14]Florida Hospital Cancer Institute, Orlando, FL

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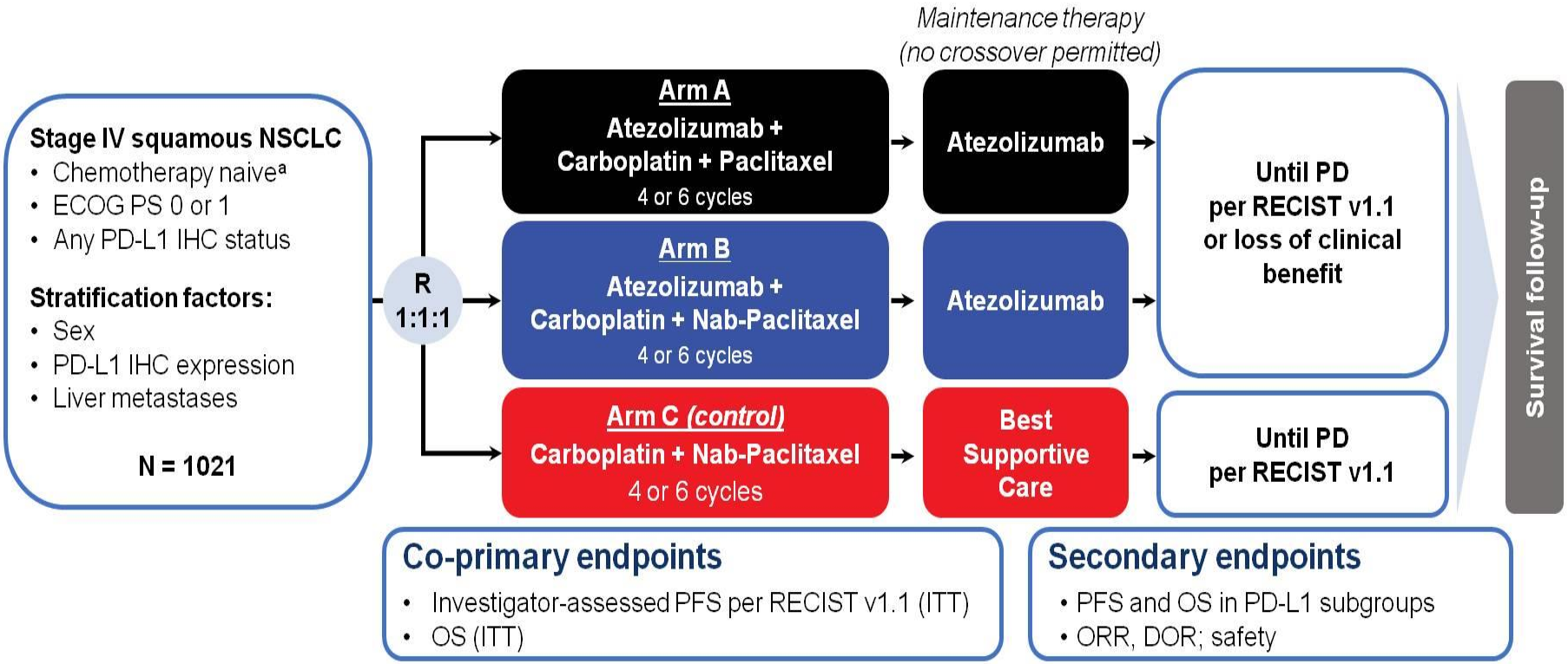
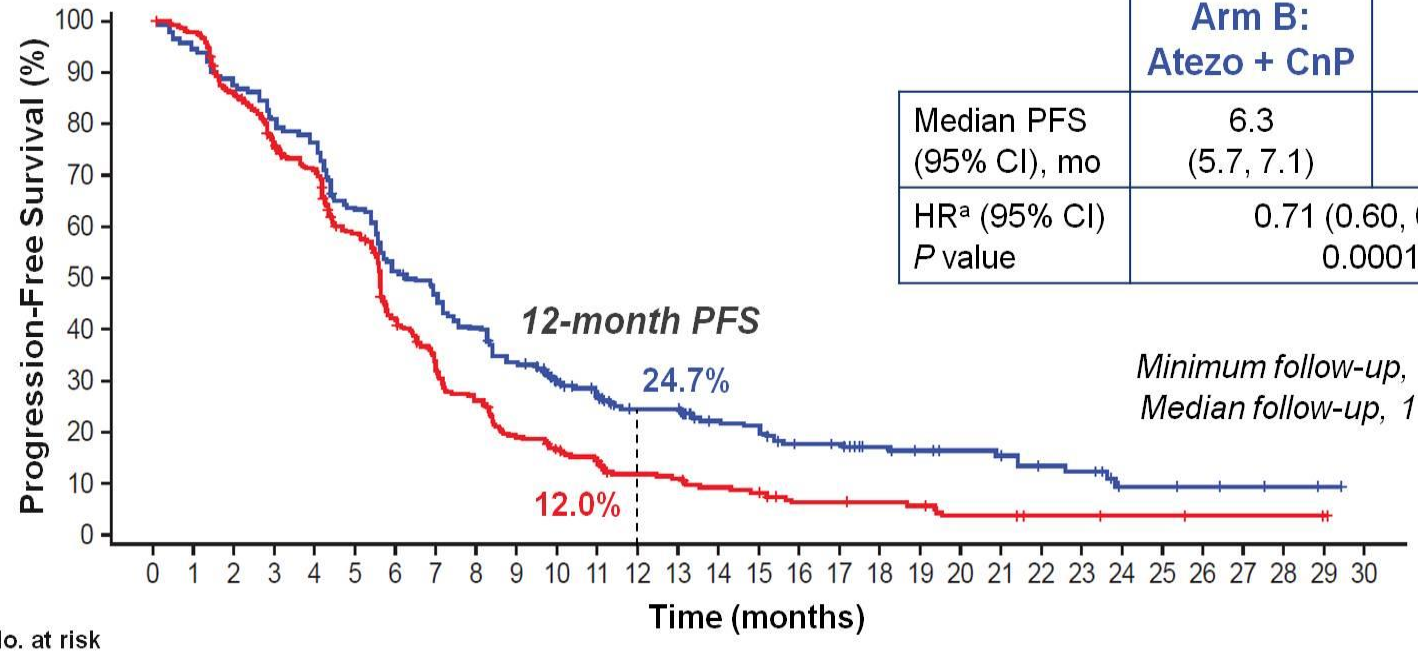
IMpower131: Study Design



Atezolizumab 1200 mg IV q3w; carboplatin AUC 6 IV q3w; nab-paclitaxel 100 mg/m^2 IV qw; paclitaxel 200 mg/m^2 IV q3w.
[a] Patients with a sensitising *EGFR* mutation or *ALK* translocation must have disease progression or intolerance to treatment with ≥ 1 approved targeted therapies. Testing for *EGFR* mutation or *ALK* translocation was not mandatory.
[b] PD-L1 expression was evaluated using the VENTANA SP142 IHC assay.

INV-Assessed PFS in the ITT Population (Arm B vs Arm C)

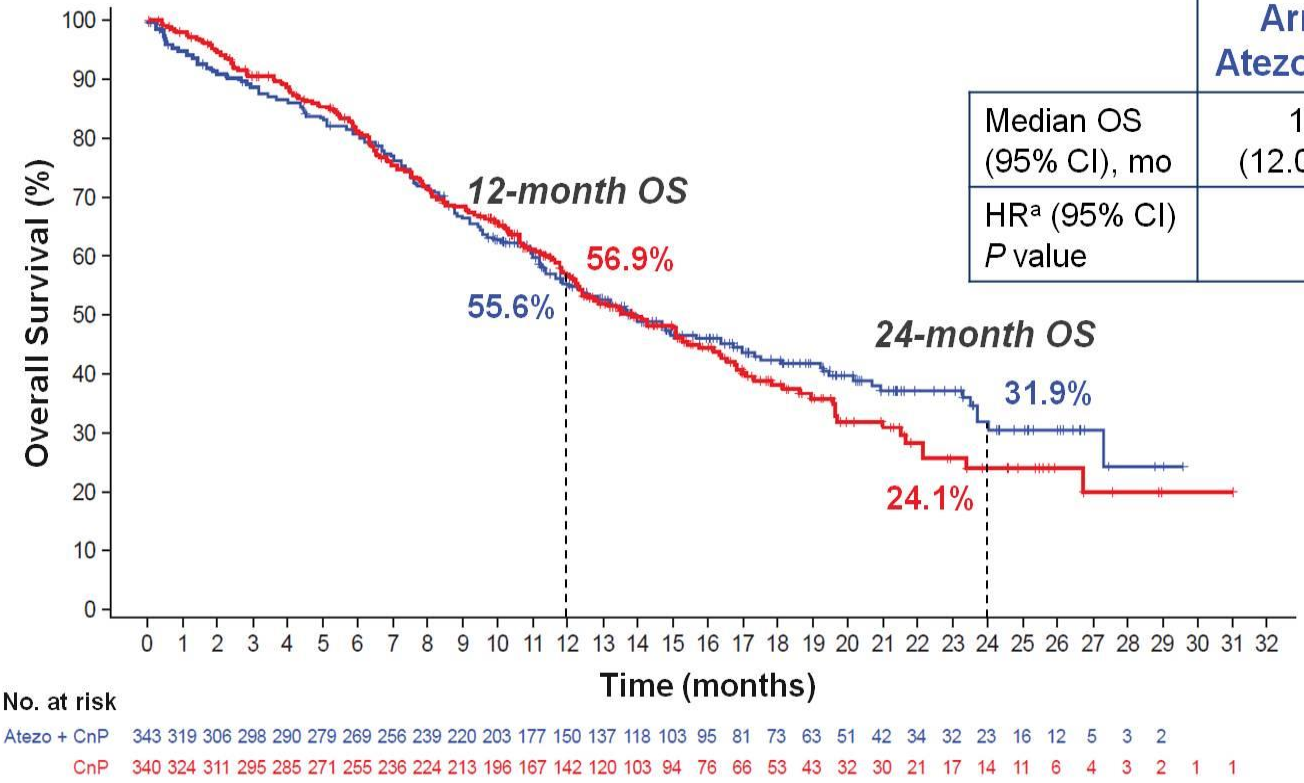


	Arm B: Atezo + CnP	Arm C: CnP
Median PFS (95% CI), mo	6.3 (5.7, 7.1)	5.6 (5.5, 5.7)
HR[a] (95% CI)	0.71 (0.60, 0.85)	
P value	0.0001	

Minimum follow-up, 9.8 mo
Median follow-up, 17.1 mo

Data cutoff: January 22, 2018.
INV, investigator. [a] Stratified HR.

First Interim OS in the ITT Population (Arm B vs Arm C)



	Arm B: Atezo + CnP	Arm C: CnP
Median OS (95% CI), mo	14.0 (12.0, 17.0)	13.9 (12.3, 16.4)
HR[a] (95% CI)	0.96 (0.78, 1.18)	
P value	0.6931	

Data cutoff: January 22, 2018.
[a] Stratified HR.

Presented By Robert Jotte at 2018 ASCO Annual Meeting

Summary

- IMpower131 met the co-primary endpoint of investigator-assessed PFS with atezolizumab + CnP (Arm B) vs CnP (Arm C) in the ITT population
- PFS benefit in Arm B vs Arm C was observed across all PD-L1–expressing subgroups and was enriched in subgroups with higher PD-L1 expression
- Atezolizumab + CnP has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified
- OS continues to be followed, with the next interim OS analysis anticipated later in 2018

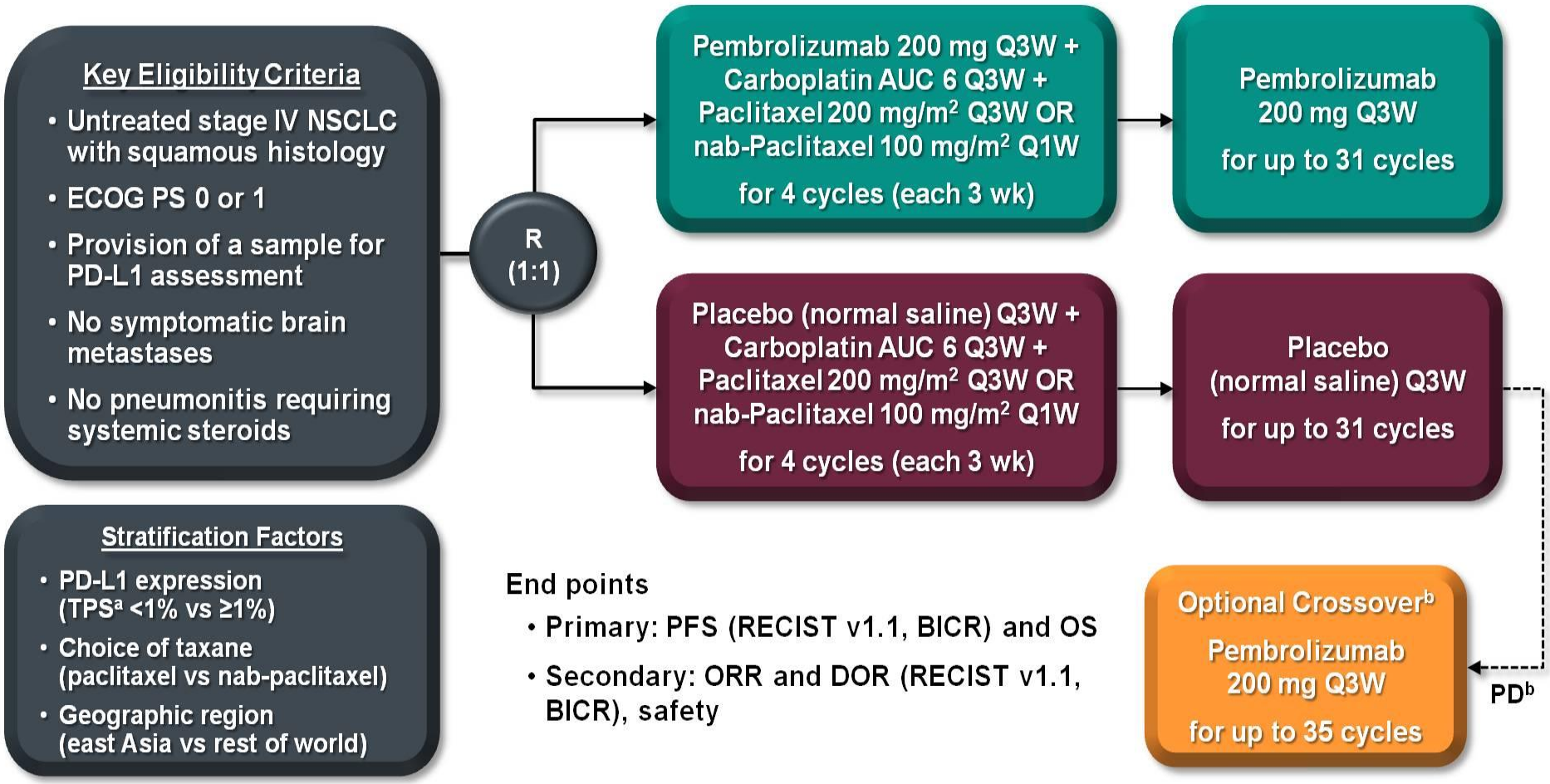
KEYNOTE-407: Phase 3 Study of Carboplatin-Paclitaxel/Nab-Paclitaxel With or Without Pembrolizumab for Metastatic Squamous NSCLC

Luis Paz-Ares,[1] Alexander Luft,[2] Ali Tafreshi,[3] Mahmut Gümüş,[4] Julien Mazières,[5] Barbara Hermes,[6] Filiz Çay Senler,[7] Andrea Fülöp,[8] Jeronimo Rodriguez Cid,[9] Shunichi Sugawara,[10] Ying Cheng,[11] Silvia Novello,[12] Balazs Halmos,[13] Yue Shentu,[14] Xiaodong Li,[14] Gregory M Lubiniecki,[14] Bilal Piperdi,[14] Dariusz Kowalski[15]

[1]Hospital Universitario 12 de Octubre, Madrid, Spain; [2]Leningrad Regional Clinical Hospital, St. Petersburg, Russia; [3]Wollongong Hospital, Wollongong, NSW, Australia; [4]Kartal Research and Training Hospital, Istanbul, Turkey; [5]Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [6]Universitätskinikum Tübingen, Tuebingen, Germany; [7]Ankara University, Ankara, Turkey; [8]Országos Korányi TBC és Pulmonológiai Intézet, Budapest, Hungary; [9]Oncology Center, Medica Sur Hospital, Mexico City, Mexico; [10]Sendai Kousei Hospital, Sendai, Japan; [11]Cancer Hospital of Jilin Province, Changchun, China; [12]University of Turin, Orbassano, Italy; [13]Albert Einstein College of Medicine, Bronx, NY, USA; [14]Merck & Co., Inc., Kenilworth, NJ, USA; [15]Maria Skłodowska-Curie Institute of Oncology, Warsaw, Poland

Presented By Luis Paz-Ares at 2018 ASCO Annual Meeting

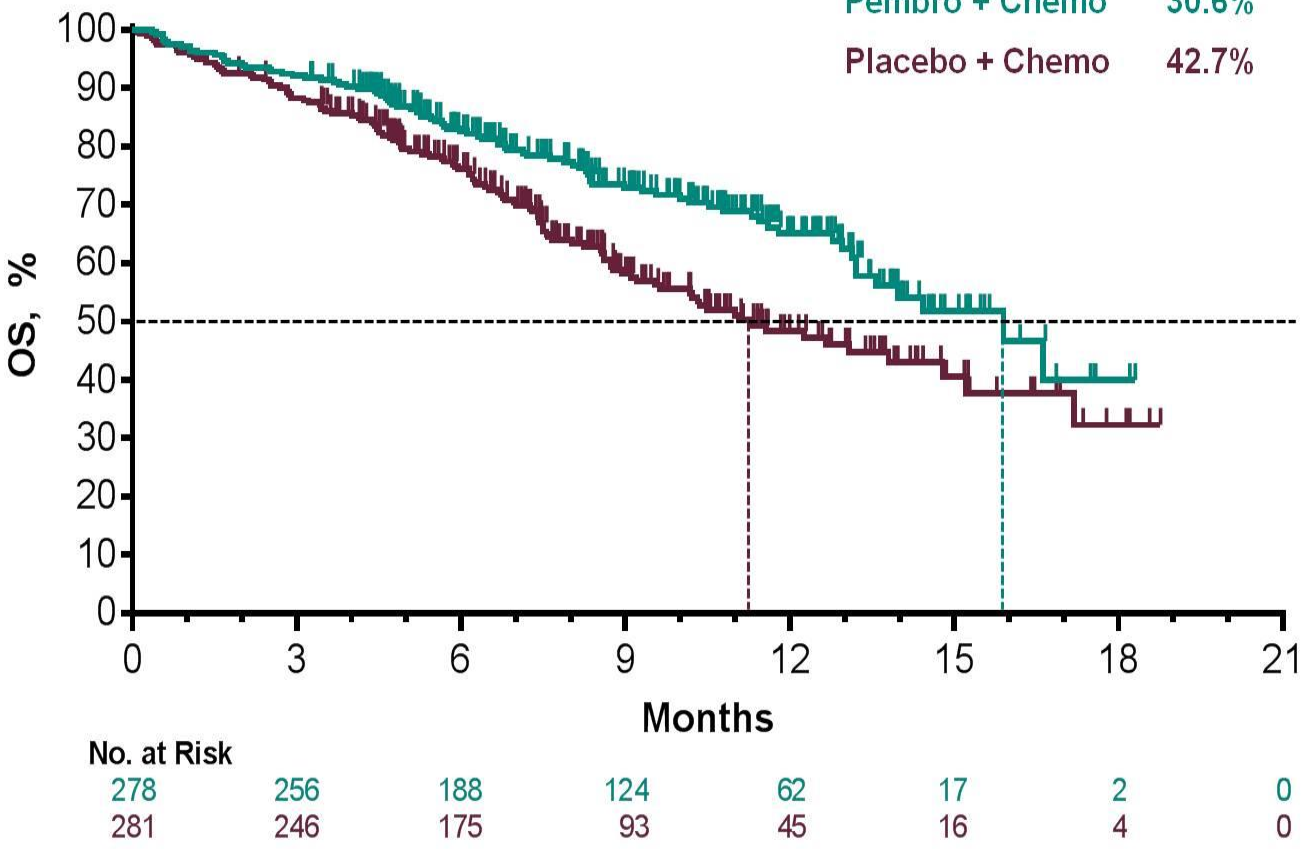
KEYNOTE-407 Study Design (NCT02775435)



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

Overall Survival at IA2, ITT

	Events	HR (95% CI)	*P*
Pembro + Chemo	30.6%	0.64 (0.49-0.85)	0.0008
Placebo + Chemo	42.7%		



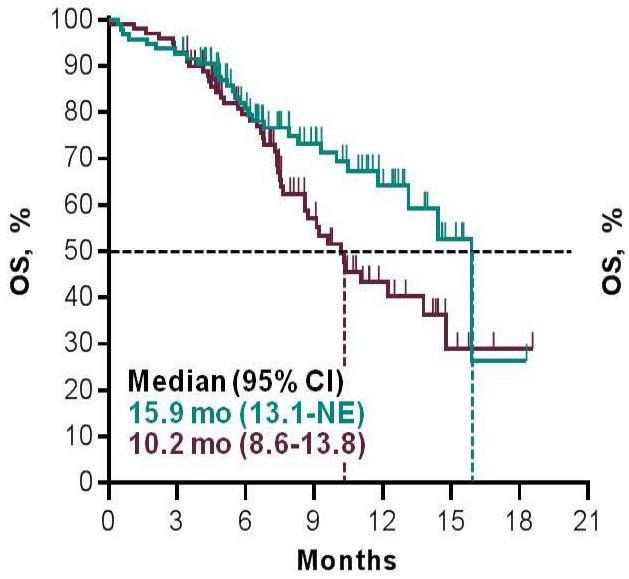
No. at Risk							
278	256	188	124	62	17	2	0
281	246	175	93	45	16	4	0

Data cutoff date: Apr 3, 2018.

Overall Survival at IA2 by PD-L1 TPS

TPS <1%

	Events	HR (95% CI)
Pembro + Chemo	30.5%	0.61 (0.38-0.98)
Placebo + Chemo	44.4%	

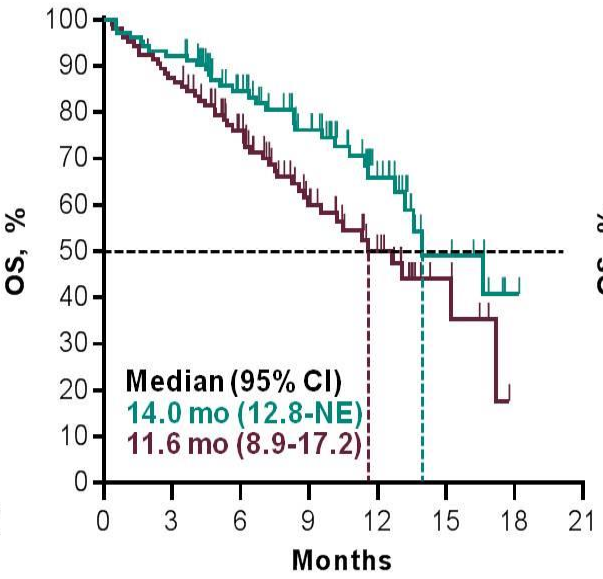


No. at Risk

95	88	62	41	20	5	1	0
99	92	63	32	14	4	1	0

TPS 1-49%

	Events	HR (95% CI)
Pembro + Chemo	30.1%	0.57 (0.36-0.90)
Placebo + Chemo	43.3%	

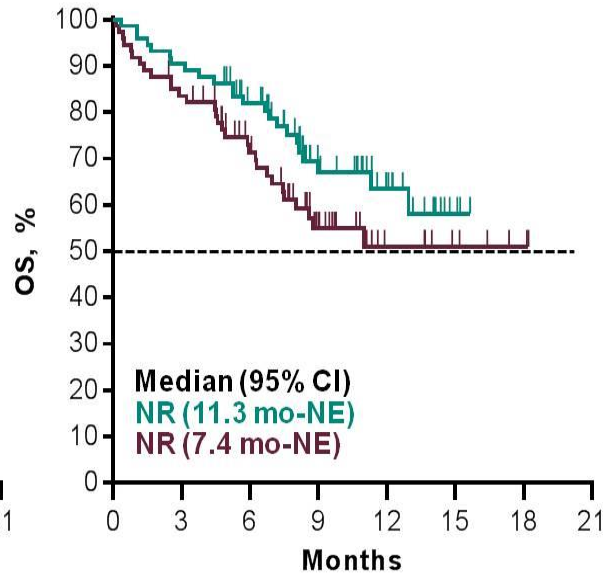


No. at Risk

103	95	68	50	25	9	1	0
104	90	66	37	21	6	0	0

TPS ≥50%

	Events	HR (95% CI)
Pembro + Chemo	31.5%	0.64 (0.37-1.10)
Placebo + Chemo	41.1%	

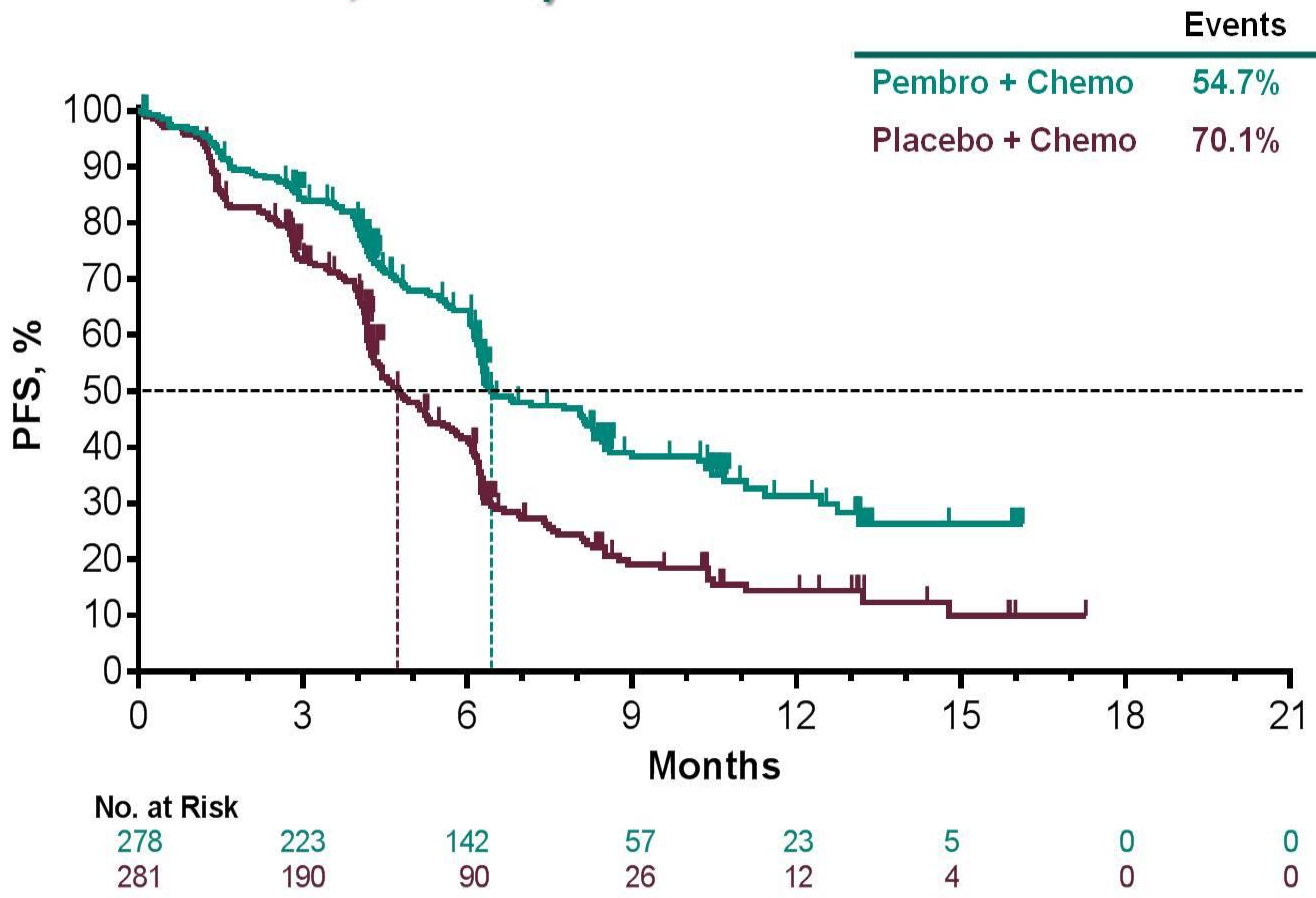


No. at Risk

73	66	53	28	15	3	0	0
73	60	42	21	9	5	2	0

Data cutoff date: Apr 3, 2018.

Progression-Free Survival at IA2, ITT (RECIST v1.1, BICR)



BICR, blinded, independent central review. Data cutoff date: Apr 3, 2018.

Summary and Conclusions

- Pembrolizumab plus chemotherapy significantly improved OS (HR 0.64) over chemotherapy alone
  - Benefit was observed irrespective of PD-L1 TPS: HR 0.61 for TPS <1%, 0.57 for TPS 1-49%, and 0.64 for TPS ≥50%
- PFS (HR 0.56) and ORR (*P* = 0.0004) were also improved with pembrolizumab plus chemotherapy and responses were more durable
- AE frequency and severity were mostly similar between arms
  - Observed events consistent with known safety profiles of pembrolizumab and chemotherapy, with no new safety signals identified
  - Rates of discontinuation due to AEs were higher in the pembrolizumab plus chemotherapy arm, but generally low overall
  - Immune-mediated AEs were more frequent in the pembrolizumab arm, with frequency and severity consistent with those observed for pembrolizumab monotherapy
- Data suggest pembrolizumab plus carboplatin and paclitaxel or nab-paclitaxel should become a new standard-of-care for first-line treatment of metastatic squamous NSCLC, irrespective of PD-L1 expression

Conclusions ASCO 2018

KEYNOTE 042: Carbo/Pem vs Pembro [PD-L1 >1%].

Better OS except group PDL-1: 1-49%

IMPOWER 150: Carbo/Paclit/Bev/Atezo vs SOC.

Better OS across all levels of PD-L1

IMPOWER 131: (SQCC) Carbo/Nab-Pac/Atezo vs SOC

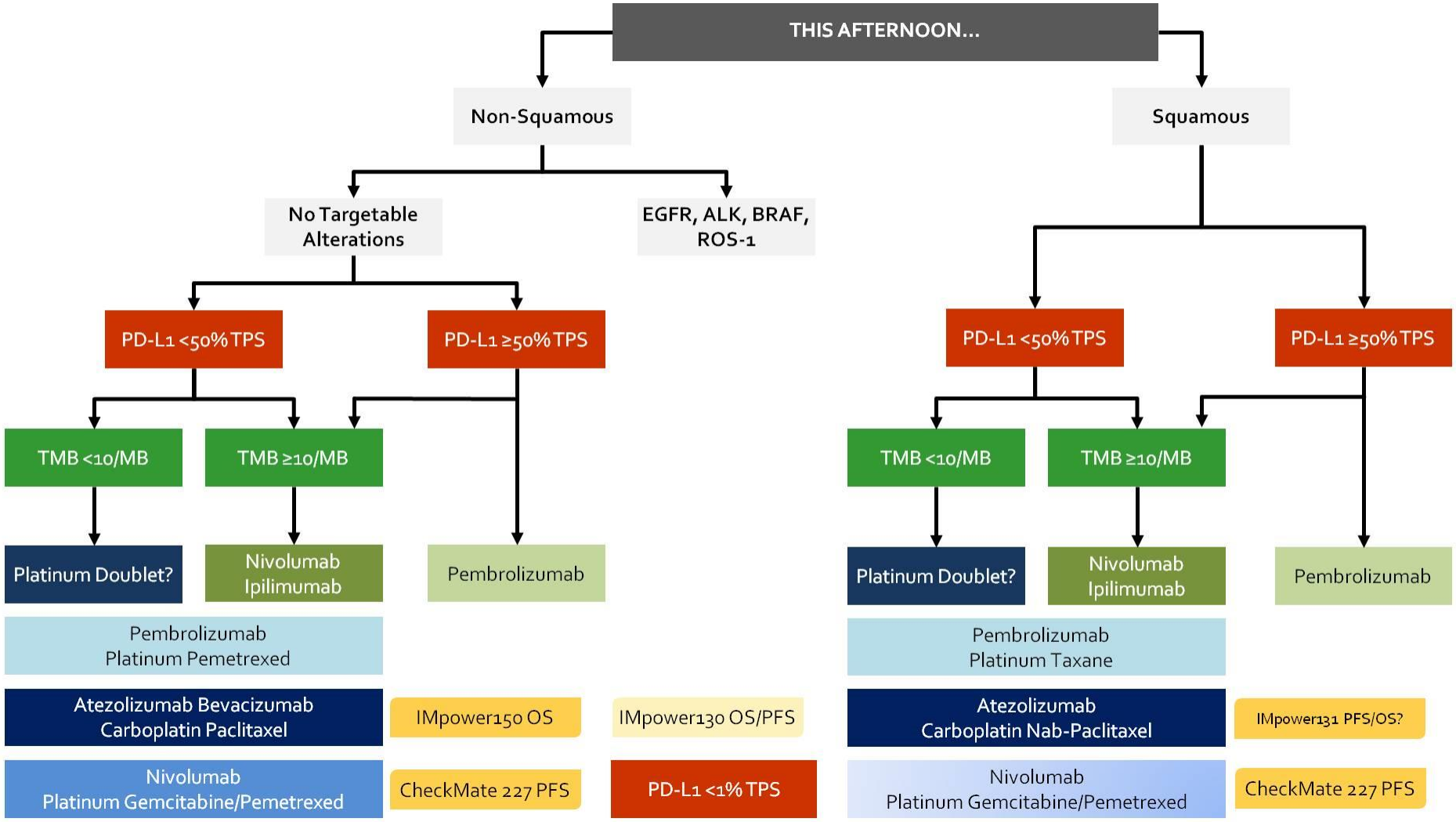
Better PFS, potential new SOC

KEYNOTE 407: (SQCC) Carbo/Paclit or Nab/Pembro vs SOC

Better OS all PD-L1 groups (NEW SOC)

Adds to KEYNOTE 189: Carbo/Pem/Pem for NSQCC and

Checkmate 227: Ipi+Nivo better PFS for all in pts high TMB



Presented By Solange Peters at 2018 ASCO Annual Meeting

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