Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Corey J Langer, MD

Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

RTP Year in Review 2022

YiR Immunotherapy and Other Nontargeted Approaches for Lung Cancer Faculty

Corey J Langer, MD
Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

Anne S Tsao, MD, MBA
Vice President, Faculty and Academic Affairs
Professor, Thoracic/Head and Neck Medical Oncology
Clinical Medical Director ad Interim, Thoracic and Orthopaedic Center
Director, Mesothelioma Program
The University of Texas MD Anderson Cancer Center
Houston, Texas

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Genentech, a member of the Roche Group, and Regeneron Pharmaceuticals Inc and Sanofi Genzyme.

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mersana Therapeutics Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

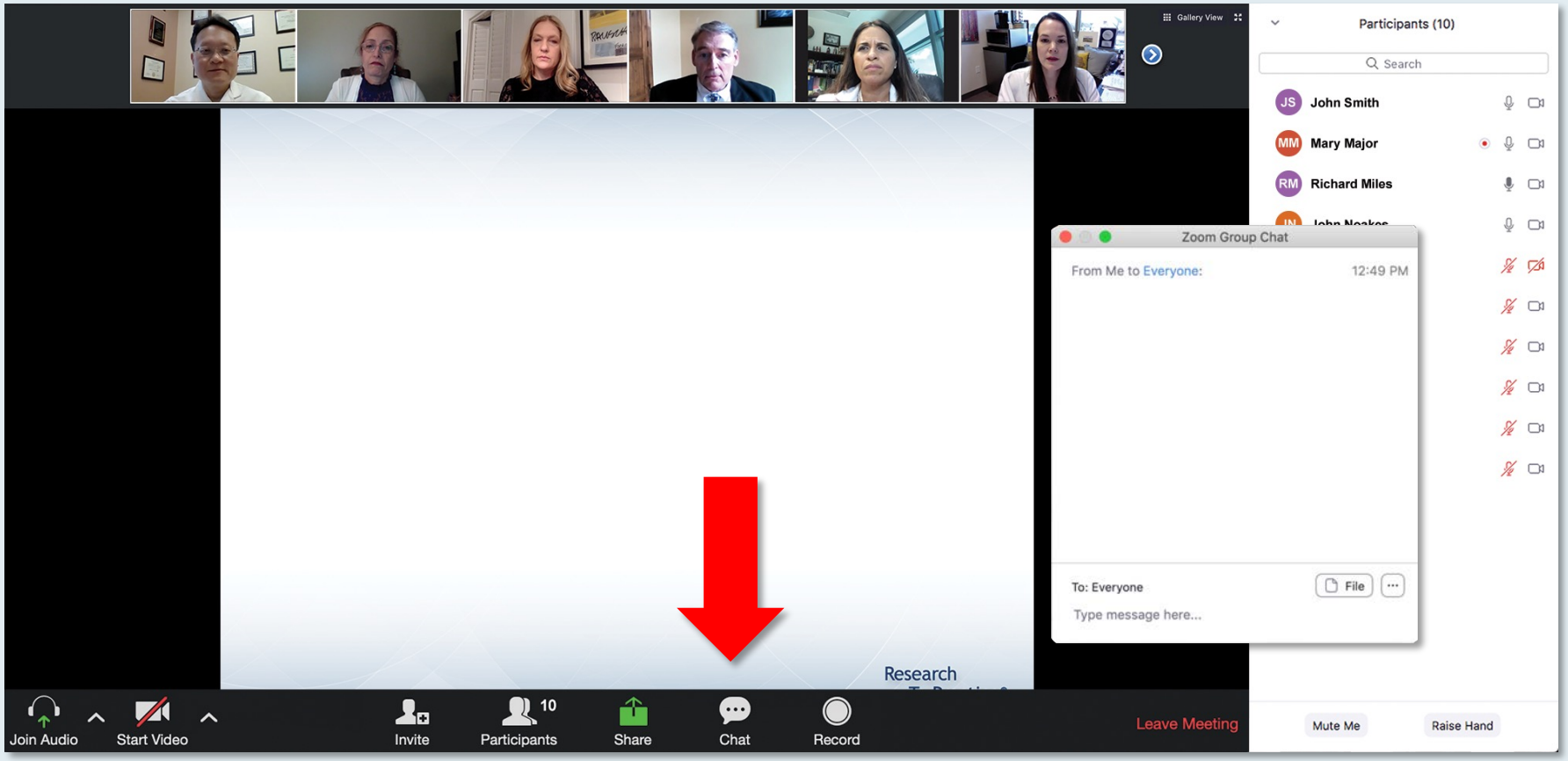
Dr Langer — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Exelixis Inc, Genentech, a member of the Roche Group, Merck, Novocure Inc, Regeneron Pharmaceuticals Inc, Takeda Pharmaceuticals USA Inc
Consulting Agreements	Abbott Laboratories, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, EMD Serono Inc, Exelixis Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Guardant Health, Hospira Inc, Jazz Pharmaceuticals Inc, Merck, Novartis, Novocure Inc, Pfizer Inc, Regeneron Pharmaceuticals Inc, Takeda Pharmaceuticals USA Inc
Contracted Research	Advantagene Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Inovio Pharmaceuticals Inc, Lilly, Mirati Therapeutics, Takeda Pharmaceuticals USA Inc, Trizell
Data and Safety Monitoring Board/Committee	Lilly, Oncocyte

Dr Tsao — Disclosures

Advisory Committee	AstraZeneca Pharmaceuticals LP, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, EMD Serono Inc, Epizyme Inc, Genentech, a member of the Roche Group, Huron, Lilly, Merck, Novartis, Roche Laboratories Inc, Seagen Inc, SELLAS Life Sciences, Takeda Pharmaceuticals USA Inc
Research Grant	Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, EMD Serono Inc, Epizyme Inc, Genentech, a member of the Roche Group, Lilly, Merck, Polaris Group, Seagen Inc, Takeda Pharmaceuticals USA Inc

We Encourage Clinicians in Practice to Submit Questions

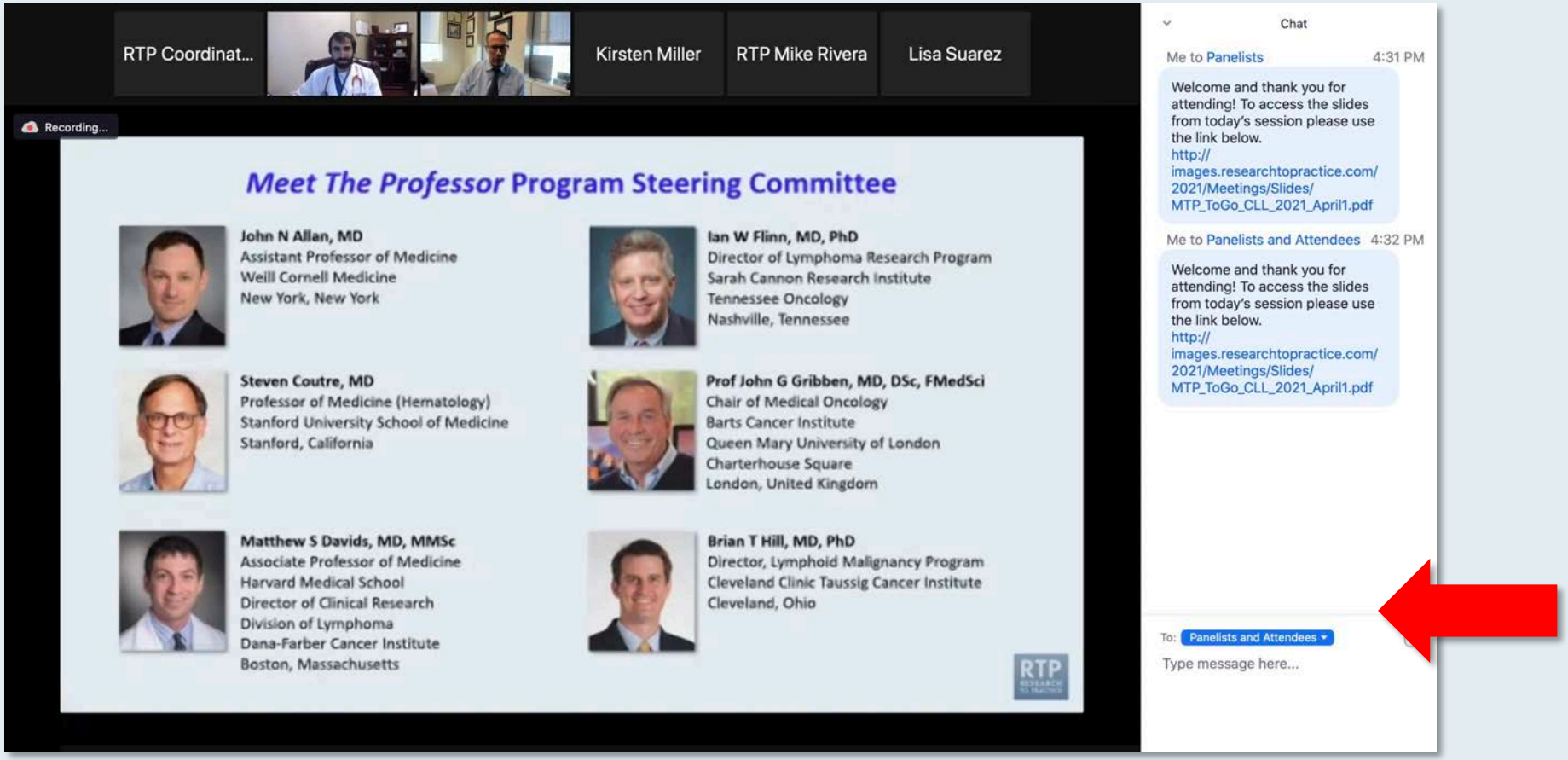


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

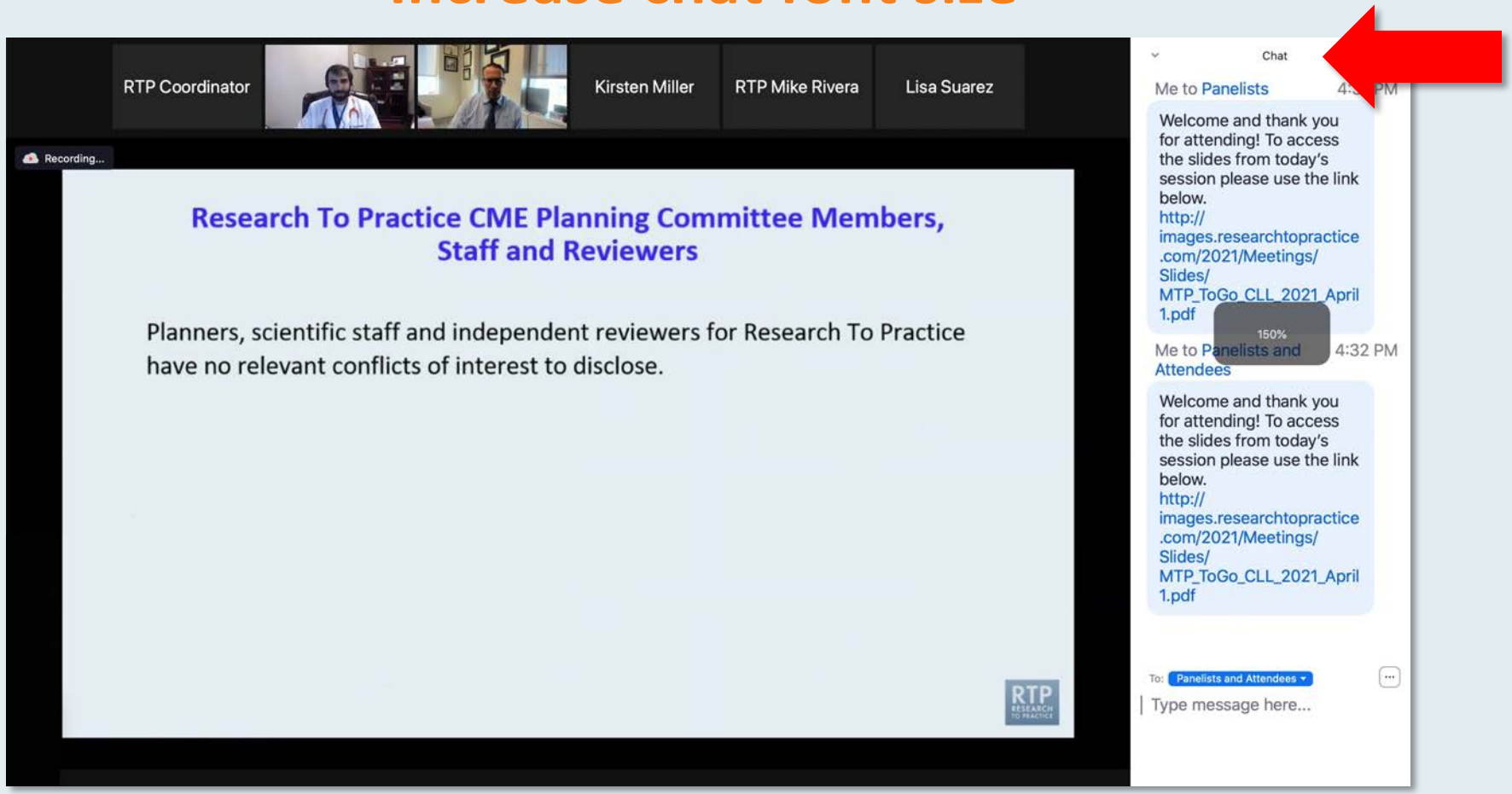


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Increase chat font size



Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty

Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator

Kristen K Ciombor, MD, MSCI

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, January 20, 2022
9:15 PM – 10:45 PM ET

Faculty

Yelena Y Janjigian, MD
Eric Van Cutsem, MD, PhD
Harry H Yoon, MD

Moderator

Samuel J Klempner, MD

RTP
RESEARCH
TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hepatobiliary Cancers (Part 3 of a 3-Part Series)

Friday, January 21, 2022
9:15 PM – 10:45 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD
Robin K Kelley, MD

Moderator

Tanios Bekaii-Saab, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Chronic Lymphocytic Leukemia

Tuesday, January 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Lindsey Roeker, MD

Jeff Sharman, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Promising Investigational Agents and Strategies for Patients with Metastatic Non-Small Cell Lung Cancer Who Experience Disease Progression on Immune Checkpoint Inhibitor Therapy

Wednesday, January 26, 2022
5:00 PM – 6:00 PM ET

Faculty

Edward B Garon, MD, MS

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Thursday, January 27, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel A Pollyea, MD, MS
Gail J Roboz, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP Year in Review 2022

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Corey J Langer, MD

Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

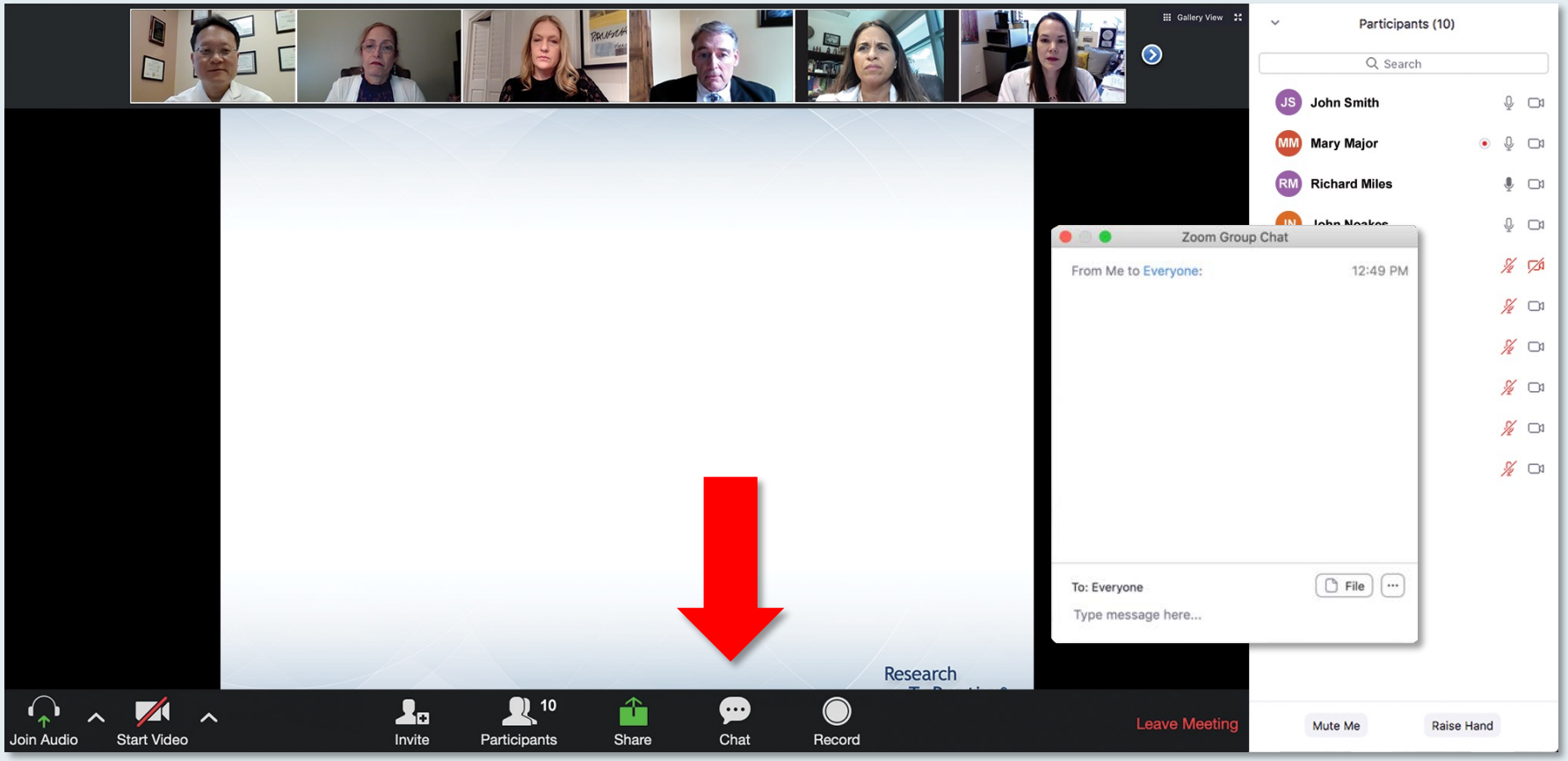
RTP Year in Review 2022

YiR Immunotherapy and Other Nontargeted Approaches for Lung Cancer Faculty

Corey J Langer, MD
Director of Thoracic Oncology
Abramson Cancer Center
Professor of Medicine
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania

Anne S Tsao, MD, MBA
Vice President, Faculty and Academic Affairs
Professor, Thoracic/Head and Neck Medical Oncology
Clinical Medical Director ad Interim, Thoracic and Orthopaedic Center
Director, Mesothelioma Program
The University of Texas MD Anderson Cancer Center
Houston, Texas

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty

Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator

Kristen K Ciombor, MD, MSCI

RTP RESEARCH TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, January 20, 2022
9:15 PM – 10:45 PM ET

Faculty

Yelena Y Janjigian, MD
Eric Van Cutsem, MD, PhD
Harry H Yoon, MD

Moderator

Samuel J Klempner, MD

RTP
RESEARCH
TO PRACTICE

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Hepatobiliary Cancers (Part 3 of a 3-Part Series)

Friday, January 21, 2022
9:15 PM – 10:45 PM ET

Faculty

Ghassan Abou-Alfa, MD, MBA
Richard S Finn, MD
Robin K Kelley, MD

Moderator

Tanios Bekaii-Saab, MD

RTP
RESEARCH TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Chronic Lymphocytic Leukemia

Tuesday, January 25, 2022
5:00 PM – 6:00 PM ET

Faculty

Lindsey Roeker, MD

Jeff Sharman, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Promising Investigational Agents and Strategies for Patients with Metastatic Non-Small Cell Lung Cancer Who Experience Disease Progression on Immune Checkpoint Inhibitor Therapy

Wednesday, January 26, 2022
5:00 PM – 6:00 PM ET

Faculty

Edward B Garon, MD, MS

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Acute Myeloid Leukemia and Myelodysplastic Syndromes

Thursday, January 27, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel A Pollyea, MD, MS
Gail J Roboz, MD

Moderator

Neil Love, MD

RTP Year in Review 2022

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology

Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Thursday, January 13, 2022
5:00 PM – 6:00 PM ET

Faculty

Corey J Langer, MD

Anne S Tsao, MD, MBA

Moderator

Neil Love, MD

RTP Year in Review 2022

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

- KEYNOTE-091: Adjuvant pembrolizumab
- IMpower010: Adjuvant atezolizumab – FDA indication
- CheckMate 816: Neoadjuvant nivolumab/chemotherapy
- PACIFIC: Durvalumab consolidation
- PACIFIC R
- COAST: Durvalumab-based consolidation

Phase III KEYNOTE-091 Trial Meets One of Its Dual Primary Endpoints of DFS for the Adjuvant Treatment of Stage IB-IIIA NSCLC

Press Release: January 10, 2022

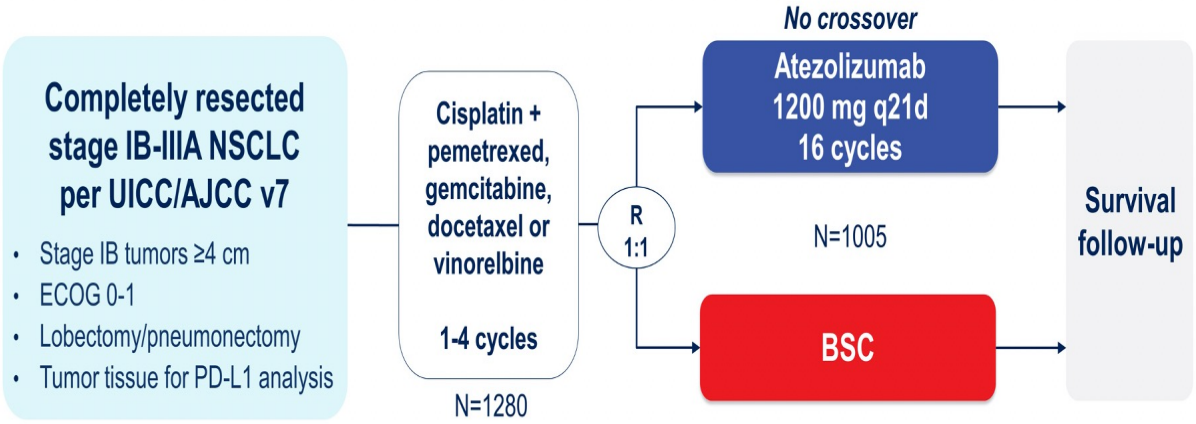
"The European Organisation for Research and Treatment of Cancer (EORTC) and the European Thoracic Oncology Platform (ETOP) today announced that the Phase 3 KEYNOTE-091 trial, also known as EORTC-1416-LCG/ETOP-8-15 – PEARLS, investigating pembrolizumab, met one of its dual primary endpoints of disease-free survival (DFS) for the adjuvant treatment of patients with stage IB-IIIA non-small cell lung cancer (NSCLC) following surgical resection regardless of PD-L1 expression. Based on an interim analysis review conducted by an independent Data Monitoring Committee, adjuvant treatment with pembrolizumab resulted in a statistically significant and clinically meaningful improvement in DFS compared with placebo in the all-comer population of patients with stage IB-IIIA NSCLC.

At the interim analysis, there was also an improvement in DFS for patients whose tumors express PD-L1 (tumor proportion score [TPS] ≥50%) treated with pembrolizumab compared to placebo; however, this dual primary endpoint did not meet statistical significance per the pre-specified statistical plan. The trial will continue to analyze DFS in patients whose tumors express high levels of PD-L1 (TPS ≥50%) and evaluate overall survival (OS), a key secondary endpoint."

https://finance.yahoo.com/news/merck-keytruda-pembrolizumab-showed-statistically-114500130.html

Resectable NSCLC: Adjuvant Immunotherapy

IMpower010: study design



Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

imAEs occuring in ≥1% of patients

	Atezolizumab (n=495)		BSC (n=495)	
n (%)	Any grade	Grade 3-4	Any grade	Grade 3-4
Any immune-mediated AEs	256 (51.7)[b]	39 (7.9%)	47 (9.5)	5 (0.6)
Rash	91 (18.4)	7 (1.4)	11 (2.2)	0
Hepatitis (diagnosis and laboratory abnormalities)	86 (17.4)	20 (4.0)	22 (4.4)	1 (0.2)
Hepatitis (laboratory abnormalities)	81 (16.4)	16 (3.2)	21 (4.2)	1 (0.2)
Hepatitis (diagnosis)	7 (1.4)	4 (0.8)	1 (0.2)	0
Hypothyroidism	86 (17.4)	0	3 (0.6)	0
Hyperthyroidism	32 (6.5)	2 (0.4)	4 (0.8)	0
Pneumonitis	19 (3.8)[c]	4 (0.8)	3 (0.6)	0
Infusion-related reaction	7 (1.4)	1 (0.2)	0	0
Adrenal insufficiency	6 (1.2)	2 (0.4)	0	0

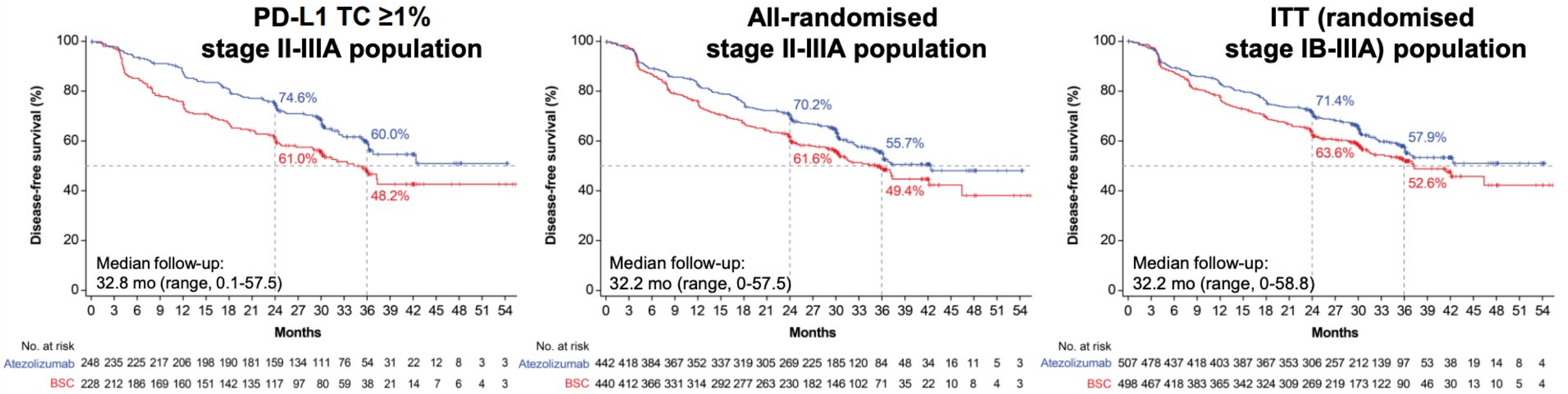
Clinical cutoff: January 21, 2021. [a] Data are from the safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). [b] Includes 2 (0.4%) Grade 5 events. [c] Includes 1 (0.2%) Grade 5 event.

Safety was consistent with prior data.
7.9% grade 3-4 imAE with atezolizumab

Wakelee et al. ASCO 2021 Abstract 8500; Felip et al. Lancet 398: 1344-1357, Oct 2021

Courtesy of Anne S Tsao, MD, MBA

IMpower010: Atezolizumab improves DFS in stages II-IIIA



	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[b]	0.02[c]	

	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[d]	

Atezolizumab conveys DFS benefit in:
Stage II-IIIA PDL1 ≥ 1% (HR 0.66)
Stage II-IIIA (HR 0.79)

Wakelee et al. ASCO 2021 Abstract 8500; Felip et al. Lancet 398: 1344-1357, Oct 2021

Courtesy of Anne S Tsao, MD, MBA

Neoadjuvant Nivolumab with Chemotherapy Significantly Improves Event-Free Survival for Patients with Resectable NSCLC in the Phase III CheckMate 816 Trial

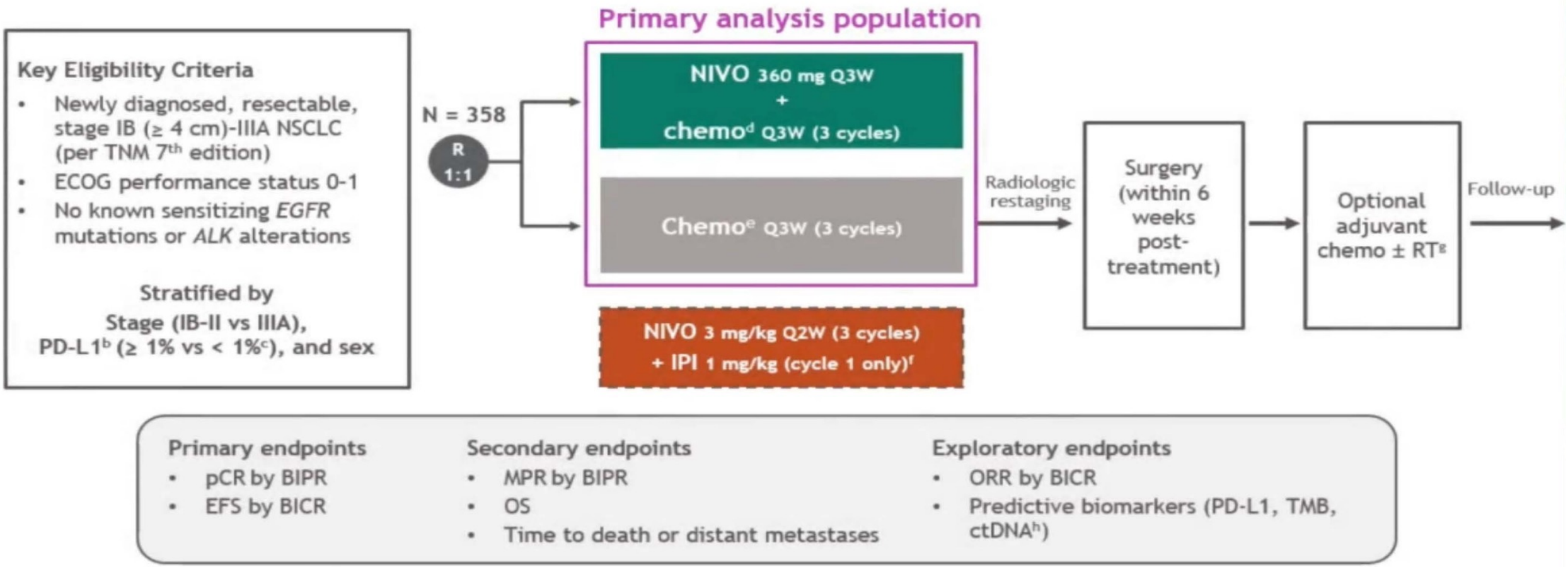
Press Release: November 8, 2021

"The Phase 3 CheckMate -816 trial met the primary endpoint of improved event-free survival (EFS) in patients with resectable stage IB to IIIA non-small cell lung cancer (NSCLC). In a prespecified interim analysis, nivolumab plus chemotherapy showed a statistically significant and clinically meaningful improvement in EFS compared to chemotherapy alone when given before surgery. This combination previously showed a significant improvement of pathologic complete response (pCR), the trial's other primary endpoint…

'CheckMate -816 is the first Phase 3 trial with an immunotherapy-based combination to demonstrate a statistically significant and clinically meaningful benefit as a neoadjuvant treatment for patients with non-metastatic non-small cell lung cancer. The combination of nivolumab plus chemotherapy first showed a statistically significant improvement in pathologic complete response rate without impacting surgical outcomes and has now extended the time patients live free of disease progression, recurrence or death,' said Abderrahim Oukessou, MD, vice president, thoracic cancers development lead. 'The event-free survival data from CheckMate -816 strengthen the evidence for the potential of nivolumab-based therapies to improve long-term clinical outcomes when used in the earlier stages of non-metastatic cancers.'"

https://news.bms.com/news/corporate-financial/2021/Neoadjuvant-Opdivo-nivolumab-Plus-Chemotherapy-Significantly-Improves-Event-Free-Survival-in-Patients-with-Resectable-Non-Small-Cell-Lung-Cancer-in-Phase-3-CheckMate--816-Trial/default.aspx

Resectable NSCLC: Neoadjuvant CheckMate 816



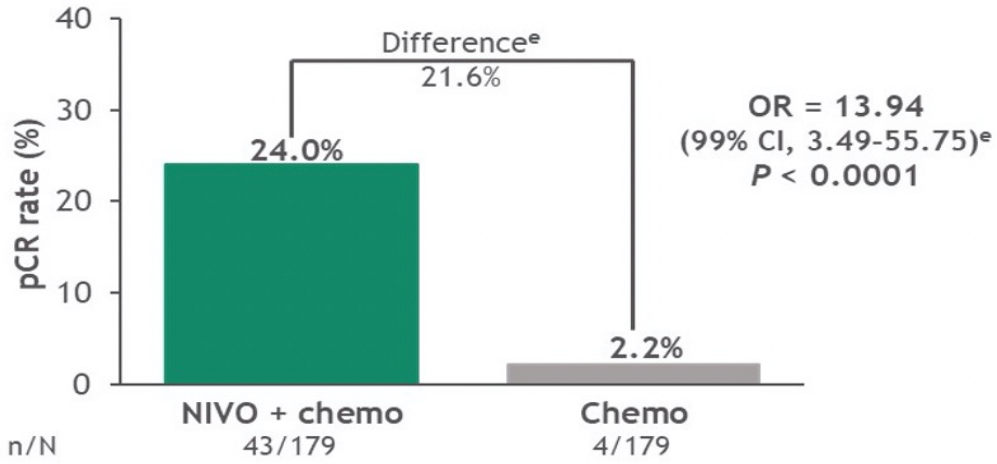
pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes
MPR: ≤ 10% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes

Forde et al. AACR 2021 Abstract CT003

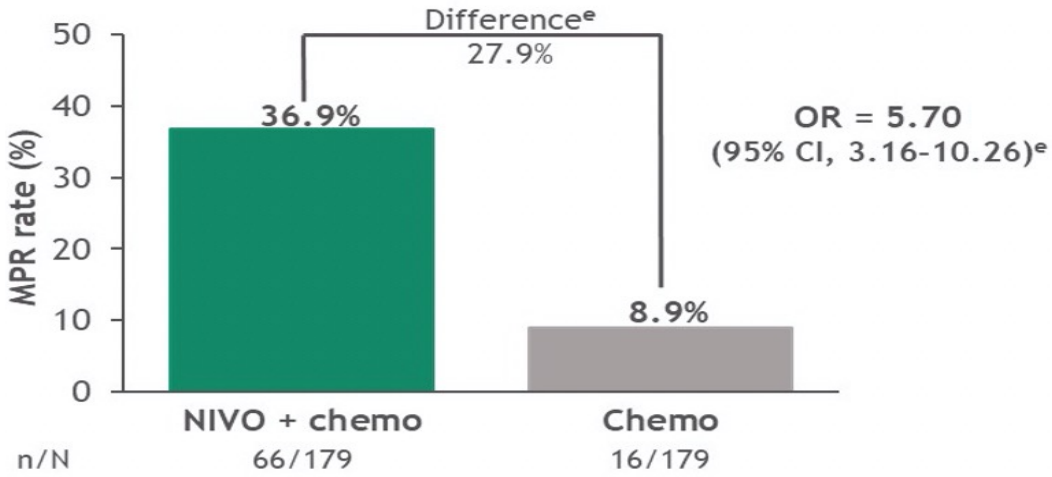
Courtesy of Anne S Tsao, MD, MBA

CheckMate 816 Nivolumab + Chemo improves pCR, MPR, ORR

pCR[b,c] in ITT (ypT0N0)[d]



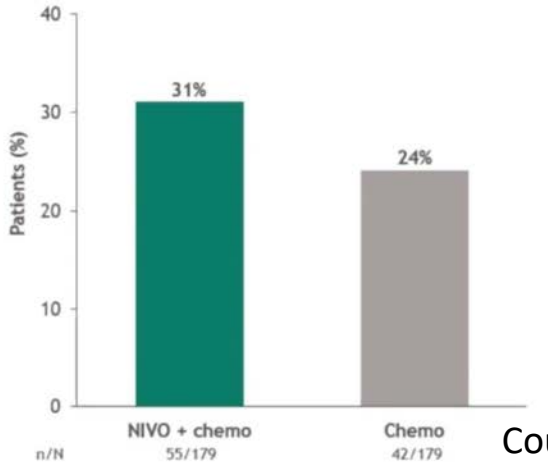
MPR[b,f] in ITT[d]



Objective response rate

Patients, n (%)	NIVO + chemo (n = 179)	Chemo (n = 179)
ORR[a]	96 (54)[b]	67 (37)[b]
Best overall response		
Complete response	1 (1)	3 (2)
Partial response	95 (53)	64 (36)
Stable disease	70 (39)	88 (49)
Progressive disease	8 (4)	11 (6)
Not evaluable	1 (1)	1 (1)
Not reported	4 (2)	12 (7)

Patients with radiographic down-staging[c]

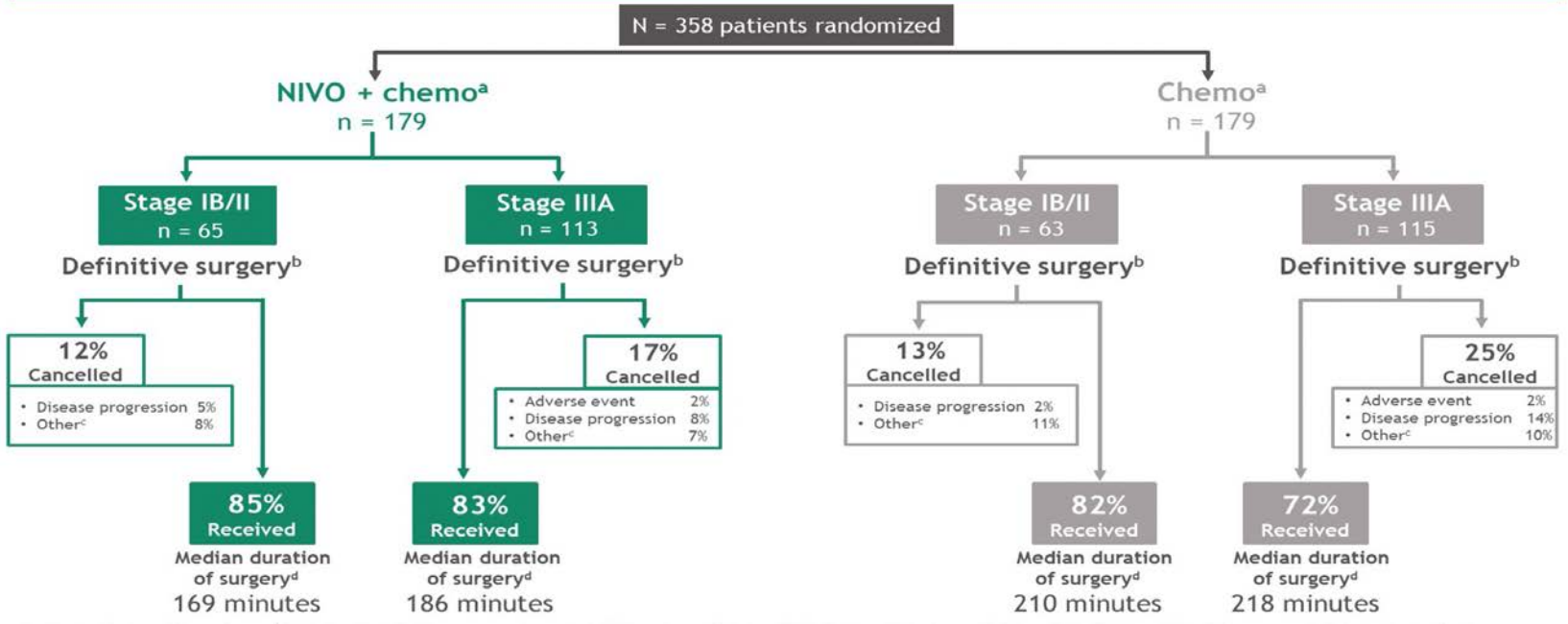


Forde et al. AACR 2021 Abstract CT003; Spicer et al. ASCO 2021 Abstract 8503

Courtesy of Anne S Tsao, MD, MBA

CheckMate 816

No difference in surgical delays, complications or hospital stay



Median time from last neoadjuvant dose to surgery nivo+chemo 5.3 weeks (4.6-6) vs chemo 5 weeks (4.6-5.9)

	NIVO + chemo (n = 135)	Chemo (n = 124)
Length of hospital stay, median (IQR), days	10.0 (7.0-14.0)	10.0 (7.0-14.5)
Length of hospital stay by surgery type,[a] median (IQR), days		
Lobectomy	10.0 (7.0-15.0)	9.0 (6.0-14.0)
Pneumonectomy	10.0 (8.0-13.0)	11.0 (9.0-16.0)
Other[b]	8.5 (4.0-13.0)	9.0 (7.0-14.0)
Length of hospital stay per region,[c,d] median (IQR), days		
North America	4.0 (4.0-7.0)	6.0 (4.0-8.0)
Europe	9.5 (8.0-14.0)	13.0 (7.0-18.0)
Asia	11.0 (9.0-16.0)	13.0 (10.0-16.0)

Spicer et al. ASCO 2021 Abstract 8503

Courtesy of Anne S Tsao, MD, MBA

Local-regional NSCLC: PACIFIC 5-year update shows continued PFS & OS benefit

- Unresectable Stage III NSCLC without progression after definitive platinum-based cCRT* (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumor tissue for PD-L1 testing†

Patients enrolled irrespective of PD-L1 status

N = 713 randomized

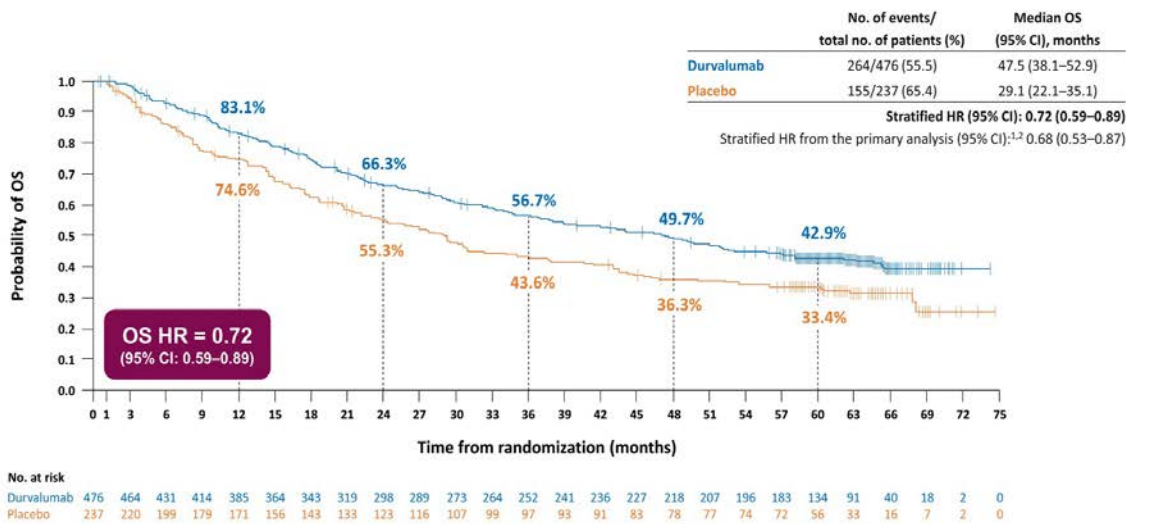
1–42 days post-cCRT

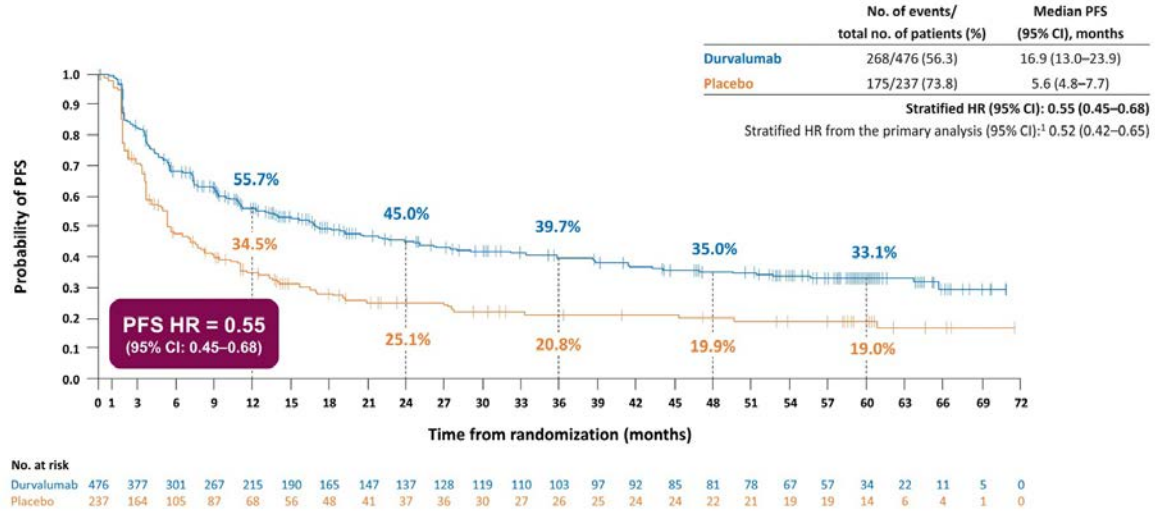
R

2:1 randomization, stratified by age, sex, and smoking history

Durvalumab
10 mg/kg q2w for up to 12 months
N = 476

Placebo
q2w for up to 12 months
N = 237



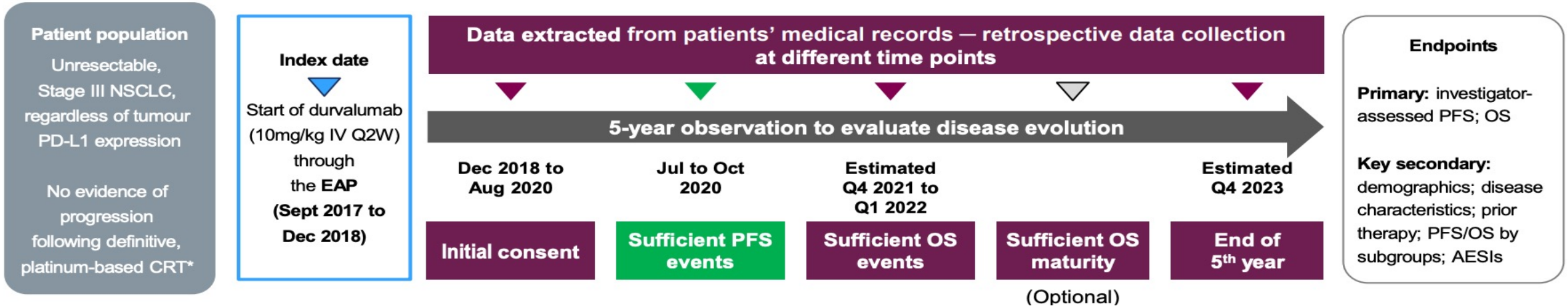


Spigel et al. ASCO 2021 Abstract 8511

Courtesy of Anne S Tsao, MD, MBA

PACIFIC-R (NCT 03798535):

An international, observational study



- **1,399 patients** included in the **full analysis set (FAS)** from **290 active sites** in **11 participating countries**
  - France (n=342), Spain (244)†, Australia (165), Netherlands (155), Belgium (118), Italy (116), Israel (92), Germany (62), UK (54), Norway (36), and Switzerland (15)

Median time to initiate durvalumab = **56 days**
Median durvalumab infusions = **22**
Median durvalumab duration = **335 days**
20.1% > 12 months
4.4% > 14 months

PACIFIC-R* **Median PFS 21.7 months** vs PACIFIC 16.9 months

16.7% treatment discontinuation due to AE
9.5% Pneumonitis permanent discontinuation
5.2% pneumonitis temporary discontinuation
=> 71.3% required corticosteroids

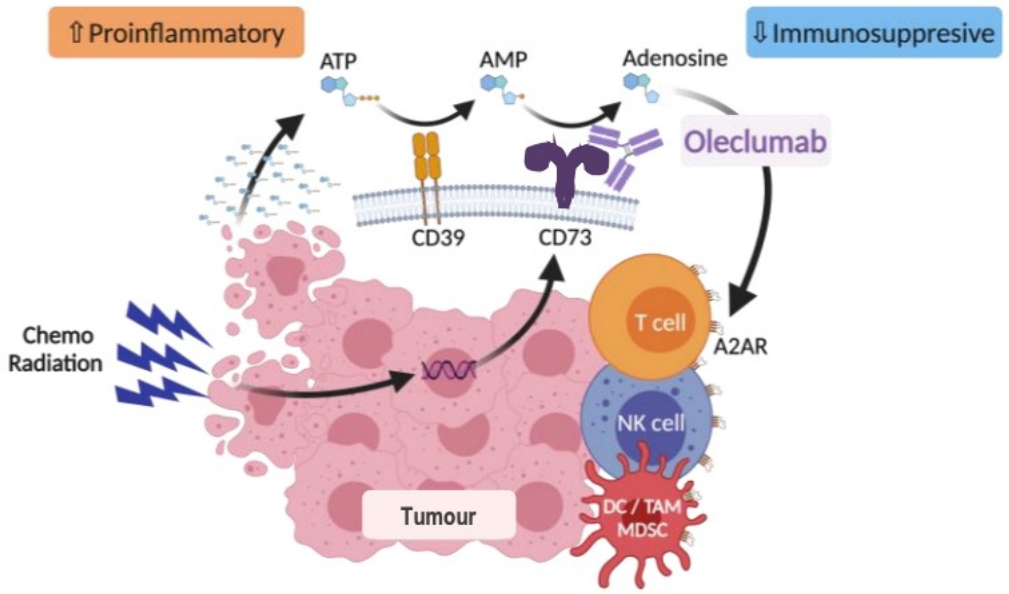
*PACIFIC-R had challenges in data collection: Germany/UK did not collect deaths on 50, RECIST not consistently used, assessments for progression not consistently collected – pandemic led to less visits for assessment.

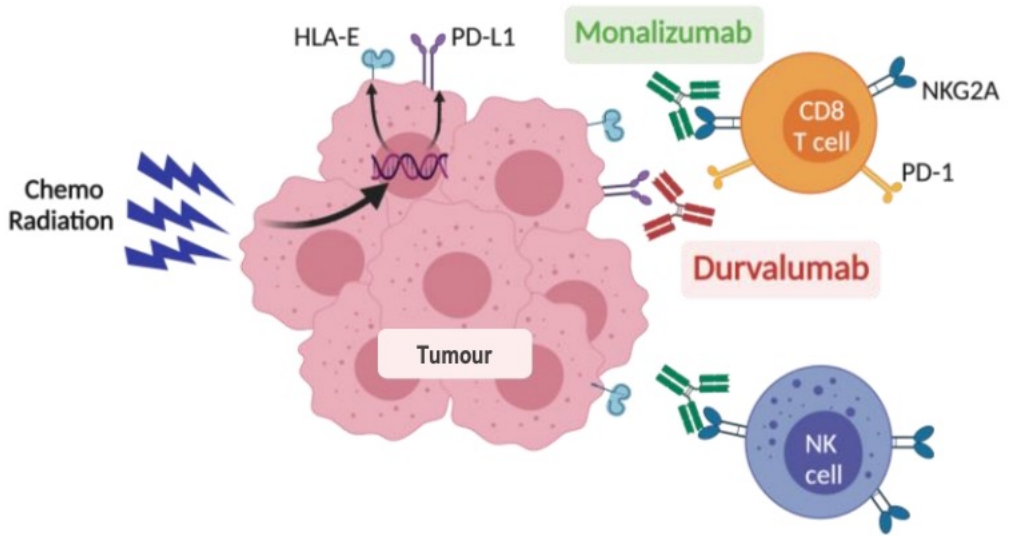
Girard et al. ESMO 2021 Abstract 1171MO

Courtesy of Anne S Tsao, MD, MBA

COAST (Combination Platform Study in Unresectable Stage III NSCLC; NCT03822351)

Phase 2 study of durvalumab alone or combined with the anti-CD73 mAb oleclumab or anti-NKG2A mAb monalizumab as consolidation therapy





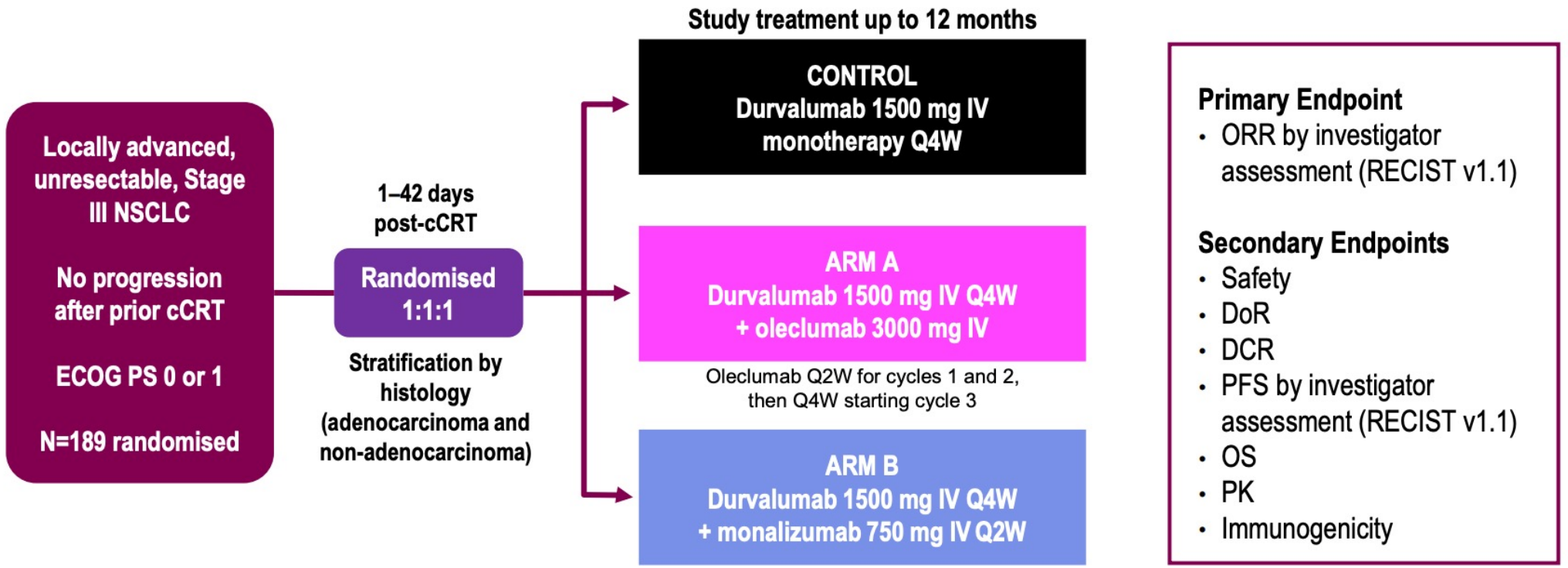
Oleclumab, anti-CD73,
Reduces extracellular adenosine production
Promotes antitumour immunity

Monalizumab blocks NKG2A to reduce inhibition of NK and CD8+ T cells.

Martinez-Marti et al. ESMO 2021 Abstract LBA42

Courtesy of Anne S Tsao, MD, MBA

COAST: Phase 2



A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumour activities in an early phase setting

Between Jan 2019 and Jul 2020, 189 patients were randomised of whom 186 received D (n=66), D+O (n=59) or D+M (n=61)

Martinez-Marti et al. ESMO 2021 Abstract LBA42

Courtesy of Anne S Tsao, MD, MBA

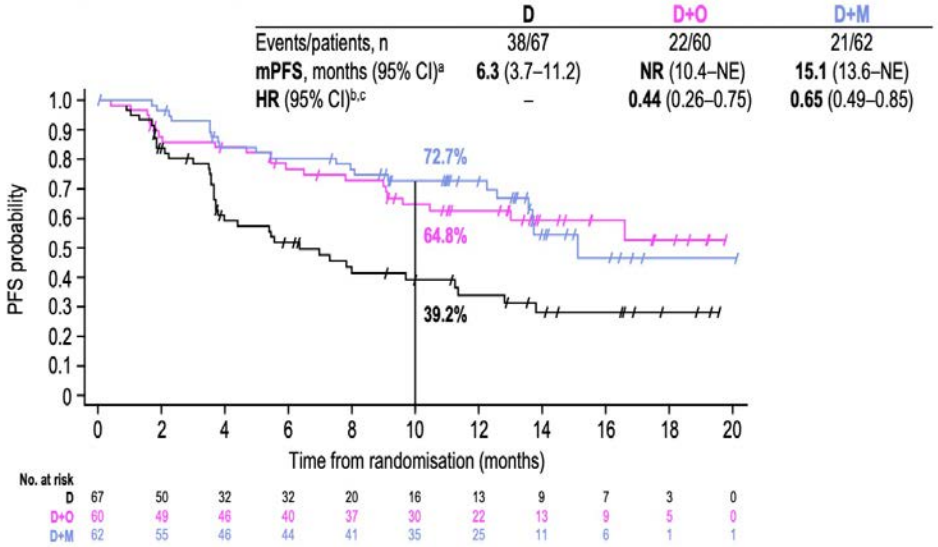
COAST Results favor D+O and D+M for PFS with no significant increase in toxicity

Antitumor activity	D (n=67)	D+O (n=60)	D+M (n=62)
Confirmed ORR	17.9	30	35.5
DCR 16 weeks	58.2	81.7	77.4
Median DoR (months)	NR	12.9	NR
mPFS	6.3	NR	15.1
HR	-	0.44	0.65

Incidence, n (%)	D (N=66)	D+O (N=59)	D+M (N=61)
Any TEAEs	65 (98.5)	57 (96.6)	61 (100)
Grade ≥3 TEAEs	26 (39.4)	24 (40.7)	17 (27.9)
Study drug-related AEs	49 (74.2)	46 (78.0)	50 (82.0)
Study drug-related SAEs	6 (9.1)	7 (11.9)	5 (8.2)
AEs leading to discontinuation	11 (16.7)	9 (15.3)	9 (14.8)
Deaths[a,b]	7 (10.6)	4 (6.8)	3 (4.9)

[a]All reported deaths within 90 days post-last dose, regardless of relationship to study drug
[b]In total, 4 deaths were related to study drug, 2 (pneumonitis and radiation pneumonitis) in the D arm, 1 (pneumonitis) in the D+O arm, and 1 (myocardial infarction) in the D+M arm

PFS by investigator assessment
(interim analysis; ITT population)



Martinez-Marti et al. ESMO 2021 Abstract LBA42

Courtesy of Anne S Tsao, MD, MBA

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma

Agenda

Module 2: NSCLC — Metastatic Disease

- Follow-up of older first- and second-line trials: PD-1, tumor mutational burden (TMB)
- Cemiplimab
- POSEIDON: Chemotherapy/durvalumab/tremelimumab
- Correlation of immune adverse events and antitumor effect
- Datopotamab deruxtecan (Dato-DXd)
- Plinabulin
- Tiragolumab

First-Line Treatment of Metastatic NSCLC

- Optimal PD-1 assay, choice of agent, TMB
- Long-term survival/cure
- Benefit of immunotherapy: Adenocarcinoma versus squamous
- Monotherapy versus chemotherapy/immunotherapy
- Options for PD-1-negative disease
- Ipilimumab/nivolumab; durvalumab/tremelimumab
- Correlation of immune adverse events with efficacy
- Second-line treatment: Docetaxel with or without ramucirumab; Dato-DXd

• EMPOWER-Lung 1 Study Design (NCT03088540)

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

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

R 1:1

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

PD → Optional continuation of cemiplimab + 4 cycles of chemotherapy

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

PD → Optional crossover to cemiplimab monotherapy

Follow-up

N=710

Five interim analyses were prespecified per protocol

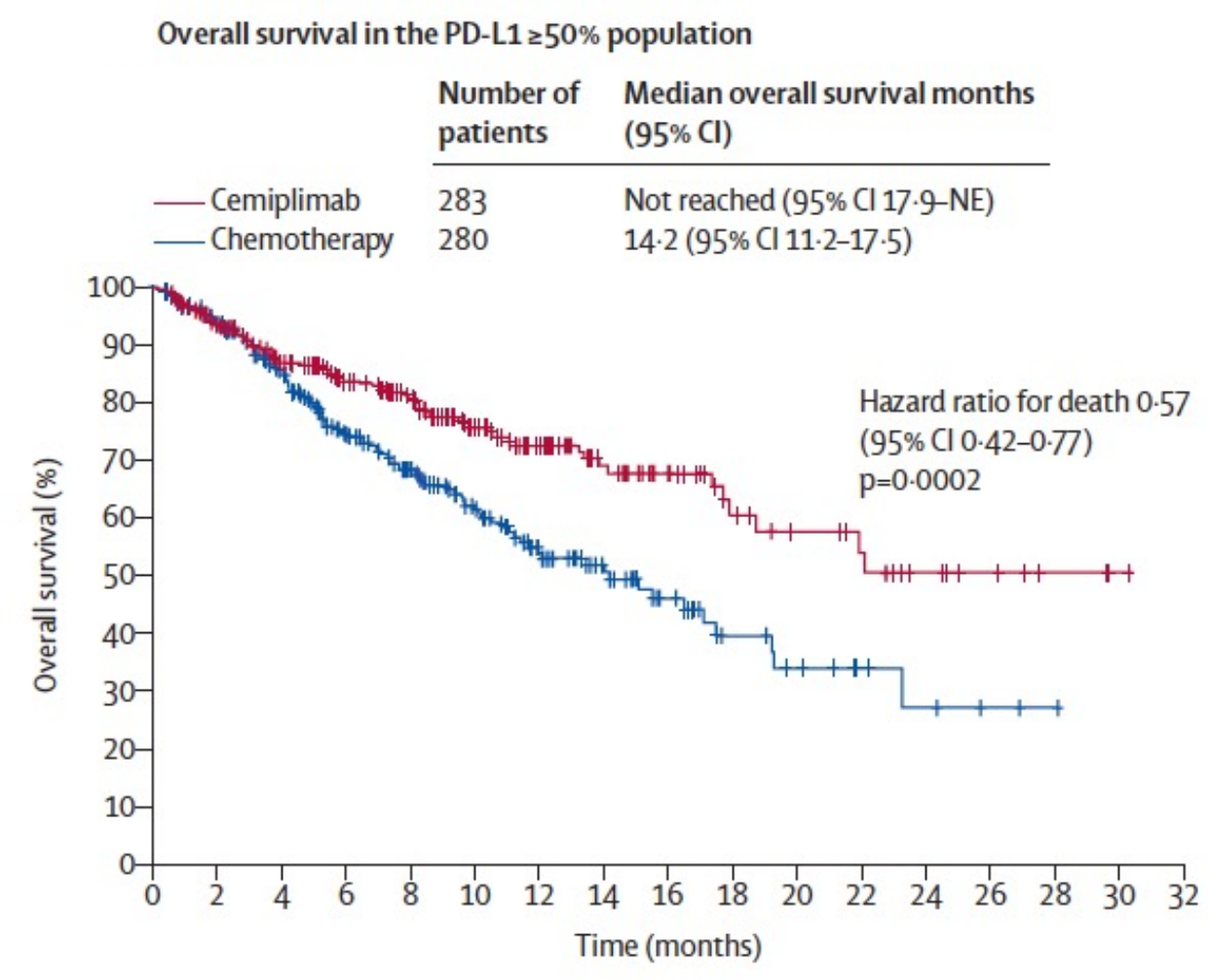
Second interim analysis (1 March 2020) presented here

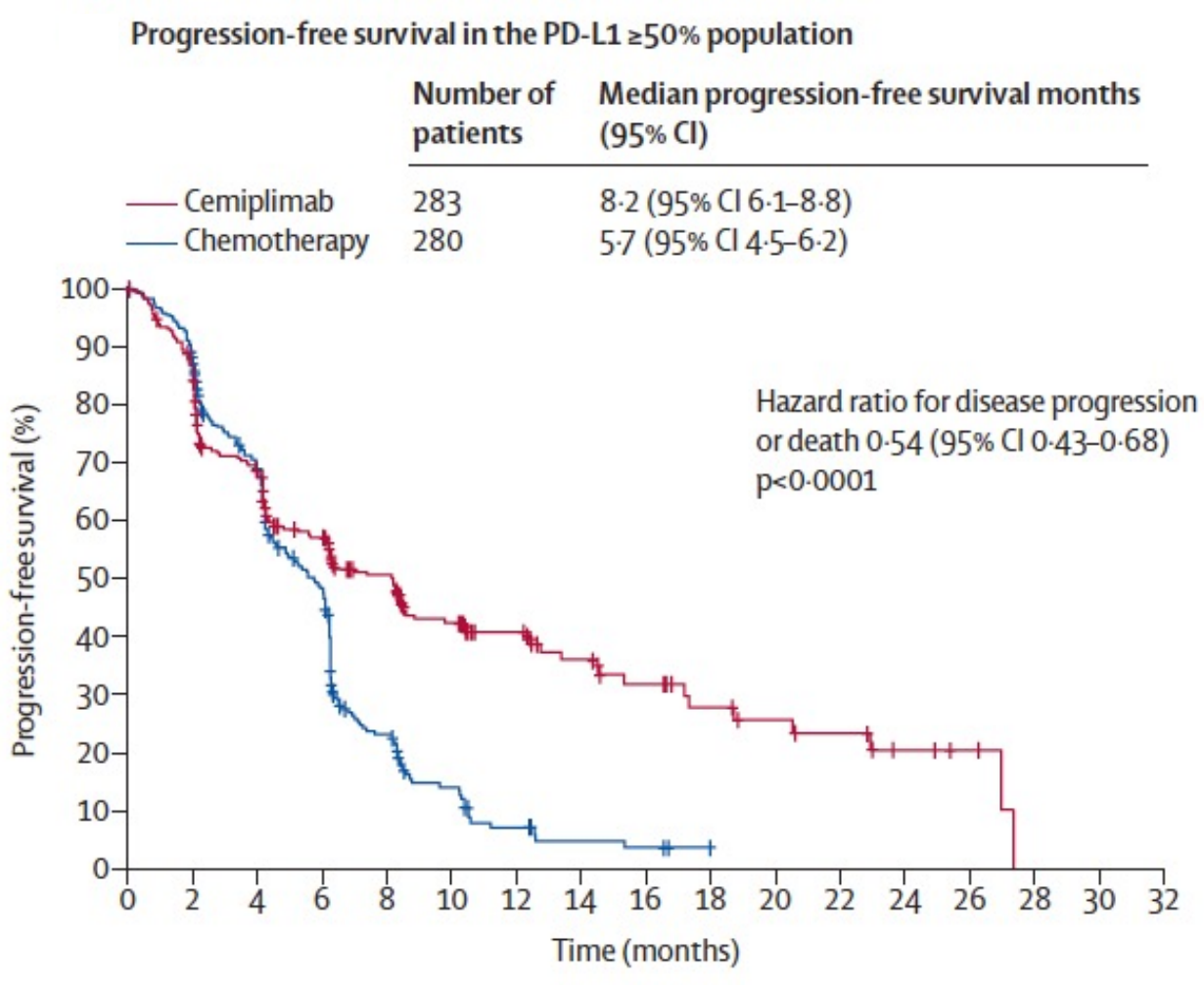
Endpoints:
- Primary: OS and PFS
- Secondary: ORR (key), DOR, HRQoL and safety

•ALK, anaplastic lymphoma kinase; chemo, chemotherapy; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HIV, human immunodeficiency virus; HRQoL, health-related quality of life; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; R, randomised; ROS1, c-ros oncogene 1; ROW, rest of the world.

Courtesy of Corey J Langer, MD

EMPOWER-Lung 1: Survival





Sezer A et al. *Lancet* 2021;397:592-604.

VIRTUAL 2020 ESMO congress

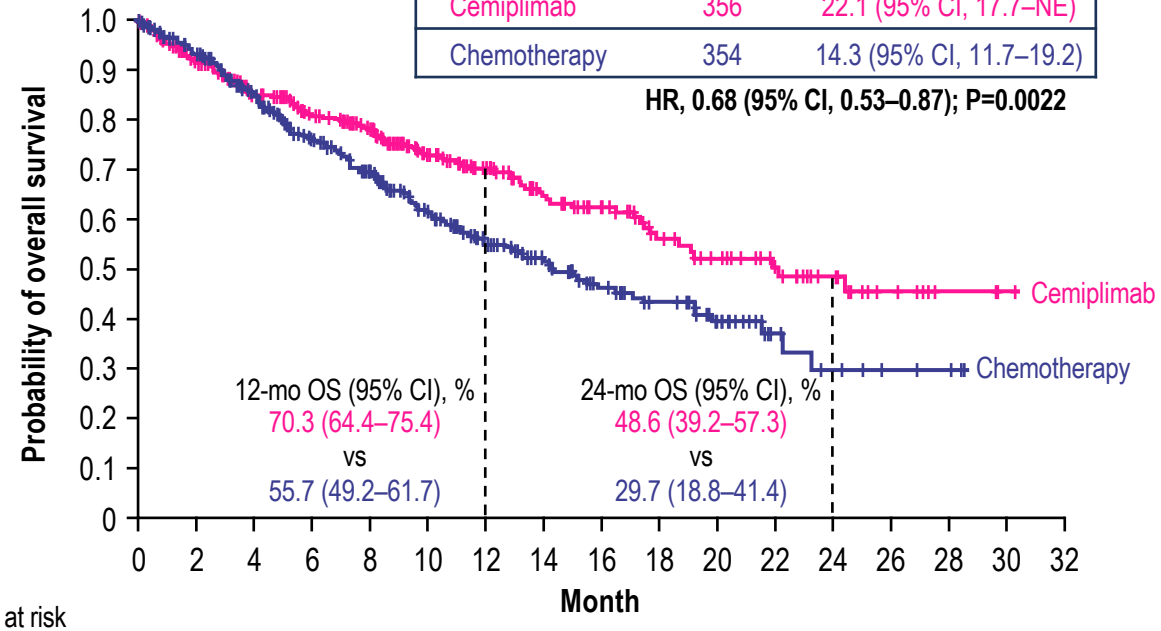
EMPOWER

• Overall Survival

ITT

	No. of Patients	Median OS (95% CI) *mo*
Cemiplimab	356	22.1 (95% CI, 17.7–NE)
Chemotherapy	354	14.3 (95% CI, 11.7–19.2)

HR, 0.68 (95% CI, 0.53–0.87); P=0.0022



No. at risk

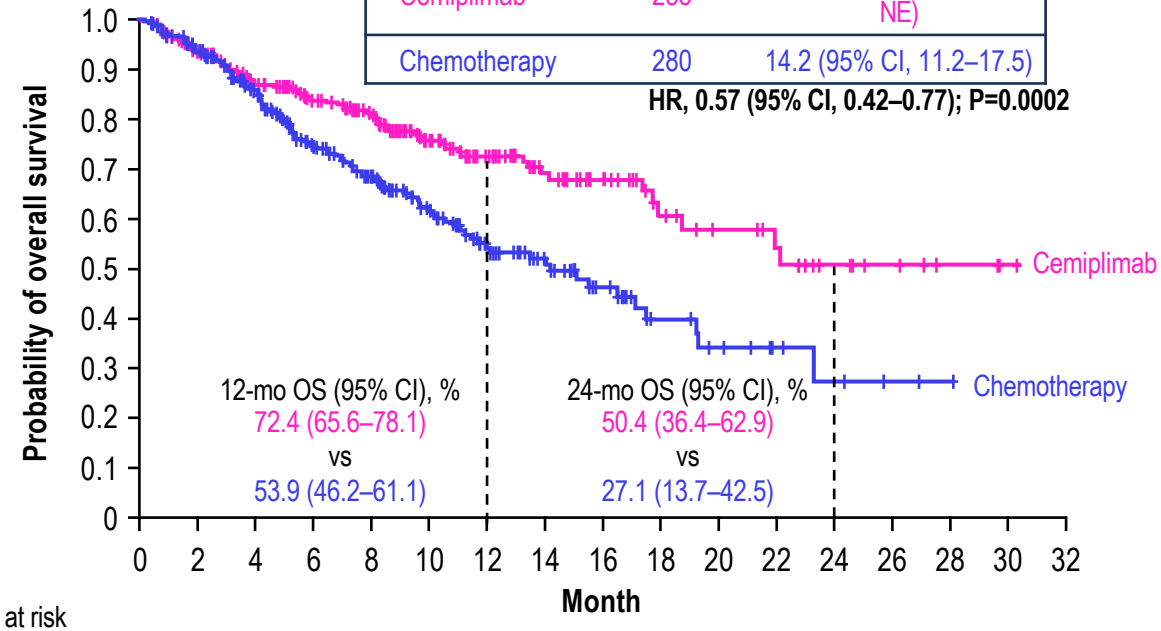
Cemiplimab	356	304	254	223	198	147	120	87	71	48	37	27	18	8	3	1	0
Chemotherapy	354	303	254	205	172	126	93	73	52	41	27	12	7	4	3	0	0

Median duration of follow-up:
Cemiplimab → 13.1 months (range: 0.1–31.9)
Chemotherapy → 13.1 months (range: 0.2–32.4)

PD-L1 ≥50% ITT

	No. of Patients	Median OS (95% CI) *mo*
Cemiplimab	283	Not reached (95% CI, 17.9–NE)
Chemotherapy	280	14.2 (95% CI, 11.2–17.5)

HR, 0.57 (95% CI, 0.42–0.77); P=0.0002



No. at risk

Cemiplimab	283	244	203	177	154	108	83	55	42	24	18	15	10	6	3	1	0
Chemotherapy	280	239	198	153	125	87	57	41	25	15	11	6	4	2	1	0	0

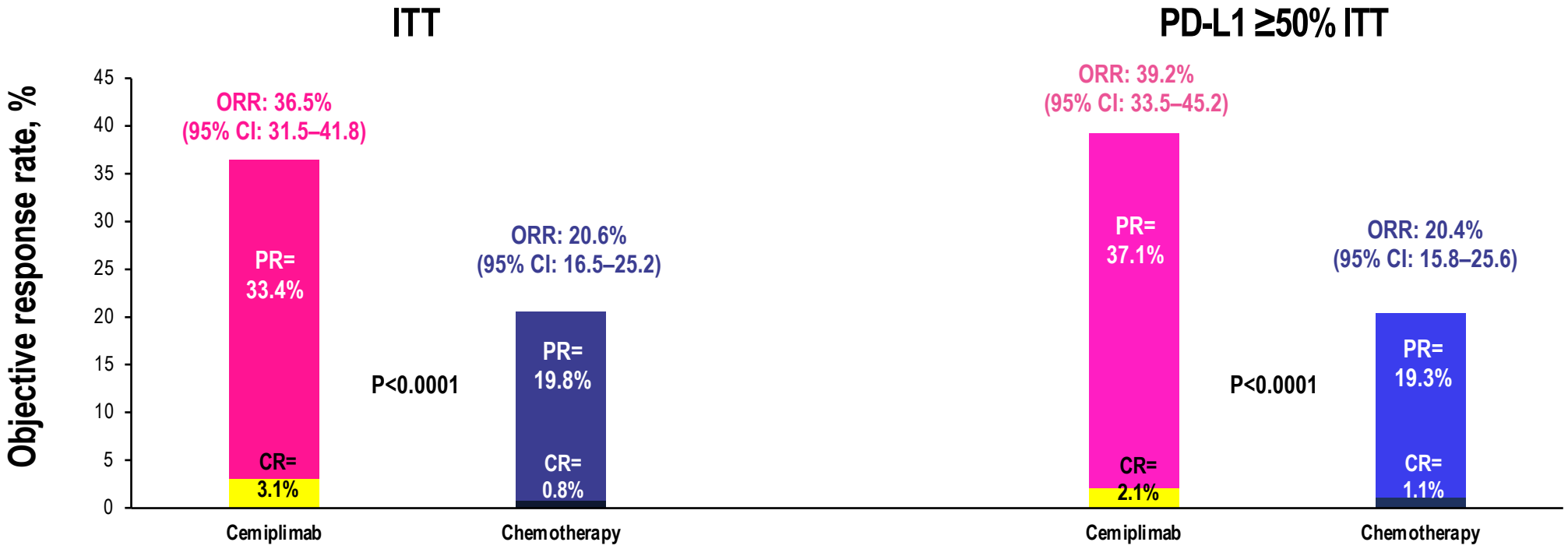
Median duration of follow-up:
Cemiplimab → 10.8 months (range: 0.1–31.9)
Chemotherapy → 10.2 months (range: 0.2–29.5)

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

•CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, month; NE, not evaluable; OS, overall survival;
•PD-L1, programmed cell death-ligand 1.

Courtesy of Corey J Langer, MD

• Tumour Response and DOR



	Cemiplimab	Chemotherapy	Cemiplimab	Chemotherapy
n (%), unless stated	ITT (n=356)	ITT (n=354)	PD-L1 ≥50% ITT (n=283)	PD-L1 ≥50% ITT (n=280)
Median DOR, months (95% CI)	21.0 (14.9–NE)	6.0 (4.3–6.4)	16.7 (12.5–22.8)	6.0 (4.3–6.5)
Median observed time to response, months (range)	2.1 (1.4–10.4)	2.1 (1.4–6.7)	2.1 (1.4–10.4)	2.1 (1.4–6.3)

•CI, confidence interval; CR, complete response; DOR, duration of response; ITT, intention-to-treat; NE, not evaluable; ORR, objective response rate; PD-L1, programmed cell death-ligand 1; PR, partial response.

Courtesy of Corey J Langer, MD

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

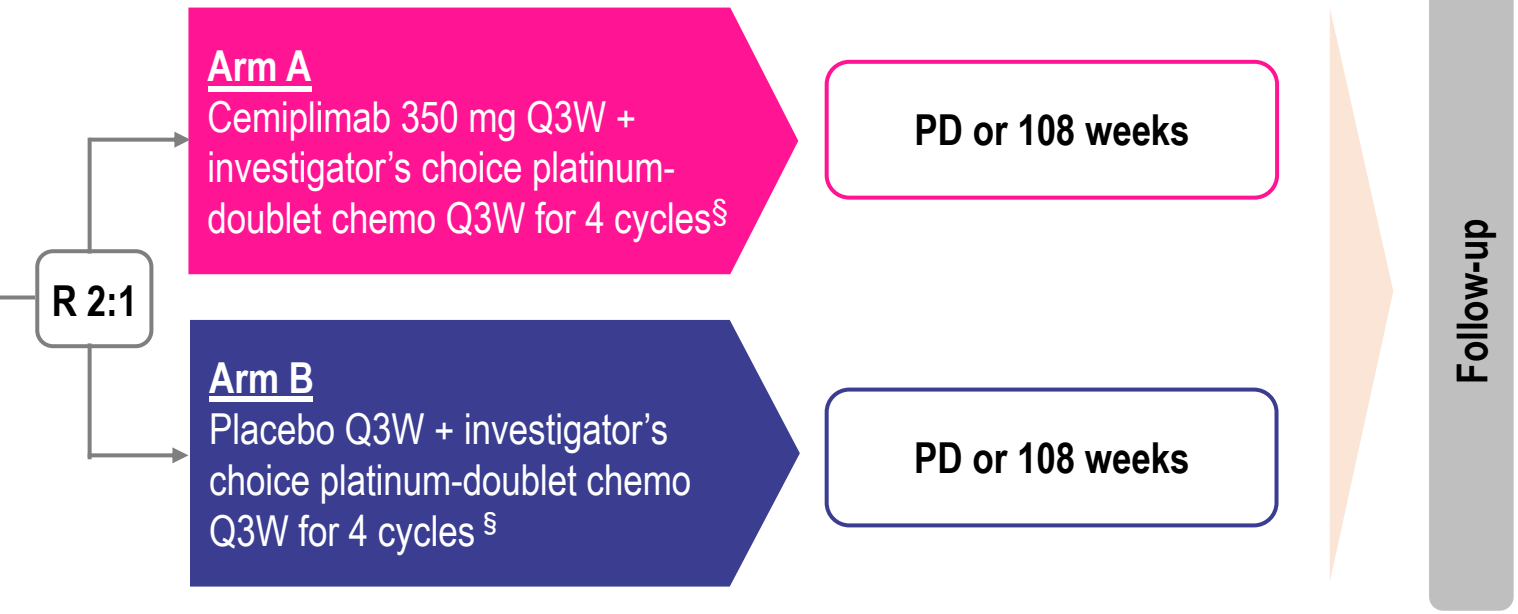
EMPOWER-Lung 3 (Part 2) Study Design (NCT03409614)

Background: Cemiplimab (a high-affinity, fully human anti–PD-1) is approved as first-line monotherapy for advanced NSCLC with PD-L1 ≥50% (EMPOWER-Lung 1 Study[1])

Key eligibility criteria
- Treatment-naive advanced NSCLC (non-squamous and squamous histology; Stage IIIb/c†, IV)
- Any PD-L1 expression
- No *EGFR*, *ALK*, or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases‡

Stratification factors
- PD-L1 expression: <1% vs 1–49% vs ≥50%
- Histology: non-squamous vs squamous

Endpoints
- Primary: OS
- Key secondary: PFS and ORR
- Additional secondary: DOR, BOR, safety, and PRO



N=466

Two interim analyses were prespecified per protocol
Second interim analysis (14 June 2021) presented here

†Patient not a candidate for definitive chemoradiation. ‡Patient must have neurologically returned to baseline (except for residual signs or symptoms related to the CNS treatment). §For patients with non-squamous NSCLC, pemetrexed is mandatory as maintenance therapy for those patients initially assigned to receive a pemetrexed-containing regimen. *ALK*, anaplastic lymphoma kinase gene; BOR, best overall response; chemo, chemotherapy; CNS, central nervous system; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor gene; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PRO, patient-reported outcomes; Q3W, every 3 weeks; R, randomised; *ROS1*, c-ros oncogene 1.

1. Sezer A et al. *Lancet* 2021;397:592–604.

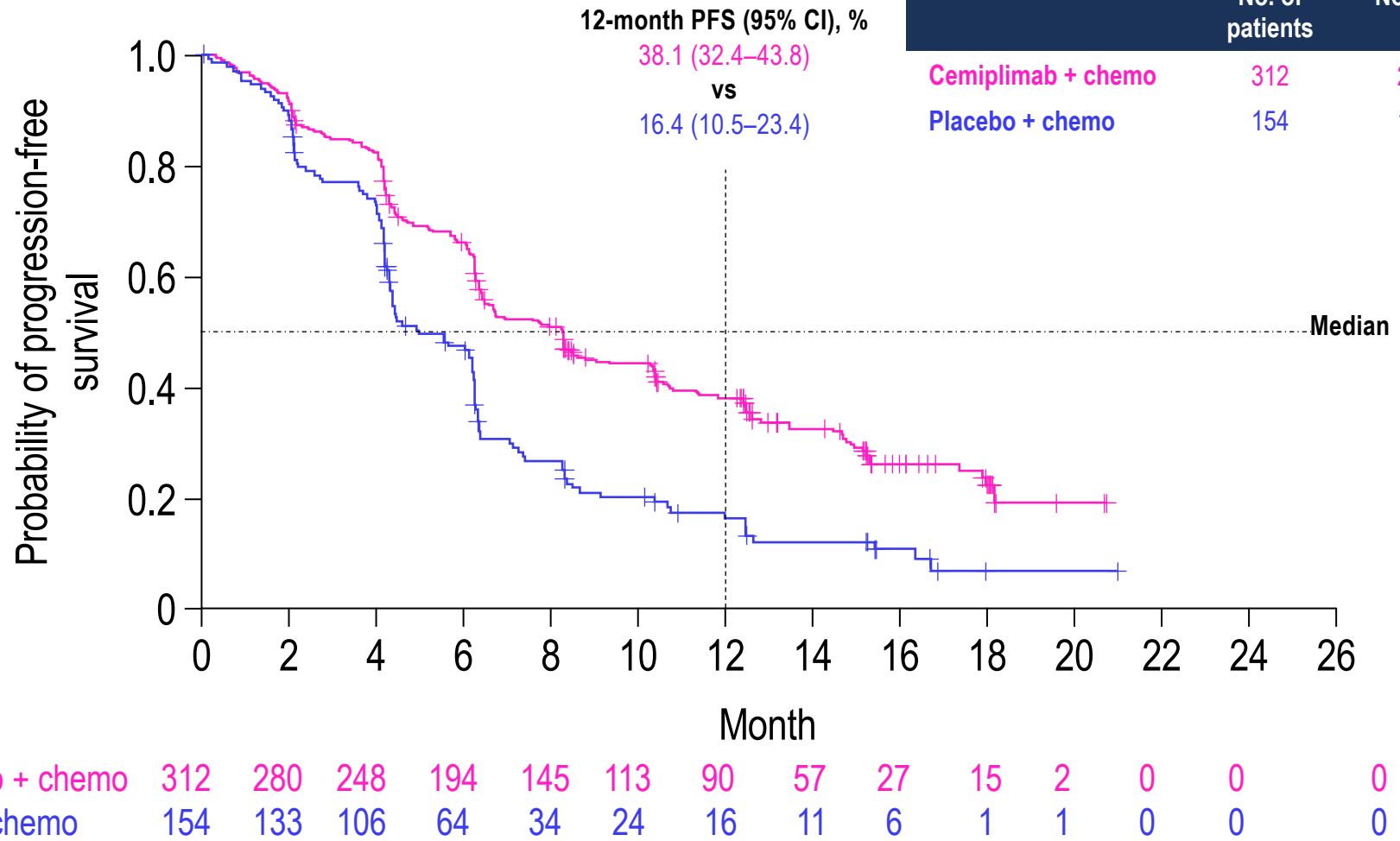
Courtesy of Corey J Langer, MD

Progression-Free Survival

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

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

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



No. at risk:

Cemiplimab + chemo	312	280	248	194	145	113	90	57	27	15	2	0	0	0
Placebo + chemo	154	133	106	64	34	24	16	11	6	1	1	0	0	0

Data cut-off date: 14 June 2021

2021 ESMO congress

Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

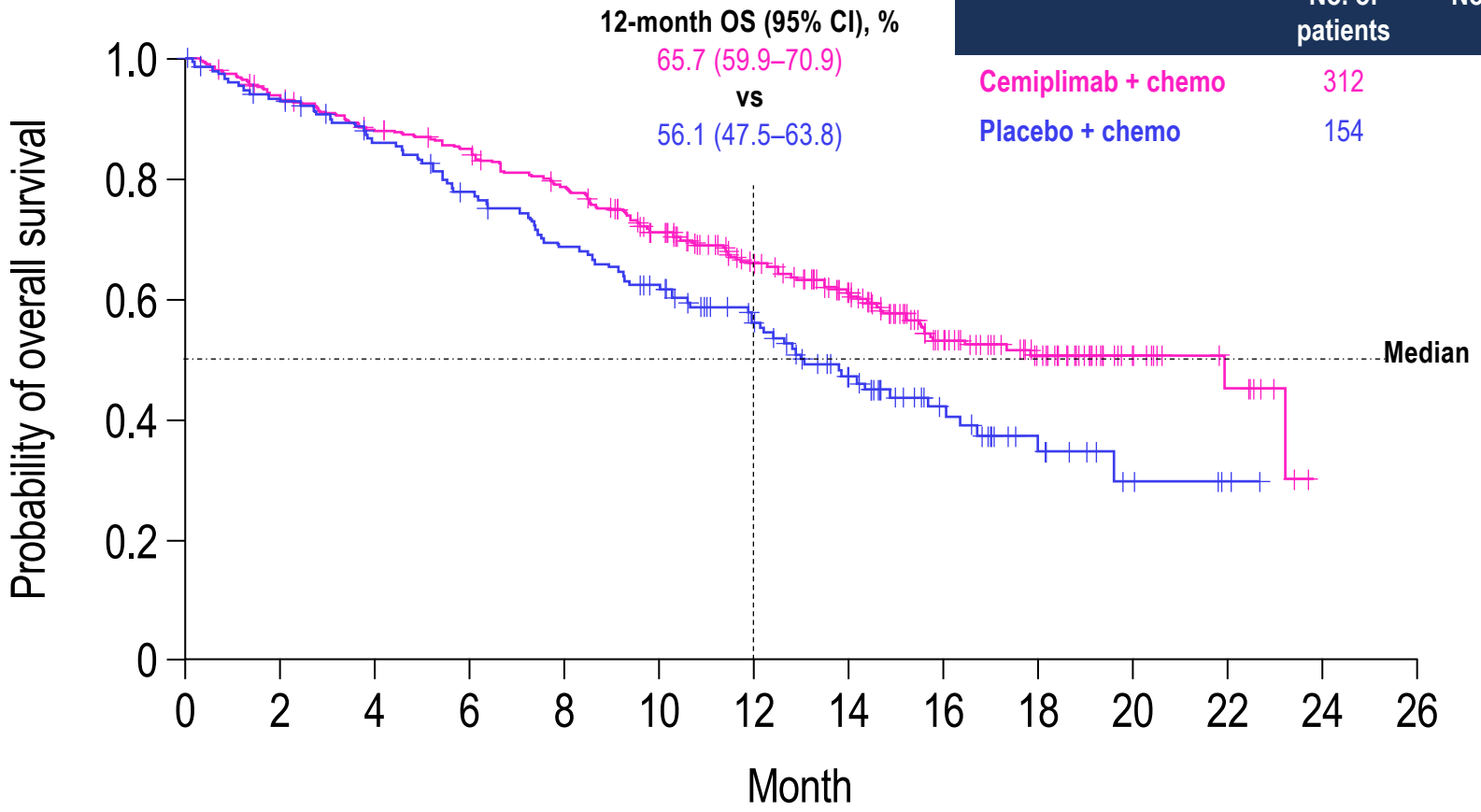
Courtesy of Corey J Langer, MD

Overall Survival

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

	No. of patients	No. of events, n (%)	OS, median (95% CI), months
Cemiplimab + chemo	312	132 (42.3)	21.9 (15.5–NE)
Placebo + chemo	154	82 (53.2)	13.0 (11.9–16.1)

HR (95% CI) = 0.71 (0.53–0.93); *P*=0.014



No. at risk:

Cemiplimab + chemo	312	289	269	256	233	199	162	131	86	52	18	8	0	0
Placebo + chemo	154	141	126	112	98	85	65	46	26	14	5	2	0	0

Data cut-off date: 14 June 2021

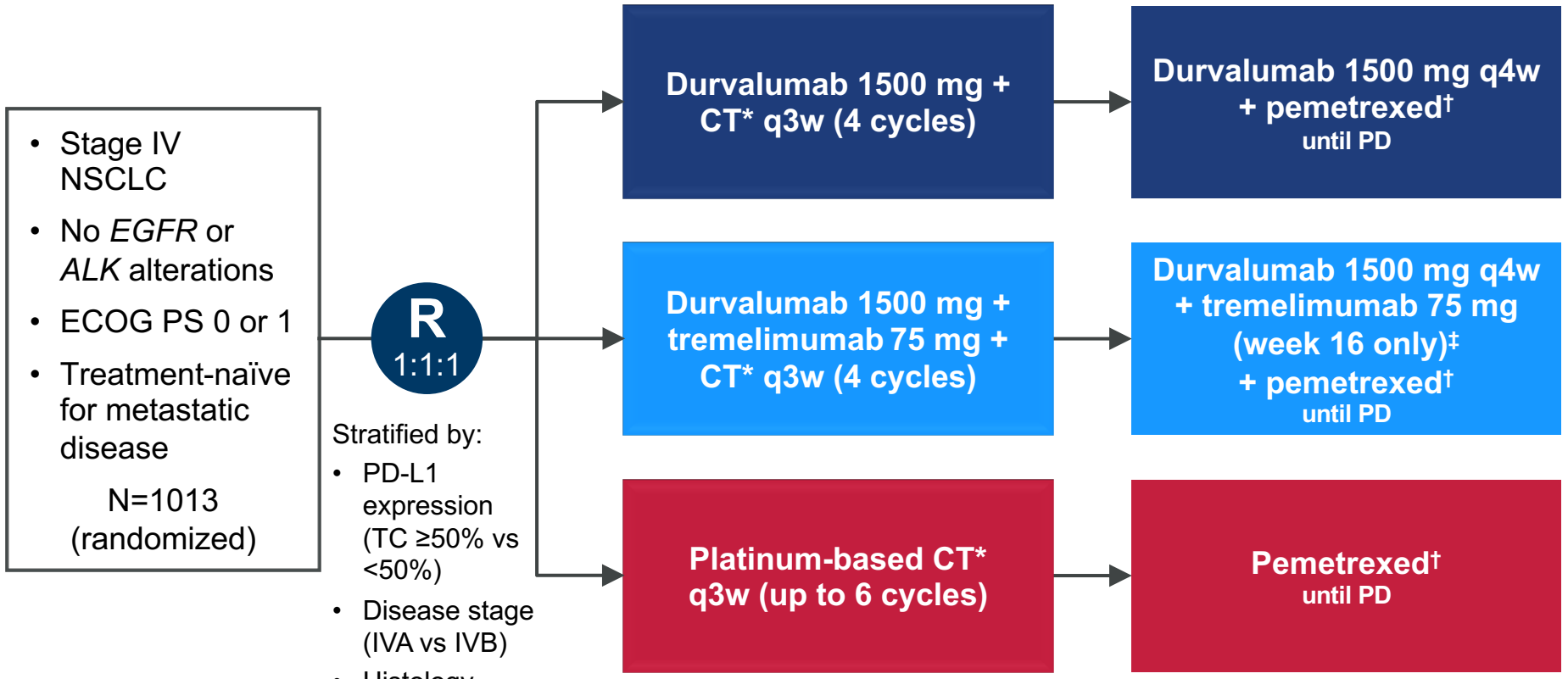
2021 ESMO congress

Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; OS, overall survival.

Courtesy of Corey J Langer, MD

POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study



Primary endpoints
- PFS by BICR (D+CT vs CT)
- OS (D+CT vs CT)

Key secondary endpoints
- PFS by BICR (D+T+CT vs CT)
- OS (D+T+CT vs CT)
- OS in patients with bTMB ≥20 mut/Mb (D+T+CT vs CT)

Additional secondary endpoints
- ORR, DoR, and BOR by BICR
- PFS at 12 months
- HRQoL
- Safety and tolerability

*CT options: gemcitabine + carboplatin/cisplatin (squamous), pemetrexed + carboplatin/cisplatin (non-squamous), or nab-paclitaxel + carboplatin (either histology); †Patients with non-squamous histology who initially received pemetrexed during first-line treatment only (if eligible); ‡Patients received an additional dose of tremelimumab post CT (5th dose)

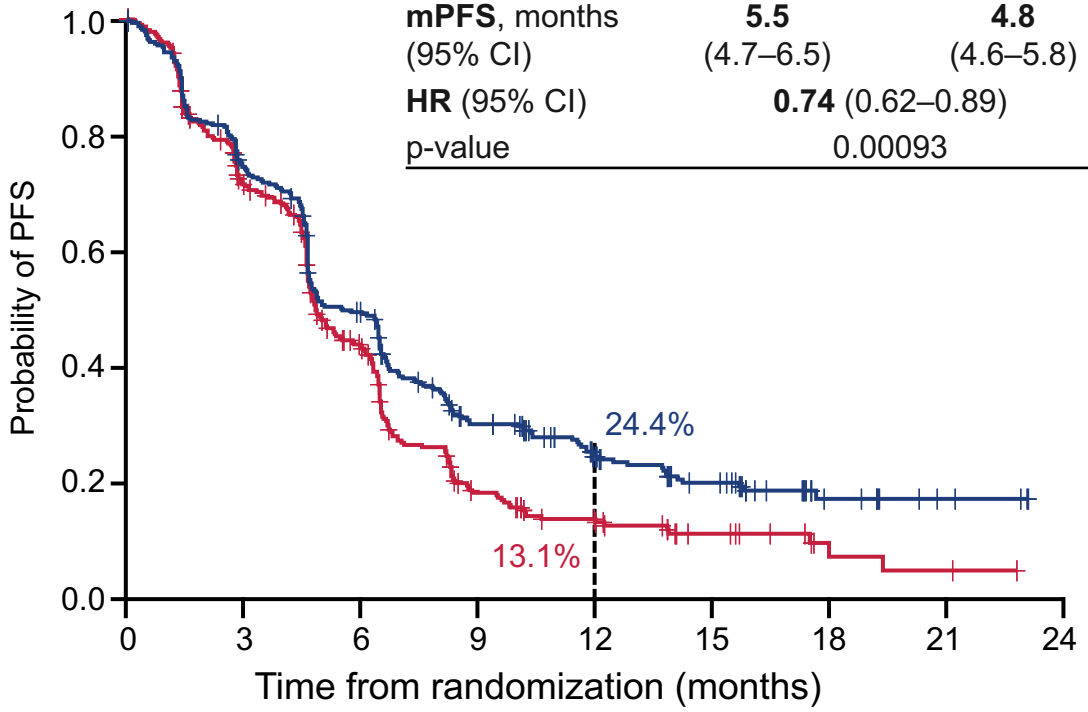
Courtesy of Corey J Langer, MD

BICR, blinded independent central review; BOR, best objective response; bTMB, blood tumor mutational burden; D, durvalumab; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; Mb, megabase; mut, mutations; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; T, tremelimumab; TC, tumor cell

Durvalumab + CT vs CT: PFS and OS

PFS

	D+CT	CT
Events, n/N (%)	253/338 (74.9)	258/337 (76.6)
mPFS, months (95% CI)	**5.5** (4.7–6.5)	**4.8** (4.6–5.8)
HR (95% CI)	**0.74** (0.62–0.89)	
p-value	0.00093	



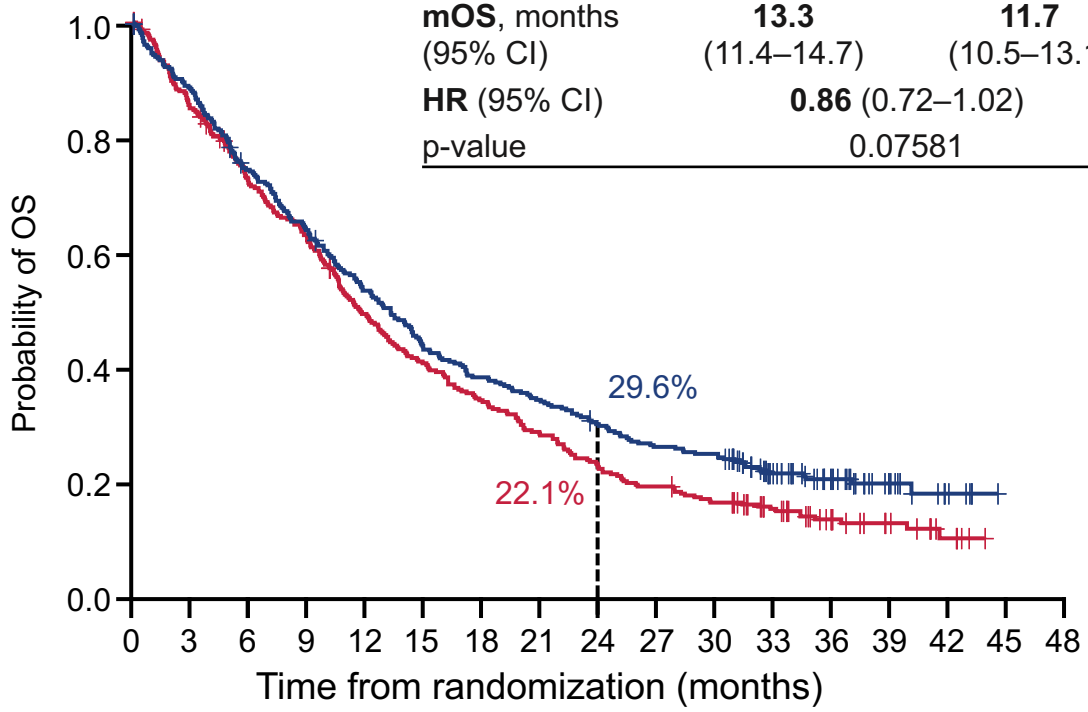
No. at risk

D+CT	338	246	158	88	53	35	11	4	0
CT	337	219	121	43	23	12	3	2	0

- Median follow-up in censored patients at DCO: 10.3 months (range 0–23.1)

OS

	D+CT	CT
Events, n/N (%)	264/338 (78.1)	285/337 (84.6)
mOS, months (95% CI)	**13.3** (11.4–14.7)	**11.7** (10.5–13.1)
HR (95% CI)	**0.86** (0.72–1.02)	
p-value	0.07581	



No. at risk

D+CT	338	296	247	212	176	142	126	112	97	85	81	51	33	15	5	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

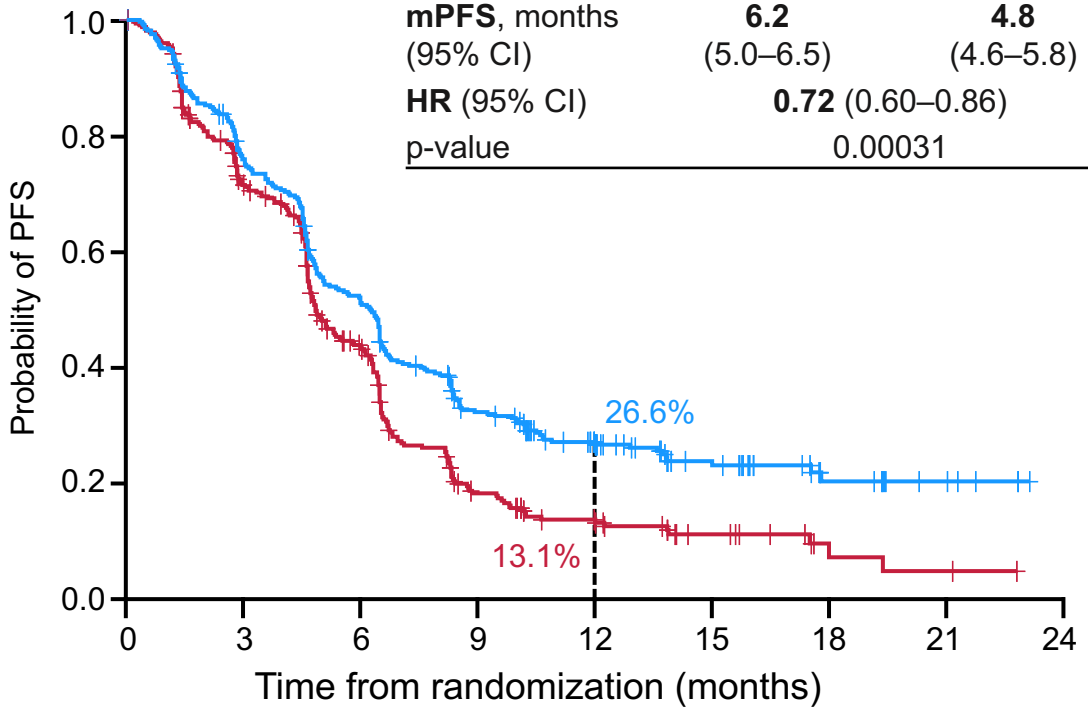
Courtesy of Corey J Langer, MD

DCO PFS FA: Jul 24, 2019; DCO OS FA: Mar 12, 2021
DCO, data cut-off; FA, final analysis; mOS, median OS; mPFS, median PFS

Durvalumab + Tremelimumab + CT vs CT: PFS and OS

PFS

	D+T+CT	CT
Events, n/N (%)	238/338 (70.4)	258/337 (76.6)
mPFS, months (95% CI)	**6.2** (5.0–6.5)	**4.8** (4.6–5.8)
HR (95% CI)	**0.72** (0.60–0.86)	
p-value	0.00031	

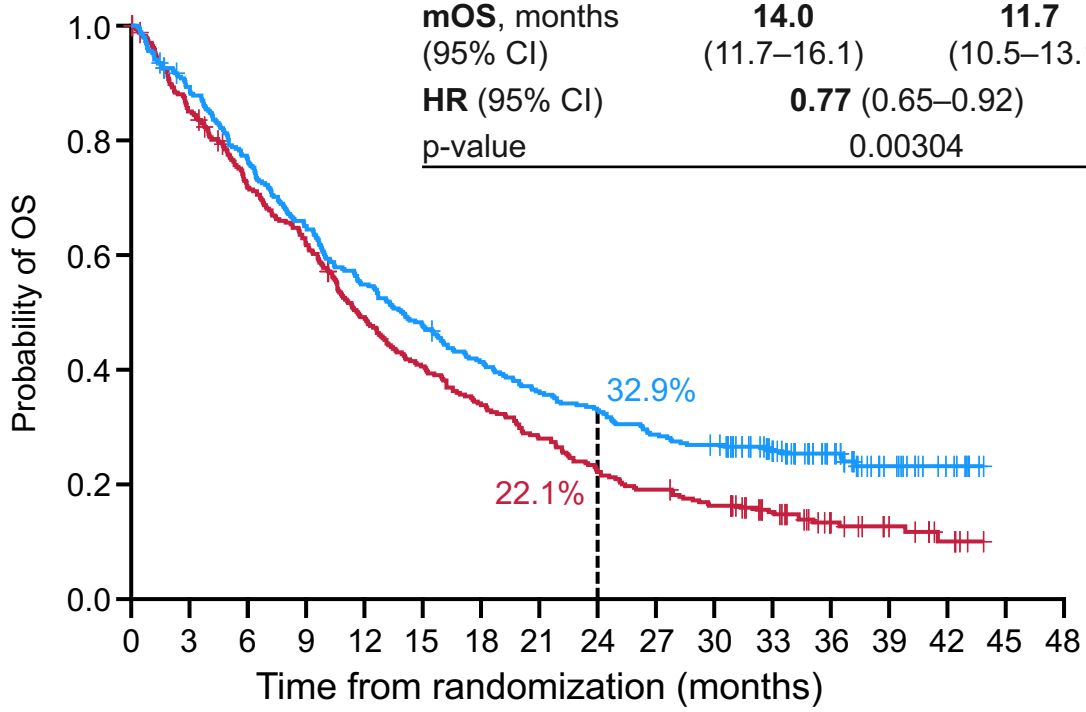


No. at risk									
D+T+CT	338	243	161	94	56	32	13	5	0
CT	337	219	121	43	23	12	3	2	0

- Median follow-up in censored patients at DCO: 10.3 months (range 0–23.1)

OS

	D+T+CT	CT
Events, n/N (%)	251/338 (74.3)	285/337 (84.6)
mOS, months (95% CI)	**14.0** (11.7–16.1)	**11.7** (10.5–13.1)
HR (95% CI)	**0.77** (0.65–0.92)	
p-value	0.00304	



No. at risk																	
D+T+CT	338	298	256	217	183	159	137	120	109	95	88	64	41	20	9	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

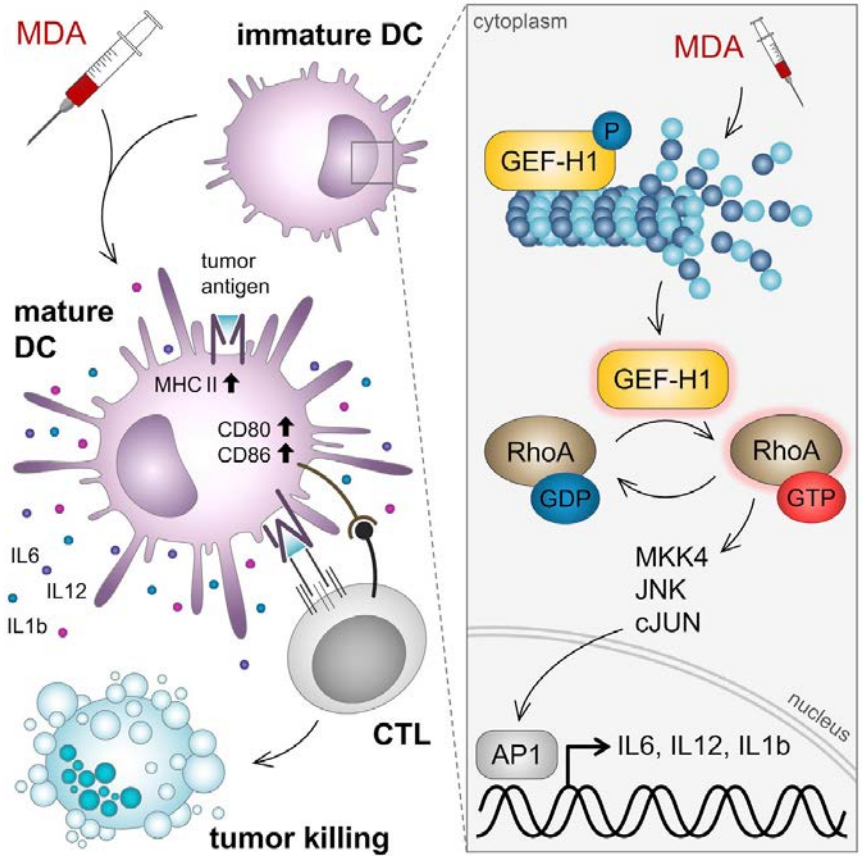
- Median follow-up in censored patients at DCO: 34.9 months (range 0–44.5)

Courtesy of Corey J Langer, MD

DCO PFS FA: Jul 24, 2019; DCO OS FA: Mar 12, 2021

Plinabulin: microtubule-targeted agent with distinct MoA

- Direct effect on tumour cells: prevents β-tubulin polymerisation into microtubules
- Vascular disrupting agent: endothelial cells disruption
- Immune functions:
  - Microtubule destabilization in dendritic cells drives DC maturation through the release of GEF-H1 from microtubules
  - Enhances cross-presentation of tumour antigens to CD8 T cells
  - Could promote TAM anti-tumour effector functions



Singh, Blood 2011; Kashyap, Cell Rep 2019; Natoli, Front Oncol 2021

Courtesy of Corey J Langer, MD

DUBLIN-3 Phase 3 Trial

DUBLIN - 3

- Non-squamous or squamous NSCLC
- Stage IIIb/IV
- ECOG performance status ≤ 2
- Progression during or after treatment with one or two treatment regimen containing platinum
- Must have at least one measurable lung lesion
- Prior checkpoint inhibitor therapy allowed
- Written consent

Brain mets allowed?

Randomized 1:1
21-day cycle
(n=599)

Stratification factors?

Only 22% of patients were previously exposed to CPI

Docetaxel + Plinabulin (N=278)

All Cycles:

Day 1:Docetaxel 75 mg/m2 + Plinabulin 30mg/m2
Day 8: Plinabulin 30mg/m2

PD

Docetaxel + Placebo (N=281)

All Cycles:

Day1: Docetaxel 75 mg/m2 + Placebo
Day 8:Placebo

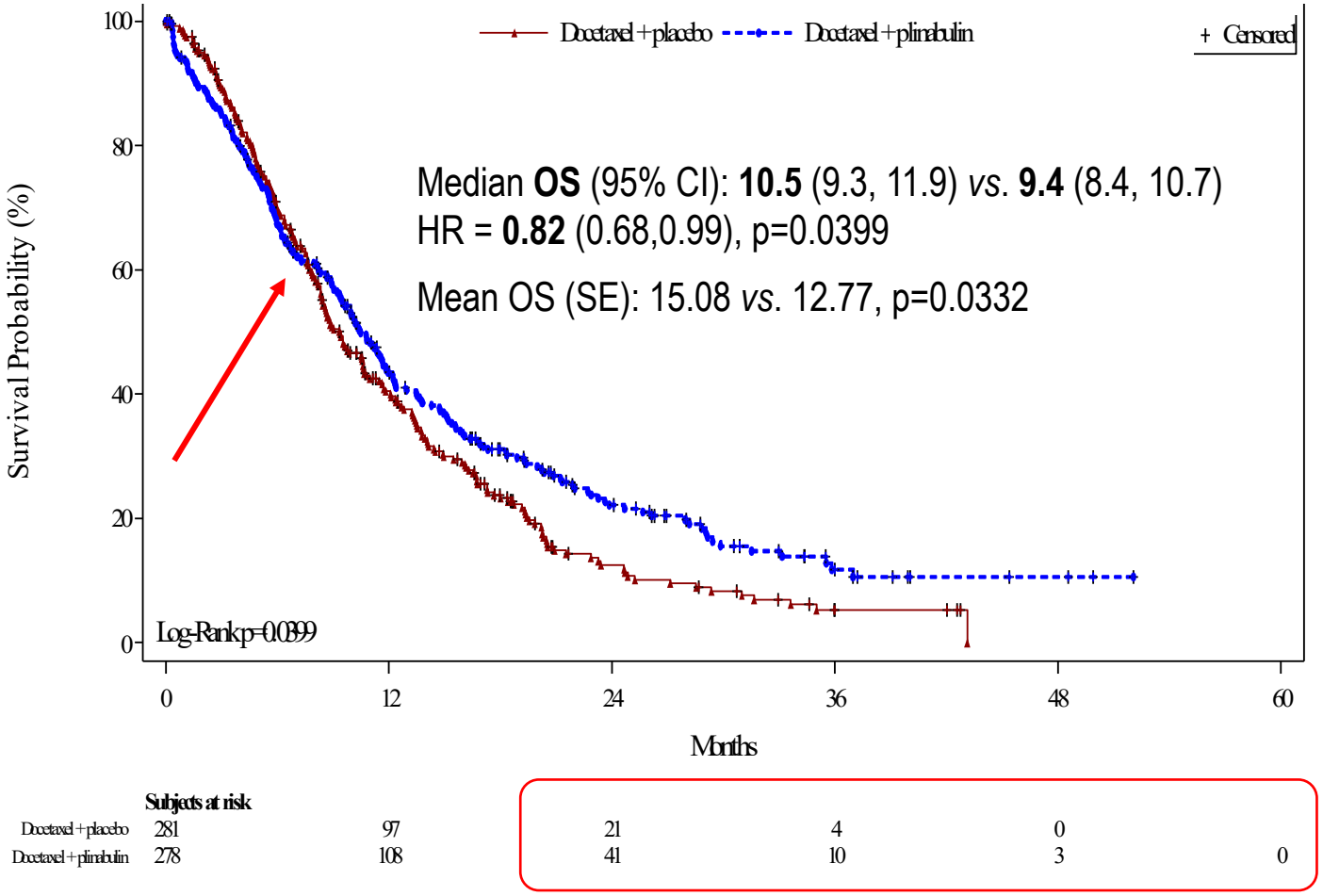
PD

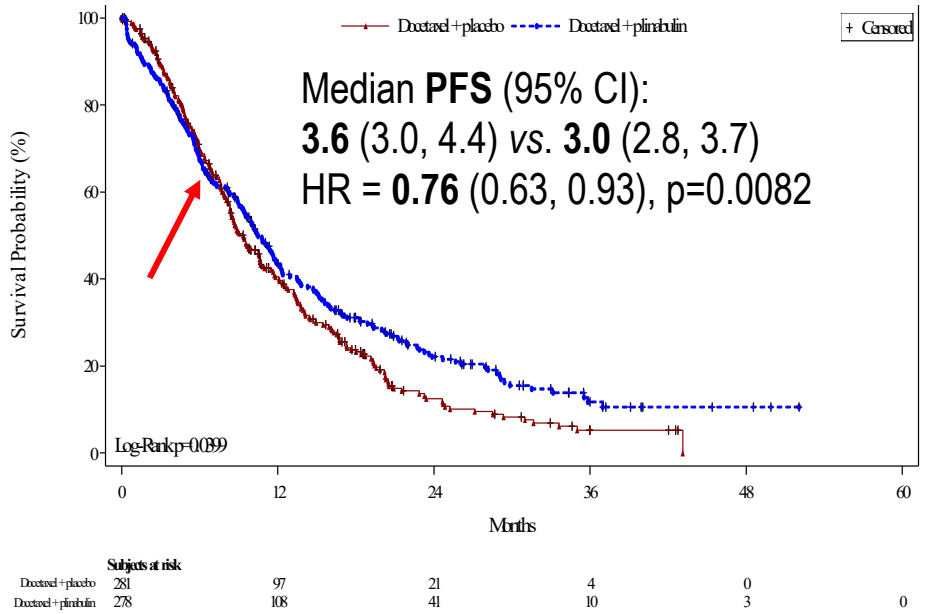
87.5% of patients from China
59.2% non-squamous NSCLC, EGFR wild-type
3.6% PS 2
75% one prior treatment line

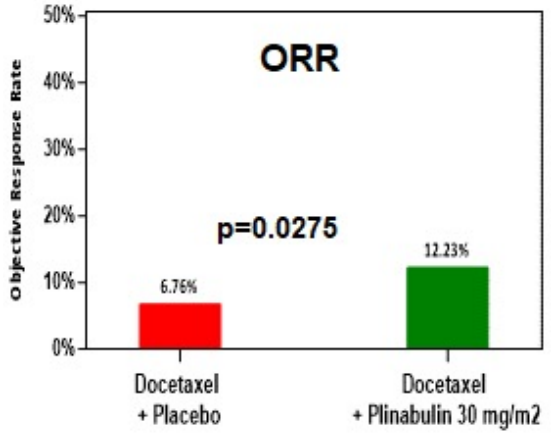
- ✓ **Primary endpoint**: Overall Survival (OS)
- ✓ **Secondary endpoints:** ORR, PFS , Percent of patients with grade 4 neutropenia on C1D8, Month 24 OS rate, Month 36 OS rate , DoR , Q-TWiST, QoL, % patients who received docetaxel >8 cycles, >10 cycles, and >12 cycles

Courtesy of Corey J Langer, MD

DUBLIN-3 Trial: main efficacy findings







Courtesy of Corey J Langer, MD

DUBLIN-3 Trial: safety of docetaxel-plinabulin combination

Safety: Treatment Related Adverse Events Reported >=10% Patients

	Docetaxel + Placebo (N=278) ; n (%)		Docetaxel+Plinabulin (30 mg/m²) (N=274) ; n (%)	
Preferred term	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**
White blood cell count decreased	183(65.8%)	130(46.8%)	156(56.9%)	75(27.4%)
Neutrophil count decreased	186(66.9%)	144(51.8%)	134(48.9%)	81(29.6%)
Nausea	63(22.7%)	0	93(33.9%)	3(1.1%)
Diarrhea	47(16.9%)	2(0.7%)	101(36.9%)	23(8.4%)
Hypertension	9(3.2%)	3(1.1%)	85(31.0%)	47(17.2%)

Q-TWiST Gain	Relative Gain to OS Restricted Mean	Relative Gain to Q-TWiST
1.93	15.11%	18.43%
	(1.72% to 30.63%)	(2.07% to 37.20%)
	p-value=0.0396	p-value=0.0393

- Clear reduction of grade 4 neutropenia (day 8, all cycles: 5.1% vs 33.6%)
- Reduction of febrile neutropenia incidence?
- Increase of non-haematological toxicities (hypertension, diarrhoea) without apparent impact on QoL

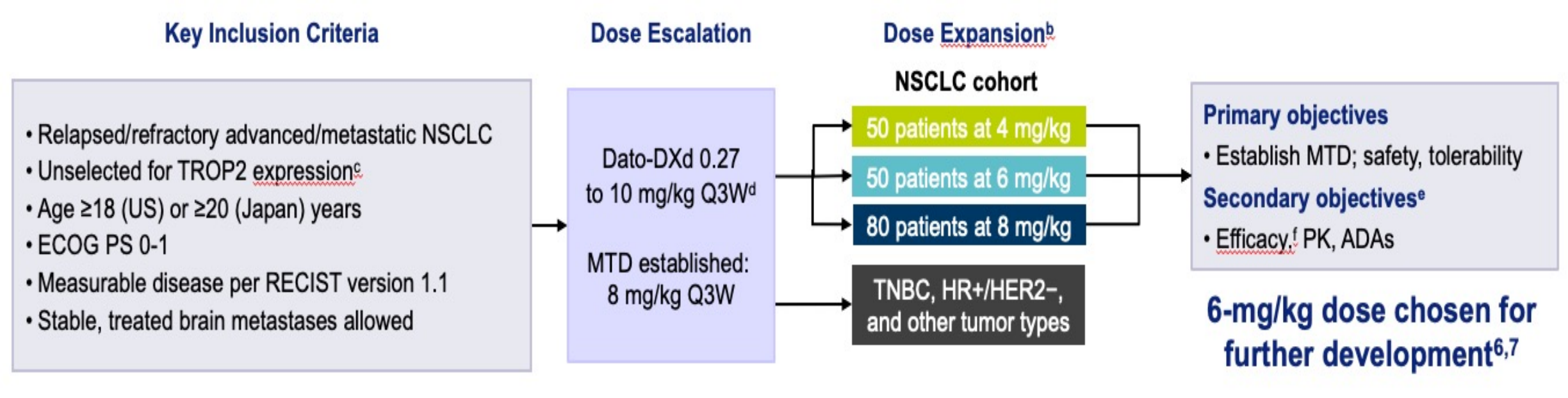
Courtesy of Corey J Langer, MD

TROPION-PanTumor01: Updated Results From the NSCLC Cohort of the Phase 1 Study of Datopotamab Deruxtecan in Solid Tumors

Garon E et al.

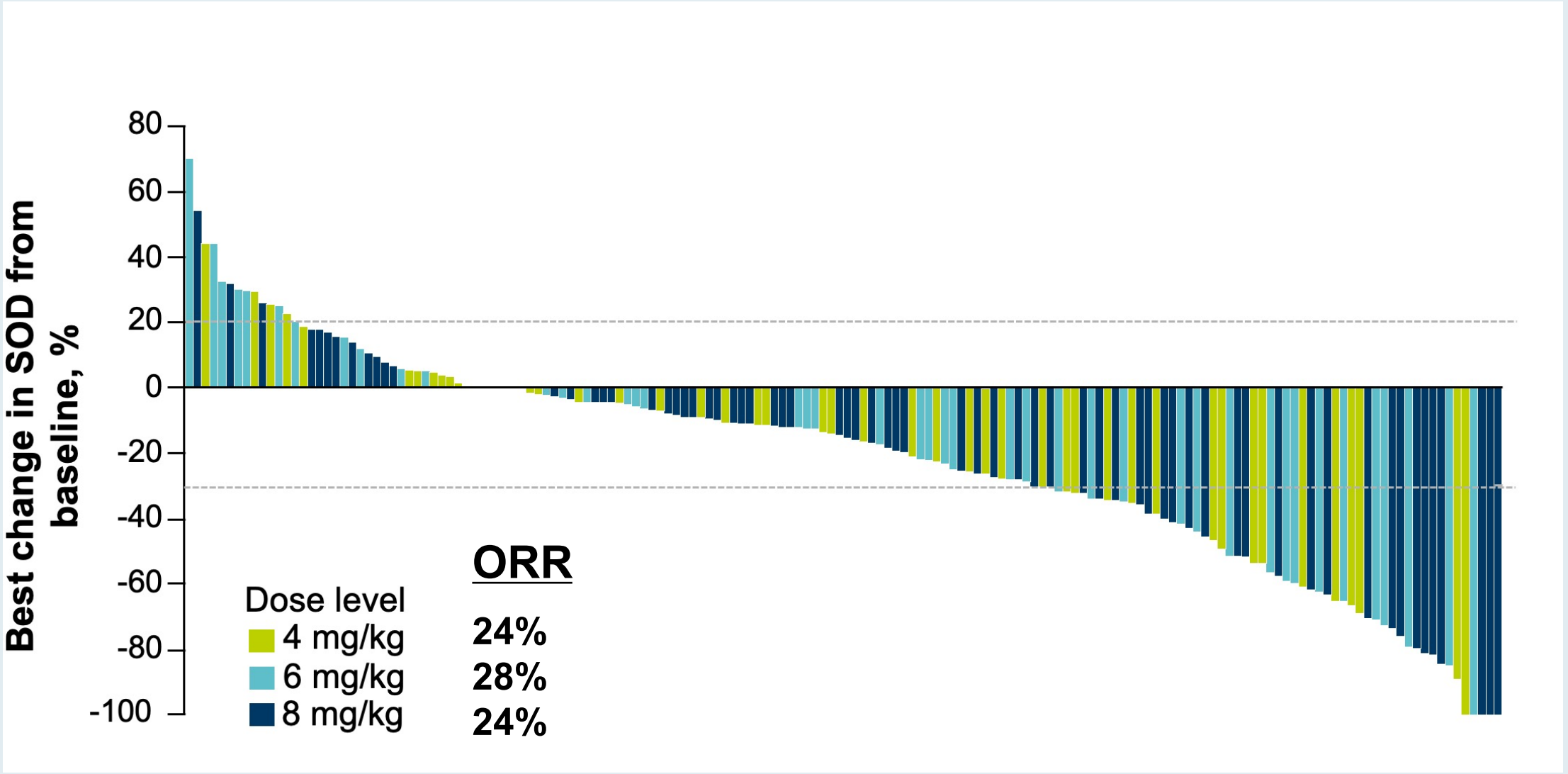
WCLC 2021;Abstract MA03.02.

TROPION-PanTumor01: Study Design



Garon E et al. WCLC 2021;Abstract MA03.02.

TROPION-PanTumor01: Best Change in Sum of Diameters (per BICR)

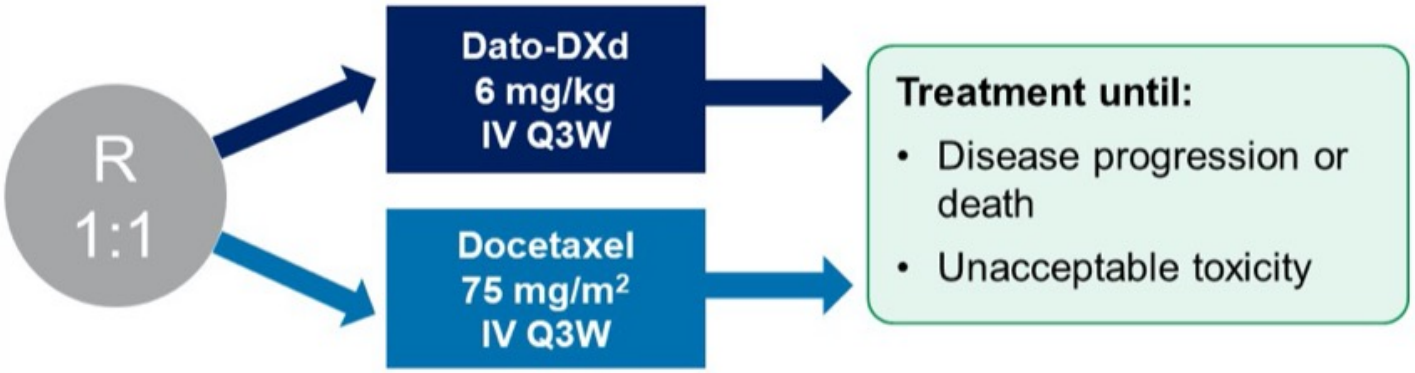


Garon E et al. WCLC 2021;Abstract MA03.02.

TROPION-Lung01: Phase III Trial Design

Patient Population (N=590)

- Advanced or metastatic NSCLC
- No *EGFR*, *ALK*, or other known actionable genomic alterations
- Previous treatment with platinum-based chemotherapy and anti–PD-1/PD-L1 immunotherapy in combination or sequentially
- Measurable disease (per RECIST version 1.1)
- ECOG PS 0 or 1



Stratified by:

- Histology (squamous vs nonsquamous)
- Immunotherapy in last regimen (yes vs no)
- Region (US/Japan/Western Europe vs rest of the world)

Yoh K et al. ASCO 2021;Abstract TPS9127.

Novel Anti-TIGIT Tiragolumab Granted FDA Breakthrough Therapy Designation in Combination with Atezolizumab for PD-L1-High NSCLC

Press Release: January 5, 2021

"Today [it was] announced that tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, has been granted Breakthrough Therapy Designation (BTD) by the US Food and Drug Administration (FDA), in combination with atezolizumab for the first-line treatment of people with metastatic non-small cell lung cancer (NSCLC) whose tumours have high PD-L1 expression with no EGFR or ALK genomic tumour aberrations. Tiragolumab is the first anti-TIGIT molecule to be granted BTD from the FDA, and the designation is based on randomised data from the phase II CITYSCAPE trial. CITYSCAPE provides the first evidence that targeting both immune inhibitory receptors, TIGIT and PD-L1, may enhance anti-tumour activity by potentially amplifying the immune response.

Tiragolumab in combination with atezolizumab has so far shown encouraging efficacy and safety in PD-L1-positive metastatic NSCLC based on data from the phase II CITYSCAPE trial, the first randomised study in the anti-TIGIT field…the combination showed an improvement in the overall response rate (ORR; 37% vs. 21% with atezolizumab alone) and a 42% reduction in the risk of disease worsening or death (progression free survival; PFS) compared with atezolizumab alone. An exploratory analysis in people with high levels of PD-L1 TPS ≥ 50% showed a clinically meaningful ORR vs. atezolizumab alone (66% vs. 24%) and median PFS was not reached (vs. 4.11 months with atezolizumab alone; HR=0.30). The data suggest that tiragolumab plus atezolizumab was generally well-tolerated, showing similar rates of all Grade 3 or more all-cause adverse events when combining the two immunotherapies compared with atezolizumab alone (48% vs. 44%)."

https://www.roche.com/media/releases/med-cor-2021-01-05.htm

Abstract LBA2

ESMO IMMUNO-ONCOLOGY

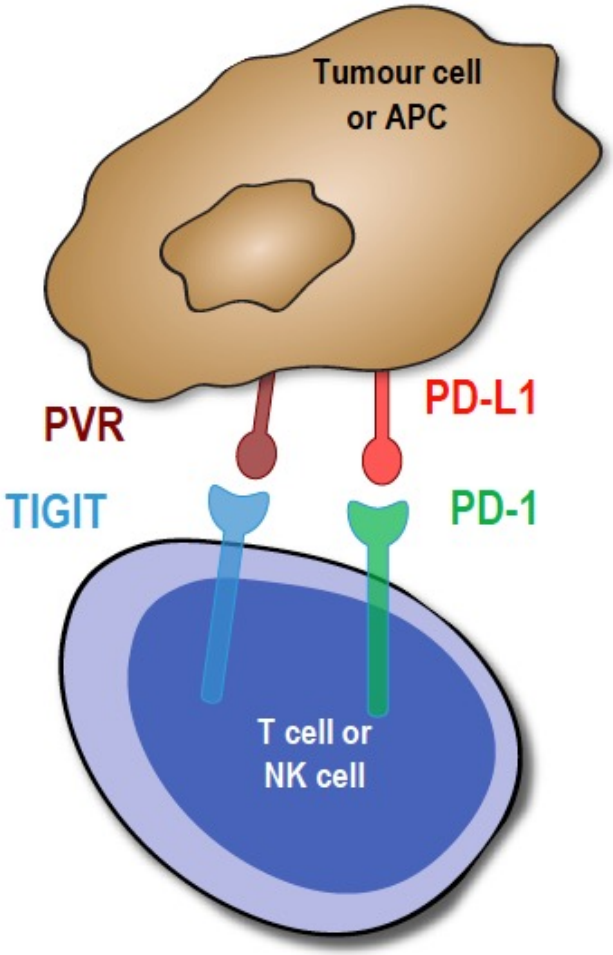
Onsite and Online Congress

Updated analysis and patient-reported outcomes from CITYSCAPE: a randomised, double-blind, Phase II study of the anti-TIGIT antibody tiragolumab + atezolizumab vs placebo + atezolizumab as first-line treatment for PD-L1+ NSCLC

Byoung Chul Cho,[1] Delvys Rodriguez-Abreu,[2] Maen Hussein,[3] Manuel Cobo,[4] Anjan Patel,[5] Nevena Secen,[6] Gregory Gerstner,[7] Dong-Wan Kim,[8] Yun-Gyoo Lee,[9] Wu-Chou Su,[10] Elizabeth Huang,[11] Namrata Patil,[12] Meilin Huang,[12] Zoe Zhang,[12] Xiaohui Wen,[12] Diana Mendus,[12] Tien Hoang,[12] Raymond Meng,[12] Melissa Johnson[13]

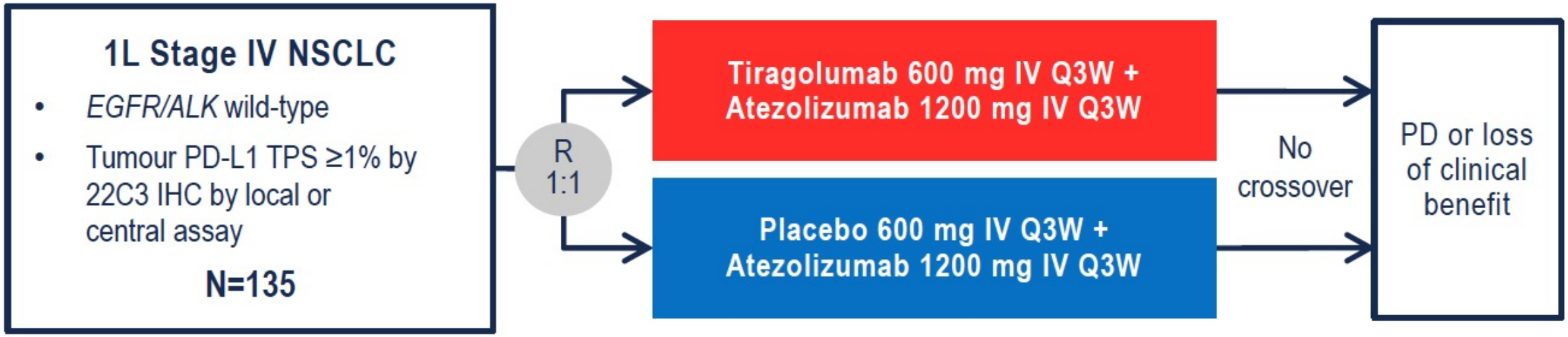
CITYSCAPE: Background

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a novel inhibitory immune checkpoint present on activated T cells and NK cells in multiple cancers.[1–3] TIGIT expression correlates with PD-1, especially in tumour-infiltrating T cells
- Tiragolumab is a fully human IgG1/kappa anti-TIGIT monoclonal antibody with an intact Fc region that blocks the binding of TIGIT to its receptor PVR
- We hypothesise that anti-TIGIT antibodies, such as tiragolumab, could restore the anti-tumour response and may amplify the activity of anti-PD-L1/PD-1 antibodies
- CITYSCAPE (NCT03563716) is the first randomised Phase II study of an anti-TIGIT antibody. At the primary analysis, tiragolumab + atezolizumab showed a clinically meaningful improvement in ORR and PFS in the ITT population compared with atezolizumab monotherapy. This was maintained after a further 5 months of follow-up, with a greater magnitude of improvement seen in the PD-L1 TPS ≥50% subgroup[4]
- Tiragolumab has been granted Breakthrough Therapy Designation (BTD) by the US FDA, in combination with atezolizumab for first-line treatment of patients with metastatic NSCLC whose tumours have high PD-L1 expression with no *EGFR* or *ALK* genomic tumour aberrations
- Here, we present an updated analysis with ~30 months of follow-up, including OS, updated PFS and safety analyses and patient-reported outcomes (PROs)



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Phase II Trial Schema



Stratification factors
- PD-L1 TPS (1–49% vs ≥50%)
- Histology (non-squamous vs squamous)
- Tobacco use (yes vs no)

Co-primary endpoints
- ORR and PFS

Key secondary endpoints
- Safety, DOR, OS

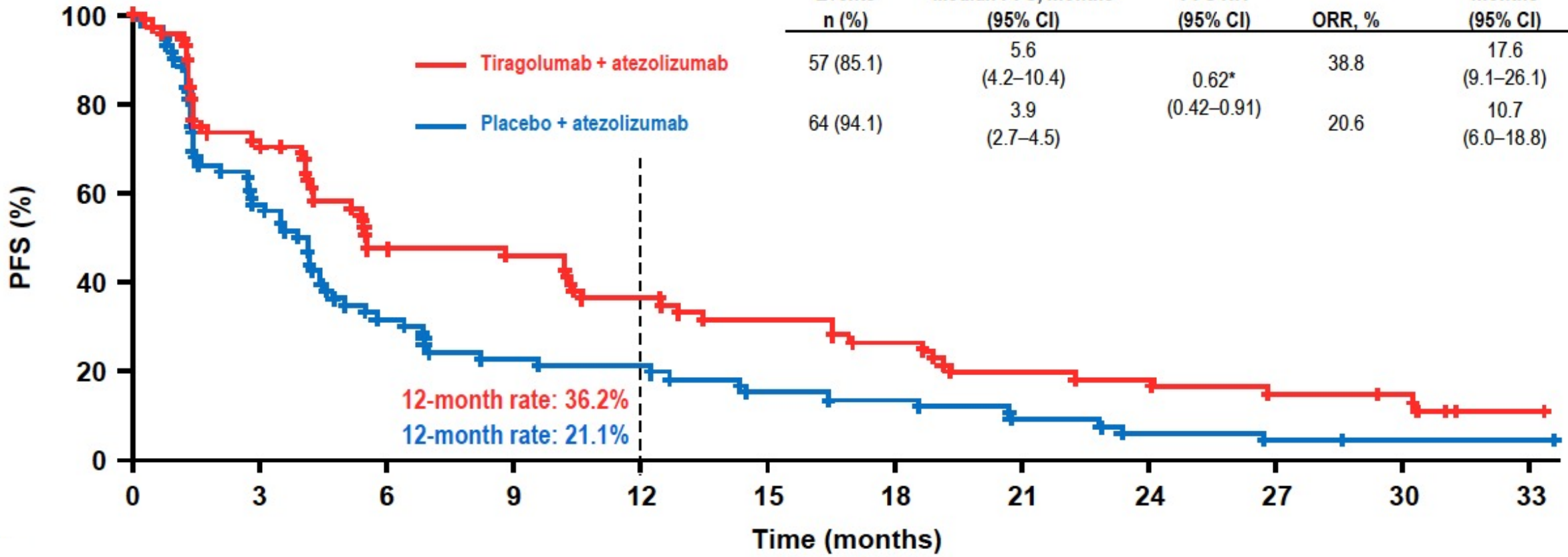
Exploratory endpoints
- Efficacy analysis by PD-L1 status, PROs

Primary analysis[1]
- Cut-off date of 30 June 2019
- Median follow-up of 5.9 months

Updated analysis
- Follow-up performed to assess safety and efficacy
- Cut-off date of 16 August 2021
- Median follow-up of 30.4 months

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Investigator-Assessed PFS – ITT Population



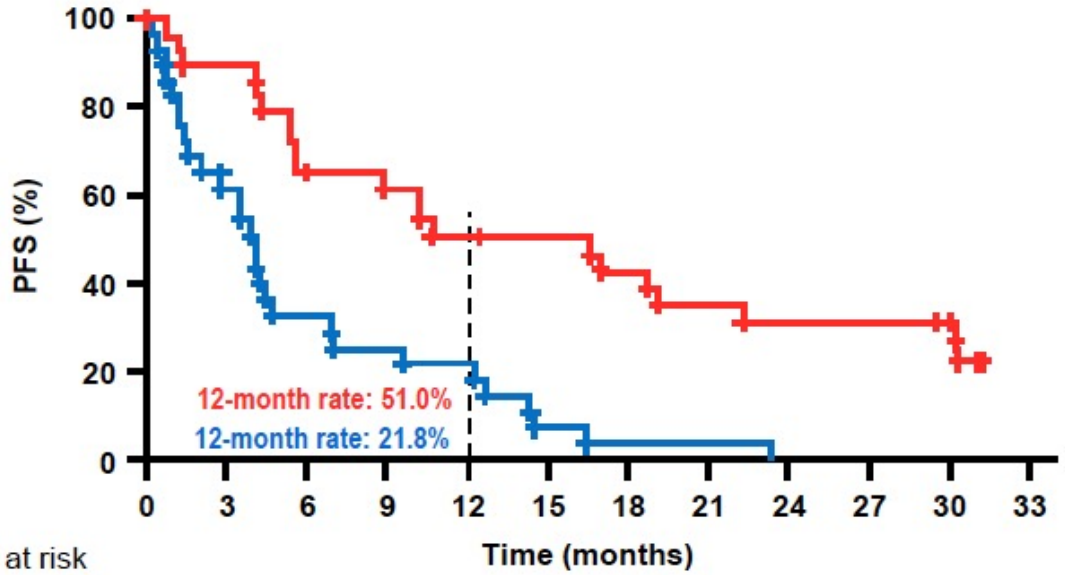
	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tiragolumab + atezolizumab	57 (85.1)	5.6 (4.2–10.4)	0.62* (0.42–0.91)	38.8	17.6 (9.1–26.1)
Placebo + atezolizumab	64 (94.1)	3.9 (2.7–4.5)		20.6	10.7 (6.0–18.8)

Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

CITYSCAPE: Investigator-Assessed PFS – PD-L1 Subgroups

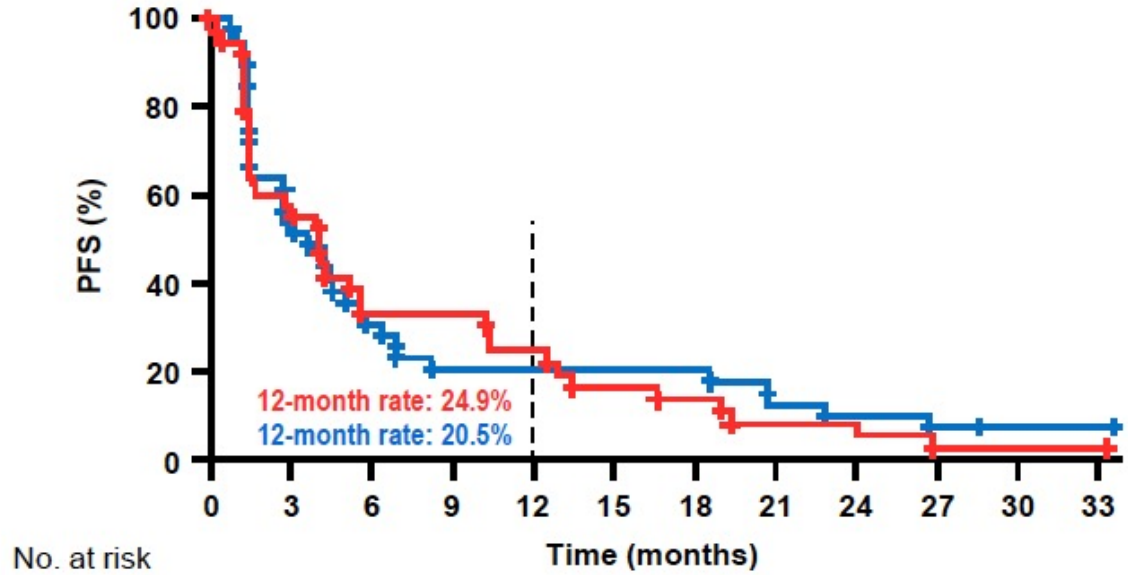
PD-L1 TPS ≥50% (n=58)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	21 (72.4)	16.6 (5.5–22.3)	0.29* (0.15–0.53)	69.0	15.7 (9.1–NE)
Placebo + atezo	28 (96.6)	4.1 (2.1–6.8)		24.1	8.2 (5.6–10.4)



PD-L1 TPS 1–49% (n=77)

	Events n (%)	Median PFS, months (95% CI)	PFS HR (95% CI)	ORR, %	Median DOR, months (95% CI)
Tira + atezo	36 (94.7)	4.0 (1.6–5.6)	1.07* (0.67–1.71)	15.8	17.8 (8.3–24.2)
Placebo + atezo	36 (92.3)	3.6 (1.4–5.5)		17.9	18.8 (15.9–22.8)



Cho BC et al. ESMO Immuno-Oncology 2021;Abstract LBA2.

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma

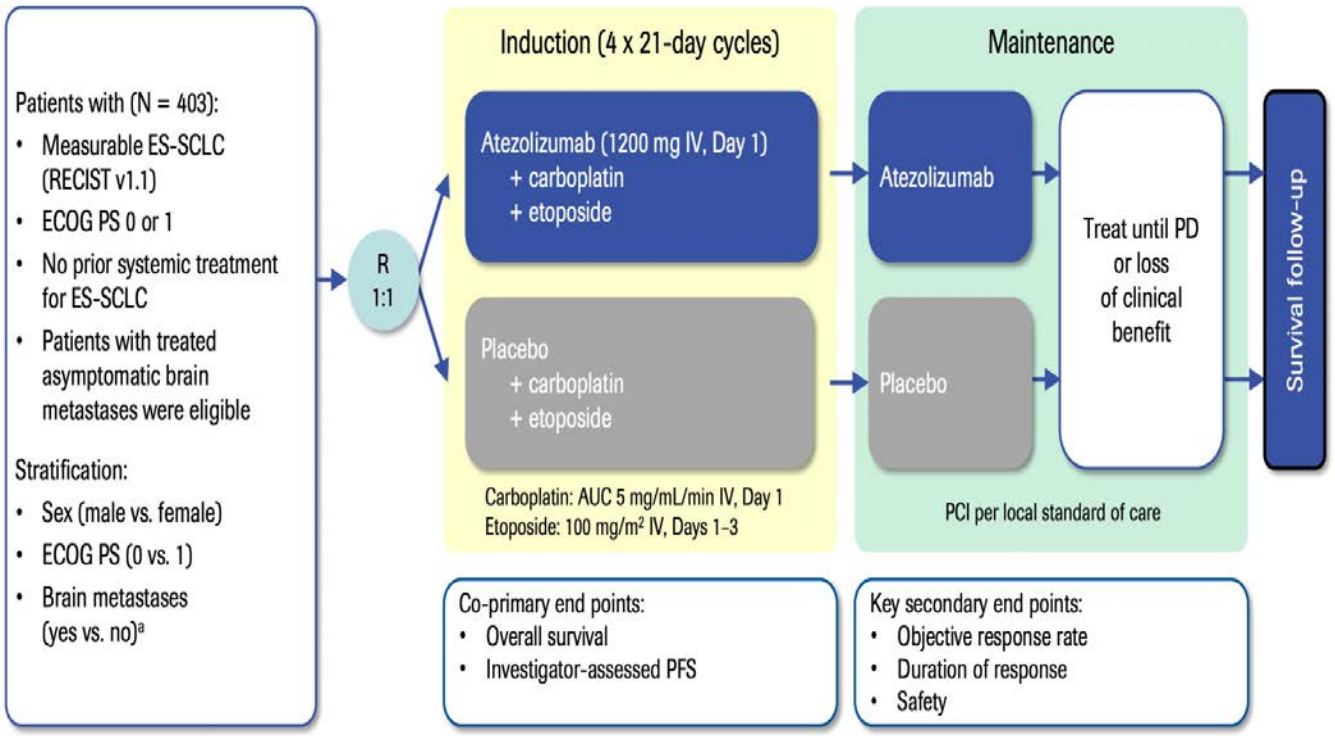
Agenda

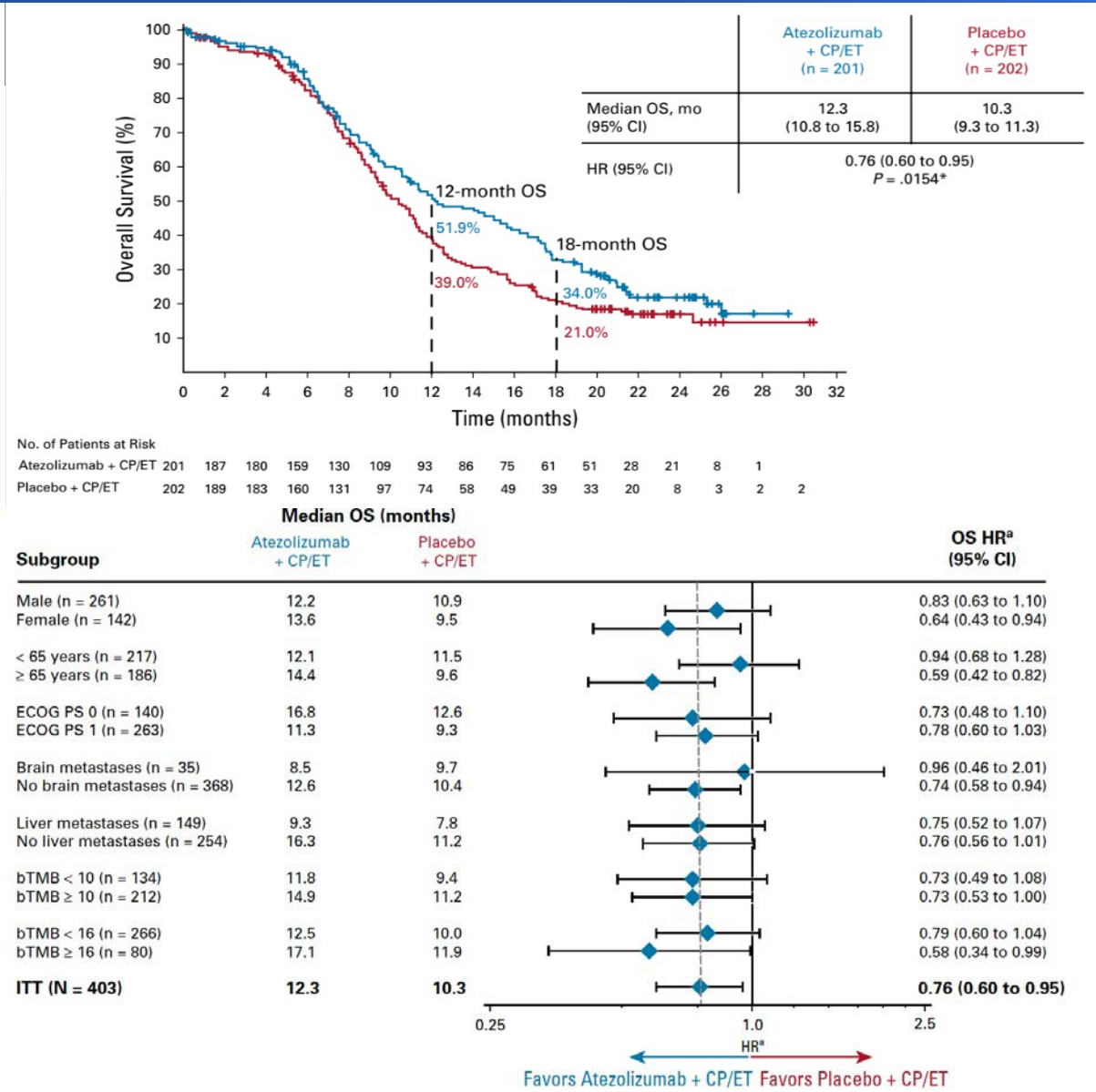
Module 3: Small Cell Lung Cancer (SCLC)

- Follow-up of chemotherapy/immunotherapy trials for extensive-stage SCLC
- ATLANTIS: Second-line lurbinectedin with docetaxel
- Trilaciclib

IMpower133 Update continues to show OS benefit

Carbo-etoposide +/- atezolizumab in ES-SCLC





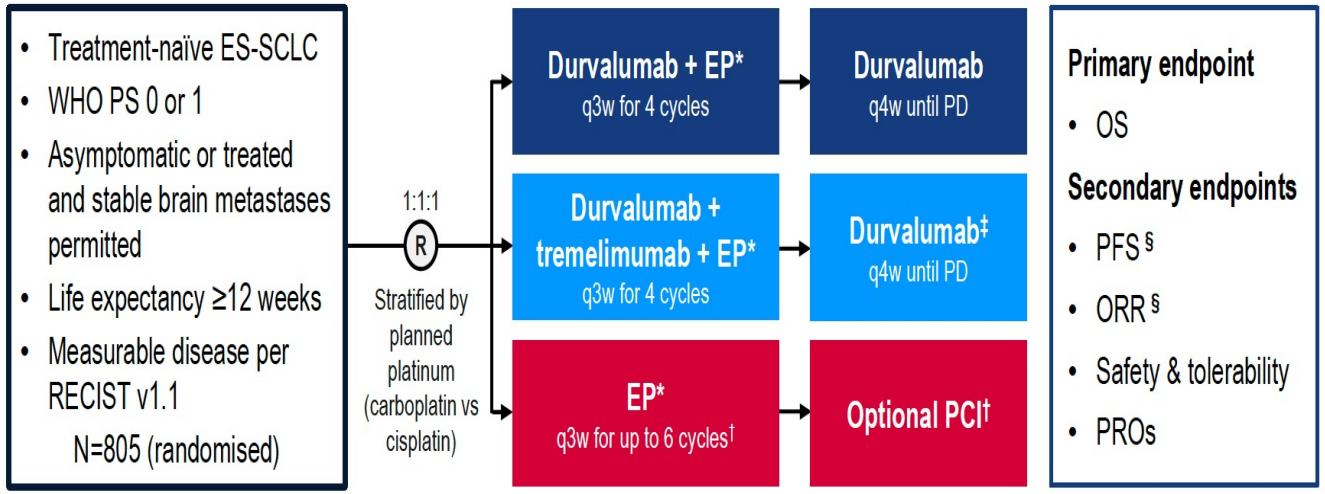
Neither PDL1 IHC status nor blood TMB were predictive of a response to carbo-etoposide-atezolizumab.

Liu et al. JCO 39: 619-630, 2021

Courtesy of Anne S Tsao, MD, MBA

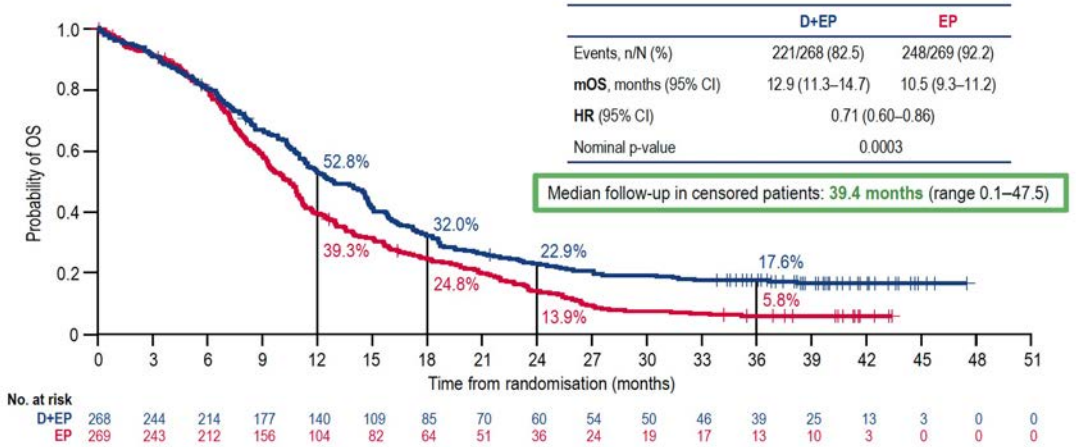
CASPIAN: 3-year update shows OS benefit

platinum-etoposide + durvalumab +/- tremelimumab

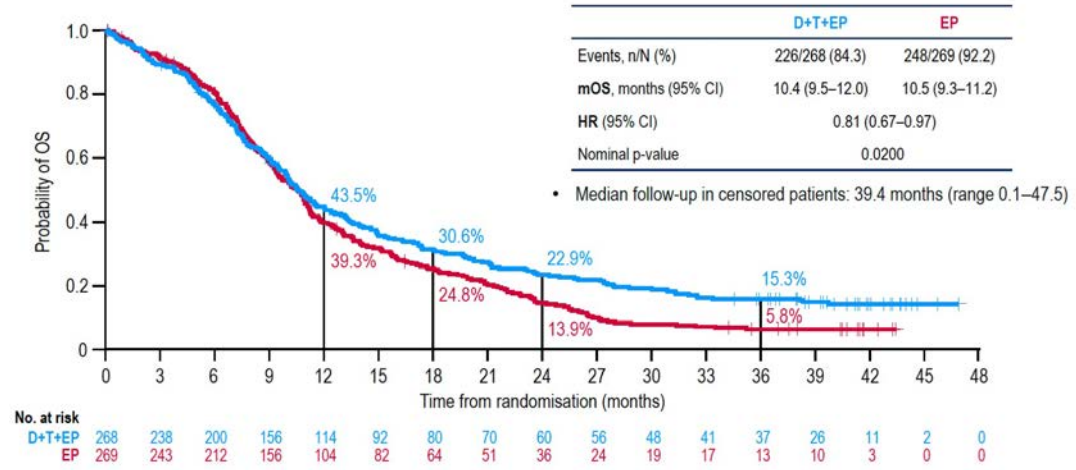


	D+EP (n=265)	D+T+EP (n=266)	EP (n=266)
Serious AEs (all cause), n (%)*	86 (32.5)	126 (47.4)	97 (36.5)
Febrile neutropenia	12 (4.5)	11 (4.1)	12 (4.5)
Pneumonia	6 (2.3)	16 (6.0)	11 (4.1)
Anaemia	5 (1.9)	9 (3.4)	12 (4.5)
Thrombocytopenia	1 (0.4)	6 (2.3)	9 (3.4)
Hyponatremia	2 (0.8)	9 (3.4)	4 (1.5)
Neutropenia	2 (0.8)	5 (1.9)	7 (2.6)
Diarrhoea	2 (0.8)	7 (2.6)	4 (1.5)
Pulmonary embolism	1 (0.4)	7 (2.6)	0
AEs leading to death (all cause), n (%)†	14 (5.3)	29 (10.9)	16 (6.0)
Treatment-related AEs leading to death	6 (2.3)	12 (4.5)	2 (0.8)

3-year Overall Survival Update: D+EP vs EP



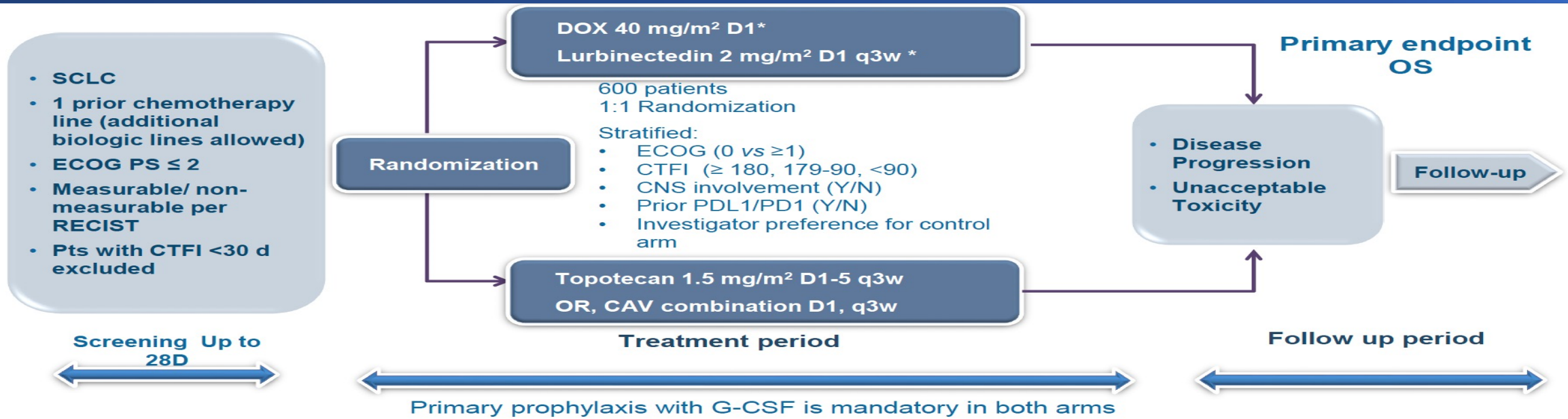
3-year Overall Survival Update: D+T+EP vs EP



Courtesy of Anne S Tsao, MD, MBA

Paz-Ares et al. ESMO 2021, Abstract LBA61

ATLANTIS: 2nd line SCLC doxorubicin + lurbinectedin vs topotecan or CAV



ATLANTIS did not reach its primary endpoint

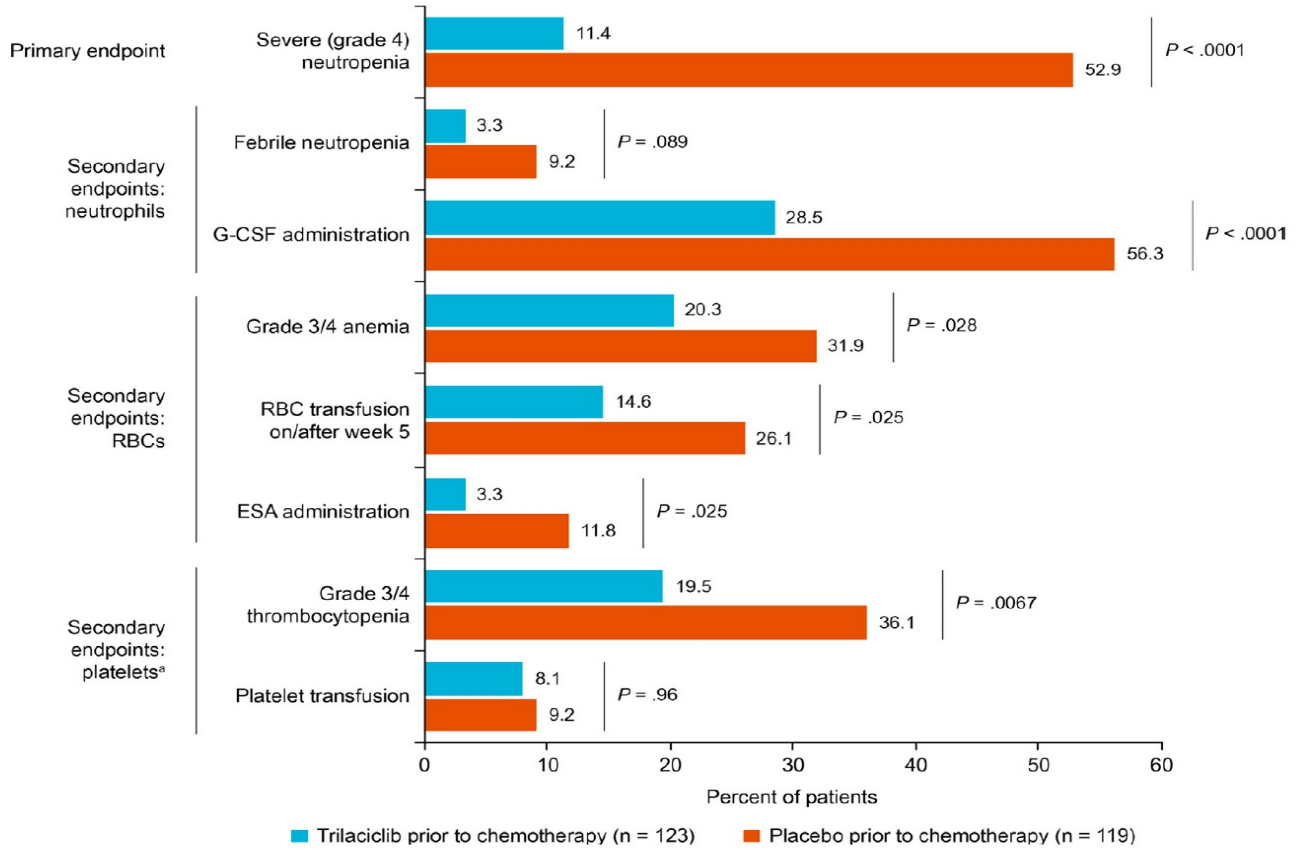
Outcome	Lurbinectedin + Doxorubicin (n=307)	Control (n=306)	
Median OS	8.6	7.6	HR 0.967, p=0.7032
Median PFS	4	4	HR 0.831, p=0.0437
PFS 6 month	31.3	24.4	0.0851
PFS 12 month	10.8	4.4	0.0129

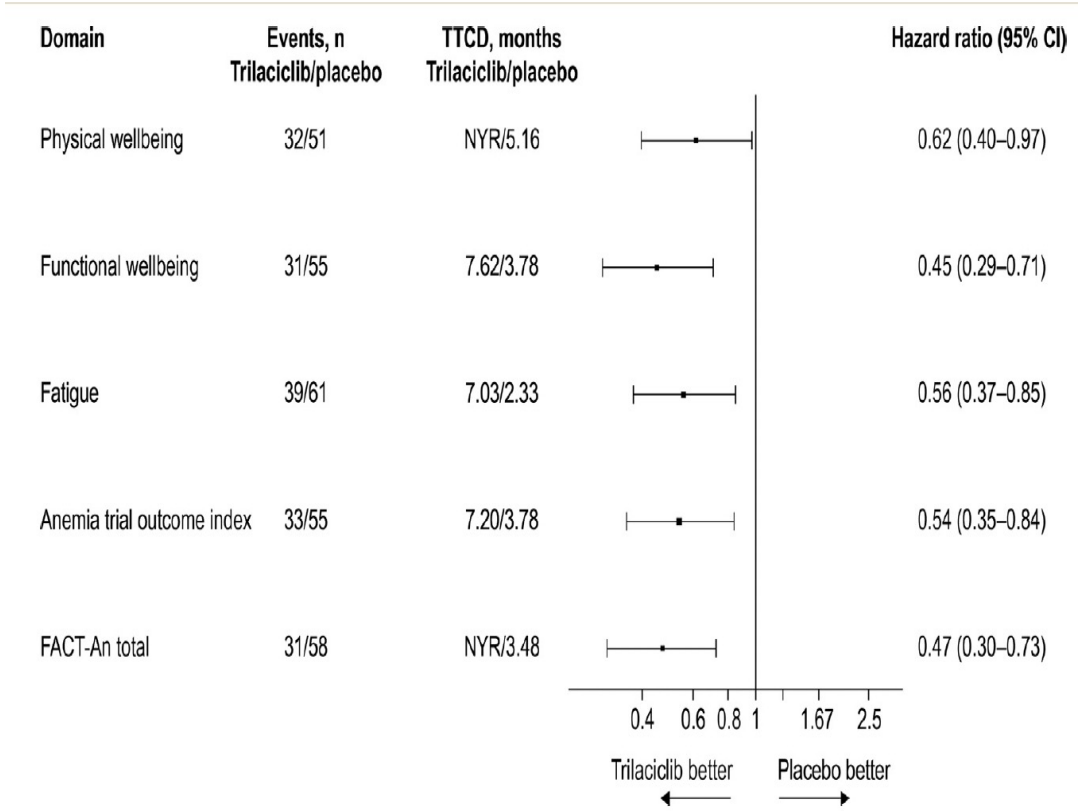
Courtesy of Anne S Tsao, MD, MBA

Paz-Ares et al. IASLC 2021, Abstract PL02.03

Trilaciclib in ES-SCLC improves outcomes

- Trilaciclib is an intravenous CDK4/6 inhibitor that protects against myelosuppression from chemotherapy.
- Data was pooled from 3 phase II randomized placebo-controlled studies (NCT02499770, NCT03041311, and NCT02514447) and analyzed retrospectively





Courtesy of Anne S Tsao, MD, MBA

Weiss et al. Clinical Lung Cancer, 22 (5): 449-460, Sept 2021

Agenda

Module 1: Non-Small Cell Lung Cancer (NSCLC) — Localized Disease

Module 2: NSCLC — Metastatic Disease

Module 3: Small Cell Lung Cancer

Module 4: Mesothelioma

Agenda

Module 4: Mesothelioma

- CheckMate 743: Nivolumab/ipilimumab – Update with histology
- SWOG-1619: Neoadjuvant chemotherapy/atezolizumab

CheckMate 743: Mesothelioma 3-year update shows OS, PFS, DoR benefit

Key eligibility criteria
- Unresectable MPM
- No prior systemic therapy
- ECOG PS 0-1

Stratified by
Histology (epithelioid vs non-epithelioid) and gender

N = 605 → R 1:1
- n = 303: **NIVO** 3 mg/kg Q2W + **IPI** 1 mg/kg Q6W (for up to 2 years)
- n = 302: **Cisplatin** or **carboplatin** + **pemetrexed** Q3W[b] (6 cycles)

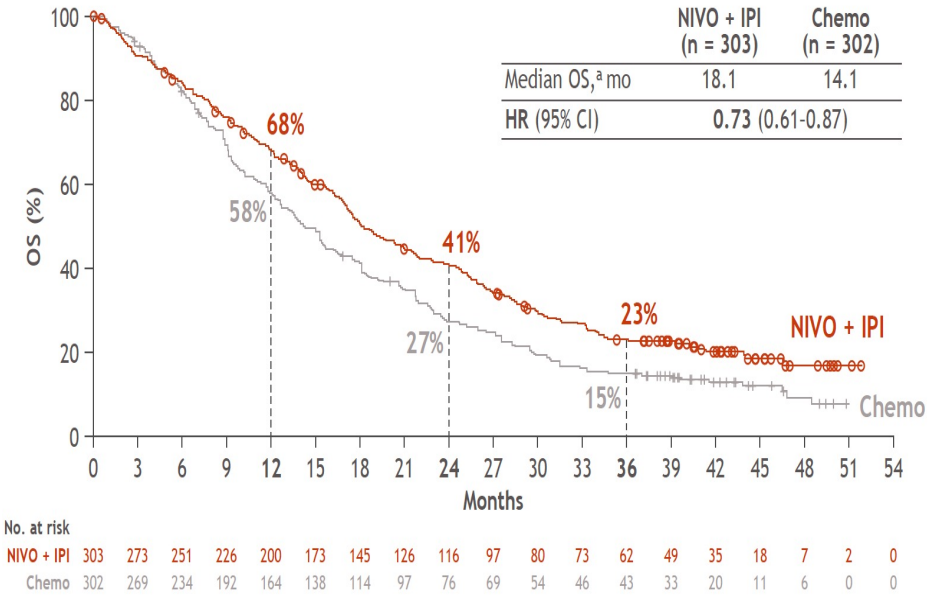
Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

Primary endpoint
- OS

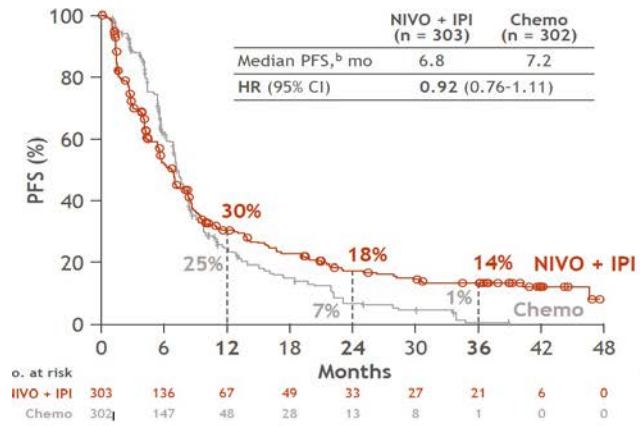
Secondary endpoints
- ORR, DCR, and PFS by BICR
- Efficacy by PD-L1[c] expression

Exploratory endpoints
- Safety and tolerability
- Biomarkers

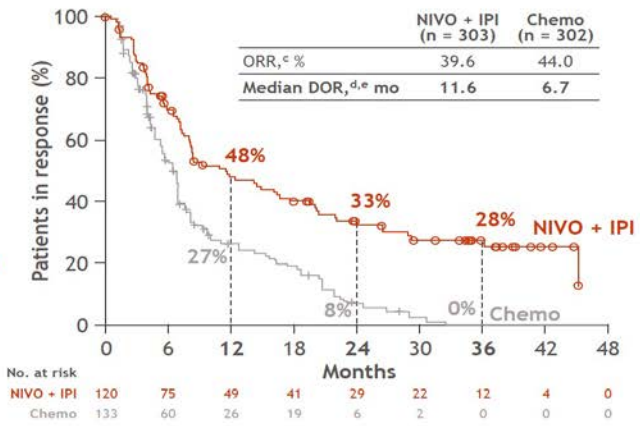
ITT Overall Survival



PFS[a]



ORR/DOR[a]

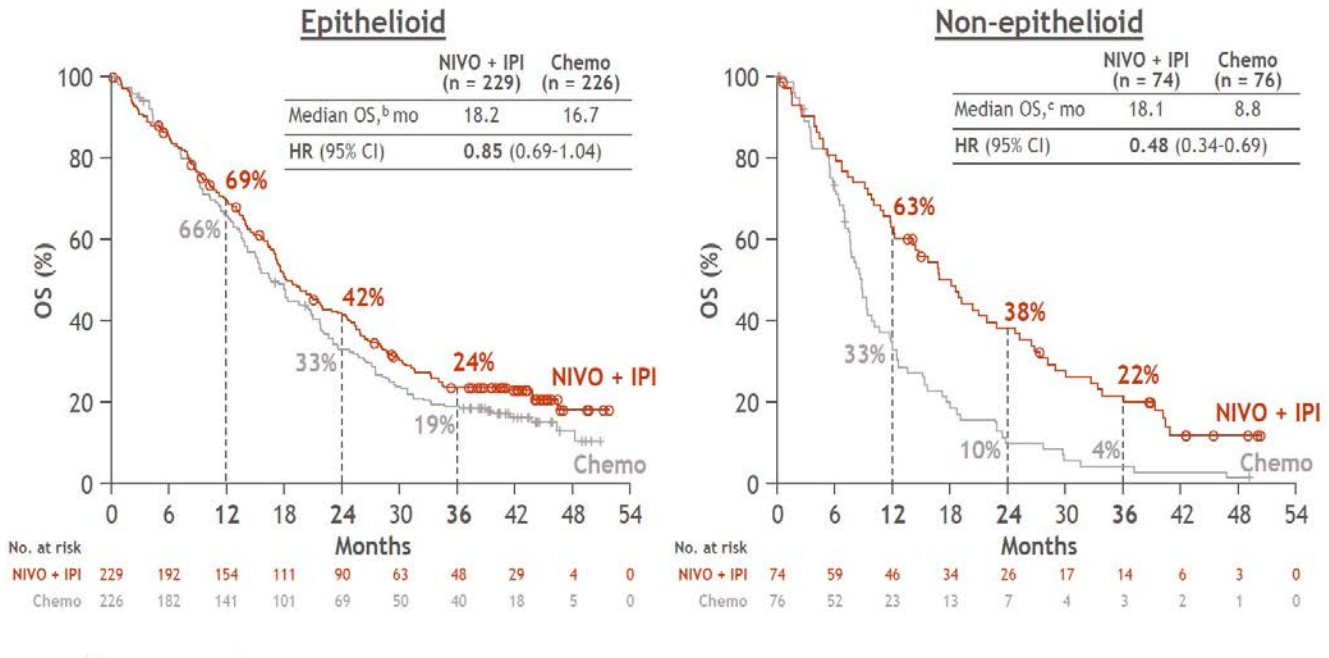


- 3-year OS rate 23% with ipi-nivo vs 15%
- 28% of responders have an ongoing response at 3 years
- TMB does not predict for benefit

Courtesy of Anne S Tsao, MD, MBA

Peters et al. ESMO 2021, AbstractLBA65

CheckMate 743: 3-year update by histology



Clinical Implications:

- Greatest magnitude of benefit seen in non-epithelioid histology
- Ipi-nivo would be a frontline choice for non-epithelioid patients unless rapid debulking is needed
- Epithelioid patients can receive either chemo +/- bevacizumab or ipi-nivo as 1st line therapy

Conclusion CheckMate 743

- New SOC for mesothelioma
- 3-year update survival results confirm the clinical benefit
- Mesothelioma is an immunogenic disease

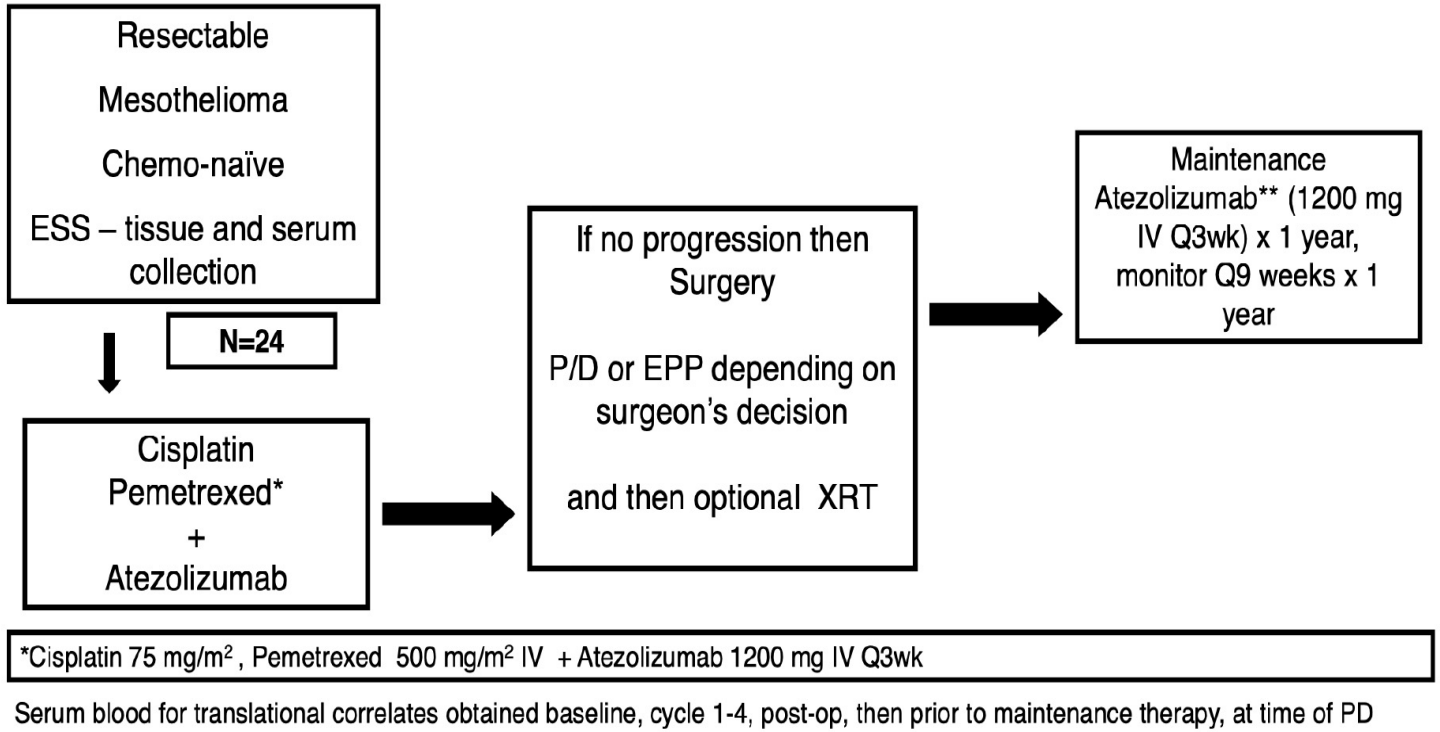
Future Research Directions:

1) Combination I/O with chemo backbones
2) Sequencing studies on chemo vs I/O
3) Novel targets – T cell CART

Courtesy of Anne S Tsao, MD, MBA

SWOG 1619

Neoadjuvant cisplatin-pemetrexed-atezolizumab



- 4 cycles of neoadjuvant cisplatin-pemetrexed-atezolizumab successfully delivered in 21 eligible and evaluable patients.
  - 18 patients (radiographic SD or PR) proceeded to surgical resection
  - 16 patients received maintenance atezolizumab
  - Median f/u time 10.3 months, median PFS 18.6 months and median OS has not been reached.
  - To date, no delayed treatment related adverse events > grade 3 reported.

S1619 Clinical Implications and Future Research Directions:

- No new safety signals from the CPA regimen nor atezolizumab maintenance therapy.
- Neoadjuvant therapy trials in this patient population are needed.
- Translational studies are pending to identify predictive biomarkers.

Courtesy of Anne S Tsao, MD, MBA

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET

Faculty

Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD

Moderator

Kristen K Ciombor, MD, MSCI

RTP RESEARCH TO PRACTICE

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

RTP Year in Review 2022