Best of ASCO- Lung Cancer

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Disclosures

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- Research Funding: Genentech/Roche, Merck, Novartis, Exelixis, Boehringer Ingelheim, Nektar Therapeutics, Takeda

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Presented by: Joel Neal, MD, PhD

Early stage/meso/small cell abstracts

Small Cell Lung Cancer

Abstract #8506: Phase 2 Study of Pembrolizumab in Advanced Small-Cell Lung Cancer: KEYNOTE-158

- Pembrolizumab in 2nd line SCLC

Abstract #8507: Efficacy and safety of rovalpituzumab tesirine in patients With DLL3-expressing, ≥ 3rd line small cell lung cancer: Results from the phase 2 TRINITY study

- "Rova-T" in 3rd line SCLC

Mesothelioma

Abstact #8503: DREAM-A phase 2 trial of DuRvalumab with first line chEmotherApy in Mesothelioma with a safety run in

- Platinum/pemetrexed/durvalumab in First line Mesothelioma

Early Stage Non-Small Cell Lung Cancer

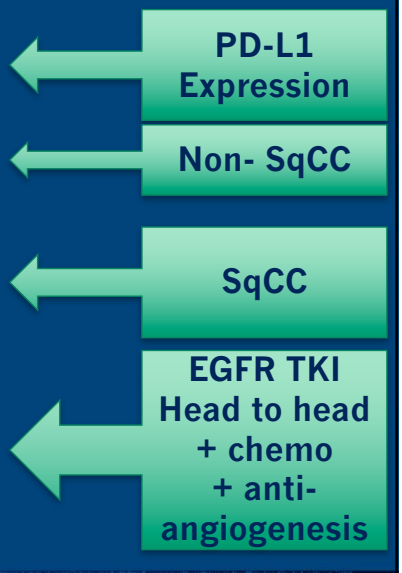
Abstract # 8502: Pragmatic Study of a Lymph Node (LN) Collection Kit for Non-Small Cell Lung Cancer (NSCLC) Resection

- Surgical optimization of node collection

Slide courtesy of Karen Kelly, MD

Metastatic NSCLC abstracts

- IO (+/-) combinations
  - KEYNOTE-042 (Abstract LBA4)
    - Platinum/pemetrexed vs pembro in PDL1 >1%
  - CheckMate-227 (Abstract 9001)
    - Nivo/ipi vs Nivo/chemo vs chemo in PDL1 <1%
  - IMPOWER-150 (Abstract 9002)
    - Carbo/pac/bev +/- atezo in non-squamous
  - KEYNOTE-407 (Abstract105)
    - Carbo/(nab)-pac +/- pembro in Squamous
  - IMPOWER-131 (LBA9000)
    - Carbo/(nab)-pac +/- atezo in Squamous
- EGFR TKI (+/- combinations)
  - NEJ026 (Abstract 9006)
    - Erlotinib +/- bevacizumab in EGFR mutant NSCLC
  - NEJ009 (Abstract 9005)
    - Carbo/pem/gefitinib vs gefitinib in EGFR mutant NSCLC
  - ARCHER 1050 (Abstract 9004)
    - Dacomitinib vs gefitinib for EGFR mutant NSCLC



Slide Courtesy of Sai-Hong Ignatius Ou

Abstract #8506: Phase 2 Study of Pembrolizumab in Advanced Small-Cell Lung Cancer: KEYNOTE-158

Hyun Cheol Chung,[1] Jose Lopez-Martin,[2] Steven Kao,[3] Wilson H. Miller Jr,[4] Willeke Ros,[5] Bo Gao,[6] Aurelien Marabelle,[7] Maya Gottfried,[8] Alona Zer,[9] Jean-Pierre Delord,[10] Nicolas Penel,[11] Shadia I. Jalal,[12] Lei Xu,[13] Susan Zeigenfuss,[13] Scott K. Pruitt,[13] Sarina A. Piha-Paul[14]

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Presented by: Hyun Cheol Chung, MD

KEYNOTE-158 (NCT02628067): Phase 2 Multicohort Study of Pembrolizumab for Advanced Solid Tumors

Patients
- Unresectable and/or metastatic SCLC
- Progression on or intolerance to standard therapy
- ECOG PS 0 or 1
- ≥1 measurable lesion
- Evaluable tumor sample for biomarker assessments
- No autoimmune disease or noninfectious pneumonitis

→ Pembrolizumab 200 mg IV Q3W → Treat for 2 years[a] or until progression,[b] intolerable toxicity, or study withdrawal → Survival follow-up

Primary endpoint[c]: ORR (RECIST v1.1, central review)
Secondary endpoints: PFS, OS, duration of response, safety
Exploratory endpoints: Efficacy in biomarker subgroups
Response assessed every 9 weeks year 1; every 12 weeks thereafter

[a]If SD or better when pembrolizumab discontinued and subsequently have PD, patients may be eligible to resume pembrolizumab for ≤1 year.
[b]If clinically stable, patients are to remain on pembrolizumab until PD is confirmed on a second scan performed ≥4 weeks later.
[c]The point estimate and exact Clopper-Pearson CI were calculated.

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Presented by: Hyun Cheol Chung, MD

Antitumor Activity (RECIST v1.1, Independent Central Review[a])

	Overall N = 107	PD-L1–Positive N = 42	PD-L1–Negative N = 50
ORR, % (95% CI)	18.7 (11.8–27.4)	**35.7** (21.6–52.0)	**6.0** (1.3–16.5)
Best overall response, n (%)			
Complete response	3 (3)	2 (5)	1 (2)
Partial response	17 (16)	13 (31)	2 (4)
Stable disease	12 (11)	3 (7)	7 (14)
Progressive disease	62 (58)	22 (52)	29 (58)

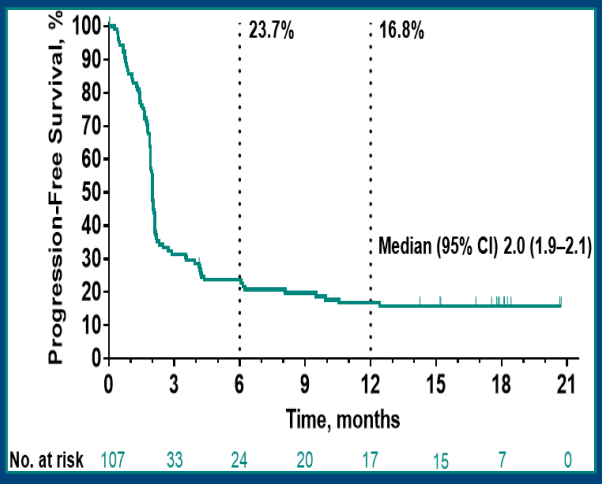
[a]Only confirmed responses are included.
Data cutoff date: January 15, 2018

12 patients (73%) had DOR ≥12 mo

Presented by: Hyun Cheol Chung, MD

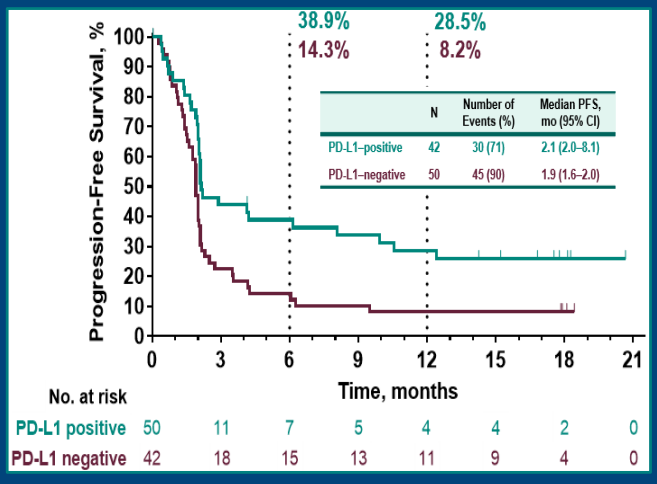
Progression-Free Survival

(RECIST v1.1, Independent Central Review)



Data cutoff date: January 15, 2018

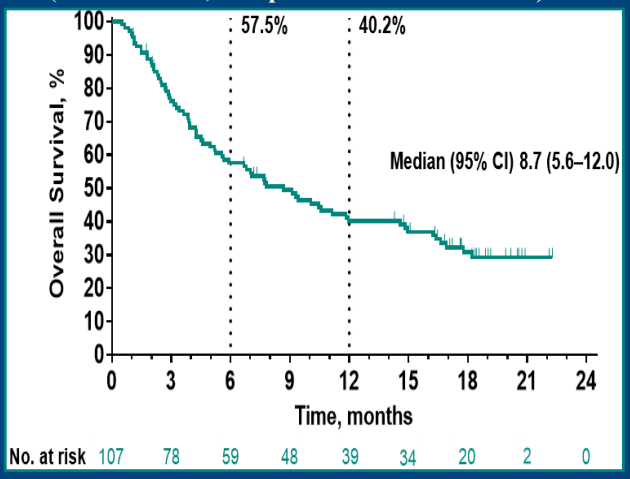
Tumor PD-L1 Status



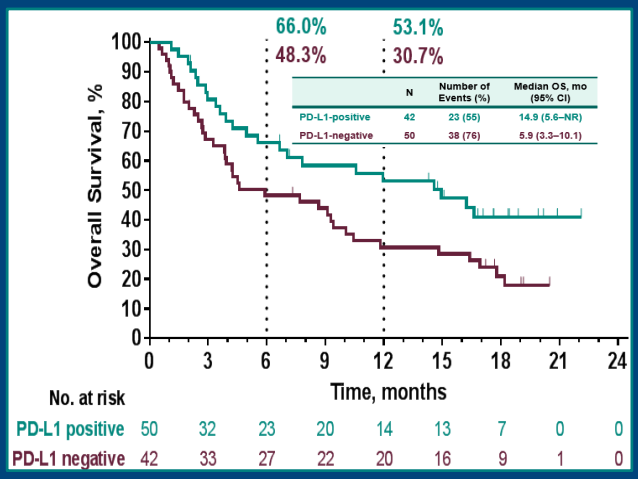
Presented by: Hyun Cheol Chung, MD

Overall Survival by Tumor PD-L1 Status

(RECIST v1.1, Independent Central Review)



Tumor PD-L1 Status



Data cutoff date: January 15, 2018

Presented by: Hyun Cheol Chung, MD

Discussion points

- Should pembrolizumab (or other immunotherapy) be used in second line SCLC?
  - Yes – though response rates still relatively modest, both nivo and nivo/ipi are in NCCN guidelines
- Does PD-L1 affect the treatment decision?
  - Data are mixed between trials but might help prioritize second line use (vs chemotherapy options)

Presented by: Joel Neal

Role for Immunotherapy in Relapsed SCLC Fleeting

Media / Press Releases

Sunday, Jun 24, 2018

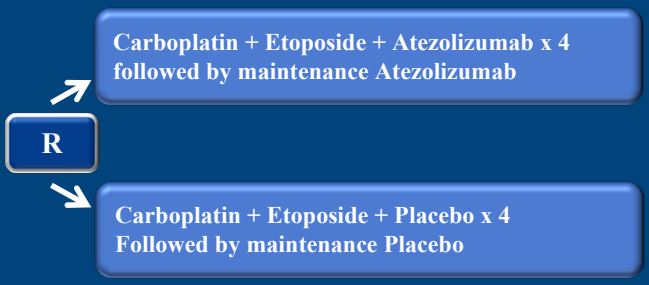
Genentech's TECENTRIQ in Combination with Chemotherapy Helped People with Previously-Untreated Extensive-Stage Small Cell Lung Cancer Live Significantly Longer Compared to Chemotherapy

IMpower133 is the first Phase III study with an immunotherapy-based combination to show improvement in overall survival and progression-free survival in the initial treatment of extensive-stage small cell lung cancer (ES-SCLC)

There has been limited treatment progress for people with ES-SCLC in the past 20 years

Data will be submitted to health authorities globally, including the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA)

South San Francisco, CA -- June 24, 2018 --



Slide courtesy of Karen Kelly, MD

Abstract 8507: Efficacy and safety of rovalpituzumab tesirine (Rova-T™) in patients with DLL3-expressing, ≥ 3rd line small cell lung cancer: Results from the Phase 2 TRINITY study

David P. Carbone[1], Daniel Morgensztern[2], Sylvestre Le Moulec[3], Rafael Santana-Davila[4], Neal Ready[5], Christine L. Hann[6], Bonnie S. Glisson[7], Afshin Dowlati[8], Charles M. Rudin[9], Laurent Greillier[10], Satwant Lally[11], Sreeni Yalamanchili[11], Jürgen Wolf[12], Ramaswamy Govindan[2], Benjamin Besse[13,14]

[1]Ohio State University, Columbus, OH, USA; [2]Washington University, St. Louis, MO, USA; [3]Institut Bergonié Centre Régional de Lutte Contre Le Cancer de Bordeaux et Sud Ouest, Bordeaux, France; [4]University of Washington, Seattle, WA, USA; [5]Duke University Medical Center, Durham, NC, USA; [6]Johns Hopkins University, Baltimore, MD, USA; [7]MD Anderson Cancer Center, Houston, TX, USA; [8]University Hospitals Case Medical Center, Cleveland, OH, USA; [9]Memorial Sloan Kettering Cancer Center, NY, NY, USA; [10]Assistance Publique—Hopitaux de Marseille, Aix Marseille University, Marseille, France; [11]AbbVie Stemcentrx, South San Francisco, CA, USA; [12]University Hospital of Cologne, Cologne, Germany; [13]Institut Gustave Roussy, Villejuif, France; [14]Paris-Sud University, Orsay, France

Presented by: David Carbone, MD

TRINITY: A Phase 2, Single-Arm Study of Rova-T in DLL3-Expressing, Relapsed/Refractory SCLC

Key Eligibility Criteria
- DLL3-positive* SCLC
- Relapsed or refractory disease
- ≥ 2 previous regimens
- ≥ 1 platinum-based regimen
- ECOG Performance Status 0-1
- Stable CNS metastases allowed

→ **N = 339**
Rova-T
0.3 mg/kg IV
q6w x 2[a]

Primary Endpoints
- Objective response rate (ORR)
- Overall survival (OS)

Secondary Endpoints
- Duration of response (DOR)
- Clinical benefit rate (CBR)
- Progression-free survival (PFS)

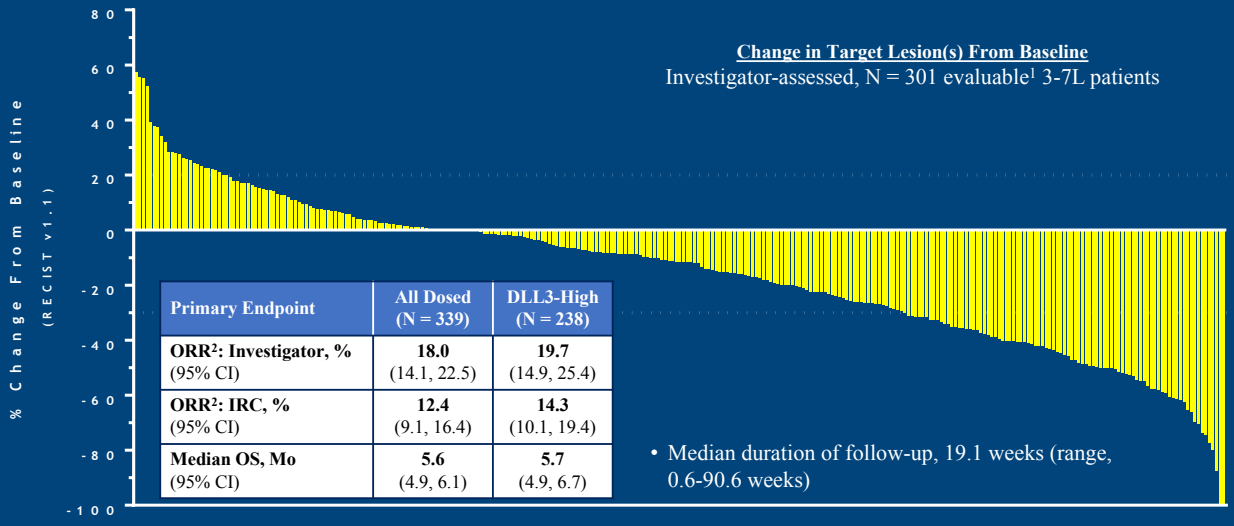
- Study was powered to detect a 25% best overall response rate in DLL3-high Pts with a Simon's two-stage design
- Study size was increased to ensure adequate enrollment of 3L Pts

Focus on DLL3-high (*i.e.* ≥ 75% cells DLL3+):
- Pre-specified subgroup analysis
- Companion Dx assay cut-off

*Clinical trial mouse antibody-based immunohistochemistry assay.
[a]Re-treatment with 2 cycles of Rova-T was permitted for patients who tolerated the initial 2 doses, exhibited SD or better, received no other systemic anticancer therapy after Rova-T, and progressed ≥ 12 weeks after the 2nd initial dose.
CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; IHC, immunohistochemistry; IV, intravenous; q6w, every 6 weeks.

Presented by: David Carbone, MD

TRINITY: Primary Endpoint Analyses



Change in Target Lesion(s) From Baseline
Investigator-assessed, N = 301 evaluable[1] 3-7L patients

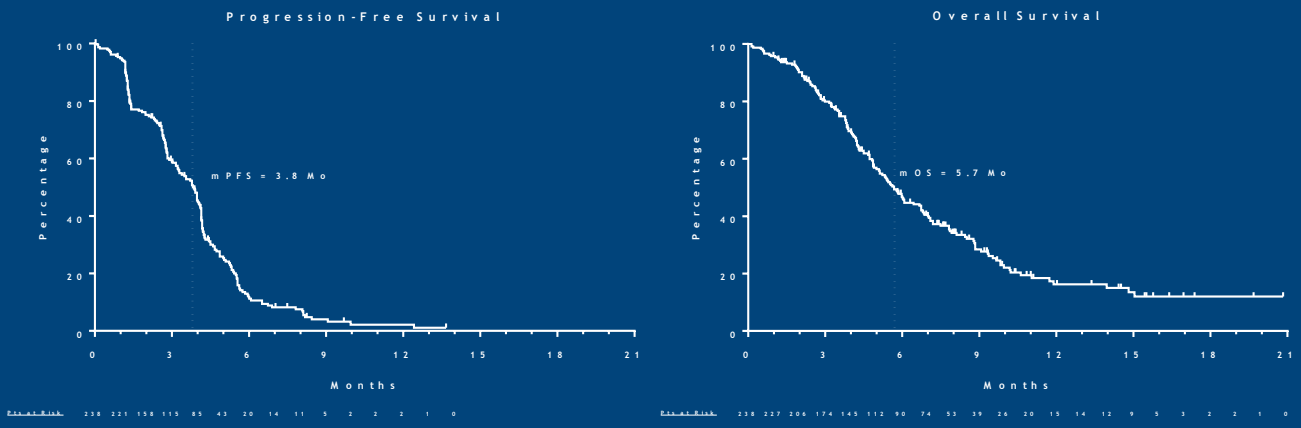
Primary Endpoint	All Dosed (N = 339)	DLL3-High (N = 238)
ORR[2]: Investigator, % (95% CI)	**18.0** (14.1, 22.5)	**19.7** (14.9, 25.4)
ORR[2]: IRC, % (95% CI)	**12.4** (9.1, 16.4)	**14.3** (10.1, 19.4)
Median OS, Mo (95% CI)	**5.6** (4.9, 6.1)	**5.7** (4.9, 6.7)

- Median duration of follow-up, 19.1 weeks (range, 0.6-90.6 weeks)

1. Patients who had a baseline scan and at least 1 follow-up scan with an evaluable response.
2. Confirmed CR+ PR per RECIST v1.1

Presented by: David Carbone, MD

IRC-Assessed PFS & OS Among DLL3-High Patients, All Lines



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Presented by: David Carbone, MD

Summary of TEAEs

TEAEs, Any Grade ≥ 15% Patients	All Patients, N = 339	
	Any n (%)	Drug-Related n (%)
Fatigue	130 (38%)	96 (28%)
Photosensitivity reaction	**123 (36%)**	**120 (35%)**
Pleural effusion	**109 (32%)**	**95 (28%)**
Peripheral edema	**104 (31%)**	**89 (26%)**
Decreased appetite	103 (30%)	53 (16%)
Nausea	88 (26%)	55 (16%)
Dyspnea	84 (25%)	33 (10%)
Thrombocytopenia	83 (25%)	74 (22%)
Constipation	75 (22%)	15 (4%)
Vomiting	59 (17%)	28 (8%)
Anemia	58 (17%)	44 (13%)
Cough	55 (16%)	7 (2%)
Hypoalbuminemia	53 (16%)	40 (12%)
Pericardial effusion	**50 (15%)**	**42 (12%)**
Abdominal pain	49 (15%)	18 (5%)
Asthenia	49 (15%)	40 (12%)

TEAEs, Grade 3/4 ≥ 10 Patients	All Patients, N = 339	
	Any n (%)	Drug-Related n (%)
Thrombocytopenia	38 (11%)	37 (11%)
Photosensitivity reaction	23 (7%)	23 (7%)
Anemia	16 (5%)	12 (4%)
Fatigue	15 (4%)	12 (4%)
Pleural effusion	15 (4%)	14 (4%)

- Serosal effusions were managed primarily through standard drainage procedures; steroids, NSAIDs, and colchicine also used
- History of effusions may be identified risk factor for Gr3+ Rova-T-related effusions

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Presented by: David Carbone, MD

Discussion points

- What is the role for rovalpituzumab tesirine in SCLC?
  - Appears to have unique activity in DLL3 positive SCLC

Presented by: Joel Neal

NHMRC Clinical Trials Centre

ALTG Australasian Lung Cancer Trials Group

National Centre for Asbestos Related Diseases an Australian Research Cooperative

Abstract #8503
DREAM

A phase 2 trial of DuRvalumab with first line chEmotherApy in Mesothelioma with a safety run in

AK Nowak, WJ Lesterhuis, BGM Hughes, C Brown, PS Kok, K O'Byrne, T John, N Pavlakis, S Kao, S Yip, WS Lam, D Karikios, A Langford, M Stockler

Presented by: Anna Nowak, MD

Current Status of Advanced Mesothelioma

- 3,000 patients/year in United States
- Incidence has peaked in US but it has not peaked overall in industrialized nations
- 38,400 deaths/year worldwide projected

Year	Phase	Regimen	N	HR	Median OS	ORR	6 mo PFS	Median PFS
2003	Randomized Phase III (Vogelzang)	Pemetrexed/CDDP vs CDDP	448	.77 p=.020	12.1 mo	41.3%	~48%	5.7 mo
2016	Randomized Phase III (Zalcman)	Pemetrexed/CDDP Bevacizumab vs Pemetrexed/CDDP	448	.77 (0.62-0.95) p=0.0167	18.8 mo	NR	~80%	9.2 mo
2017	Randomized Phase II (Nowak)	Pemetrexed/CDDP vs Nintedanib vs Pemetrexed/CDDP	62	.77 (0.46-1.29) p=0.319	18.3 mo	57%	75%	9.7 mo

- Second line treatment options single cytotoxic agents, nivolumab, nivolumab/ipilimumab

Slide courtesy of Karen Kelly, MD

Study Schema

Single-arm, multicentre phase II trial, N=56

Population

1st line MPM
Non-surgical
ECOG PS 0-1
No PD-L1 selection

Exclusions

AID, steroids, prior IO agent

Induction

Cisplatin 75mg/m² + Pemetrexed 500mg/m² + Durvalumab 1125mg q3w

6 cycles

→

Maintenance

Durvalumab 1125mg q3w x 52 w

(Until PD or toxicity)

17 cycles

Outcomes

PFS6*

OTRR (CR + PR)*
Toxicity
PFS*
OS

* mRECIST for MPM, mirRC

- 2-stage Simon's design: **31 in stage 1**, additional 23 in stage 2,
- The regimen would be worthy of pursuit if the true PFS6 rate was 65% or higher, but not if it was 45% or lower
- 90% power with a one-sided type 1 error rate of 5%

Presented by: Anna Nowak, MD

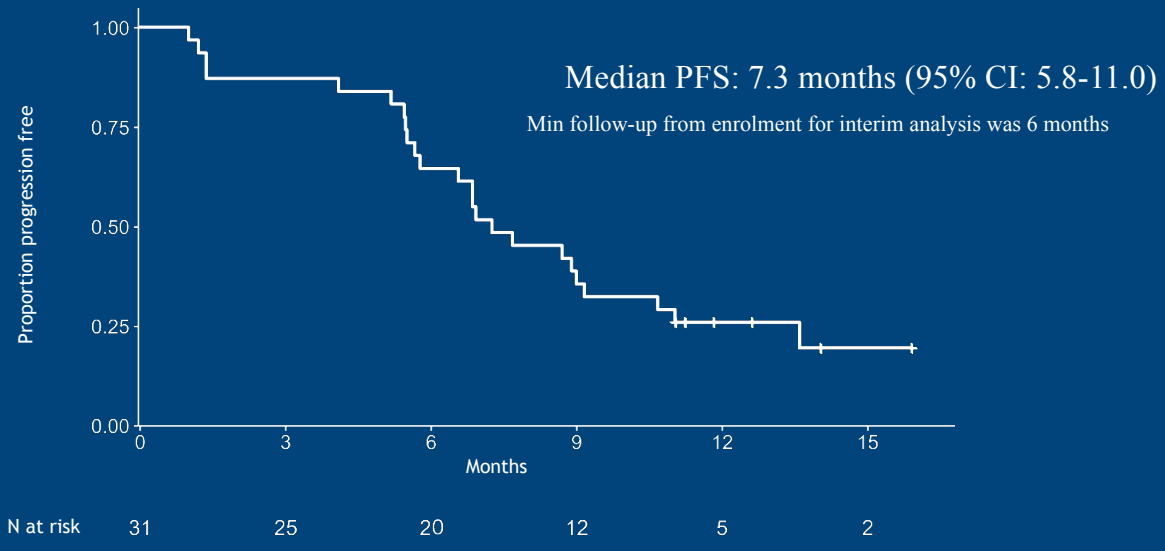
Objective tumour response in the first 31 participants

	Best single response (%)	Confirmed response mRECIST (%)	Confirmed response iRECIST (%)
Complete response	0 (0%)	0 (0%)	0 (0%)
Partial response	20 (65%)	17 (55%)	18 (58%)
Stable disease	7 (23%)	9 (29%)	9 (29%)
Progressive disease	4 (13%)	5 (16%)	4 (13%)
Total	31	31	31

Chemotherapy Intensity	N= 31	Intensity
No. of patients who		
Completed 6 doses of cisplatin	21 (68%)	95%
Converted to carboplatin	5 (16%)	n/a
No. of durvalumab doses, median (range)	12 (1-18)	94%

Presented by: Anna Nowak, MD

Progression free survival 6 months = 65%



Median PFS: 7.3 months (95% CI: 5.8-11.0)

Min follow-up from enrolment for interim analysis was 6 months

Presented by: Anna Nowak, MD

Discussion points

- What is the role for durvalumab or other immunotherapy in malignant pleural mesothelioma?
  - Currently reasonable to use checkpoint inhibitor (any available) in second line therapy, and probably will see transition to using with chemo in front line setting soon as with NSCLC

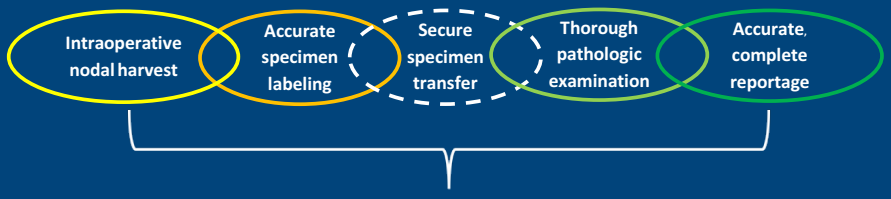
Presented by: Joel Neal

Abstract # 8502: Pragmatic Study of a Lymph Node (LN) Collection Kit for Non-Small Cell Lung Cancer (NSCLC) Resection

Raymond U. Osarogiagbon MBBS
Multidisciplinary Thoracic Oncology Program
Baptist Cancer Center, Memphis, TN

Presented by: Raymond Osarogiagbon, MBBS

Conceptual Model: The Chain of Responsibility



Self-contained, with lid

Indicates 'mandatory' stations
Checklist
Pre-labelled with anatomic nomenclature

Station-specific containers
Color-coded, named, numbered

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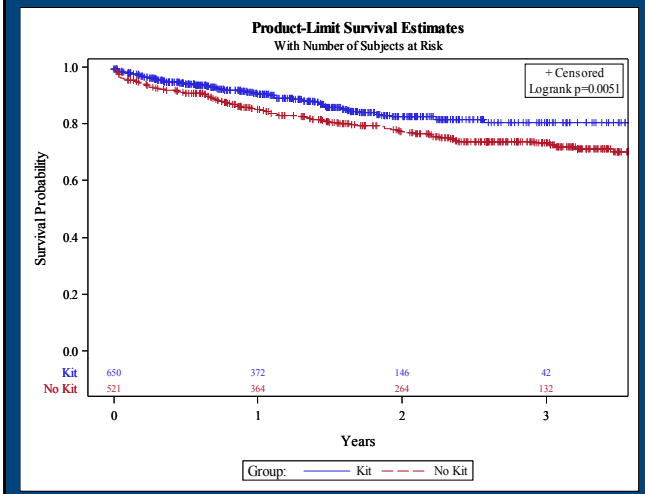
Presented by: Raymond Osarogiagbon, MBBS

Survival: Kit v Non-Kit Resections



Proportional Hazards Models

Model	Hazard Ratio	P-Value
Crude	0.67 (0.50, 0.89)	.0054
Fully Adjusted* with Surgeon Clustering	0.57 (0.42, 0.77)	0.0003

Sensitivity Analyses

Model	Hazard Ratio	P-Value
Excluding Sub-lobar Resections*	0.61 (0.44, 0.85)	0.0030
Excluding Deaths within 60 days*	0.60 (0.40, 0.90)	0.0123
Only in Adopting Surgeons*	0.54 (0.38, 0.76)	0.0005
Crude- Only in Adopting Surgeons	0.58 (0.43, 0.79)	0.0005

* Fully Adjusted Models (for age, sex, histology, tumor grade, extent of resection, Pathologic t-stage, pathologic m-stage, number of comorbidities, and type of pathologic examination (a subgroup of patients in each group received a pathologic exam with a novel gross dissection method).

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Presented by: Raymond Osarogiagbon, MBBS

Discussion points

- Should a systematic approach to lymph node collection be used during surgery to improve overall survival?
  - Yes!

Presented by: Joel Neal

Summary – SCLC/Meso/Early Stage

- Immunotherapy is an active treatment in relapsed SCLC. Awaiting its validation but with positive data in the first line setting its role in the relapsed setting is likely to become limited.
- Additional novel classes of agents are needed to treat SCLC
- At first glance the role for immunotherapy in front line mesothelioma is modest
- Predictive biomarkers will be critical to optimize immunotherapy treatment for SCLC and mesothelioma.
- A lymph node collection kit improves the quality of pathologic nodal staging and overall survival in operable lung cancer
- Increasing regional nodal staging should begin today

Presented by: Karen Kelly, MD

Metastatic NSCLC abstracts

- IO (+/-) combinations
  - KEYNOTE-042 (Abstract LBA4)
    - Platinum/pemetrexed vs pembro in PDL1 >1%
  - CheckMate-227 (Abstract 9001)
    - Nivo/ipi vs Nivo/chemo vs chemo in PDL1 <1%
  - IMPOWER-150 (Abstract 9002)
    - Carbo/pac/bev +/- atezo in non-squamous
  - KEYNOTE-407 (Abstract105)
    - Carbo/(nab)-pac +/- pembro in Squamous
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  - NEJ026 (Abstract 9006)
    - Erlotinib +/- bevacizumab in EGFR mutant NSCLC
  - NEJ009 (Abstract 9005)
    - Carbo/pem/gefitinib vs gefitinib in EGFR mutant NSCLC
  - ARCHER 1050 (Abstract 9004)
    - Dacomitinib vs gefitinib for EGFR mutant NSCLC

PD-L1 Expression

Non- SqCC

SqCC

EGFR TKI Head to head + chemo + anti-angiogenesis

Slide modicied from Sai-Hong Ignatius Ou

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]

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Gilberto Lopes

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

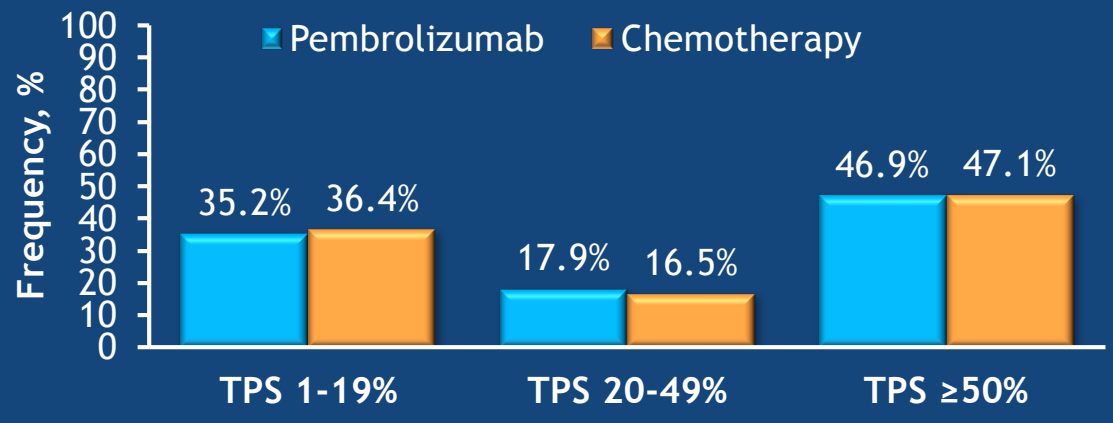
N = 637 → Pembrolizumab 200 mg Q3W for up to 35 cycles

N = 637 → Carboplatin AUC 5 or 6 Q3W + Paclitaxel 200 mg/m² Q3W[a] OR Carboplatin AUC 5 or 6 Q3W + Pemetrexed 500 mg/m² 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%

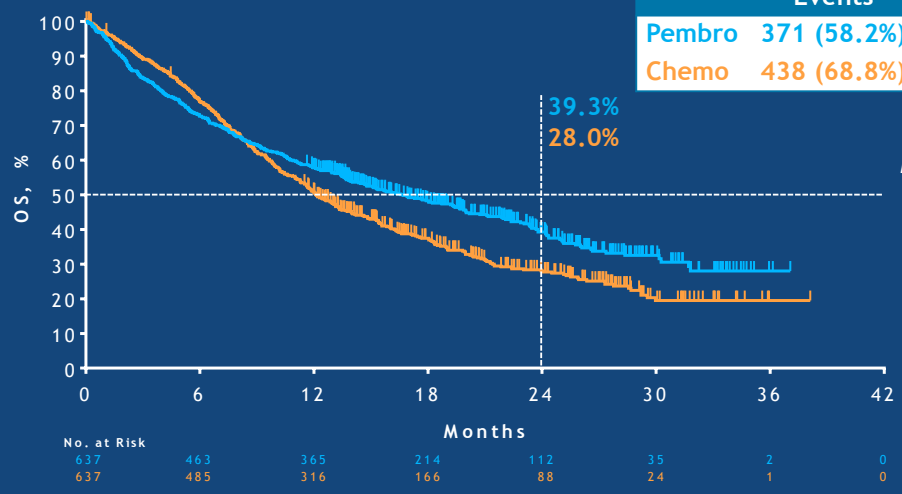
[a]Pemetrexed maintenance therapy was optional but strongly encouraged for patients with nonsquamous histology.

Frequency of PD-L1 TPS Categories: TPS ≥1% Population



Data cutoff date: Feb 26, 2018.

Overall Survival: TPS ≥1%

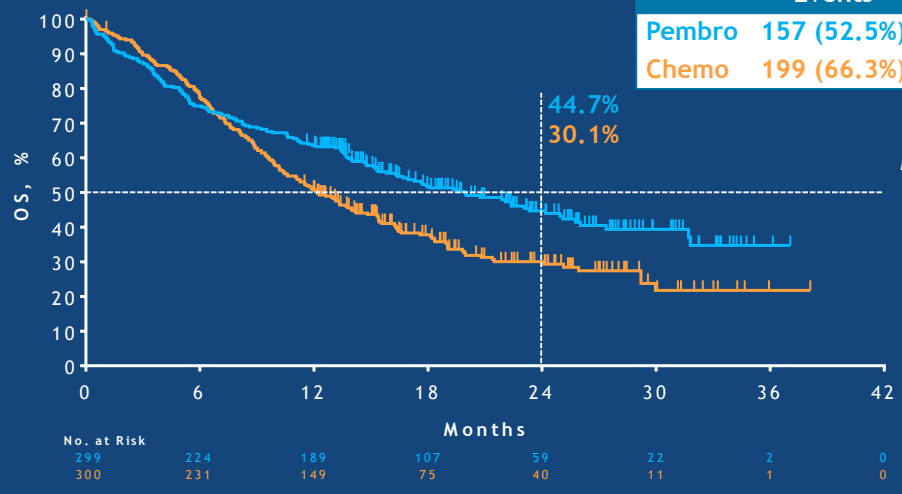


	Events	HR (95% CI)	*P*
Pembro	371 (58.2%)	0.81 (0.71-0.93)	0.0018
Chemo	438 (68.8%)		

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

Data cutoff date: Feb 26, 2018.

Overall Survival: TPS ≥50%

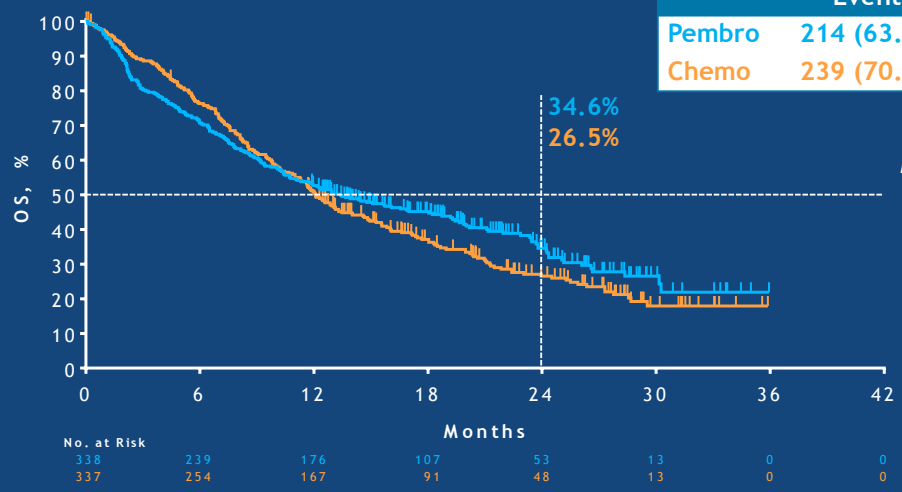


	Events	HR (95% CI)	*P*
Pembro	157 (52.5%)	0.69 (0.56-0.85)	0.0003
Chemo	199 (66.3%)		

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

Data cutoff date: Feb 26, 2018.

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.

Data cutoff date: Feb 26, 2018.

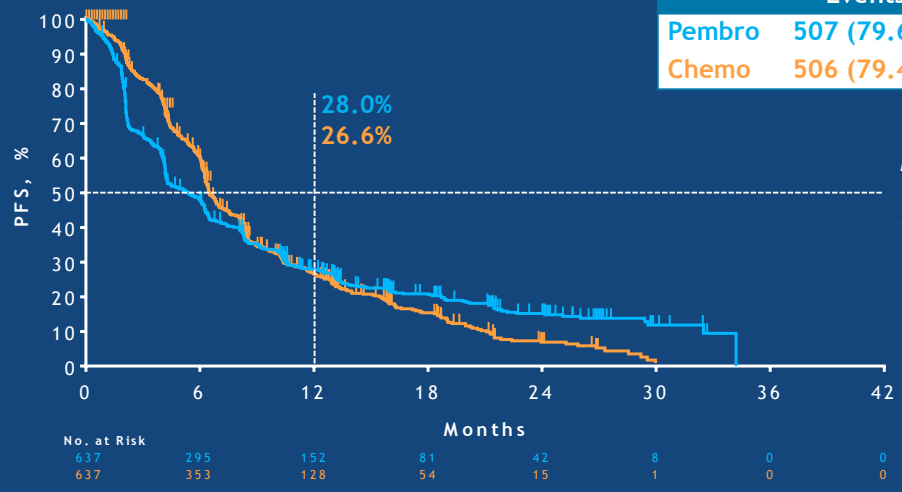
Overall Survival in Subgroups, TPS ≥1%

Subgroup	Events/Pts	Hazard Ratio (95% CI)
Overall	809/1274	0.81 (0.71-0.93)
Age		
<65 yr	444/707	0.81 (0.67-0.98)
≥65 yr	365/567	0.82 (0.66-1.01)
Sex		
Male	584/902	0.80 (0.68-0.94)
Female	225/372	0.89 (0.68-1.17)
ECOG PS		
0	215/390	0.77 (0.59-1.01)
1	594/884	0.83 (0.71-0.98)
Geographic region		
East Asia	196/370	0.79 (0.59-1.05)
Rest of world	613/904	0.82 (0.70-0.96)
Histology		
Squamous	343/492	0.75 (0.60-0.93)
Nonsquamous	466/782	0.86 (0.72-1.03)
Smoking status		
Never	163/282	1.00 (0.73-1.37)
Former	471/721	0.71 (0.59-0.86)
Current	175/271	0.95 (0.70-1.29)
Chemotherapy regimen		
Pem + Carbo	371/636	0.87 (0.71-1.07)
Pac + Carbo	438/638	0.74 (0.61-0.90)
Disease status		
Metastatic	711/1114	0.83 (0.71-0.96)
Locally adv.	98/160	0.74 (0.49-1.13)

Dotted vertical line represents the hazard ratio in the total population.

Data cutoff date: Feb 26, 2018.

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



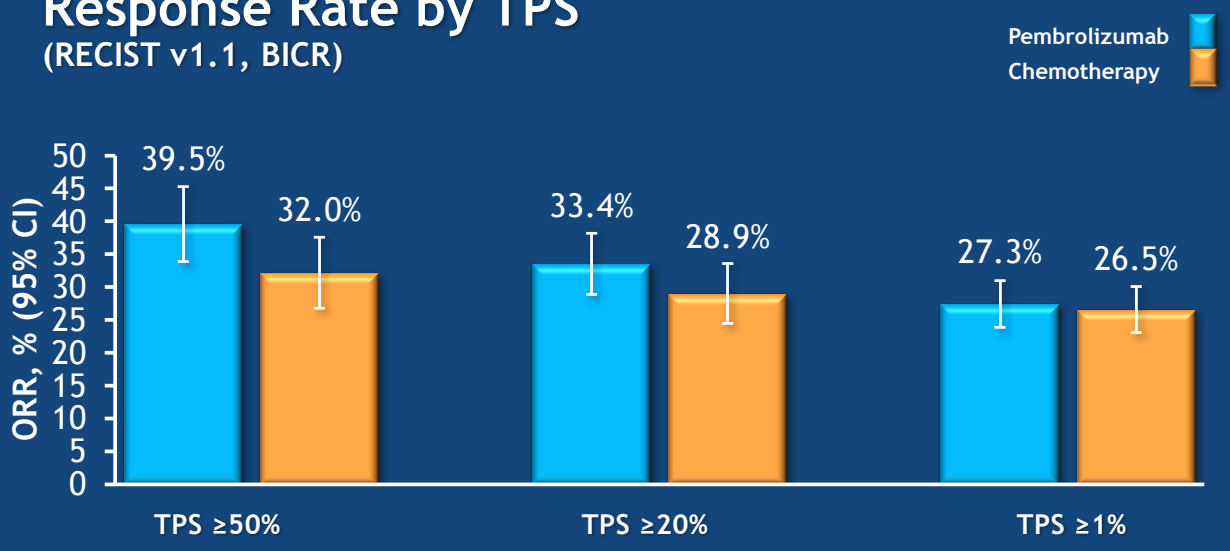
	Events	HR (95% CI)
Pembro	507 (79.6%)	1.07 (0.94-1.21)
Chemo	506 (79.4%)	

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.

Data cutoff date: Feb 26, 2018.

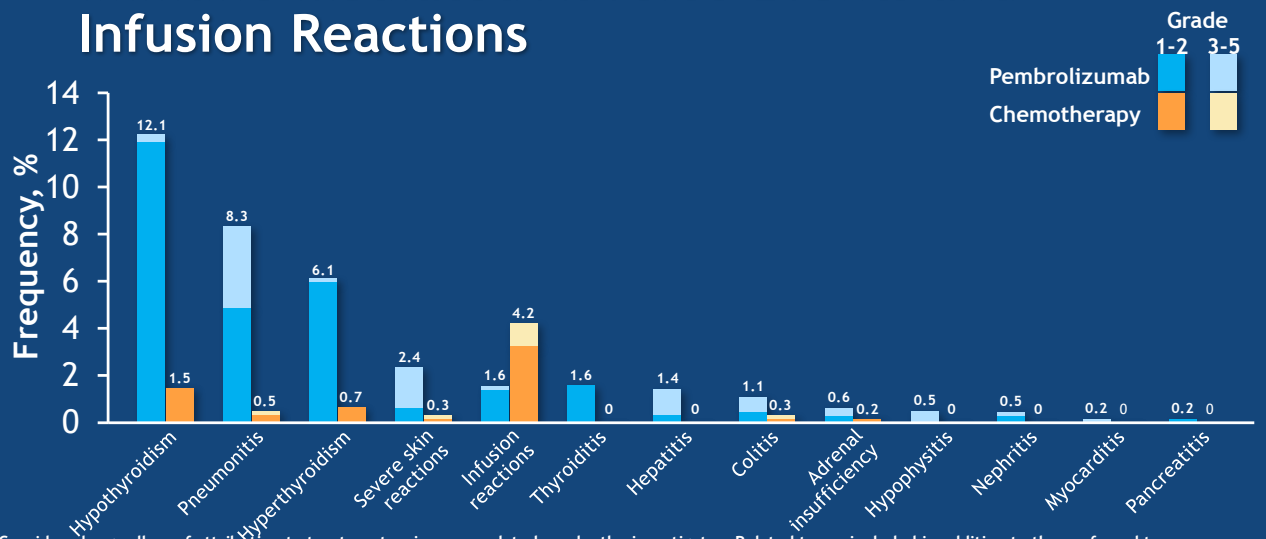
Response Rate by TPS
(RECIST v1.1, BICR)



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.

Immune-Mediated Adverse Events and Infusion Reactions



Considered regardless of attribution to treatment or immune relatedness by the investigator. Related terms included in addition to the preferred terms listed.

Data cutoff date: Feb 26, 2018.

Comparison between KN-042 (PD-L1 >=50% subset) & KN-024

	Keynote-042			Keynote-024		
	Pembro	Chemo	HR (95%CI)	Pembro	Chemo	HR (95%CI)
N	299	300		154	151	
SqCC	38.1%	39.1%		19%	18%	
Brain mets	?	?		12%	7%	
ORR	39.5%	32.0%		45%	28%	p = 0.0011
Median PFS	7.1m (5.9-9.0)	6.4m (6.1-6.9)	0.81 (0.67-0.99)	10.3m	6.0m	0.50 (0.37-0.68)
Median OS	20.0m (15.4-24.9)	12.2m (10.4-11.2)	0.69 (0.56-0.85)	NR	NR	0.60 (0.41-0.89)

Reck et al, NEJM 2016; 375: 1823-1833
Lopes ASCO 2018 (LBA 4)

Discussion points

- What is the role for pembrolizumab in the front-line treatment of NSCLC with PD-L1 treatment of >= 1%?
  - Data not strong enough for 1-49% subgroup to favor pembrolizumab over carbo/pemetrexed/pembro
- What about >= 50%?
  - Still supports choice of pembrolizumab alone for this group (but carbo/pemetrexed/pembro also an option)

Presented by: Joel Neal

2018 ASCO ANNUAL MEETING

Nivolumab + Ipilimumab, Nivolumab + Chemotherapy, and Chemotherapy in Chemo-Naive Patients With Advanced Non-Small Cell Lung Cancer and <1% Tumor PD-L1 Expression: Results From CheckMate 227

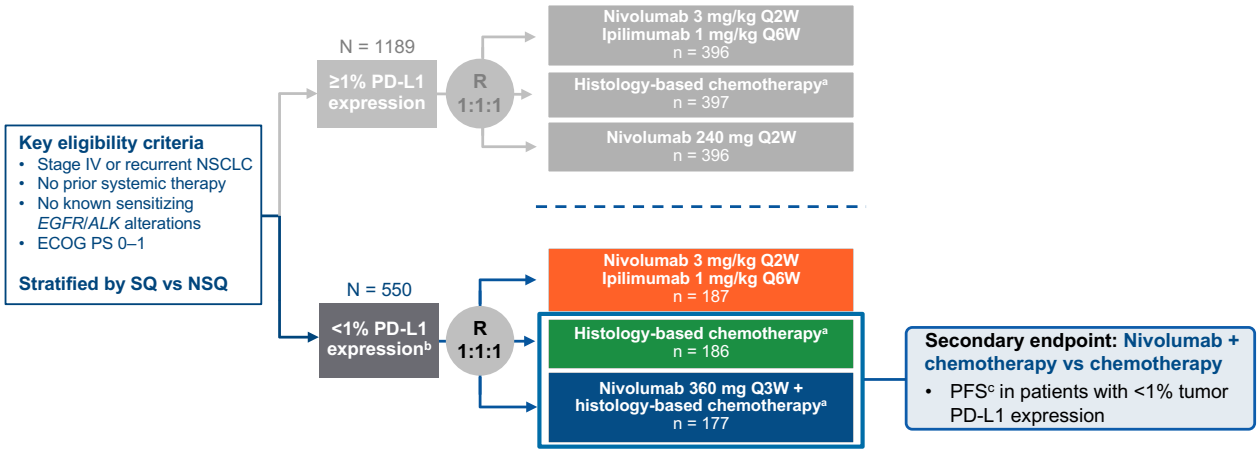
Hossein Borghaei,[1] Matthew D. Hellmann,[2] Luis Paz-Ares,[3] Suresh S. Ramalingam,[4] Martin Reck,[5] Kenneth J. O'Byrne,[6] Prabhu Bhagavatheeswaran,[7] Faith Nathan,[7] Julie Brahmer[8]

[1]Fox Chase Cancer Center, Philadelphia, PA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Hospital Universitario Doce de Octubre, CNIO, Universidad Complutense & CiberOnc, Madrid, Spain; [4]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [5]LungenClinic Grosshansdorf, German Center for Lung Research, Grosshansdorf, Germany; [6]Princess Alexandra Hospital Brisbane, Queensland, Australia; [7]Bristol-Myers Squibb, Princeton, NJ, USA; [8]Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA

2018 ASCO Annual Meeting, June 1–5, Chicago, IL

CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

CheckMate 227 Part 1 Study Design



- Co-primary endpoints: OS in PD-L1–selected populations and PFS[c] in TMB-selected populations treated with nivolumab + ipilimumab vs chemotherapy

Database lock: January 24, 2018; minimum follow-up: 11.2 months

[a]**NSQ:** pemetrexed + cisplatin or carboplatin, Q3W for ≤4 cycles, with optional pemetrexed maintenance following chemotherapy or nivolumab + pemetrexed maintenance following nivolumab + chemotherapy; **SQ:** gemcitabine + cisplatin, or gemcitabine + carboplatin, Q3W for ≤4 cycles; [b]One patient was randomized with <1% tumor PD-L1 expression in IVRS, but was subsequently found to have ≥1% tumor PD-L1 expression; [c]Per BICR

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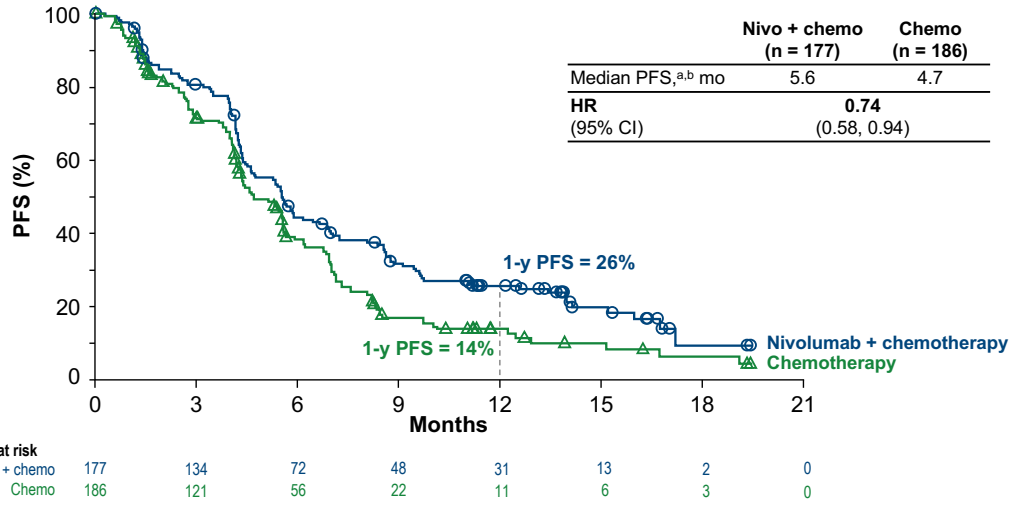
CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

PFS: Nivolumab + Chemotherapy vs Chemotherapy in Patients With <1% Tumor PD-L1 Expression

All Randomized Patients (Squamous and Non-squamous)



	Nivo + chemo (n = 177)	Chemo (n = 186)
Median PFS,[a,b] mo	5.6	4.7
HR (95% CI)	**0.74** (0.58, 0.94)	

No. at risk								
Nivo + chemo	177	134	72	48	31	13	2	0
Chemo	186	121	56	22	11	6	3	0

[a]95% CI: nivo + chemo (4.6, 6.7 mo), chemo (4.3, 5.6 mo); [b]In the nivo + ipi arm (n = 187), median (95% CI) PFS was 4.4 (3.1, 6.0), 1-y PFS was 29%, and HR vs chemo was 0.79 (0.62, 1.01)

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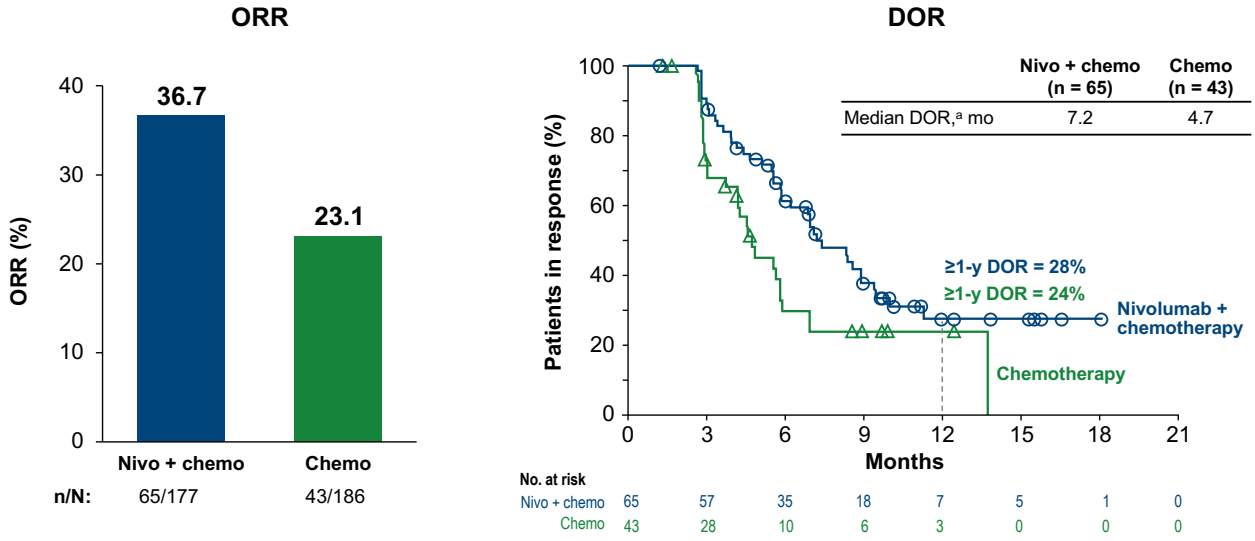
CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

ORR and DOR in Patients With <1% Tumor PD-L1 Expression



DOR per BICR; ORR was 25.1% (n/N: 47/187), median DOR was 18.0 mo (95% CI: 12.2, NR), and ≥1-y DOR was 72% in the nivo + ipi arm
[a]95% CI: nivo + chemo (5.9, 9.4 mo), chemo (3.7, 5.8 mo)

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CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

Baseline Characteristics in Patients With <1% Tumor PD-L1 Expression

	Nivolumab + chemotherapy (n = 177)	Nivolumab + ipilimumab (n = 187)	Chemotherapy (n = 186)
Median age, y	64	63	64
Female, %	27	26	33
ECOG PS,[a] %			
0	33	37	31
1	66	63	68
Smoking status, %			
Current/former smoker	84	87	85
Never smoker	15	12	15
Unknown	1	1	0
Histology, %			
Squamous	24	25	25
Non-squamous	76	75	75
TMB, %			
Evaluable	55	48	58
High (≥10 mut/Mb)	44	42	45
Low (<10 mut/Mb)	56	58	55

[a]In the chemo arm, ECOG PS for 1 patient was not reported; 1 patient in each arm was reported as ECOG PS ≥2

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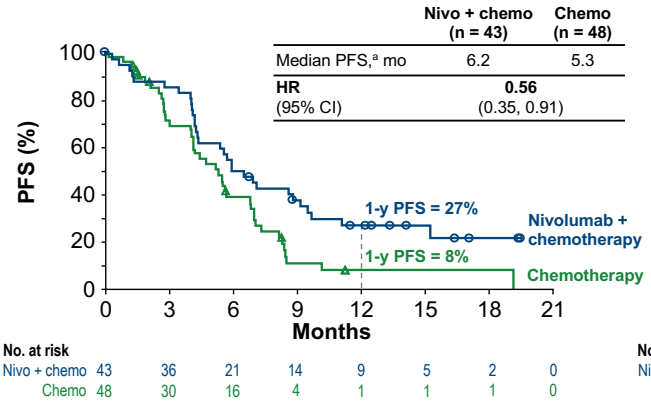
CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

PFS: Nivolumab + Chemotherapy vs Chemotherapy By TMB

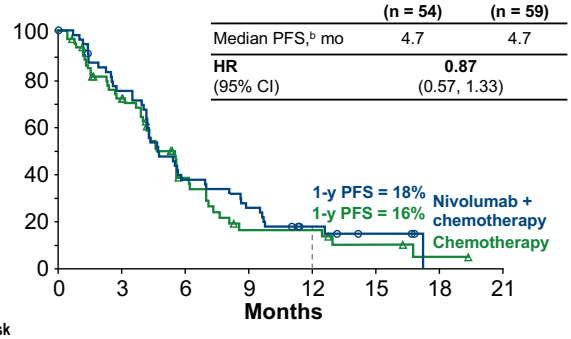
TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression



	Nivo + chemo (n = 43)	Chemo (n = 48)
Median PFS,[a] mo	6.2	5.3
HR (95% CI)	**0.56** (0.35, 0.91)	

No. at risk								
Nivo + chemo	43	36	21	14	9	5	2	0
Chemo	48	30	16	4	1	1	1	0

TMB <10 mut/Mb and <1% Tumor PD-L1 Expression



	Nivo + chemo (n = 54)	Chemo (n = 59)
Median PFS,[b] mo	4.7	4.7
HR (95% CI)	**0.87** (0.57, 1.33)	

No. at risk								
Nivo + chemo	54	38	19	13	6	3	0	0
Chemo	59	39	16	6	6	3	1	0

- TMB ≥10 mut/Mb: ORR was 60.5% with nivo + chemo and 20.8% with chemo
- TMB <10 mut/Mb: ORR was 27.8% with nivo + chemo and 22.0% with chemo

[a]95% CI: nivo + chemo (4.3, 9.1 mo), chemo (4.0, 6.8 mo); [b]95% CI: nivo + chemo (4.2, 6.9 mo), chemo (3.9, 6.2 mo)

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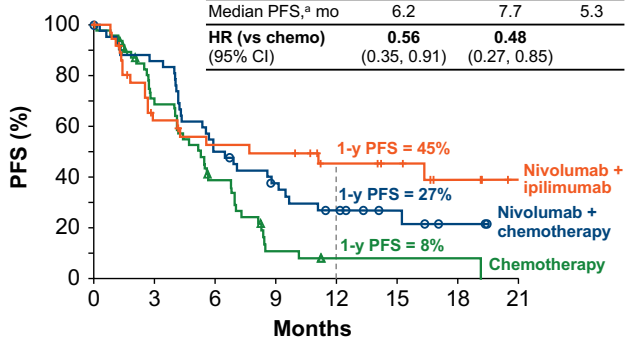
CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

PFS: Nivolumab + Chemotherapy and Nivolumab + Ipilimumab By TMB

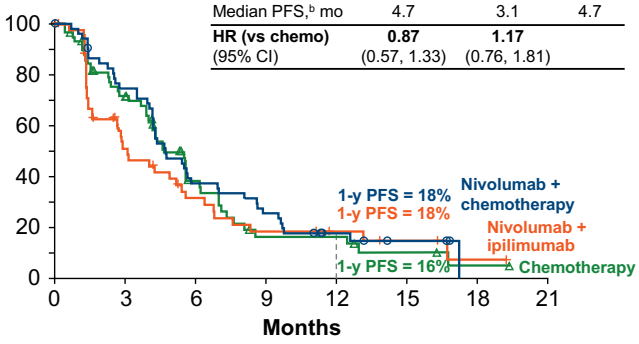
TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression



	Nivo + chemo (n = 43)	Nivo + ipi (n = 38)	Chemo (n = 48)
Median PFS,[a] mo	6.2	7.7	5.3
HR (vs chemo) (95% CI)	**0.56** (0.35, 0.91)	**0.48** (0.27, 0.85)	

No. at risk								
Nivo + chemo	43	36	21	14	9	5	2	0
Nivo + ipi	38	20	16	15	10	8	4	1
Chemo	48	30	16	4	1	1	1	0

TMB <10 mut/Mb and <1% Tumor PD-L1 Expression



	Nivo + chemo (n = 54)	Nivo + ipi (n = 52)	Chemo (n = 59)
Median PFS,[b] mo	4.7	3.1	4.7
HR (vs chemo) (95% CI)	**0.87** (0.57, 1.33)	**1.17** (0.76, 1.81)	

No. at risk								
Nivo + chemo	54	38	19	13	6	3	0	0
Nivo + ipi	52	22	12	7	5	3	1	0
Chemo	59	39	16	6	6	3	1	0

Exploratory analysis

[a]95% CI: nivo + chemo (4.3, 9.1 mo), nivo + ipi (2.7, NR mo), chemo (4.0, 6.8 mo); [b]95% CI: nivo + chemo (4.2, 6.9 mo), nivo + ipi (1.6, 5.4 mo), chemo (3.9, 6.2 mo)

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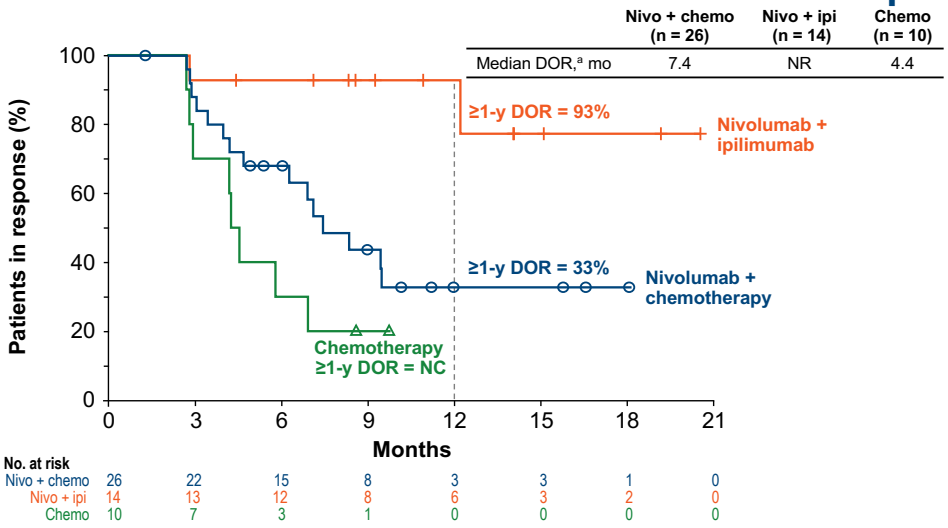
CheckMate 227: Nivo + Ipi, Nivo + Chemo, and Chemo in 1L NSCLC With <1% Tumor PD-L1 Expression

DOR: Nivolumab + Chemotherapy and Nivolumab + Ipilimumab in Patients With TMB ≥10 mut/Mb and <1% Tumor PD-L1 Expression



- ORR was 60.5% with nivo + chemo, 36.8% with nivo + ipi, and 20.8% with chemo

Exploratory analysis
[a]95% CI: nivo + chemo (4.6, NR mo), nivo + ipi (12.2, NR mo), chemo (2.7, 6.9 mo)

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Efficacy results: PD-L1 expression <1%

Patient population	# of patients	ORR	DOR (months)	PFS (months)	1-year PFS
Chemotherapy	177	23.1%	4.7	4.7	14%
Chemotherapy + nivolumab	186	36.7%	7.2	5.6 HR=0.74, 0.58-0.94	26%
Nivolumab+ ipilimumab	187	25.1%	18.0	4.4 HR=0.79, 0.62-1.01	29%

ORR and DOR for nivo/ipi (n=47)
HR vs chemotherapy

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PRESENTED BY: TOM STINCHCOMBE'S DISCUSSION SLIDE

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Discussion points

- What is the role for nivolumab + ipilimumab, or nivolumab + chemotherapy, in the front-line treatment of NSCLC with PD-L1 treatment of < 1%?
  - Positive trial compared with chemo, but not strong enough to displace carbo/pemetrexed/pembro first line
  - TMB subsets interesting but require tissue and weeks of turnaround for NGS testing (only FM validated)

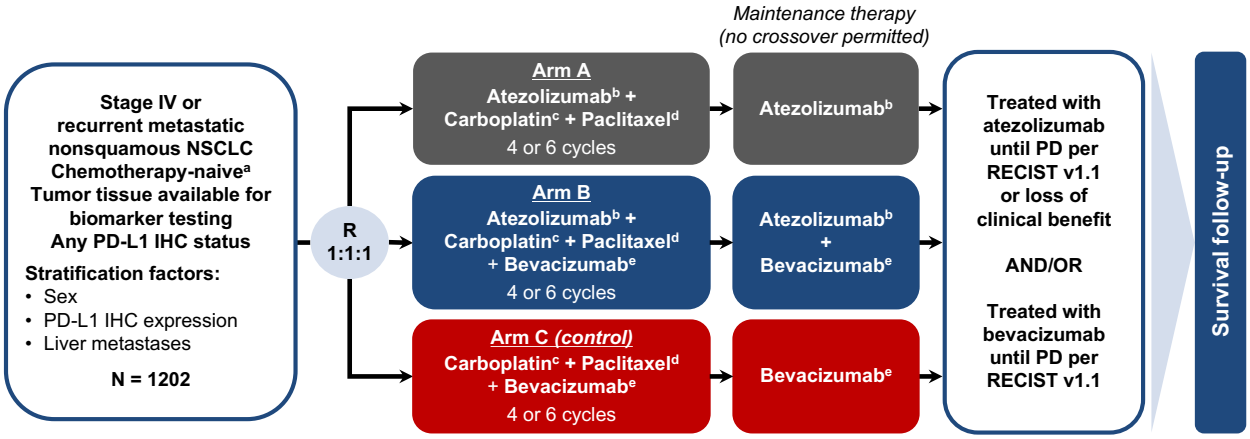
Presented by: Joel Neal

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



Treated Brain metastasis allowed

[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.

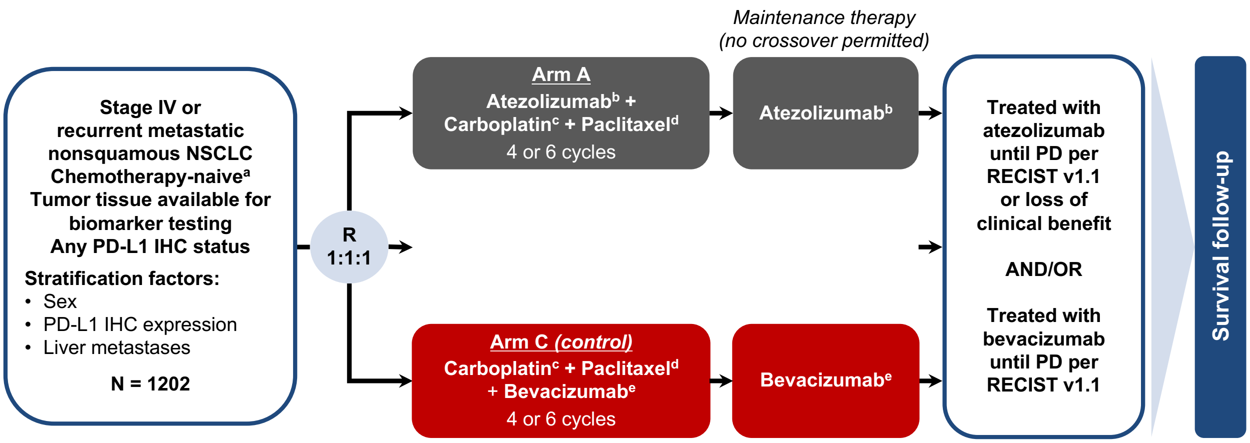
Baseline Characteristics

Baseline characteristics	Arm A: atezo + CP (N = 402)	Arm B: atezo + bev + CP (N = 400)	Arm C (*control*): bev + CP (N = 400)
Median age (range), years	63 (32-85)	63 (31-89)	63 (31-90)
Sex, male, n (%)	241 (60%)	240 (60%)	239 (60%)
ECOG PS, 0, n (%)	180 (45%)	159 (40%)	179 (45%)
Tobacco use history, n (%)			
Current smoker | Previous smoker	98 (24%) | 227 (57%)	90 (23%) | 228 (57%)	92 (23%) | 231 (58%)
Never smoker	77 (19%)	82 (21%)	77 (19%)
Liver metastases, yes, n (%)	53 (13%)	52 (13%)	57 (14%)
EGFR mutation, positive, n (%)	45 (11%)	34[a] (9%)	45 (11%)
EML4-ALK rearrangement, positive, n (%)	9 (2%)	11 (3%)	20 (5%)
Teff gene signature expression, high, n (%)[b]	177 (44%)	166 (42%)	148 (37%)
PD-L1 expression, n (%)[c]			
TC3 or IC3	68 (17%)	75 (19%)	73 (18%)
TC2/3 or IC2/3	137 (34%)	140 (35%)	133 (33%)
TC1/2/3 or IC1/2/3	213 (53%)	209 (52%)	195 (49%)
TC0 and IC0	188 (47%)	191 (48%)	205 (51%)

- Patients baseline characteristics were balanced across all arms

IC, tumour-infiltrating immune cells; TC, tumour cells.
[a] One patient had *EGFR* exon 19 deletion and also tested *ALK* positive per central lab. [b] The Teff gene signature high cut-off ≥ –1.91 was used. [c] 1 patient in Arm A had unknown PD-L1 IHC expression. TC3 or IC3 = TC ≥ 50% or IC ≥ 10% PD-L1+; TC2/3 or IC2/3 = TC or IC ≥ 5% PD-L1+; TC1/2/3 or IC1/2/3 = TC or IC ≥ 1% PD-L1+; TC0 and IC0 = TC and IC < 1% PD-L1+.
Data cutoff: January 22, 2018

IMpower150 Study Design



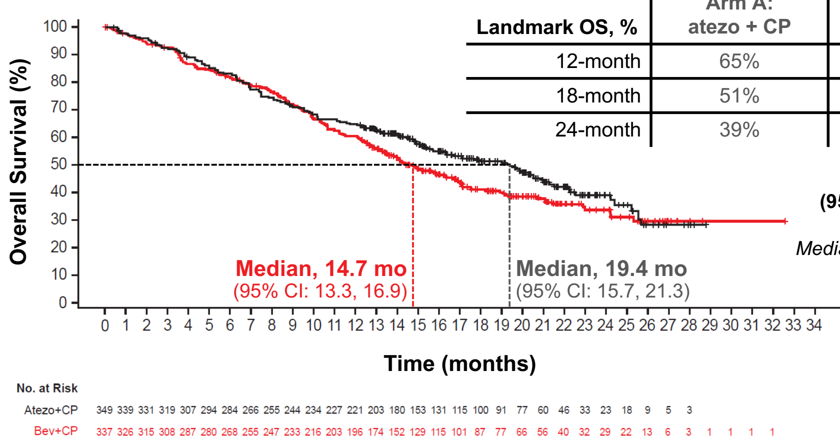
Treated Brain metastasis allowed

[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/m² IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w.

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

Arm A is carbo/pac/atezo
Arm C is carbo/pac/bev

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

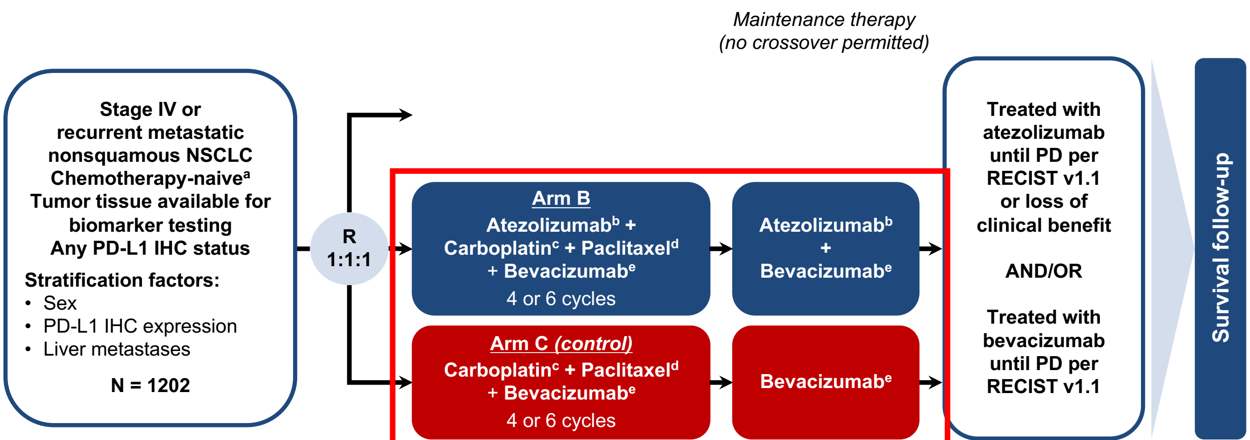


HR[a], 0.88
(95% CI: 0.72, 1.08)
***P* = 0.2041**
Median follow-up: ~20 mo

- 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

IMpower150 Study Design

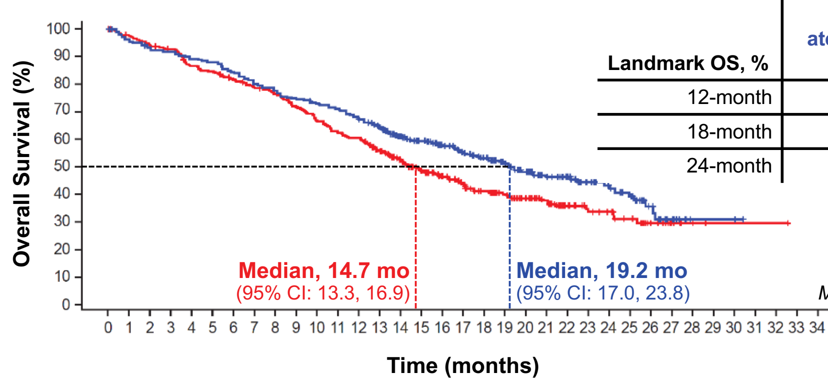


Treated Brain metastasis allowed

[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.

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

Arm B is carbo/pac/bev/atezo
Arm C is carbo/pac/bev



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

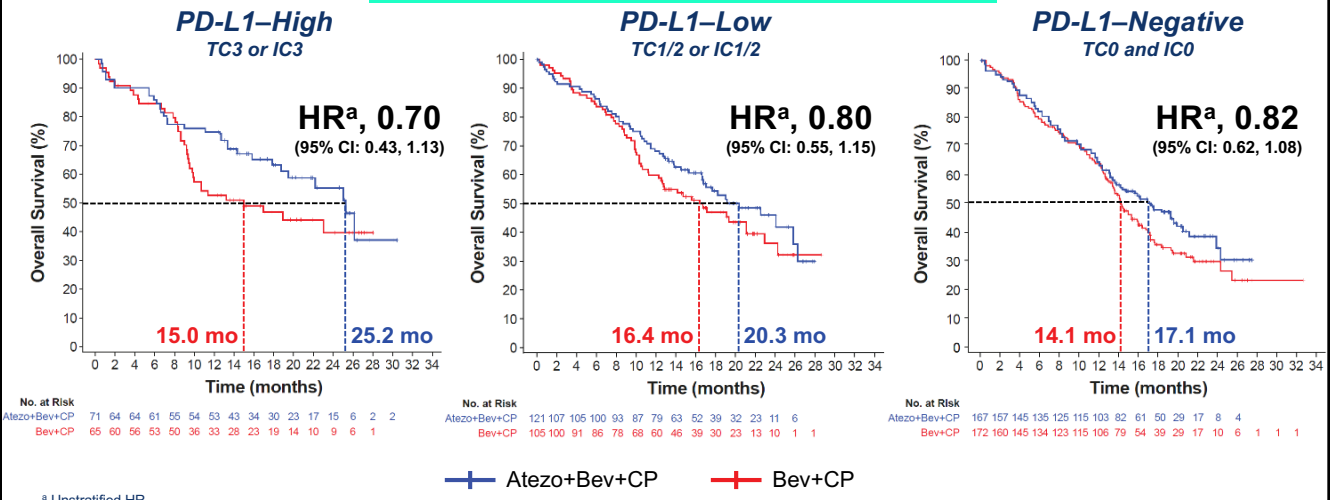
Atezo+Bev+CP	359	339	328	323	314	310	296	284	273	264	256	250	235	218	188	167	147	133	119	103	84	66	57	41	34	28	16	9	2	2	2	
Bev+CP	337	326	315	308	287	280	268	255	247	233	216	203	196	174	152	129	115	101	87	77	66	56	40	32	29	22	13	6	3	1	1	1	1

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

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

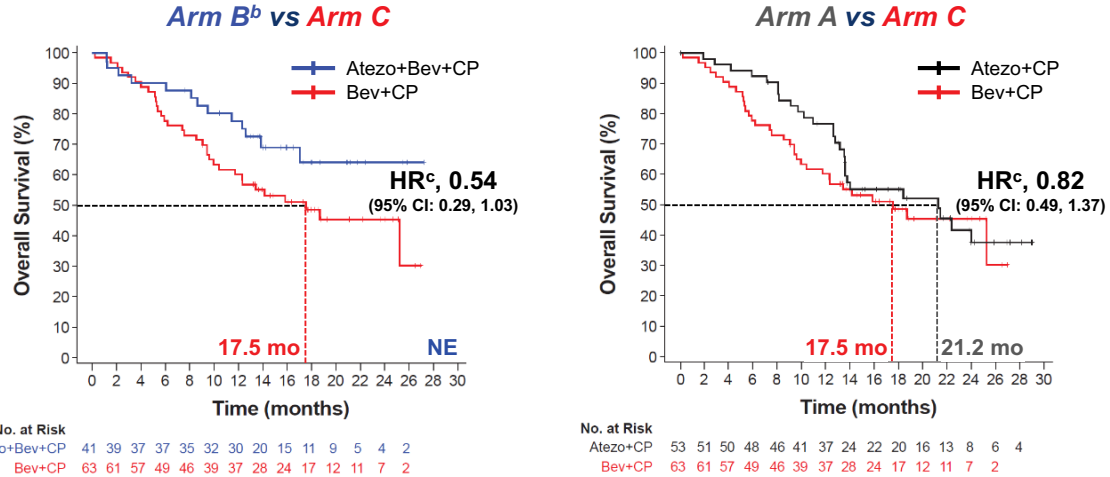
Survival Benefit Was Observed Across All PD-L1 Subgroups in the ITT-WT (Arm B vs Arm C)

All unstratified HRs crossed 1.00



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

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



[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

Discussion points

- What is the role for carboplatin/paclitaxel/bevacizumab/atezolizumab in the front-line treatment of NSCLC?
  - Strong OS data regardless of PD-L1 status but carbo/pemetrexed/pembrolizumab has fewer toxicities (no taxane or bev)
  - Consider for EGFR patients post-TKI therapy?

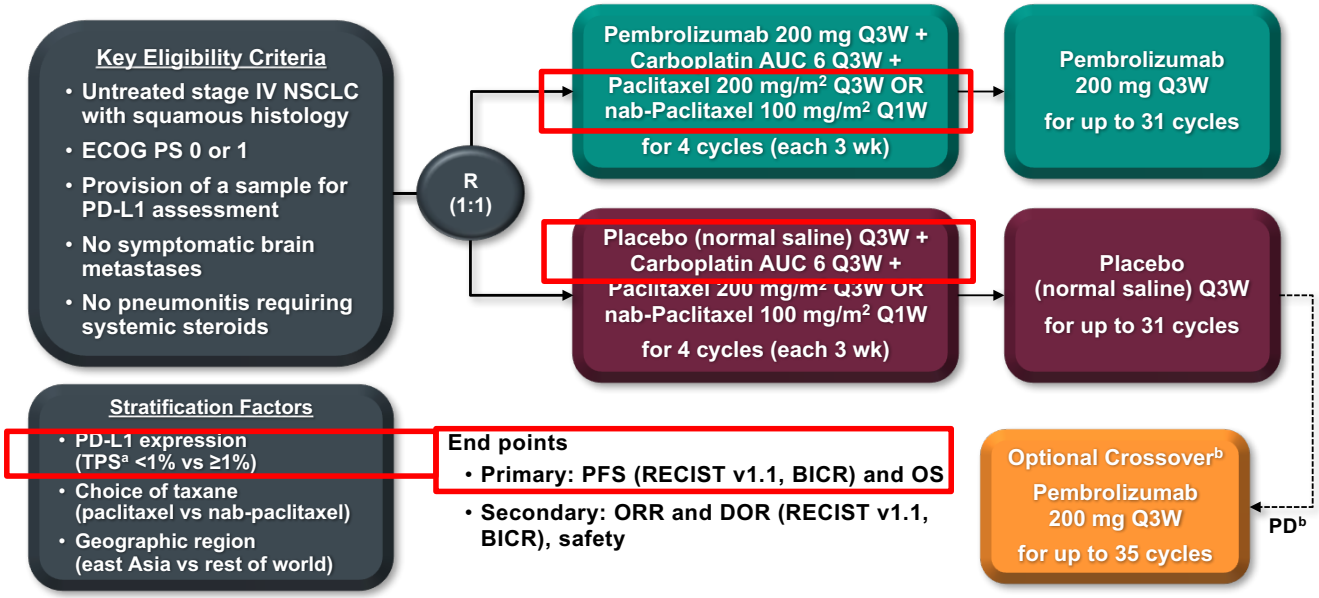
Presented by: Joel Neal

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]

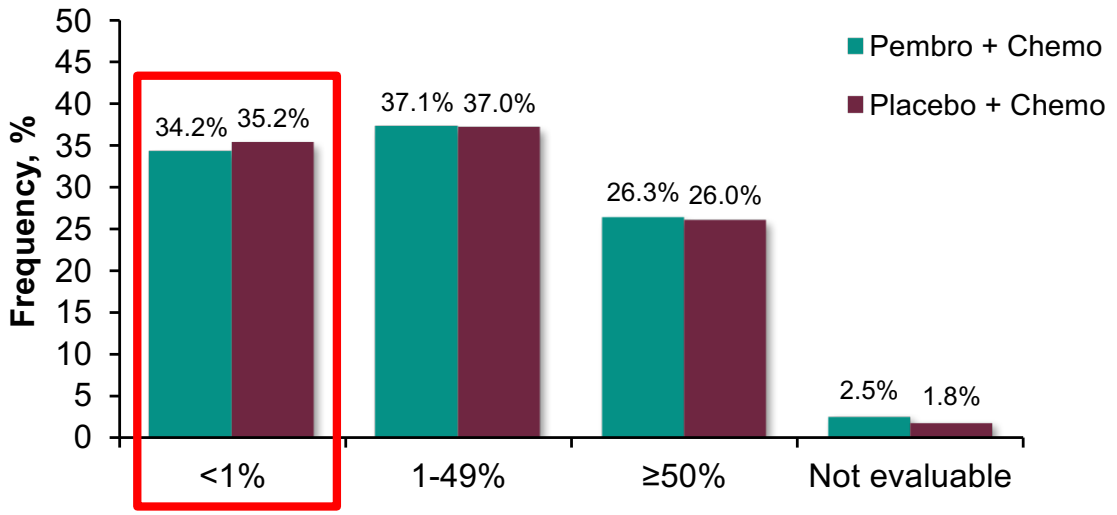
[1]Hospital Universitario 12 de Octubre, Madrid, Spain; [2]Leningrad Regional Clinical Hospital, St. Petersburg, Russia; [3]Wollongong Hospital, Wollongong, NSW, Australia; [4]Kartal Research and Training Hospital, Istanbul, Turkey; [5]Centre Hospitalier Universitaire de Toulouse, Toulouse, France; [6]Universitätskinikum 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

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.

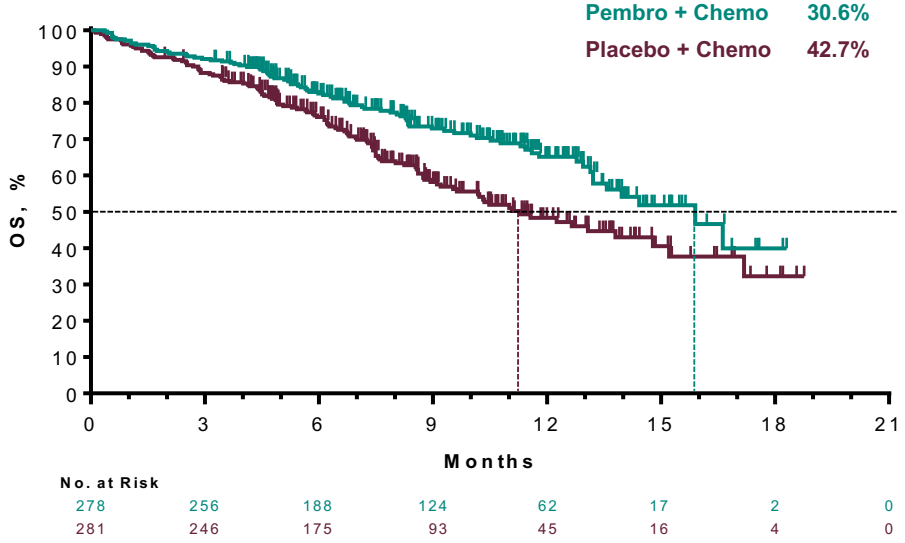
Frequency of PD-L1 TPS Categories



Not evaluable refers to specimens with an inadequate number of tumor cells or no tumor cells seen; these patients were included in the PD-L1 TPS <1% group for randomization stratification but excluded from analyses of efficacy by TPS. Data cutoff date: Apr 3, 2018.

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%		

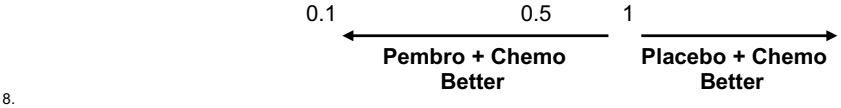


Median (95% CI)
15.9 mo (13.2-NE)
11.3 mo (9.5-14.8)

Data cutoff date: Apr 3, 2018.

Overall Survival at IA2 in Key Subgroups

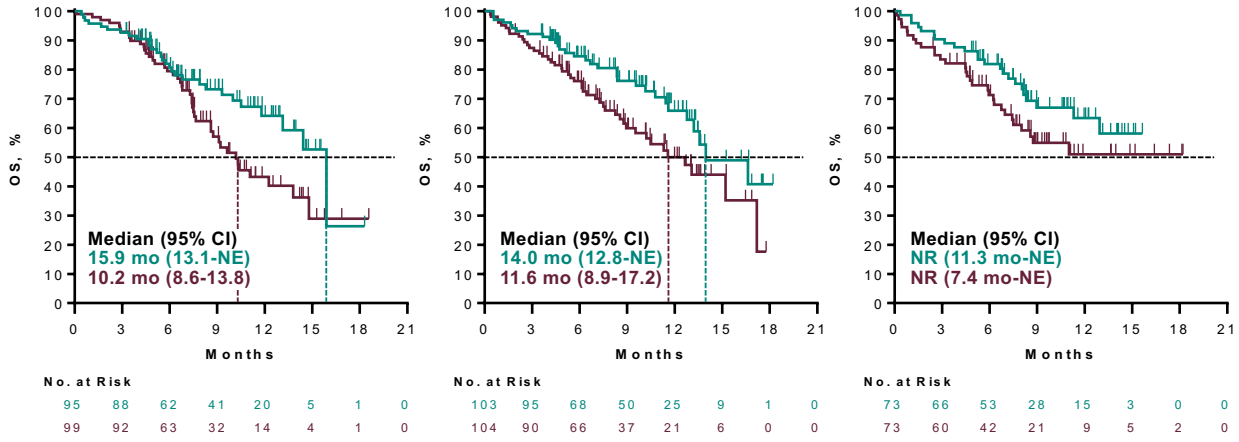
Subgroup	No. of Deaths/ No. of Patients	Hazard Ratio (95% CI)
Overall	205/559	0.64 (0.49-0.85)
Age		
<65 yrs	88/254	0.52 (0.34-0.80)
≥65 yrs	117/305	0.74 (0.51-1.07)
Sex		
Male	167/455	0.69 (0.51-0.94)
Female	38/104	0.42 (0.22-0.81)
ECOG PS		
0	48/163	0.54 (0.29-0.98)
1	157/396	0.66 (0.48-0.90)
Region of enrollment		
East Asia	34/106	0.44 (0.22-0.89)
Rest of world	171/453	0.69 (0.51-0.93)
Choice of taxane		
Paclitaxel	140/336	0.67 (0.48-0.93)
Nab-paclitaxel	65/223	0.59 (0.36-0.98)



Data cutoff date: Apr 3, 2018.

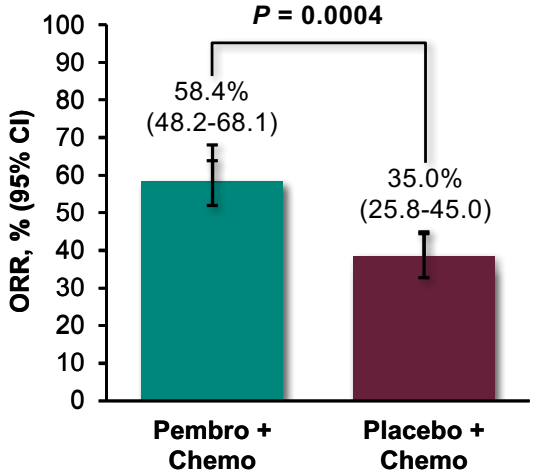
Overall Survival at IA2 by PD-L1 TPS

	TPS <1%		TPS 1-49%		TPS ≥50%	
	Events	HR (95% CI)	Events	HR (95% CI)	Events	HR (95% CI)
Pembro + Chemo	30.5%	0.61 (0.38-0.98)	30.1%	0.57 (0.36-0.90)	31.5%	0.64 (0.37-1.10)
Placebo + Chemo	44.4%		43.3%		41.1%	



Data cutoff date: Apr 3, 2018.

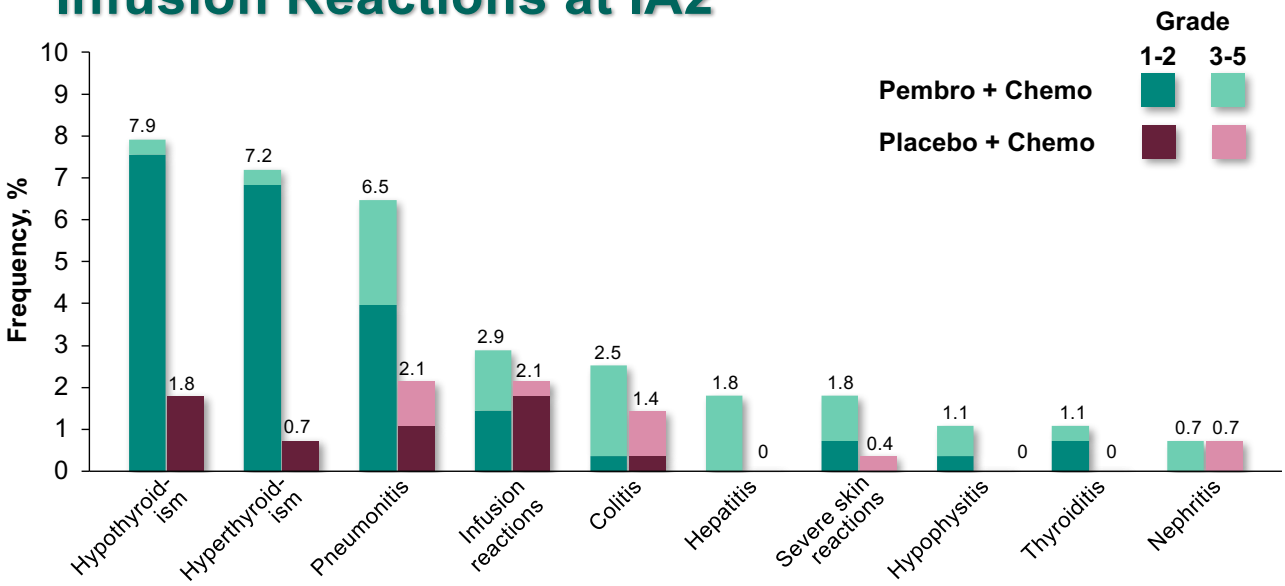
Objective Response Rate at IA2 (RECIST v1.1 by BICR)



Best Response	Pembro + Chemo (N = 278)	Placebo + Chemo (N = 281)
Complete response	4 (1.4%)	6 (2.1%)
Partial response	157 (56.5%)	102 (36.3%)
Stable disease	78 (28.1%)	104 (37.0%)
Progressive disease	17 (6.1%)	39 (13.9%)
Not evaluable[a]	6 (2.2%)	7 (2.5%)
Not assessed[b]	16 (5.8%)	23 (8.2%)

[a]Patients who had ≥1 post-baseline imaging assessment, none of which were evaluable per RECIST v1.1 by BICR. [b]Patients who did not have ≥1 post-baseline imaging assessment. Includes confirmed responses only. No alpha allocated to comparison of ORR at IA2. Data cutoff date: Apr 3, 2018.

Immune-Mediated Adverse Events and Infusion Reactions at IA2



Data cutoff date: Apr 3, 2018.

Discussion points

- What is the role for carboplatin/(nab)paclitaxel/pembrolizumab in the front-line treatment of squamous NSCLC?
  - Positive trial with OS benefit in all subgroups => this should be incorporated into practice now
  - Paclitaxel is a reasonable and more cost effective choice

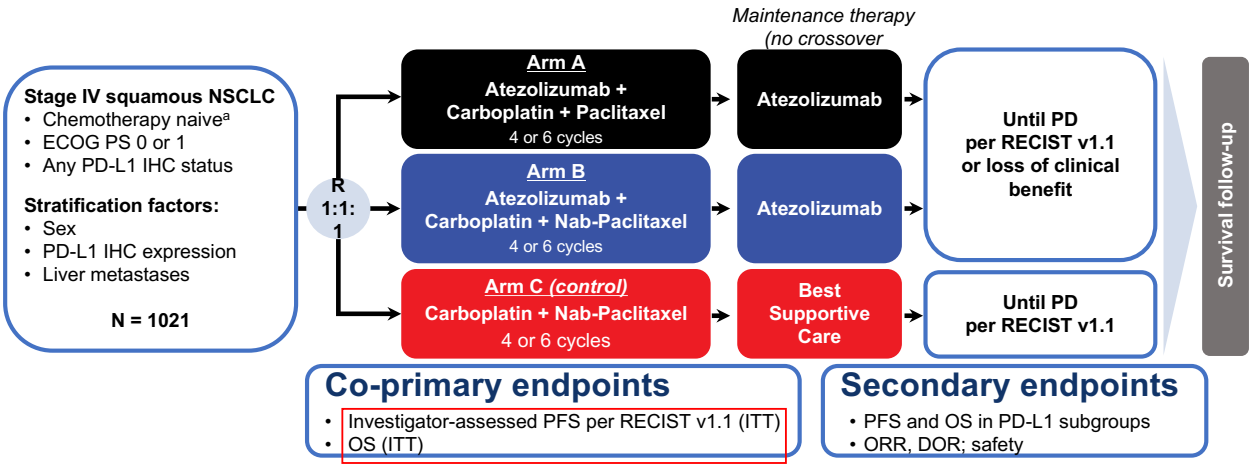
IMpower131: Primary PFS and Safety Analysis of a Randomized Phase III Study of Atezolizumab + Carboplatin + Paclitaxel or Nab-Paclitaxel vs Carboplatin + Nab-Paclitaxel as 1L Therapy in Advanced Squamous NSCLC

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

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

IMpower131: Study Design

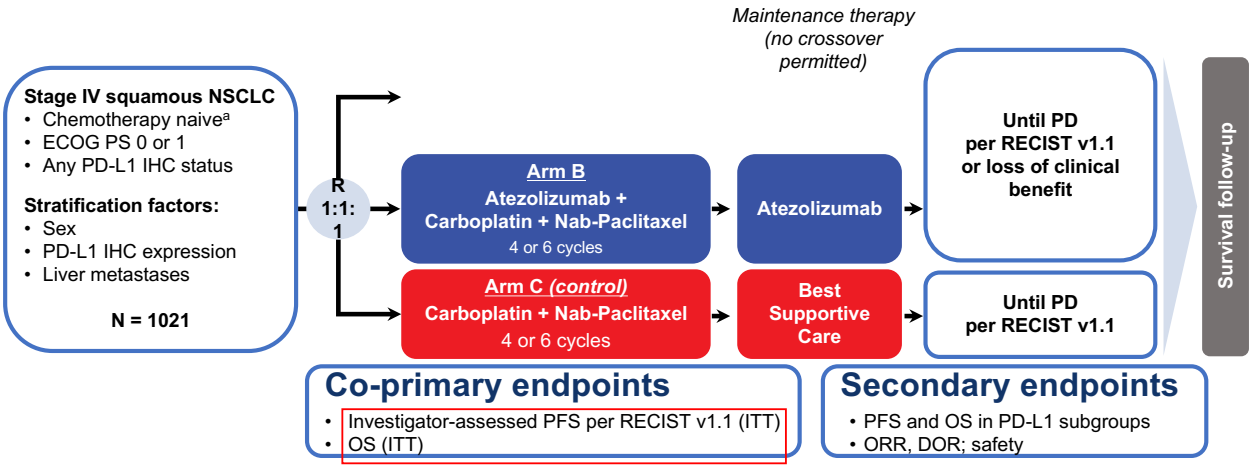


Atezolizumab 1200 mg IV q3w; carboplatin AUC 6 IV q3w; nab-paclitaxel 100 mg/m² IV qw; paclitaxel 200 mg/m² IV q3w.
[a] Patients with a sensitising *EGFR* mutation or *ALK* translocation must have disease progression or intolerance to treatment with ≥ 1 approved targeted therapies. Testing for *EGFR* mutation or *ALK* translocation was not mandatory.
[b] PD-L1 expression was evaluated using the VENTANA SP142 IHC assay.

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

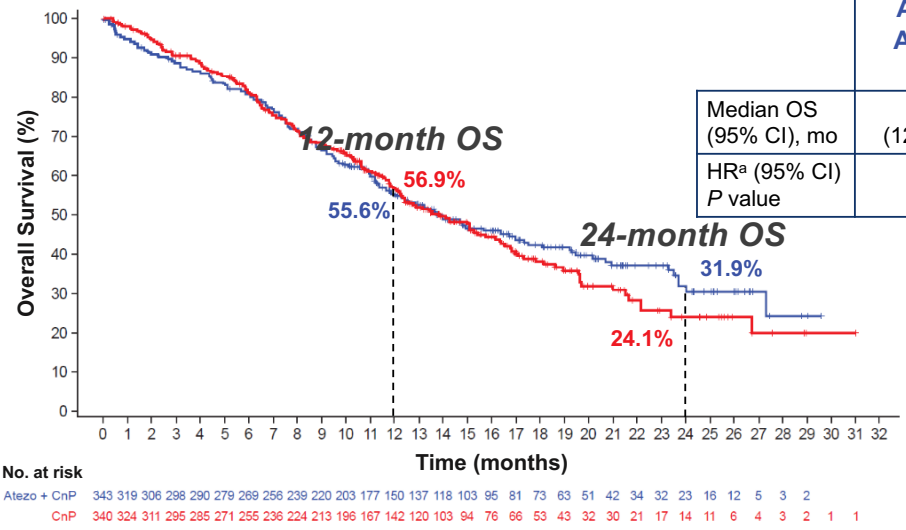
PRESENTED BY: Jotte R, et al. IMpower131 PFS Analysis. https://bit.ly/2snPEzb

IMpower131: Study Design



Atezolizumab 1200 mg IV q3w; carboplatin AUC 6 IV q3w; nab-paclitaxel 100 mg/m² IV qw; paclitaxel 200 mg/m² 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.

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

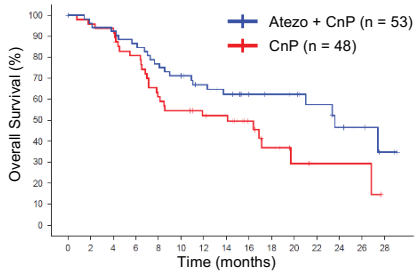


	Arm B: Atezo + CnP	Arm C: CnP
Median OS (95% CI), mo	14.0 (12.0, 17.0)	13.9 (12.3, 16.4)
HR[a] (95% CI) *P* value	0.96 (0.78, 1.18) 0.6931	

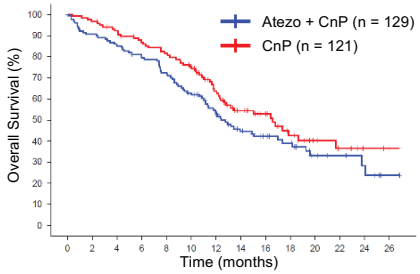
Data cutoff: January 22, 2018.
[a] Stratified HR.

First Interim OS in PD-L1 Subgroups (Arm B vs Arm C)

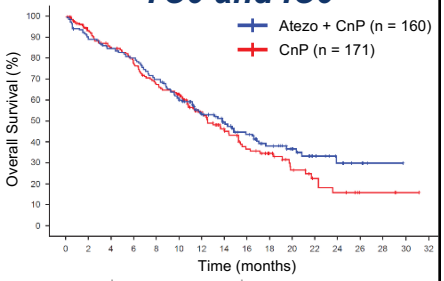
PD-L1 High TC3 or IC3



PD-L1 Low TC1/2 or IC1/2



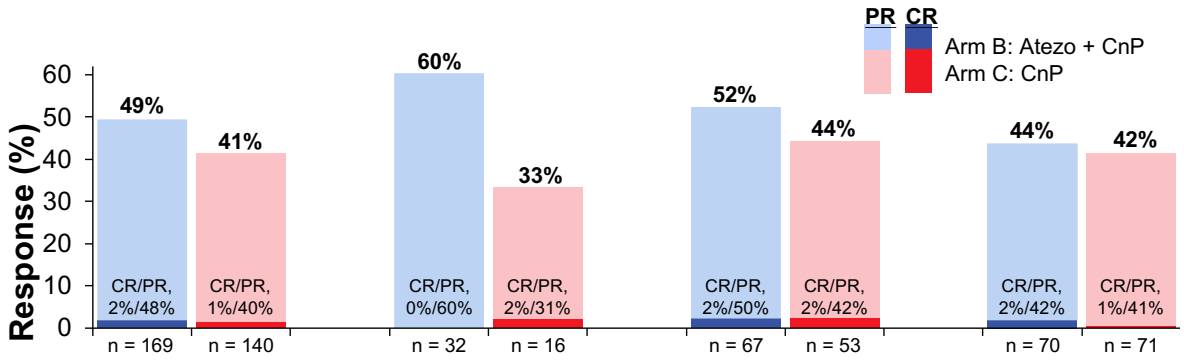
PD-L1 Negative TC0 and IC0



	Atezo + CnP	CnP	Atezo + CnP	CnP	Atezo + CnP	CnP
12-month OS	67%	52%	54%	64%	53%	53%
24-month OS	47%	30%	28%	37%	30%	16%
Median OS, mo	23.6	14.1	12.4	16.6	13.8	12.5
HR[a] (95% CI)	0.56 (0.32, 0.99)		1.34 (0.95, 1.90)		0.86 (0.65, 1.15)	

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

Confirmed Objective Response Rate and Duration of Response



	ITT Population		PD-L1 High (TC3 or IC3)		PD-L1 Low (TC1/2 or IC1/2)		PD-L1 Negative (TC0 and IC0)	
Median DOR (range), mo	7.2 (1.7-28.1+)	5.2 (2.1-27.6+)	18.7 (1.7-26.0)	5.3 (2.8-14.1)	6.9 (2.6-22.4)	5.0 (2.6-24.3)	6.9 (1.9-28.1)	5.2 (2.1-27.6)
Ongoing response, n (%)	54 (32)	23 (16)	17 (53)	4 (25)	17 (25)	6 (11)	20 (29)	13 (18)

Data cutoff: January 22, 2018.
+, censored.

Discussion points

- What is the role for carboplatin/nab-paclitaxel/atezolizumab in the front-line treatment of squamous NSCLC?
  - No preliminary OS benefit, in contrast to chemo/pembrolizumab
  - Awaiting data for paclitaxel (Arm A)

Presented by: Joel Neal

Finally *EGFR*+ NSCLC

NEJ026, NEJ009, ARCHER1050

1G + anti-angiogenesis, 1G + chemotherapy, 2G versus 1G

Slide Courtesy of Sai-Hong Ignatius Ou

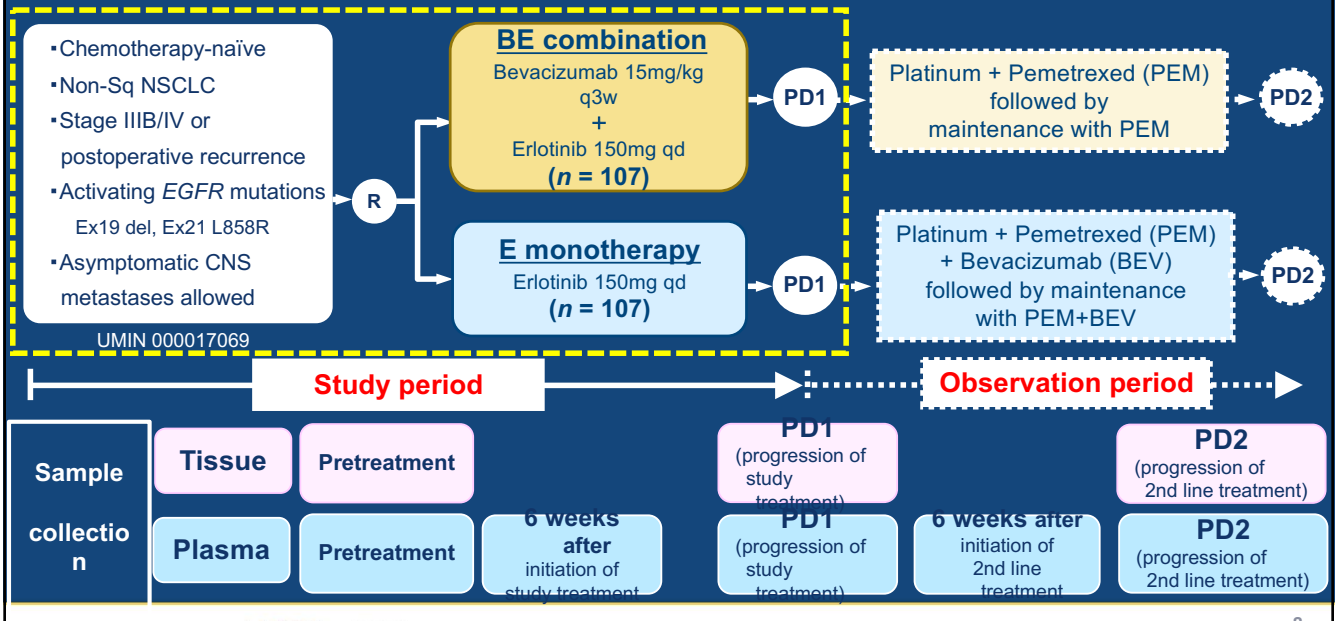
Phase III study comparing bevacizumab plus erlotinib to erlotinib in patients with untreated NSCLC harboring activating *EGFR*-mutations: NEJ 026

Naoki Furuya[1], Tatsuro Fukuhara[2], Haruhiro Saito[3], Kana Watanabe[2], Shunichi Sugawara[4], Shunichiro Iwasawa[5], Yoshio Tsunezuka[6], Ou Yamaguchi[7], Morihito Okada[8], Kouzou Yoshimori[9], Ichiro Nakachi[10], Akihiko Gemma[11], Koichi Azuma[12], Koichi Hagiwara[13], Toshihiro Nukiwa[14], Satoshi Morita[15], Kunihiko Kobayashi[7], and Makoto Maemondo[16],

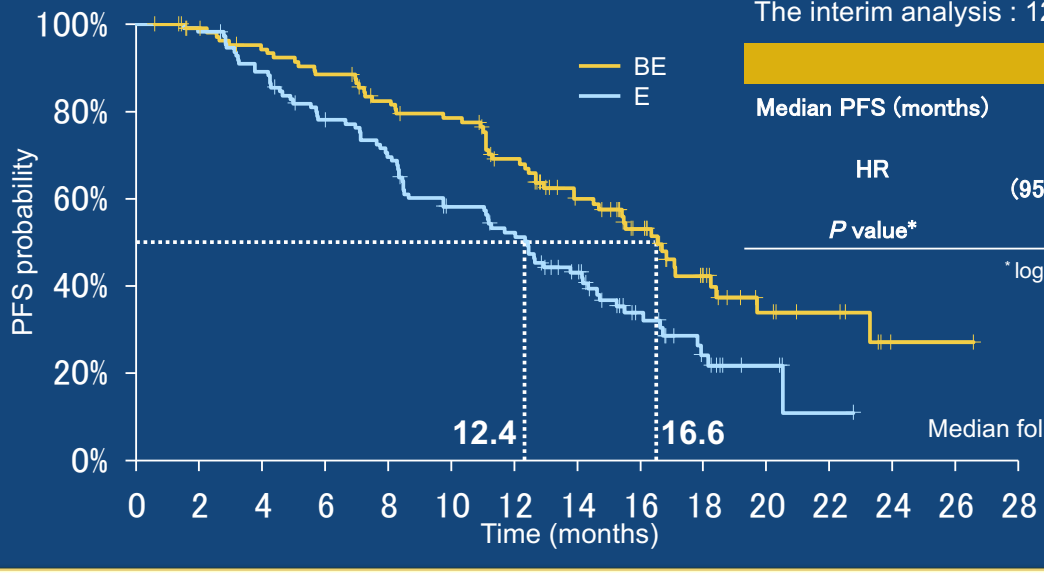
North East Japan Study Group

[1]St. Marianna University School of Medicine, [2]Miyagi Cancer Center, [3]Kanagawa Cancer Center, [4]Sendai Kousei Hospital, [5]Chiba University Hospital, [6]Ishikawa Prefectural Central Hospital, [7]Saitama Medical University International Medical Center, [8]Hiroshima University, [9]Fukujuji Hospital, JATA, [10]Saiseikai Utsunomiya Hospital, [11]Nippon Medical School, [12]Kurume University School of Medicine, [13]Jichi Medical University, [14]Tohoku University, [15]Kyoto University Graduate School of Medicine, [16]Iwate Medical University.

Study Design : NEJ 026 (Phase III study)



PFS by investigator assessment



The interim analysis : 128 events

	BE	E
Median PFS (months)	16.6	12.4
HR	0.563 (95% CI : 0.394–0.804)	
P value*	0.00057	

* log-rank test, two-sided

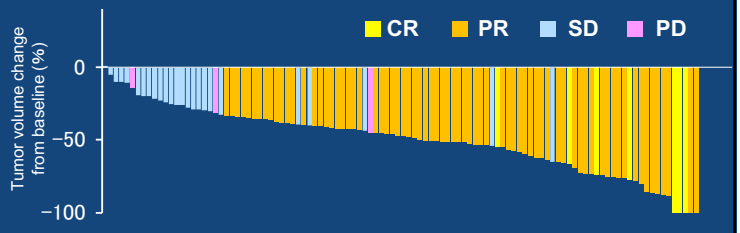
Median follow up : 12.5 months

Objective tumor response by independent review

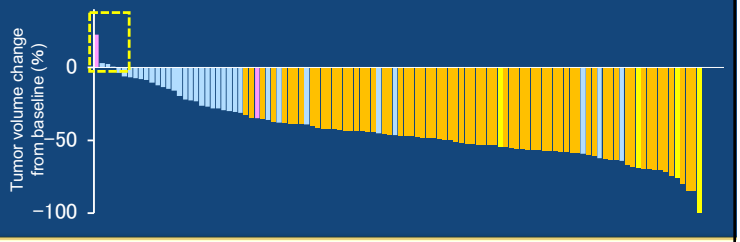
	BE (n=112)	E (n=112)	*P* value
CR	8 (7.1%)	4 (3.6%)	
PR	73 (65.2%)	70 (62.5%)	
SD	25 (22.3%)	34 (30.4%)	
PD	4 (3.6%)	2 (1.8%)	
NE	2 (1.8%)	2 (1.8%)	
ORR	72.3%	66.1%	0.311
DCR	94.6%	96.4%	0.518

* χ^2 test

BE combination



E monotherapy



Discussion points

- What is the role for adding bevacizumab to erlotinib in EGFR mutant NSCLC?
  - Awaiting data for overall survival
  - Unknown whether translates to first-line osimertinib (FLAURA), but is a potential treatment strategy

Presented by: Joel Neal

Phase III Study Comparing Gefitinib Monotherapy to Combination Therapy with Gefitinib, Carboplatin, and Pemetrexed for Untreated Patients with Advanced Non-Small Cell Lung Cancer with EGFR Mutations (NEJ009)

Atsushi Nakamura[1], Akira Inoue[2], Satoshi Morita[3], Yukio Hosomi[4], Terufumi Kato[5] Tatsuro Fukuhara[6], Akihiko Gemma[7], Kazuhisa Takahashi[8], Yuka Fujita[9], Toshiyuki Harada[10] Koichi Minato[11], Kei Takamura[12], Kunihiko Kobayashi[13], Toshihiro Nukiwa[14]

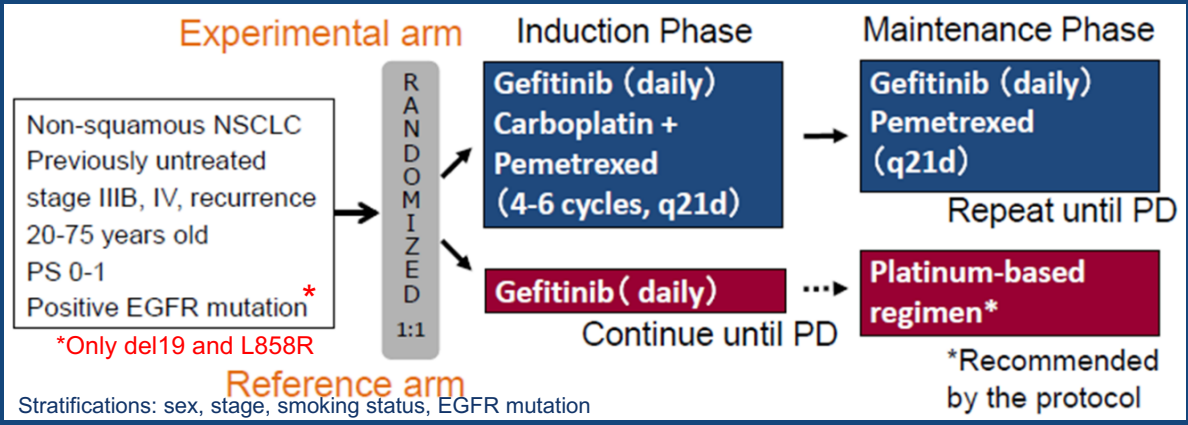
[1]Sendai Kousei Hospital, [2]Tohoku University School of Medicine, [3]Kyoto University Graduate School of Medicine [4]Tokyo Metropolitan Komagome Hospital, [5]Kanagawa Cardiovascular & Respiratory Center, [6]Miyagi Cancer Center [7]Nippon Medical School, [8]Juntendo University Graduate School of Medicine, [9]Asahikawa Medical Center [10]JCHO Hokkaido Hospital, [11]Gunma Prefectural Cancer Center, [12]Obihiro Kosei General Hospital [13]Saitama Medical University, [14]Tohoku University, Professor Emeritus

PRESENTED BY: Atsushi Nakamura

http://clicktoeditURL.com

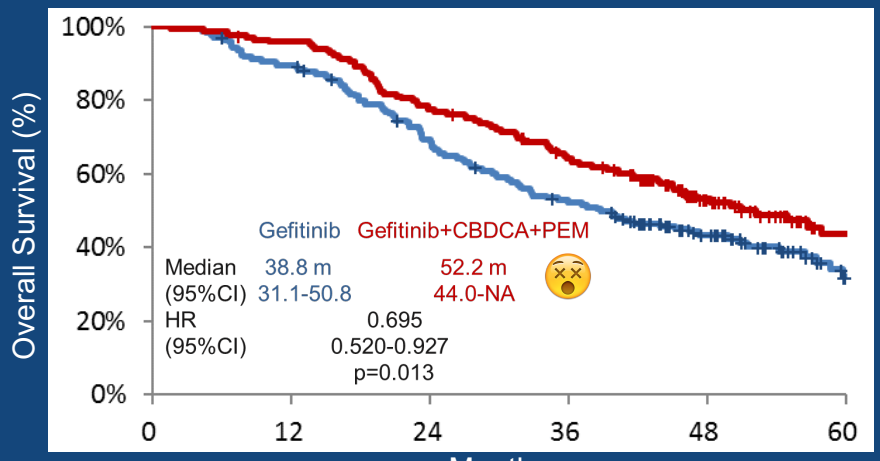
8
4

Study Design of NEJ009



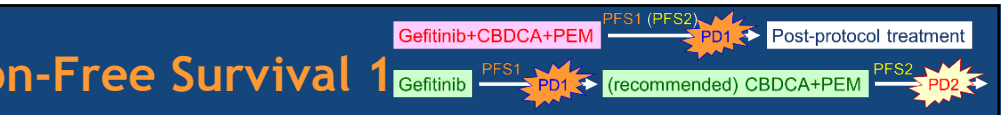
- From Oct. 2011 to Sep. 2015, 345 patients were enrolled from institutions across Japan. In Oct.2017, a number of pre-planned events for primary endpoint analysis were observed.

Overall Survival



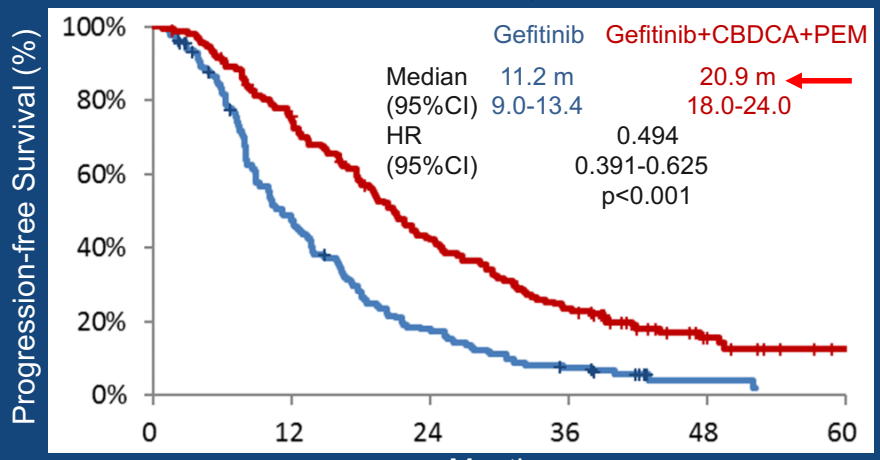
No. at Risk						
Gefitinib	172	153	115	86	50	14
Gefitinib+CBDCA+PEM	170	162	131	105	57	20

Progression-Free Survival 1



ORR (%)

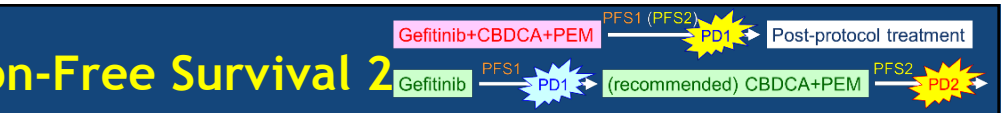
	Gefitinib	combo
CR	3.5	4.7
PR	64.0	79.3
SD	25.0	13.6
PD	4.7	1.2
ORR	67.4	84.0

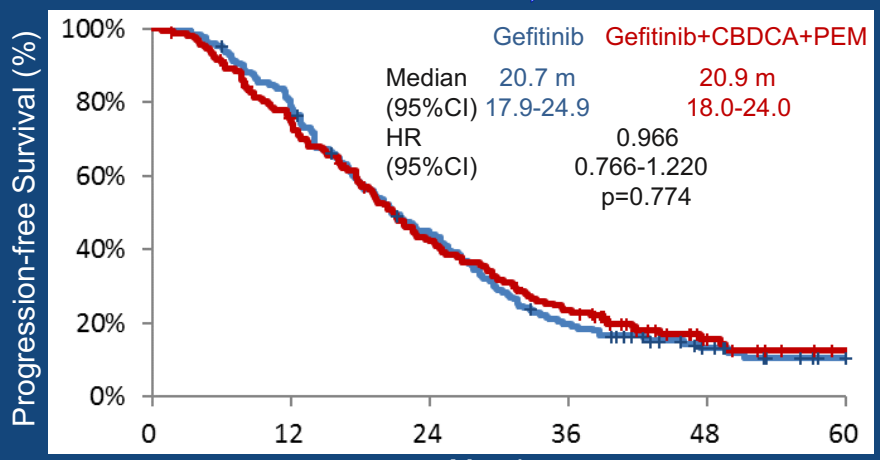


No. at Risk

Gefitinib	172	78	29	11	2	0
Gefitinib+CBDCA+PEM	169	123	68	37	10	2

Progression-Free Survival 2





No. at Risk

Gefitinib	172	135	74	32	13	2
Gefitinib+CBDCA+PEM	169	123	68	37	10	2

Discussion points

- What is the role for adding EGFR TKI to chemotherapy in the first line treatment of EGFR mutant NSCLC?
  - Not a routine practice but OS benefit is thought provoking
  - Can we extend to osimertinib + chemo first line?

Presented by: Joel Neal

Improvement in Overall Survival in a Randomized Study Comparing Dacomitinib With Gefitinib in Patients With Advanced Non-Small Cell Lung Cancer Harboring *EGFR*-Activating Mutations

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PRESENTED BY: Tony S. Mok, MD

ARCHER 1050: Study Design

- Phase 3 randomized open-label study to evaluate dacomitinib as an alternative first-line treatment for patients with advanced NSCLC with an *EGFR*-activating mutation

- Advanced NSCLC with *EGFR*-activating mutation(s)
- No prior systemic treatment of advanced NSCLC
- No CNS metastases
- No prior EGFR TKI or other TKI
- ECOG PS of 0 or 1

N = 452

R
1:1

Dacomitinib 45 mg
PO QD
(n = 227)

Gefitinib 250 mg
PO QD
(n = 225)

Primary endpoint

PFS by blinded independent review (IR)

- Target HR ≤0.667 (50%↑)
- 90% power
- 1-sided α = 0.025
- Assumed median PFS: 14.3 vs 9.5 months

Stratification factors

Race (including Asian vs non-Asian)

EGFR mutation type (exon 19 vs 21)

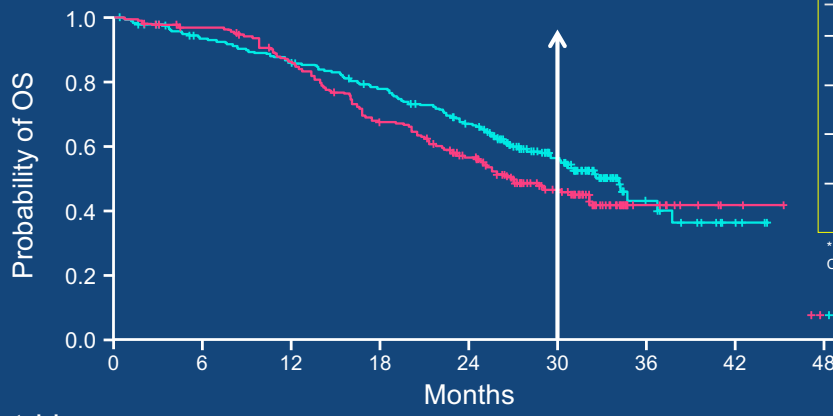
Secondary endpoints

OS

PFS (investigator assessed), ORR, DOR, TTF, Safety, PROs

ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT01774721.
CNS, central nervous system; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; ORR, objective response rate; PO, orally; PROs, patient-reported outcomes; PS, performance status; QD, once daily; R, randomized; TTF, time to treatment failure.

Final OS (Primary Analysis)



	Dacomitinib (n = 227)	Gefitinib (n = 225)
Number of deaths, n (%)	103 (45.4)	117 (52.0)
Median OS, months (95% CI)	34.1 (29.5, 37.7)	26.8 (23.7, 32.1)
HR* (95% CI)	0.760 (0.582, 0.993) 1-sided *P** = 0.0219	
OS probability at 30 months, %	56.2	46.3
CNS metastases at progression, n	1	11

* Stratified analysis.
CNS, central nervous system

No. at risk:

Dacomitinib	227	206	188	167	138	77	14	3	0
Gefitinib	225	213	186	144	113	63	12	3	0

Discussion points

- What is the role for dacomitinib in the first line treatment of EGFR mutant NSCLC?
  - Has OS benefit compared with first generation EGFR TKI's
  - Predicted benefit compared with first line osimertinib use less clear

Thank you!

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Presented by: Joel Neal