Key Considerations in the Optimal Clinical Care of Patients with Small Cell Lung Cancer

Wednesday, February 9, 2022
5:00 PM – 6:00 PM ET

Faculty

Luis Paz-Ares, MD, PhD
Jared Weiss, MD

Moderator

Neil Love, MD

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Luis Paz-Ares, MD, PhD
Chair of the Medical Oncology Department at the Hospital Universitario 12 de Octubre
Associate Professor at the Universidad Complutense
Head of the Lung Cancer Unit at the National Oncology Research Center
Madrid, Spain

Jared Weiss, MD
Professor of Medicine
UNC School of Medicine
Lineberger Comprehensive Cancer Center
Chapel Hill, North Carolina

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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Dr Love — Disclosures

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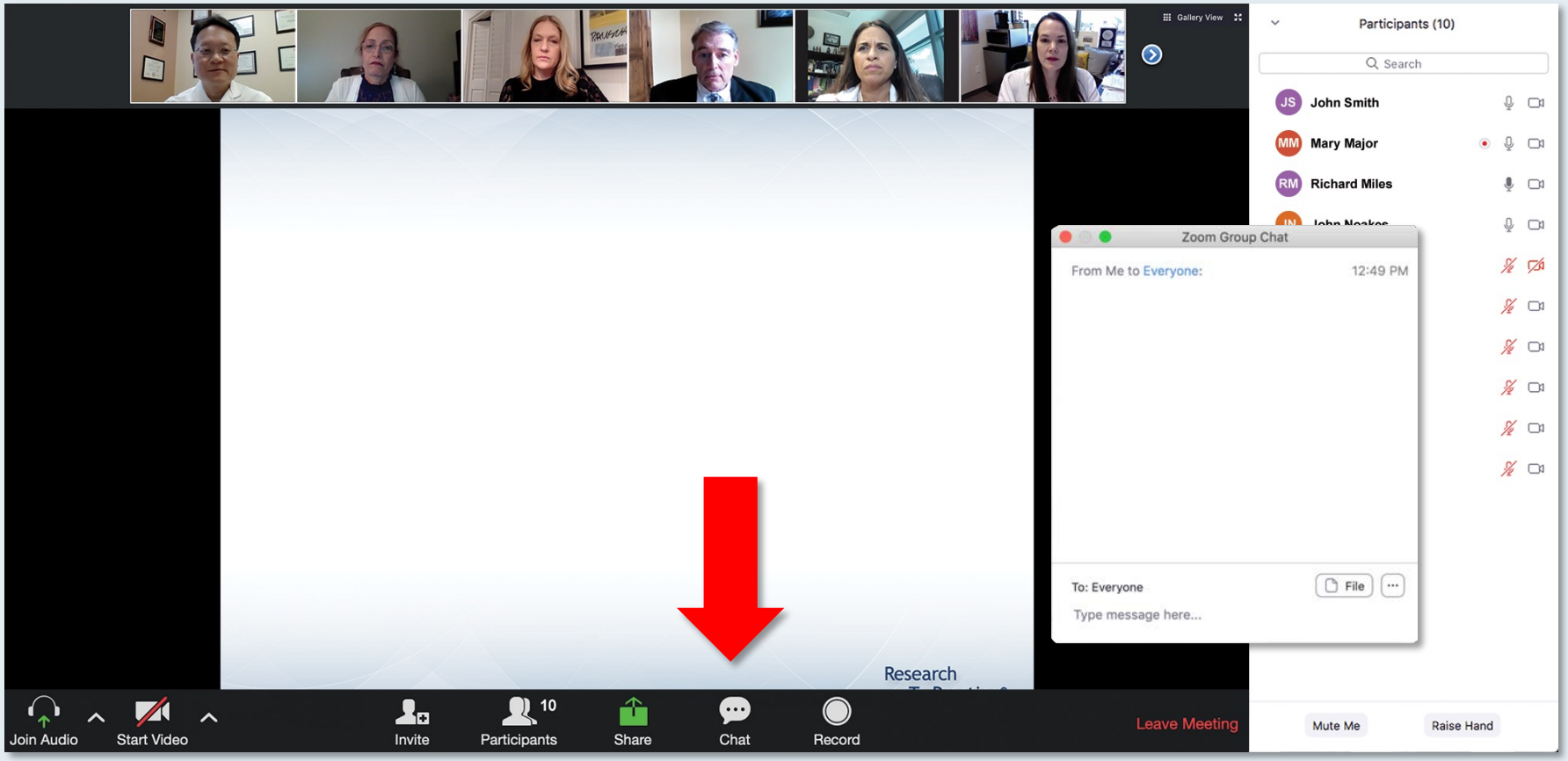

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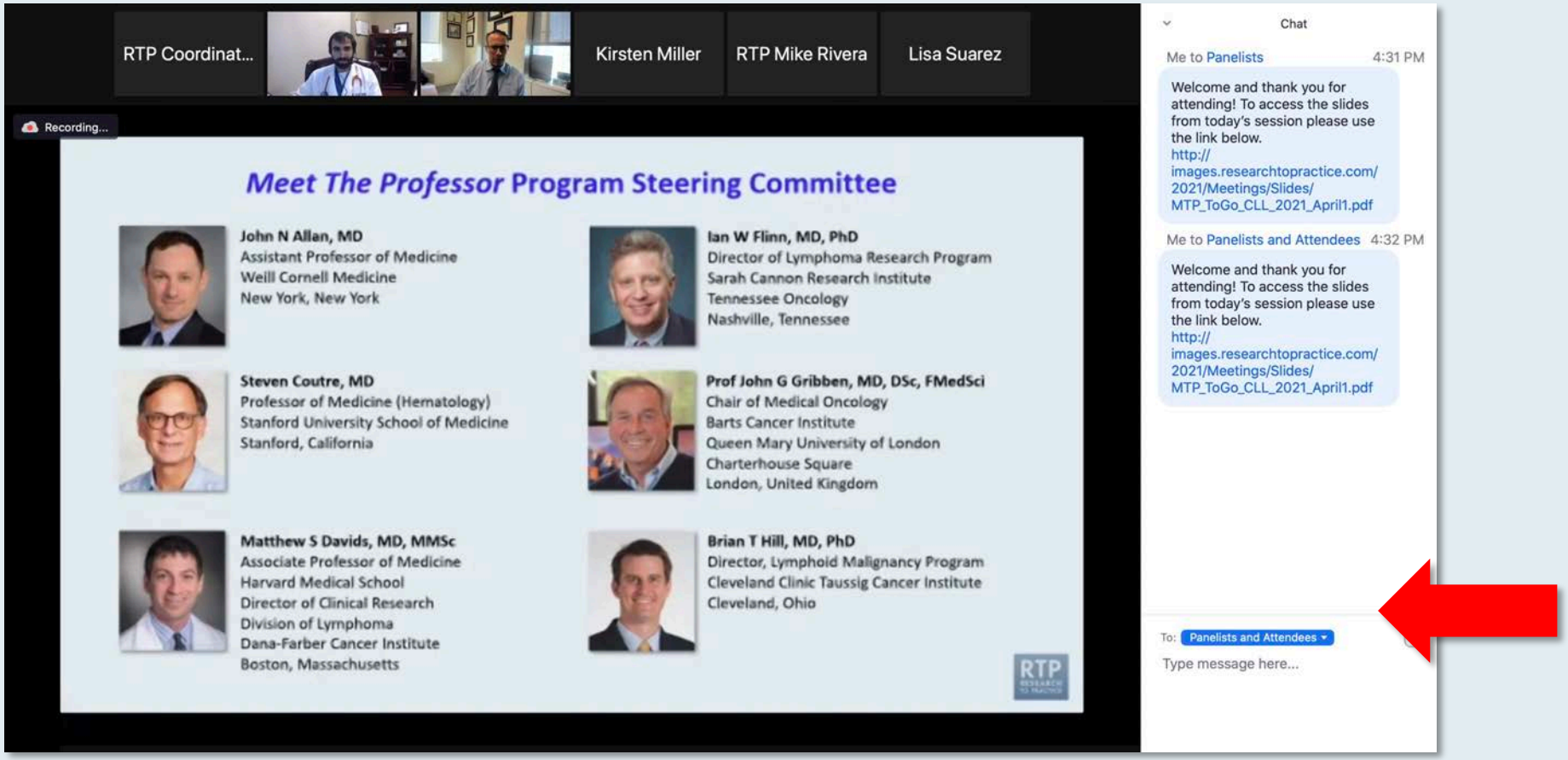
Expand chat submission box



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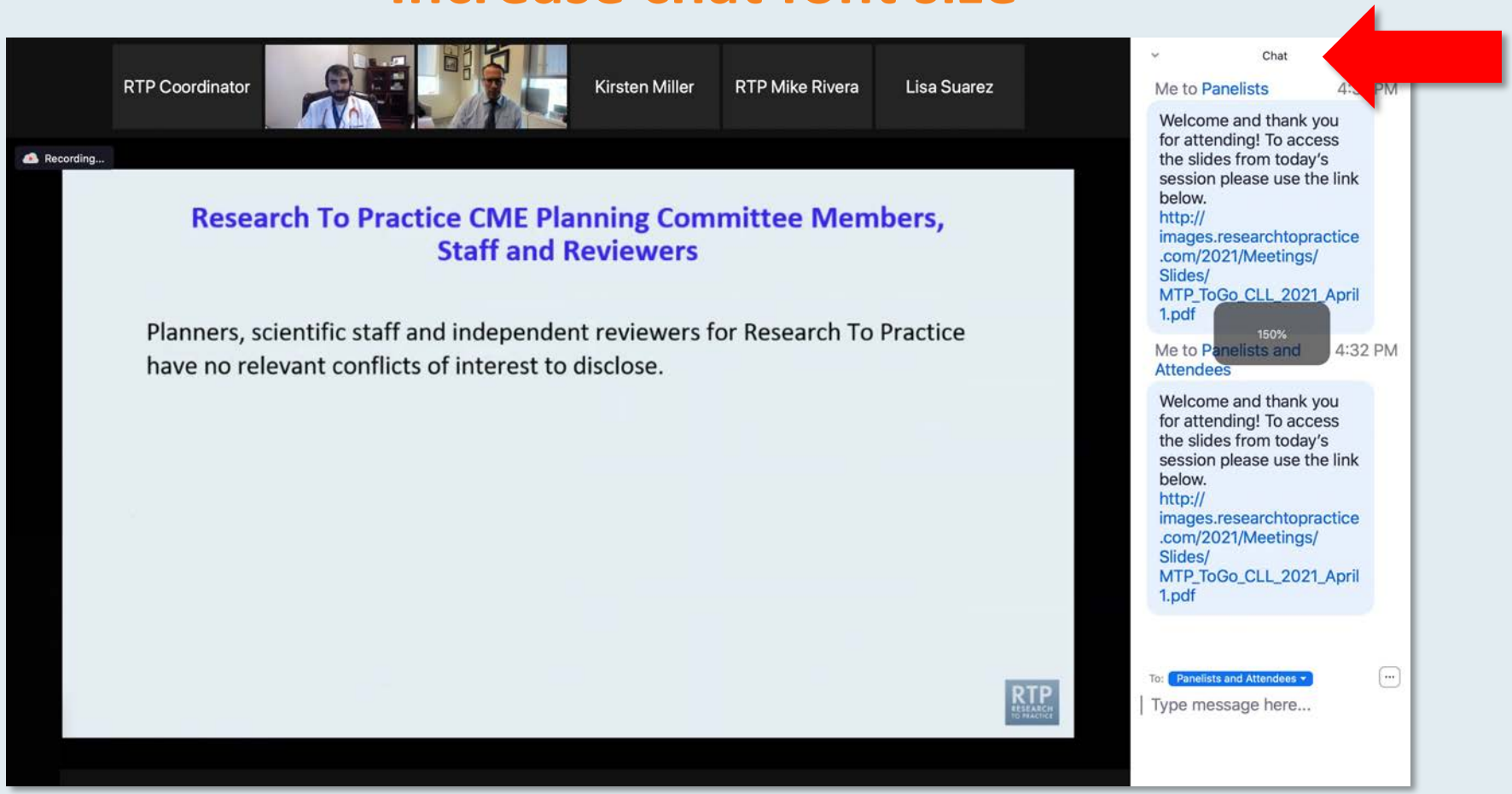

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

ONCOLOGY TODAY

WITH DR NEIL LOVE

NSCLC with EGFR Exon 20 Insertion Mutations

DR GREGORY RIELY
MEMORIAL SLOAN KETTERING CANCER CENTER

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Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the North Carolina Oncology Association and the South Carolina Oncology Society

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

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Recent Advances and Real-World Implications in Medical Oncology: Agenda

Module 1	**Chronic Lymphocytic Leukemia and Lymphomas** 8:35 AM – 9:40 AM
Module 2	**Multiple Myeloma** 9:40 AM – 10:45 AM
Module 3	**Genitourinary Cancers** 10:45 AM – 11:50 AM
Module 4	**Breast Cancer** 12:30 PM – 1:35 PM
Module 5	**Gastrointestinal Cancers** 1:35 PM – 2:40 PM
Module 6	**Lung Cancer** 2:40 PM – 3:45 PM

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Meet The Professor

Current and Future Role of Immunotherapy in the Management of Lung Cancer

Tuesday, February 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Charu Aggarwal, MD

Moderator

Neil Love, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Prostate Cancer (Part 1 of a 2-Part Series)

Thursday, February 17, 2022

7:00 PM – 9:00 PM PT

Faculty

Neeraj Agarwal, MD
Himisha Beltran, MD
Fred Saad, MD
A Oliver Sartor, MD

Moderator

Alan H Bryce, MD

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Bladder Cancer (Part 2 of a 2-Part Series)

Friday, February 18, 2022

6:30 PM – 8:00 PM PT

Faculty

Shilpa Gupta, MD
Daniel P Petrylak, MD
Guru Sonpavde, MD

Moderator

Sumanta Kumar Pal, MD

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Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Thursday, February 24, 2022
5:00 PM – 6:00 PM ET

Faculty
Amir Fathi, MD

Moderator
Neil Love, MD

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The Great Adjuvant Debate — Exploring the Role of Novel Therapies in the Management of Localized Cancer

Monday, February 28, 2022

5:00 PM – 6:00 PM ET

Faculty

Jeffrey S Weber, MD, PhD
Roy S Herbst, MD, PhD
Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Tuesday, March 1, 2022
5:00 PM – 6:00 PM ET

Faculty

Michael E Williams, MD, ScM

Moderator

Neil Love, MD

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Thank you for joining us!

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

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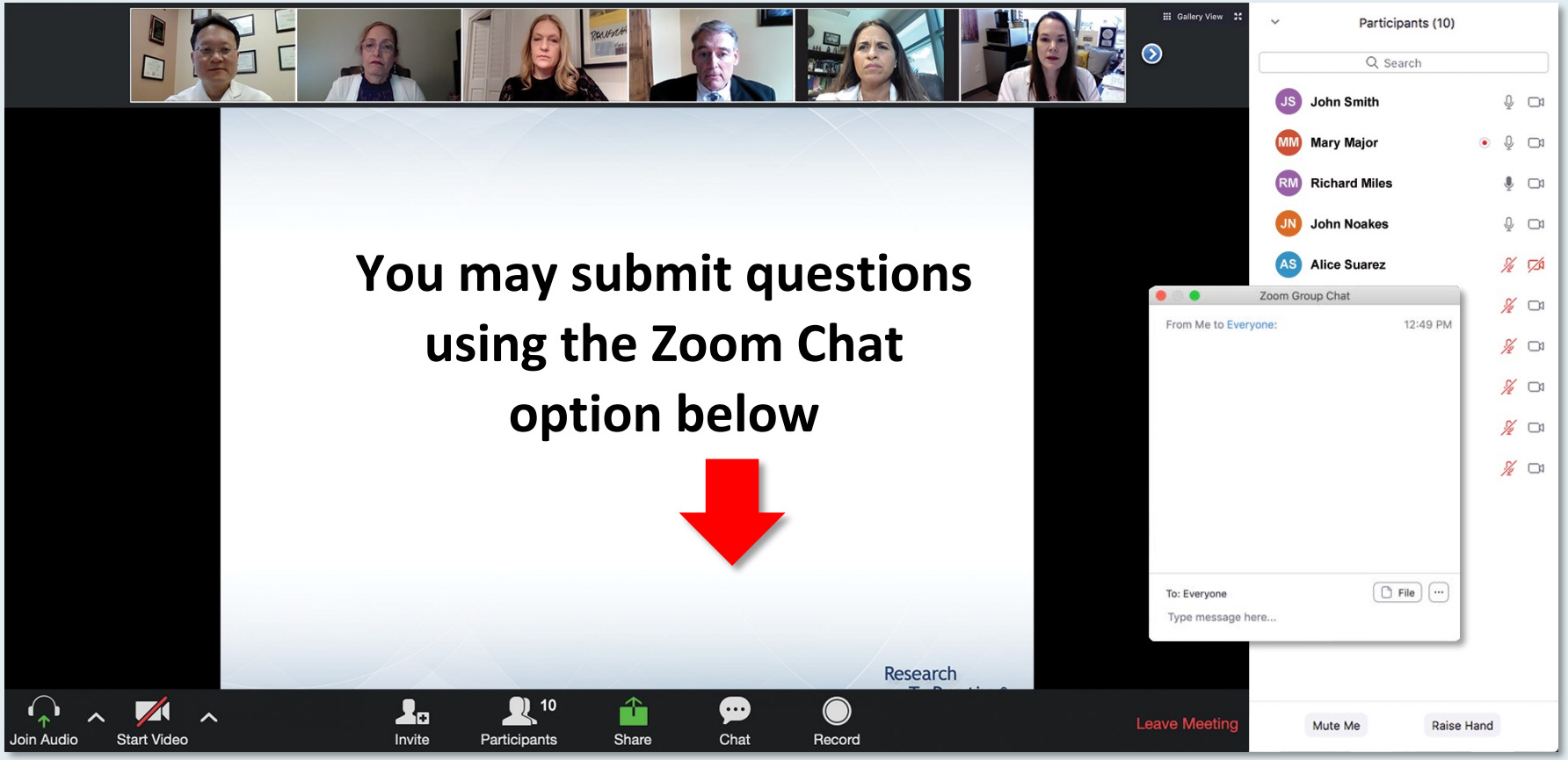

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Key Considerations in the Optimal Management of Patients with Small Cell Lung Cancer — A Case-Based Live CME Webcast and Multifaceted Enduring Resource

Luis Paz-Ares
Hospital Universitario 12 de Octubre

Recognition and Management of Adverse Events (AEs) with Available SCLC Treatments

Dr Weiss

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Agenda

Case – Dr Paz-Ares: A 69-year-old woman with newly diagnosed extensive-stage small-cell lung cancer (ES-SCLC) who receives carboplatin/etoposide/atezolizumab

Case – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab

Case – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression

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Case – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression

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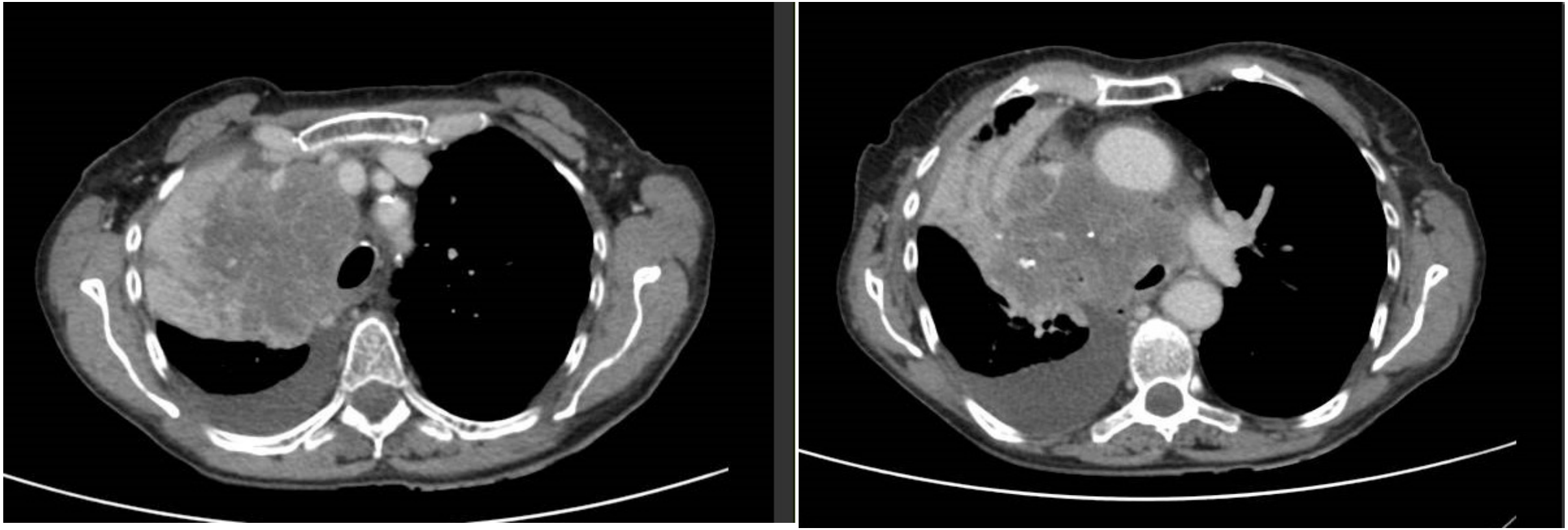
Case Presentation – Dr Paz-Ares: A 69-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/atezolizumab

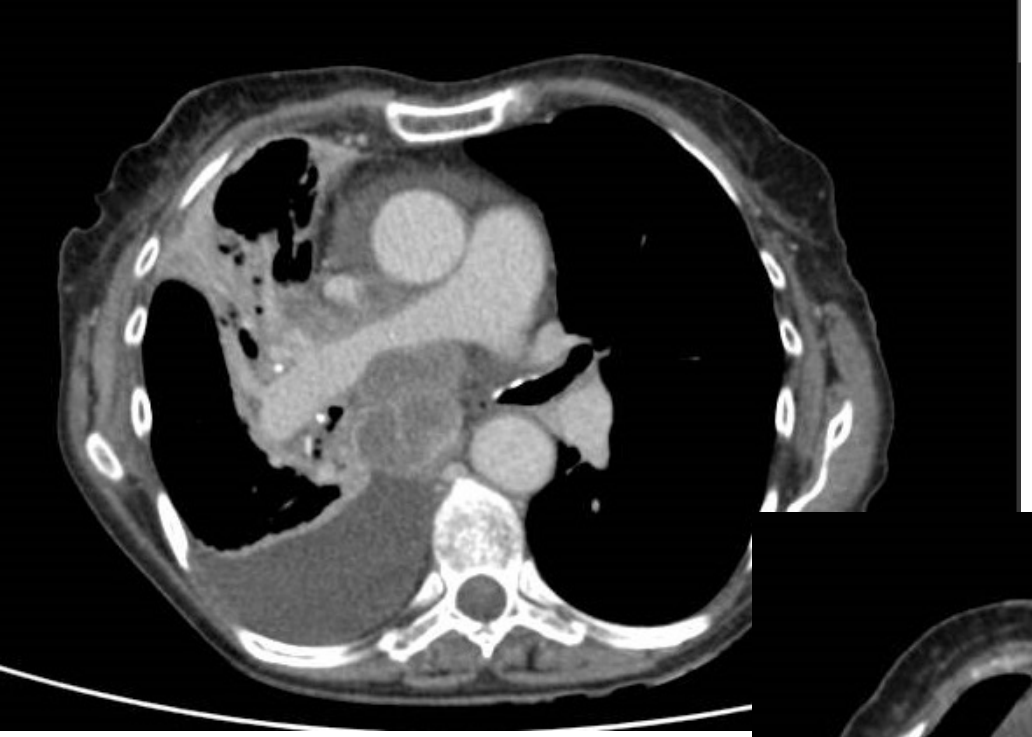
- 69 yo female
- PMH
  - Smoker (53 p/y)
  - HBP
  - Alcohol use

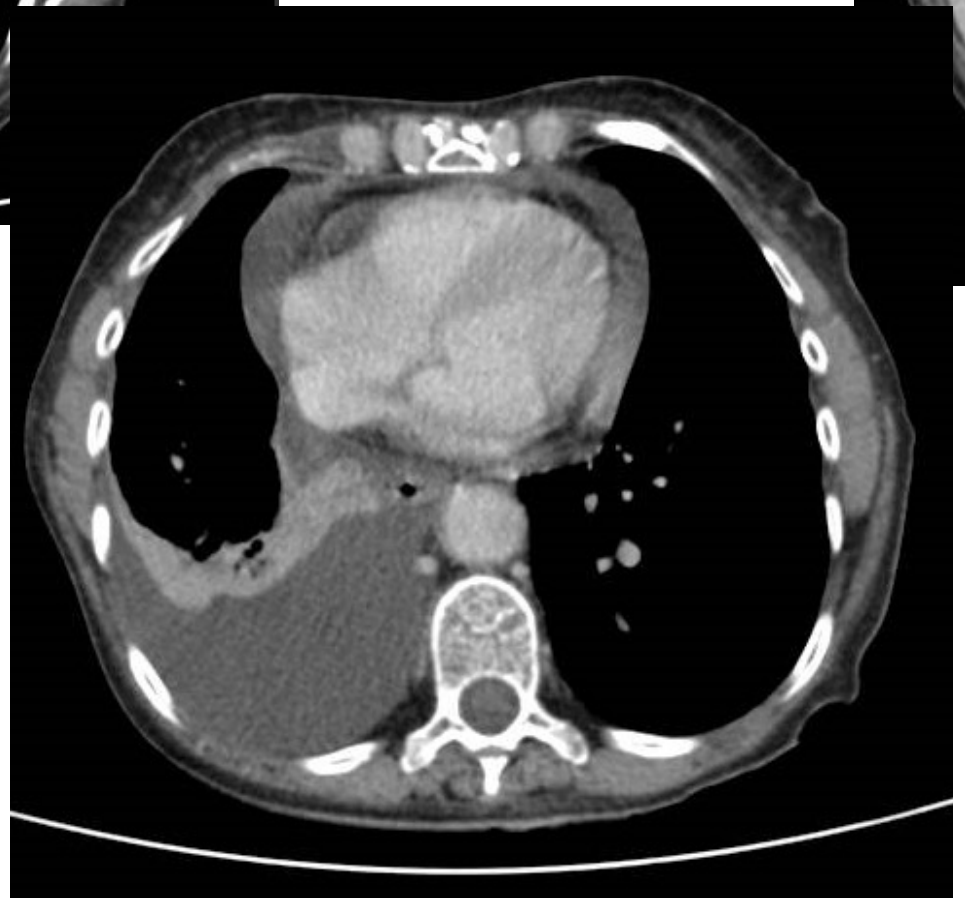
- June 2020:
  - Increased cough and dyspnea for 3 months
  - Asthenia, hyporexia
  - DX: Stage IV SCLC RUL
    (lung, mediastinal, pleural, pericardial, abdominal)

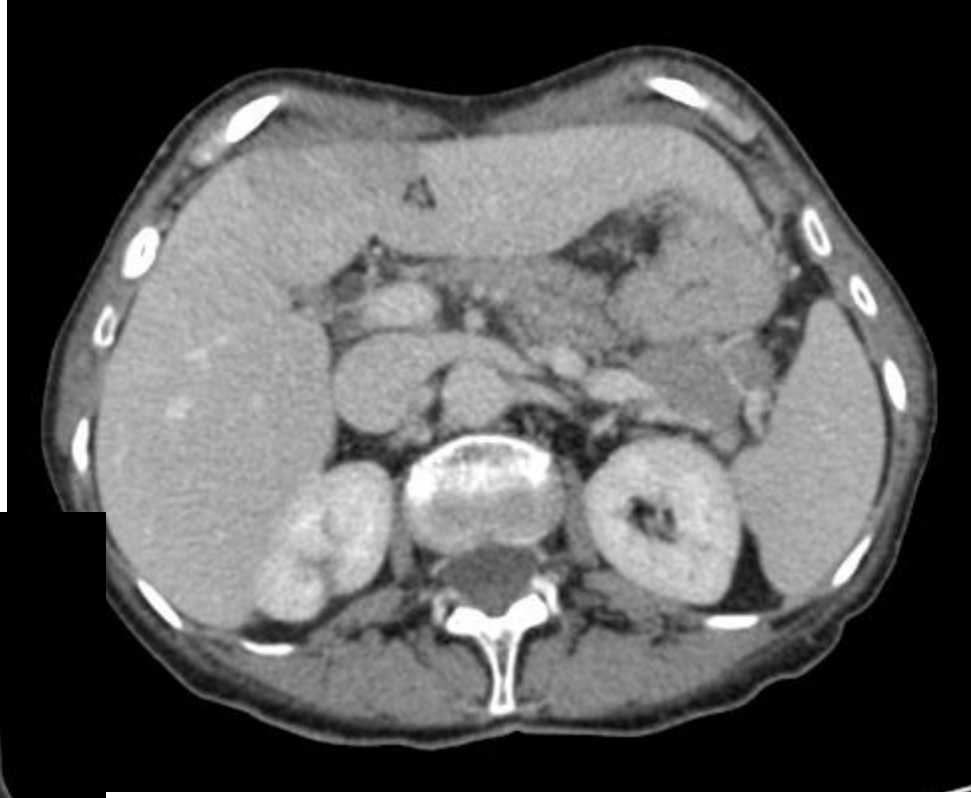
Case Presentation – Dr Paz-Ares: A 69-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/atezolizumab (continued)

June 2020 - Baseline









Courtesy of Luis Paz-Ares, MD, PhD

Case Presentation – Dr Paz-Ares: A 69-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/atezolizumab (continued)

- 69 yo female
- PMH
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- June 2020:
  - Increased cough and dyspnea for 3 months
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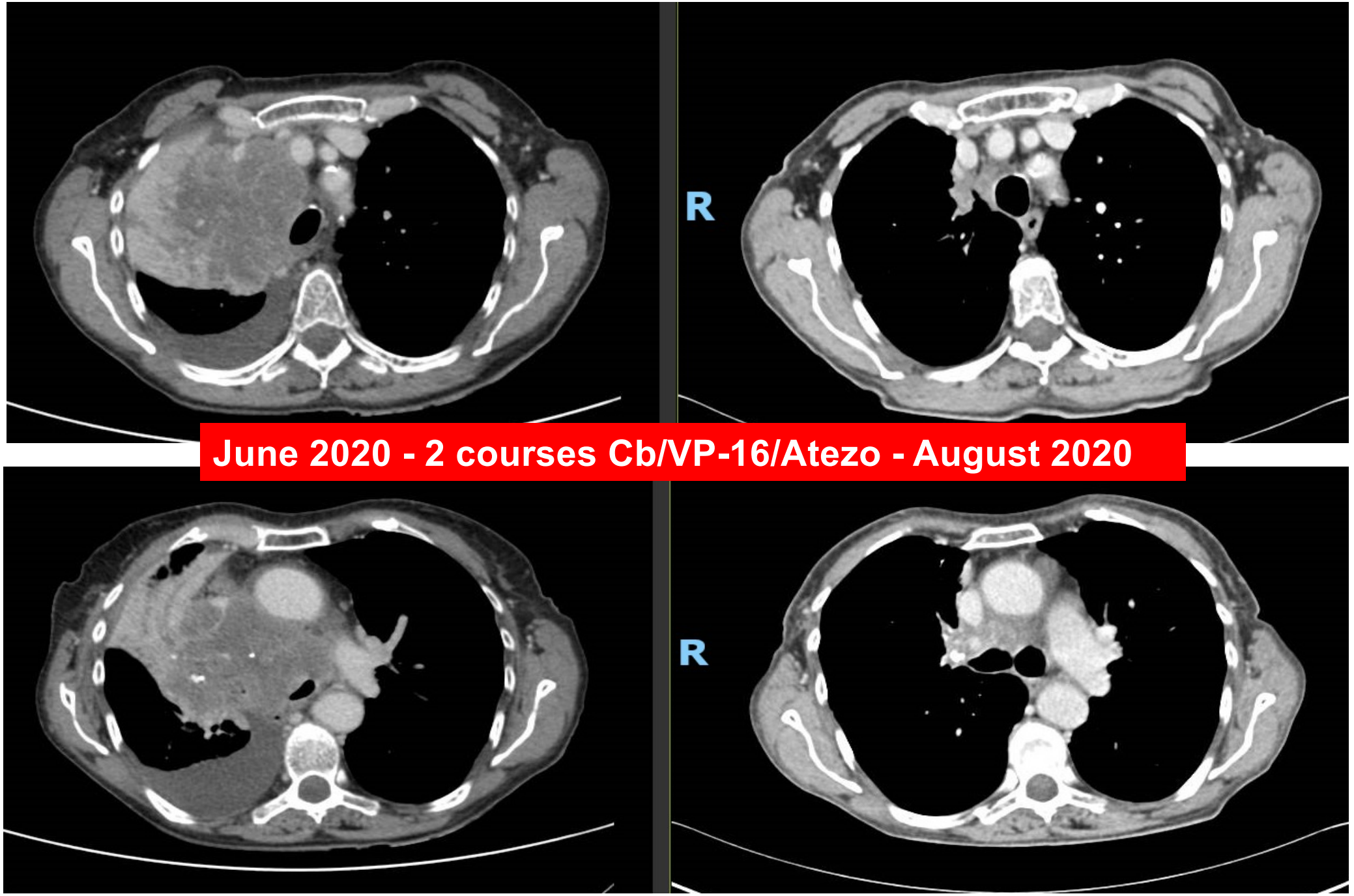
  - DX: Stage IV SCLC RUL
    (lung, mediastinal, pleural, pericardial, abdominal)

- **What would be your treatment proposal?**



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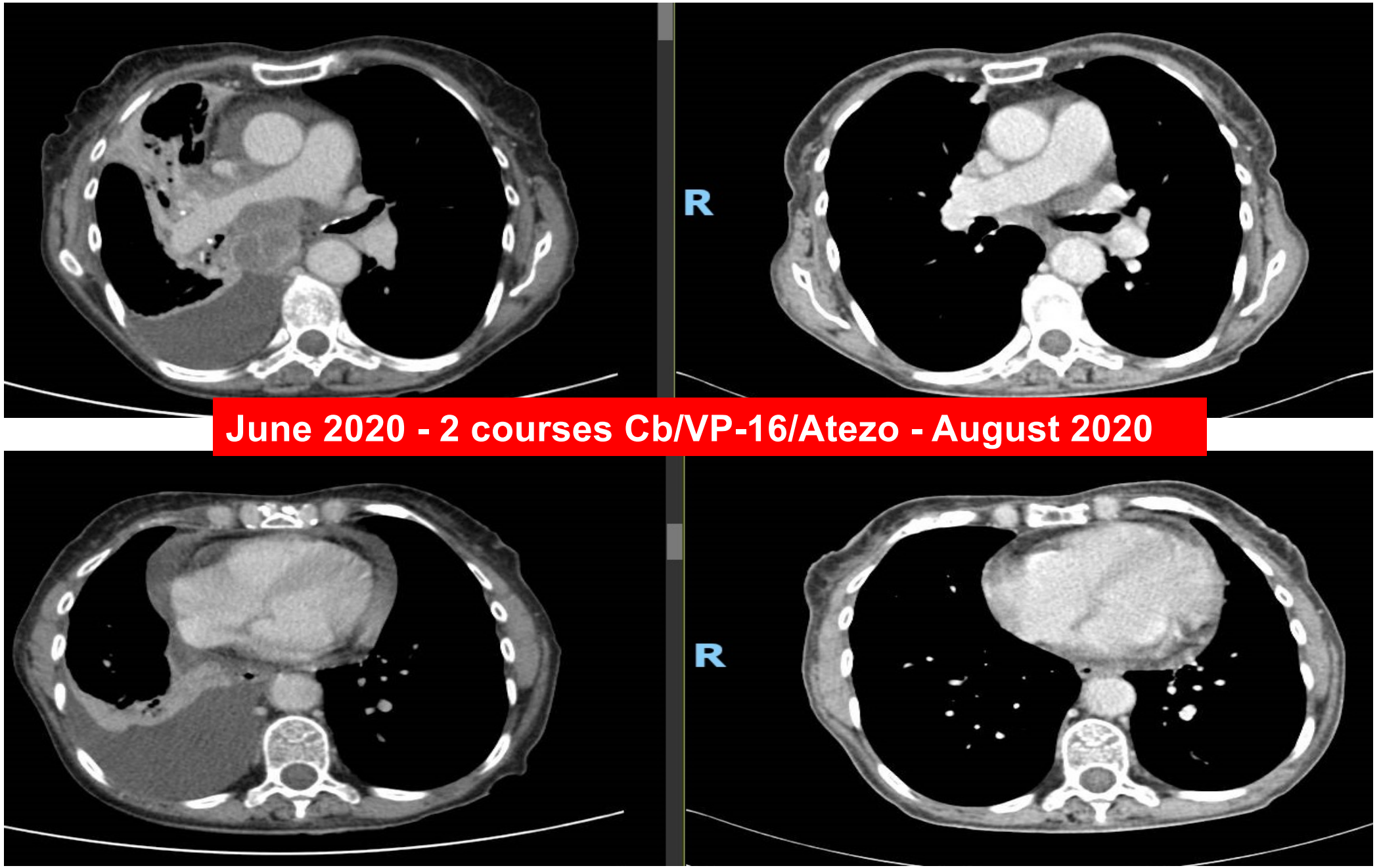

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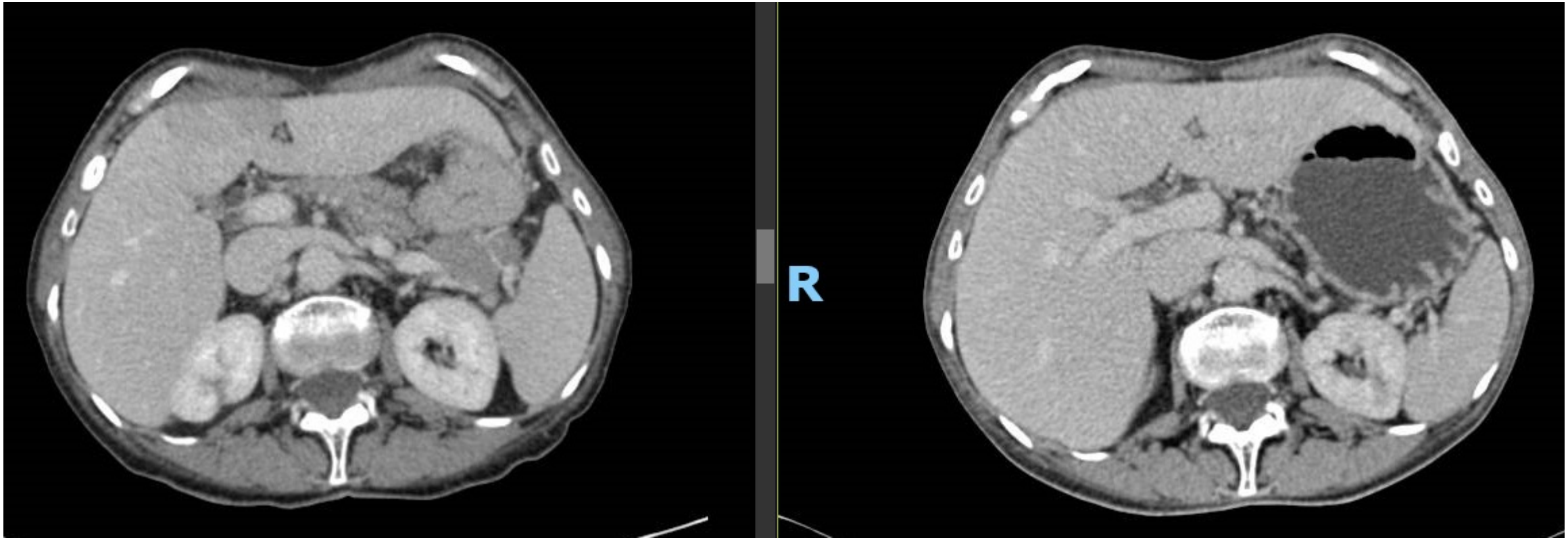
Case Presentation – Dr Paz-Ares: A 69-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/atezolizumab (continued)

June 2020 - 2 courses Cb/VP-16/Atezo - August 2020



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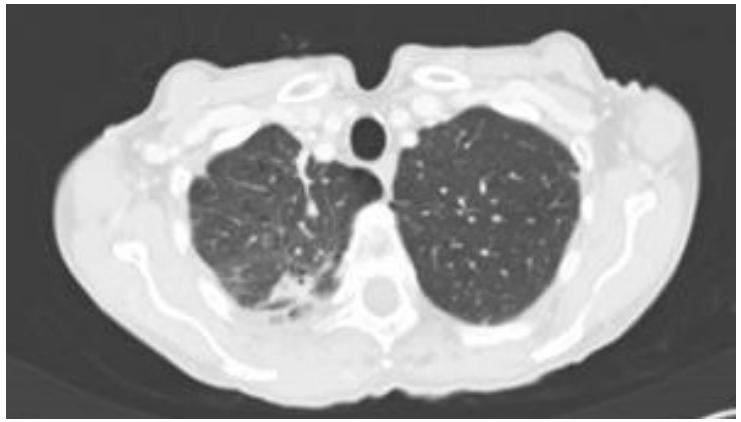
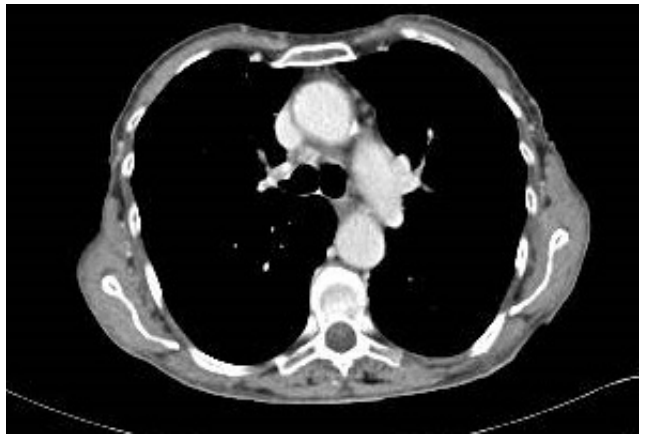
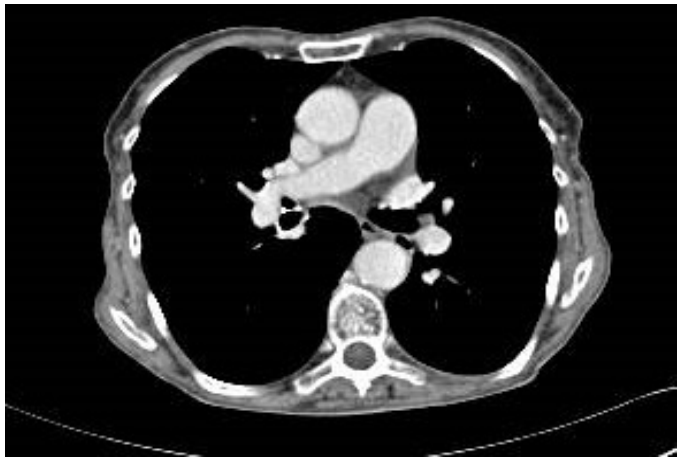
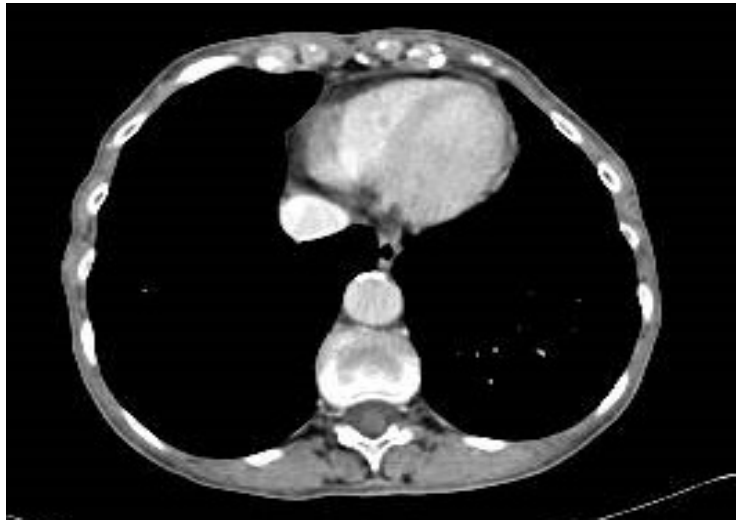
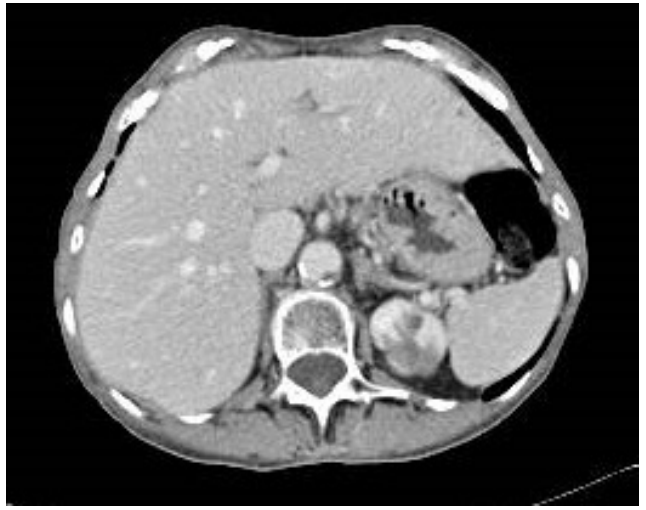
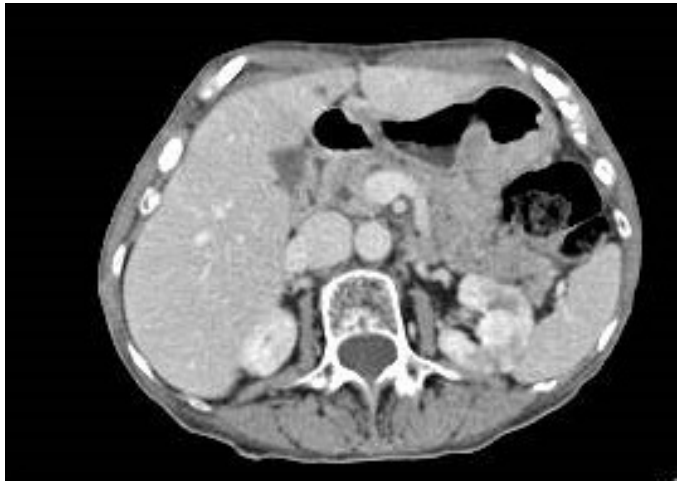
LAST CT Scan – Dec 2021

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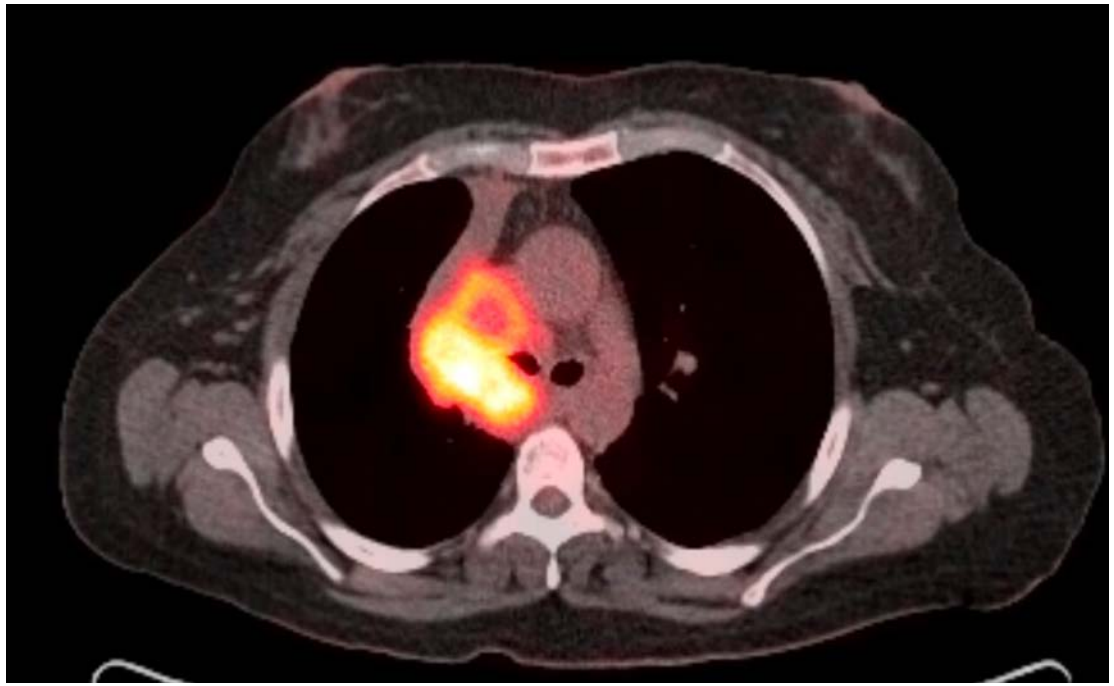
Case Presentation – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab

- A 46-year-old woman with 40 pack-year smoking history who presented to the ER with acute increase in chronic dyspnea and cough.
- Imaging demonstrated bulky central chest mass, as well as post-obstructive pneumonia. MRI brain negative for metastases.
- She was admitted to the hospital and antibiotics were started, resulting in partial improvements in her symptoms.
- PS is 1. PMH = COPD.
- Bronch/EBUS showed SCLC.
- PET demonstrated spread to contralateral lung and to liver.



Courtesy of Jared Weiss, MD

For consideration

What should be done next to palliate her dyspnea?

Airway stent

XRT

Chemotherapy

Oxygen and morphine

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab (continued)

- The patient was treated with carboplatin and etoposide. Her physician tried to order durvalumab, but it was not in inpatient formulary.
- Cough and SOB improved rapidly. The patient was discharged on the 7th hospital day.
- She returned to clinic two weeks later. Her dyspnea and cough were further improved, but she complained of:
  - Fatigue, now napping twice per day, but still able to perform her ADLs and IADLs.
  - Anorexia. Not eating as much as her family would like.
  - Nausea, partially relieved with ondansetron.

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab (continued)

- Fatigue
  - Patient was felt to be mildly hypovolemic. NS given by IV, patient asked to increase hydration PO, and a followup visit made for 1 week to reassess and for possible additional IVF.
  - Patient advised to increase activity, as tolerated.
  - Nutrition mgmt. as below.
- Anorexia
  - Nutrition consulted and advised patient to pursue small, more frequent meals.
  - Dietary counseling offered.
  - Dronabinol prescribed.
- Nausea
  - On questioning, constipation was elicited. Ca checked and was OK.
  - Patient hydrated as above.
  - Docusate and senna started twice per day.
  - Patient advised the ondansetron can be constipating. Given prochlorperazine to try in place of or in addition, as needed.
- Palliative care consulted. They provided many useful recommendations, including recognition of depression resulting in a referral to counseling.

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab (continued)

- The Patient's symptoms improved with additional supportive care.
- C2 was administered with the addition of durvalumab. Followup imaging planned for prior to a theoretical third cycle.

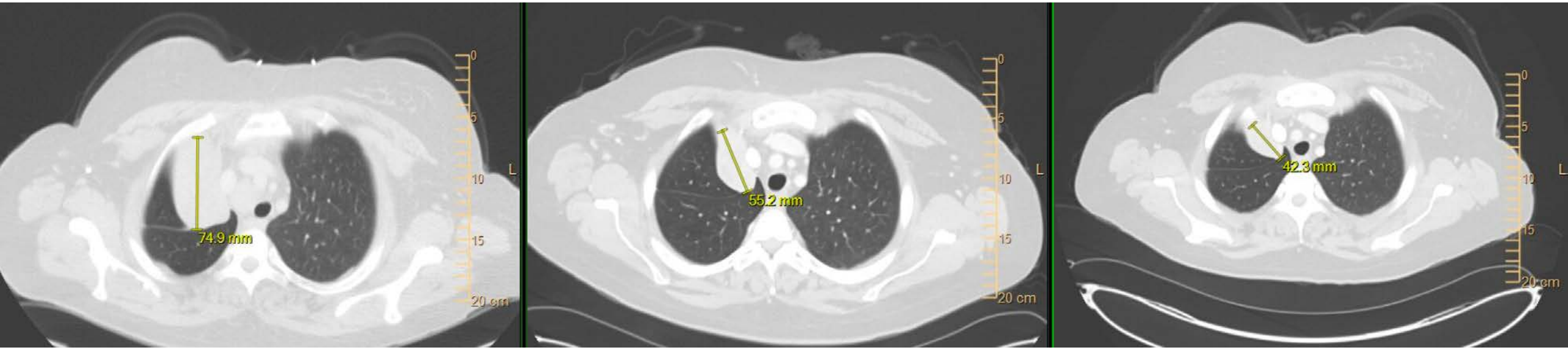
Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab (continued)

Pre C1

Pre C3

Post C4



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- Laboratory results prior to C4 demonstrated a TSH of 20, FT4 0.5. Cortisol wnl.
- On ROS, the only possibly attributable symptoms were fatigue and constipation, but the extent to which hypothyroidism contributed to these was not clear.
- Patient started on 1ug/kg levothyroxine.
- C4 and maintenance C1-2 went well. Fatigue increased.
- Followup imaging showed additional minor response. The patient initiated maintenance durvalumab. TSH decreased to 10; levothyroxine increased. Recheck planned for 6 weeks later.

Courtesy of Jared Weiss, MD

Side Effects

How much toxicity does the PDL1 inhibitor add?

What are the most common AEs?

What are the most common irAEs?

	Durvalumab + EP (n=265)		EP (n=266)	
	Any grade*	Grade 3 or 4	Any grade*	Grade 3 or 4
Any immune-mediated adverse event (grouped term), n (%)[†,‡]	52 (20%)	12 (5%)	7 (3%)	1 (<1%)
Hypothyroid events	24 (9%)	0	2 (1%)	0
Hyperthyroid events	14 (5%)	0	0	0
Pneumonitis	7 (3%)	2 (1%)	2 (1%)	1 (<1%)
Hepatic events	7 (3%)	5 (2%)	0	0
Dermatitis/rash	4 (2%)	0	2 (1%)	0
Diarrhoea/colitis	4 (2%)	1 (<1%)	1 (<1%)	0
Thyroiditis	4 (2%)	0	0	0
Type 1 diabetes mellitus	4 (2%)	4 (2%)	0	0
Adrenal insufficiency	1 (<1%)	0	0	0
Pancreatic events	1 (<1%)	1 (<1%)	0	0
Other rare/miscellaneous[§]	2 (1%)	0	0	0

	Durvalumab plus platinum–etoposide (n=265)		Platinum–etoposide (n=266)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Any event	260 (98%)	163 (62%)	258 (97%)	166 (62%)
Any serious event	82 (31%)	57 (22%)	96 (36%)	70 (26%)
Any event leading to discontinuation*	25 (9%)	7 (3%)	25 (9%)	7 (3%)
Any event leading to death†	13 (5%)	..	15 (6%)	..
Neutropenia	111 (42%)	64 (24%)	124 (47%)	88 (33%)
Anaemia	102 (38%)	24 (9%)	125 (47%)	48 (18%)
Nausea	89 (34%)	1 (<1%)	89 (33%)	5 (2%)
Alopecia	83 (31%)	3 (1%)	91 (34%)	2 (1%)
Constipation	44 (17%)	2 (1%)	51 (19%)	0
Decreased appetite	48 (18%)	2 (1%)	46 (17%)	2 (1%)
Thrombocytopenia	41 (15%)	15 (6%)	53 (20%)	25 (9%)
Fatigue	48 (18%)	4 (2%)	45 (17%)	3 (1%)
Vomiting	39 (15%)	0	44 (17%)	3 (1%)
Asthenia	40 (15%)	5 (2%)	40 (15%)	3 (1%)
Leucopenia	40 (15%)	17 (6%)	32 (12%)	14 (5%)
Dysphoea	31 (12%)	5 (2%)	28 (11%)	3 (1%)
Neutrophil count decreased	26 (10%)	17 (6%)	31 (12%)	17 (6%)
Diarrhoea	26 (10%)	3 (1%)	30 (11%)	3 (1%)
Cough	33 (12%)	2 (1%)	18 (7%)	0
Hyponatraemia	26 (10%)	10 (4%)	12 (5%)	7 (3%)
Febrile neutropenia	17 (6%)	14 (5%)	17 (6%)	17 (6%)
White blood cell count decreased	14 (5%)	4 (2%)	17 (6%)	6 (2%)
Platelet count decreased	16 (6%)	4 (2%)	14 (5%)	6 (2%)
Pneumonia	11 (4%)	5 (2%)	18 (7%)	9 (3%)
Hypertension	15 (6%)	8 (3%)	7 (3%)	1 (<1%)
Lipase increased	12 (5%)	9 (3%)	7 (3%)	4 (2%)
Amylase increased	11 (4%)	6 (2%)	2 (1%)	1 (<1%)

Paz-Ares, Lancet 2019

Courtesy of Jared Weiss, MD

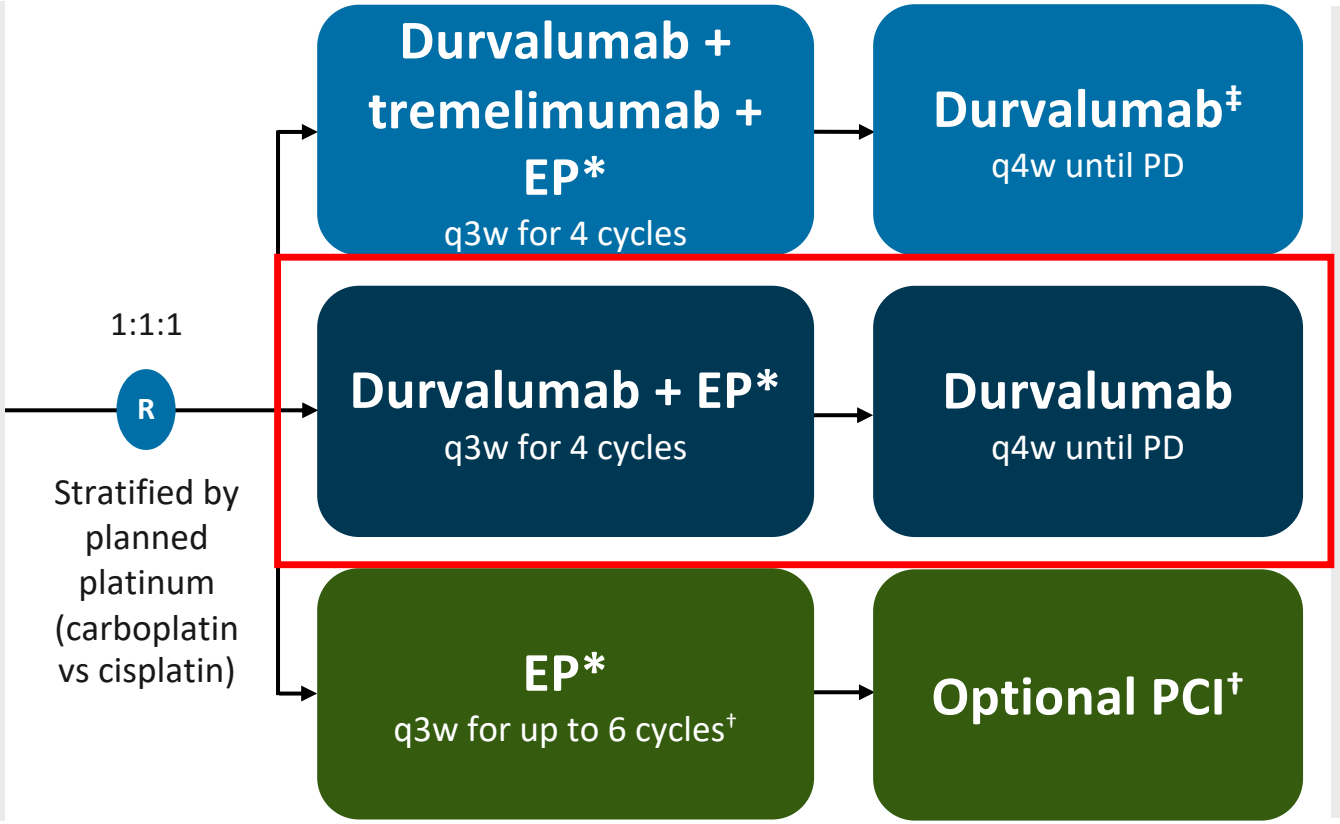
Key Relevant Data Sets

CASPIAN Study Design

Phase 3, global, randomized, open-label, active-controlled, multicentre study

- Treatment-naïve ES-SCLC
- WHO PS 0 or 1
- Asymptomatic or treated and stable brain metastases permitted
- Life expectancy ≥12 weeks
- Measurable disease per RECIST v1.1

N=805 (randomized)



Primary endpoint

- OS

Secondary endpoints

- PFS §
- ORR §
- Safety & tolerability
- PROs

*EP consists of etoposide 80–100 mg/m2 with either carboplatin AUC 5–6 or cisplatin 75–80 mg/m2, durvalumab dosed at 1500 mg, tremelimumab dosed at 75 mg
†Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion
‡Patients received an additional dose of tremelimumab post-EP; §By investigator assessment per RECIST v1.1
AUC, area under the curve; ORR, objective response rate; PCI, prophylactic cranial irradiation; PD, disease progression; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1

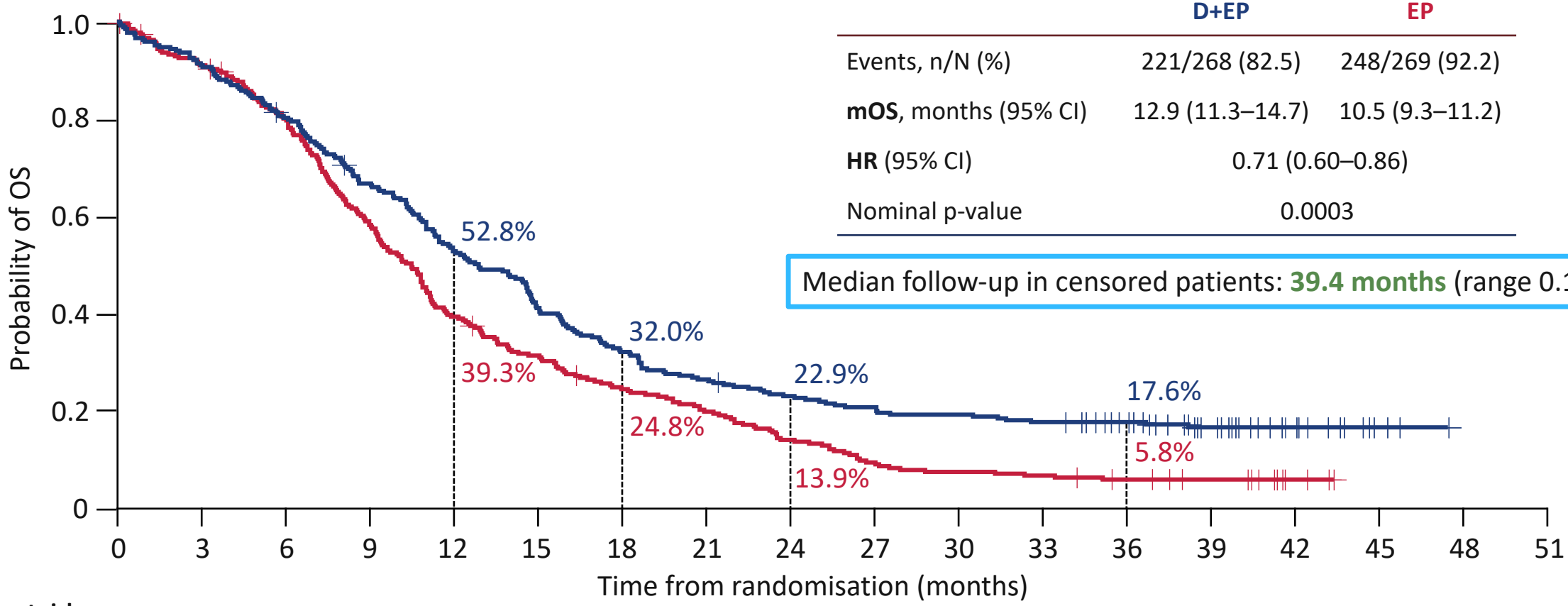
Paz-Ares L, et al. Oral presentation at ASCO 2020; abstract 9002.

Courtesy of Luis Paz-Ares, MD, PhD

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

	D+EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3–14.7)	10.5 (9.3–11.2)
HR (95% CI)	0.71 (0.60–0.86)	
Nominal p-value	0.0003	

Median follow-up in censored patients: **39.4 months** (range 0.1–47.5)



No. at risk

D+EP	268	244	214	177	140	109	85	70	60	54	50	46	39	25	13	3	0	0
EP	269	243	212	156	104	82	64	51	36	24	19	17	13	10	3	0	0	0

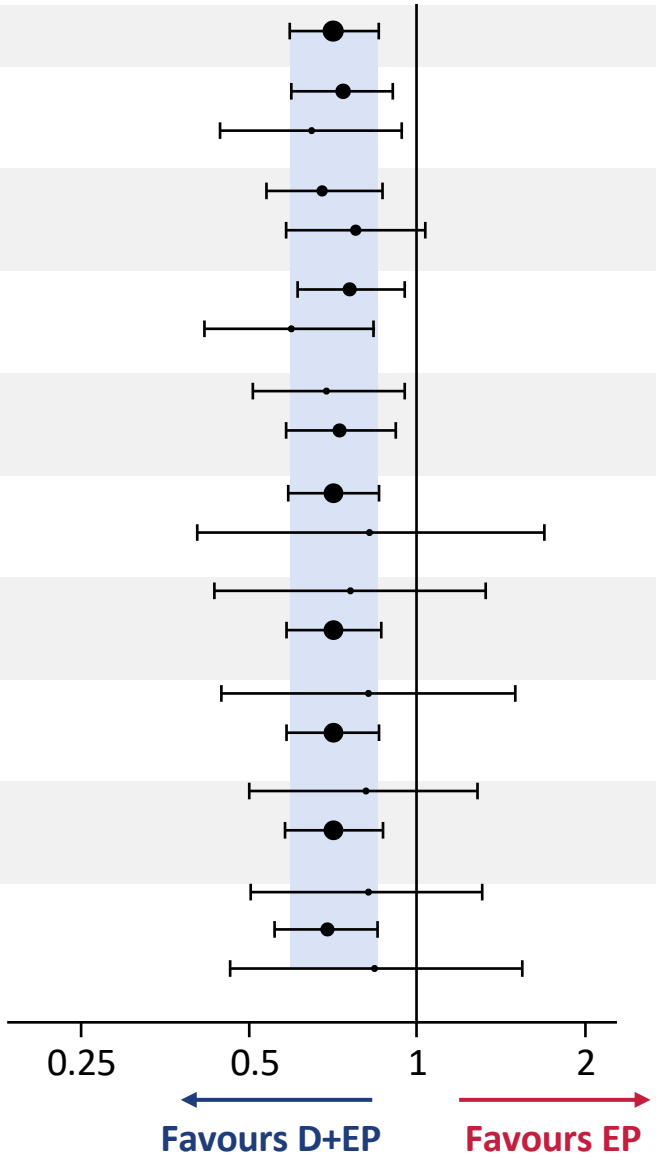
Data cutoff: 22 March 2021

Courtesy of Luis Paz-Ares, MD, PhD

Paz-Ares et al. ESMO 2021

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

		HR (95% CI)
All patients (n=537)		0.71 (0.60–0.86)
Planned platinum agent	Carboplatin (n=402)	0.74 (0.60–0.91)
	Cisplatin (n=135)	0.65 (0.45–0.94)
Age	<65 years (n=324)	0.68 (0.54–0.87)
	≥65 years (n=213)	0.78 (0.59–1.04)
Sex	Male (n=374)	0.76 (0.62–0.95)
	Female (n=163)	0.60 (0.42–0.84)
Performance status	0 (n=189)	0.70 (0.51–0.95)
	1 (n=348)	0.73 (0.58–0.92)
Smoking status	Smoker (n=500)	0.71 (0.59–0.86)
	Non-smoker (n=37)	0.82 (0.41–1.69)
Brain/CNS metastases	Yes (n=55)	0.76 (0.43–1.33)
	No (n=482)	0.71 (0.59–0.86)
AJCC disease stage at diagnosis	Stage III (n=52)	0.82 (0.45–1.49)
	Stage IV (n=485)	0.71 (0.59–0.86)
Race	Asian (n=78)	0.81 (0.50–1.28)
	Non-Asian (n=458)	0.71 (0.58–0.87)
Region	Asia (n=76)	0.82 (0.51–1.31)
	Europe (n=405)	0.69 (0.56–0.85)
	North and South America (n=56)	0.84 (0.46–1.54)



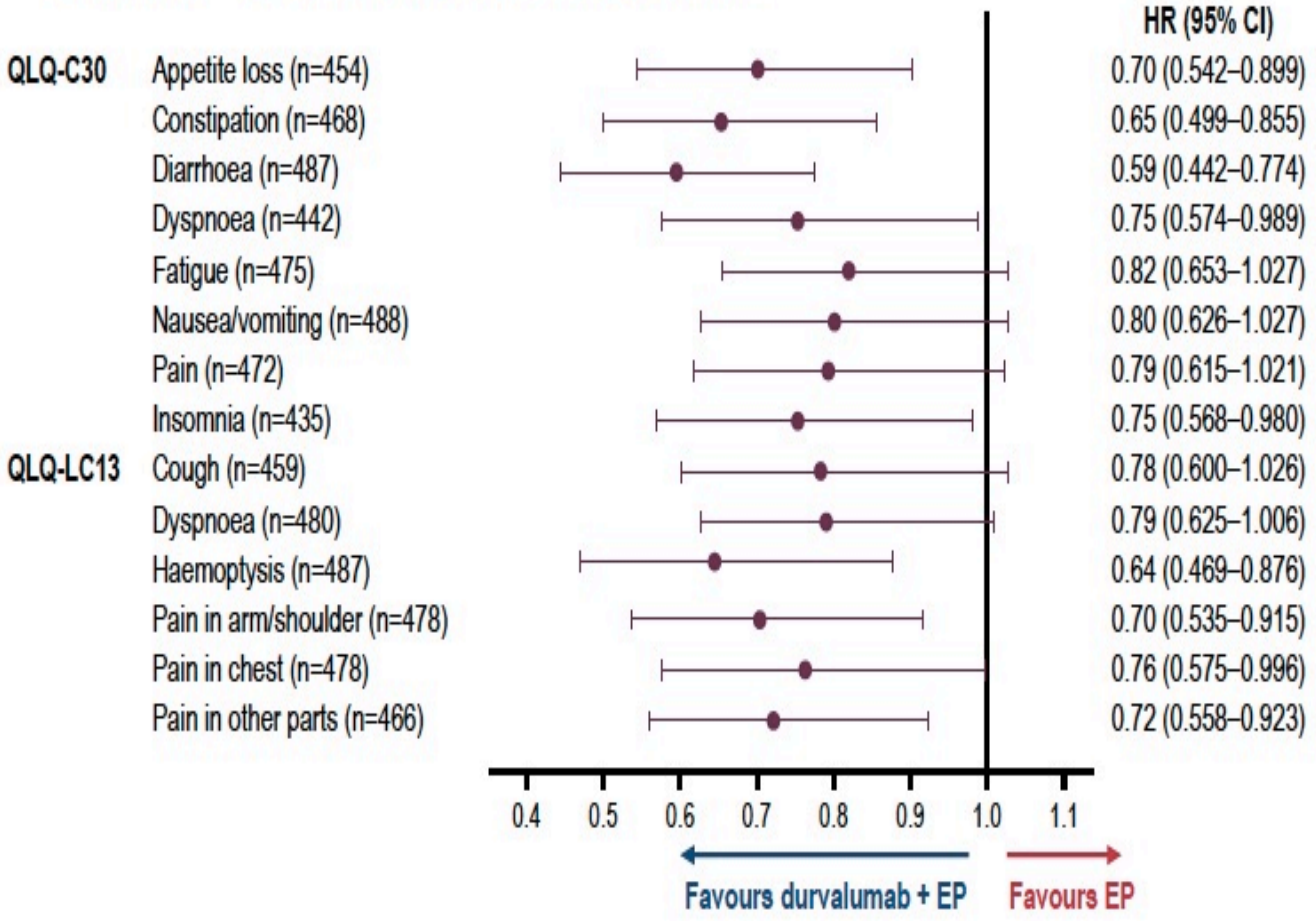
Data cutoff: 22 March 2021; Size of circle is proportional to the number of events across both treatment groups
AJCC, American Joint Committee on Cancer; CNS, central nervous system

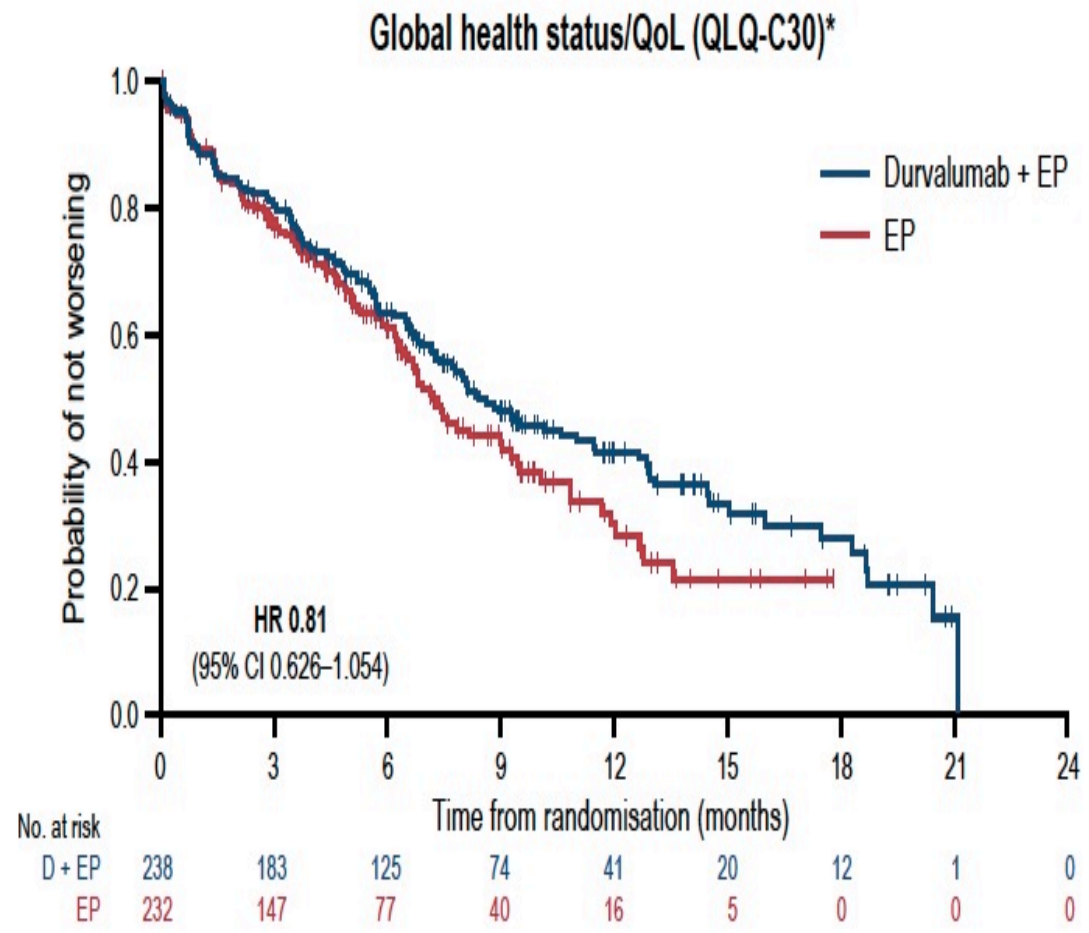
Courtesy of Luis Paz-Ares, MD, PhD

Paz-Ares et al. ESMO 2021

QoL

- Durvalumab + EP was favoured across all symptoms

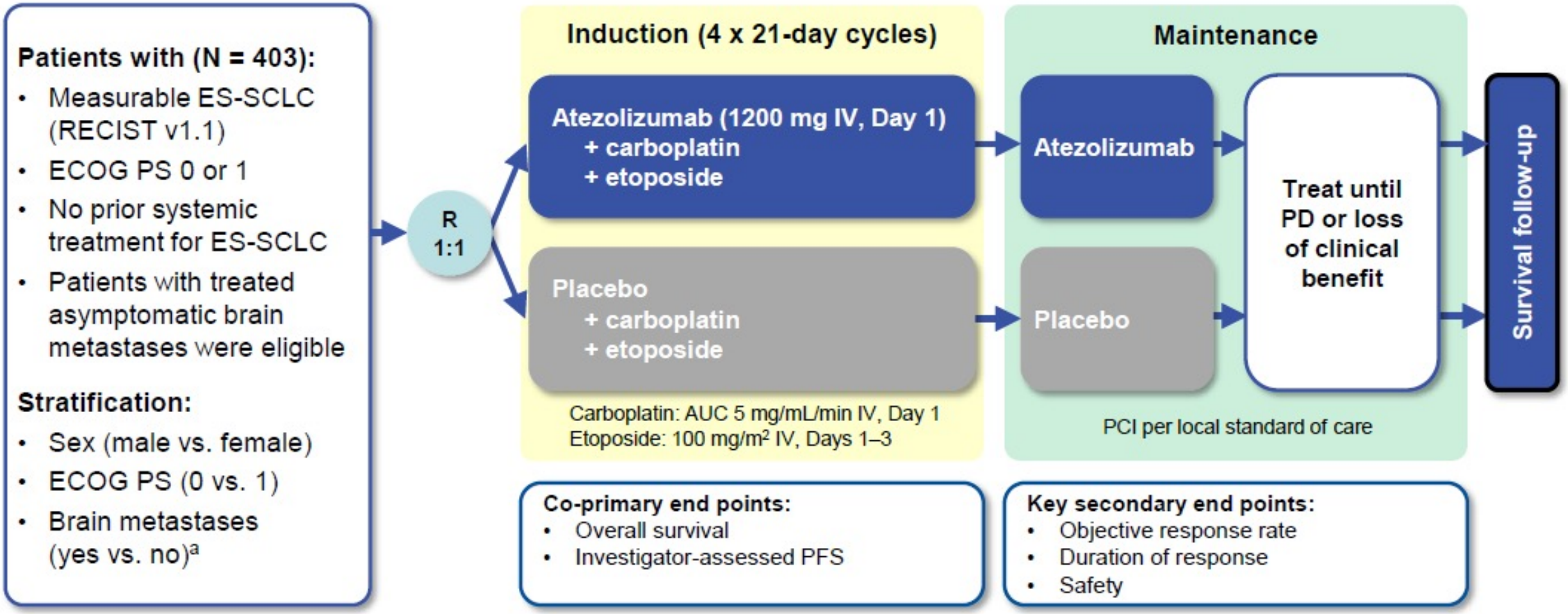




Goldman JW et al, Lancet Oncol 2021; 22:51-65.

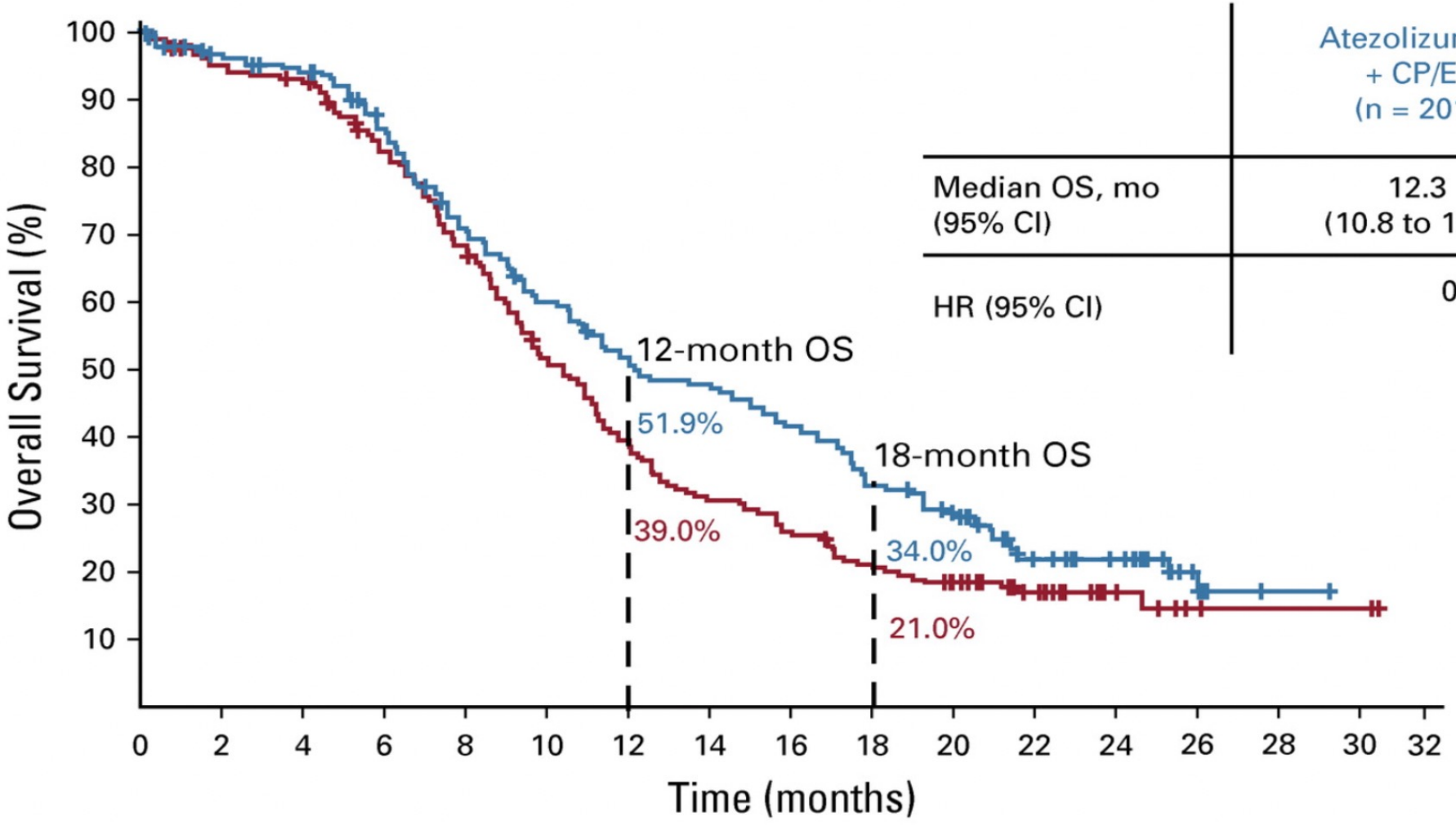
Courtesy of Luis Paz-Ares, MD, PhD

IMpower133



Courtesy of Luis Paz-Ares, MD, PhD

IMpower133: Updated Overall Survival



	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

Liu SV et al. JCO 2021(39; 6: 619-630)

IMpower133

Patients — no. (%)	Atezolizumab + CP/ET (N = 198)	Placebo + CP/ET (N = 196)
Patients with ≥ 1 AE	198 (100)	189 (96.4)
Grade 3–4 AEs	133 (67.2)	125 (63.8)
Treatment-related AEs[a]	188 (94.9)	181 (92.3)
Serious AEs	74 (37.4)	68 (34.7)
Immune-related AEs	79 (39.9)	48 (24.5)
AEs leading to withdrawal from any treatment[a]	22 (11.1)	6 (3.1)
AEs leading to withdrawal from atezolizumab/placebo	21 (10.6)	5 (2.6)
AEs leading to withdrawal from carboplatin	5 (2.5)	1 (0.5)
AEs leading to withdrawal from etoposide	8 (4.0)	2 (1.0)
Treatment-related deaths	3 (1.5)	3 (1.5)

- Median duration of treatment with atezolizumab was 4.7 months (range: 0 to 21)
- Median number of doses received:
  - Atezolizumab: 7 (range: 1 to 30)
  - Chemotherapy: 4 doses for carboplatin; 12 doses for etoposide (same for both treatment groups)

Courtesy of Luis Paz-Ares, MD, PhD

Liu, WCLC 2018

CASPIAN vs IMpower133

CASPIAN	IMpower133
• Free choice for platinum	• Only carboplatin
• Up to 6 cycles of CT	• Up to 4 cycles of CT
• Maintenance every 4 wks	• Maintenance every 3 wks
• PCI not allowed in ICI group	• PCI allowed
• 10% BM - untreated	• 9% BM - treated
• OS as primary endpoint	• OS and PFS co-primary
• Median OS 13 months	• Median OS 12.3 months
• Median PFS 5.1 months	• Median PFS 5.2 months
• AE grade ≥ 3: 62%	• AE grade ≥ 3: 58.1%

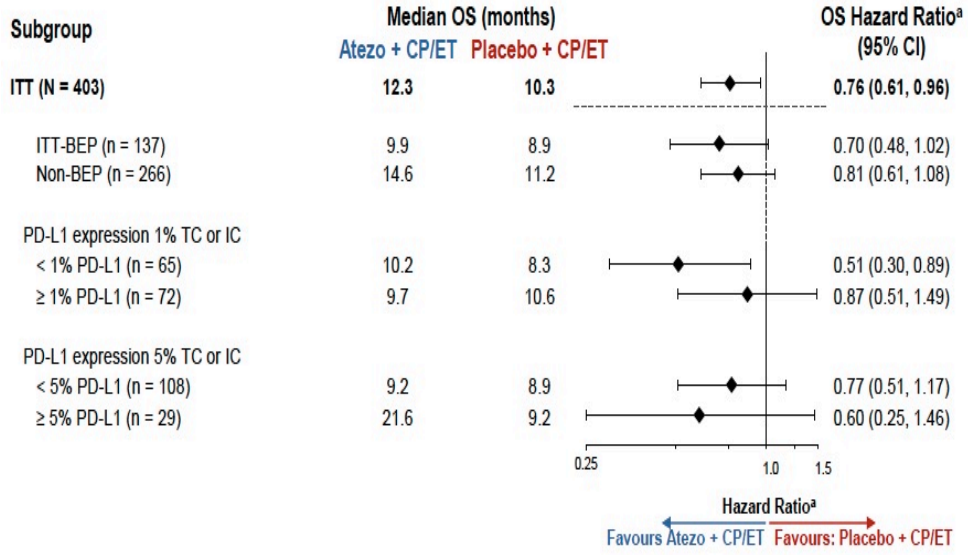
Paz-Ares L, et al. Lancet. 2019; 394: 1929-39.
Horn L, et al. N Engl J Med. 2018; 379: 2220-9.

Courtesy of Luis Paz-Ares, MD, PhD

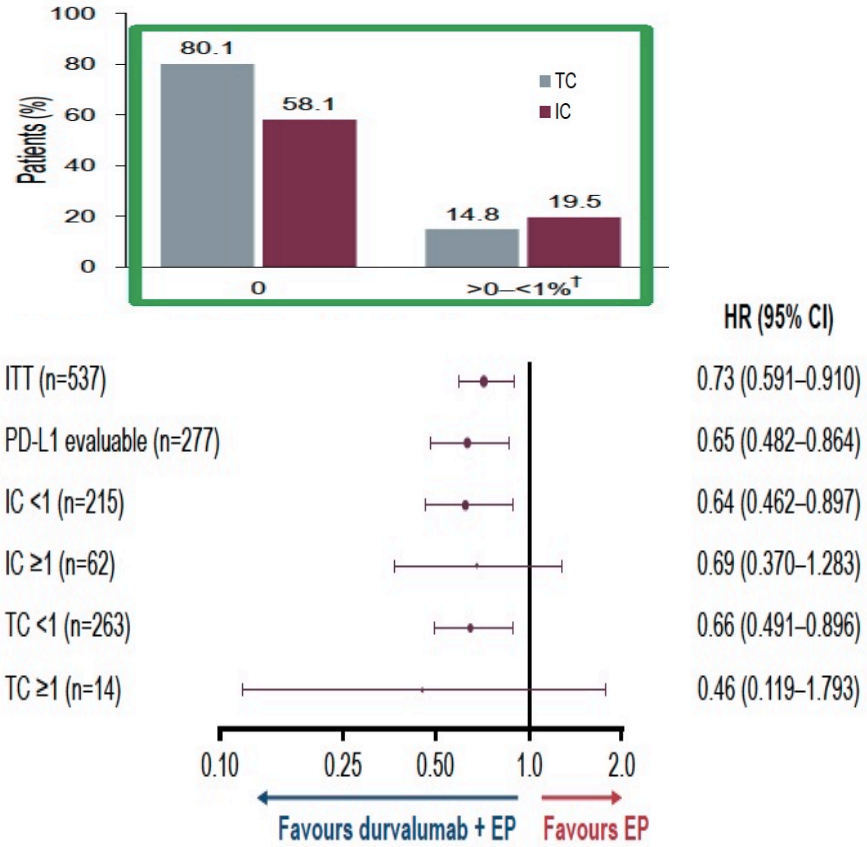
PD-L1 expression and outcome

IMpower133 PD-L1 (SP263) evaluable in 34% of ITT

PD-L1 IHC expression in ES-SCLC (n = 137)			
IC	% BEP (n)	TC	% BEP (n)
< 1%	49.6% (68)	< 1%	94.2% (129)
≥ 1%	50.4% (69)	≥ 1%	5.8% (8)



CASPIAN PD-L1 (SP263) evaluable in 59% of pts. in 3 arms



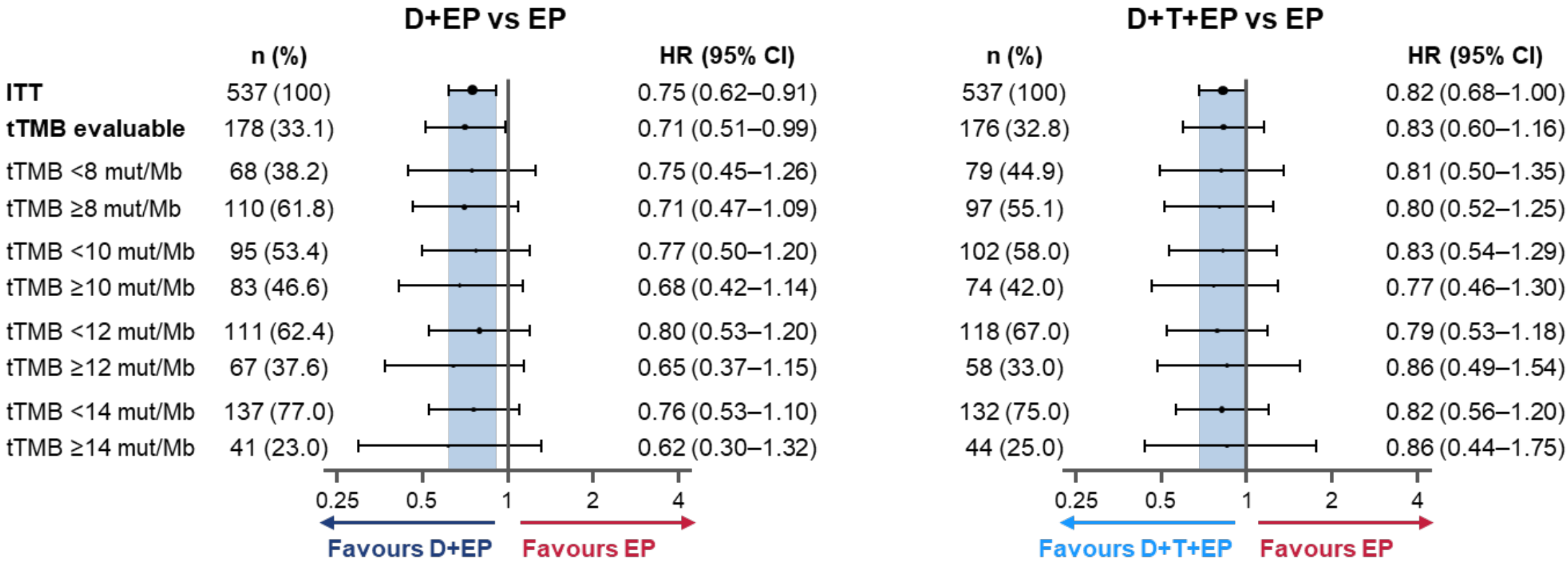
PD-L1 expression in TC is low and no significant interaction PD-L1 and outcome

- BEP, biomarker evaluable population; IC, immune cells; TC, tumor cells.
- Reck M, et al. Presented at: ESMO 2019; Abstract 2374. Paz-Ares, et al. Presented at: ESMO 2019; Abstract 3837.

Courtesy of Luis Paz-Ares, MD, PhD

CASPIAN: Overall survival based on tTMB

tTMB was not predictive of an improvement in OS for durvalumab ± tremelimumab + EP vs EP



CI, confidence interval; D, durvalumab; EP, platinum-etoposide; HR, hazard ratio; ITT, intent-to-treat; T, tremelimumab; tTMB, tissue tumour mutational burden.

Courtesy of Luis Paz-Ares, MD, PhD

Agenda

Case – Dr Paz-Ares: A 69-year-old woman with newly diagnosed extensive-stage small-cell lung cancer (ES-SCLC) who receives carboplatin/etoposide/atezolizumab

Case – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab

Case – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression

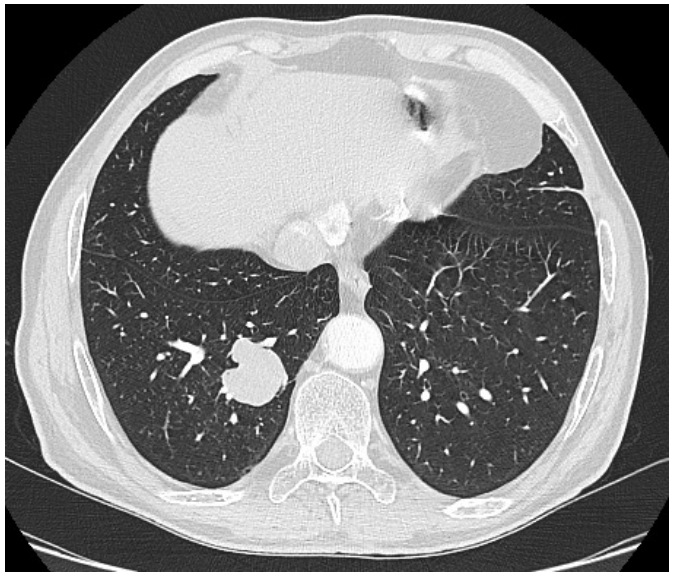
Case – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin

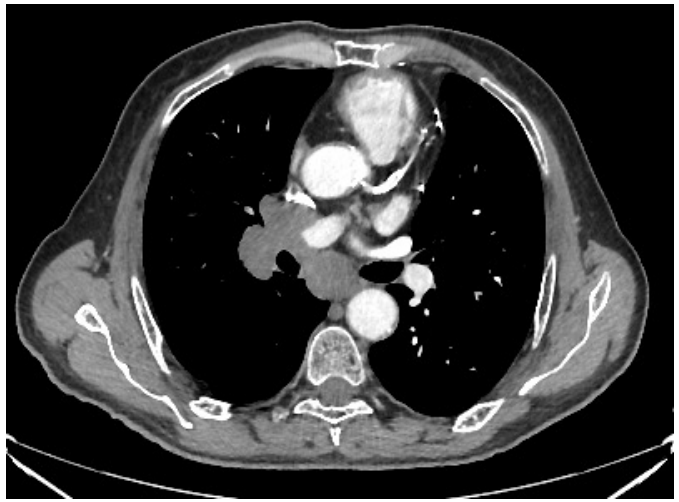
Case – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression

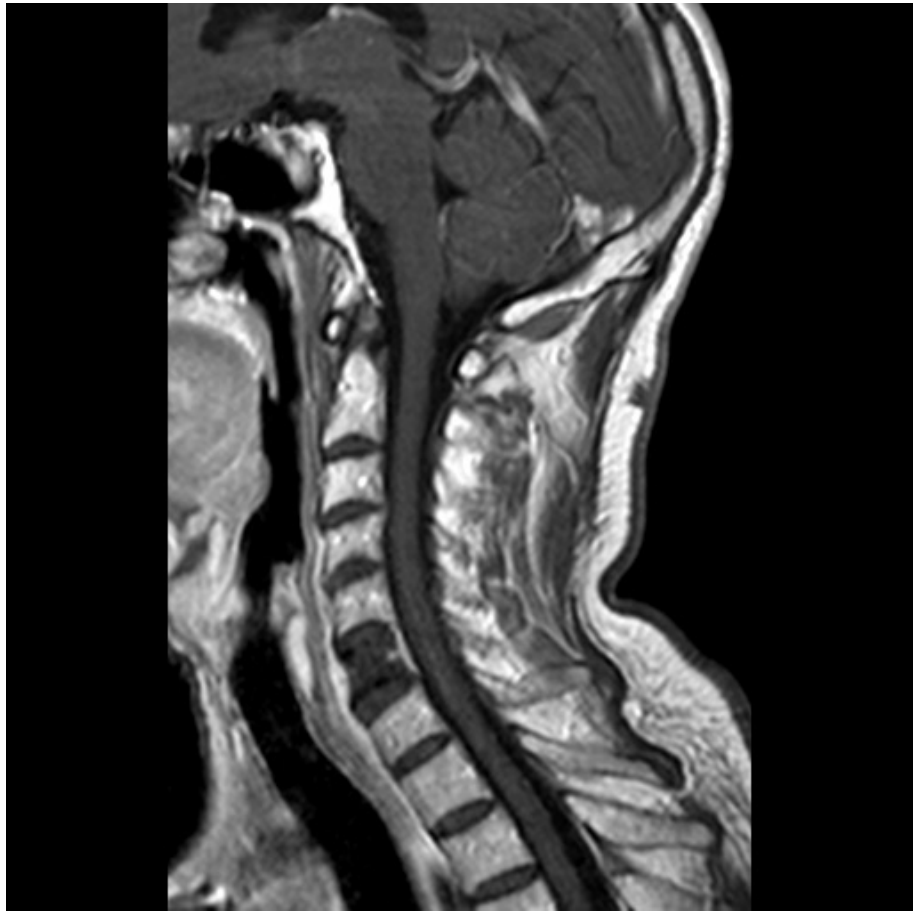
Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression

- 63 yo male
- PMH
  - Prior smoker (38 p/y)
  - HBP and dyslipemia
  - AF (Cardioverted, flecainide)
  - CAD – 3 vessel re-vascularization surgery in Aug 2009
- Jan 2018:
  - Cervical pain (2 months)
  - Stage IV SCLC of the RLL with spinal cord compression (C6)

Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)







Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)

- 63 yo male
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  - AF (Cardioverted, flecainide)
  - CAD – 3 vessel re-vascularization surgery in Aug 2009
- Jan 2018:
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  - Local hospital: **Radiation therapy (10 x 300 cGy)**

Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)

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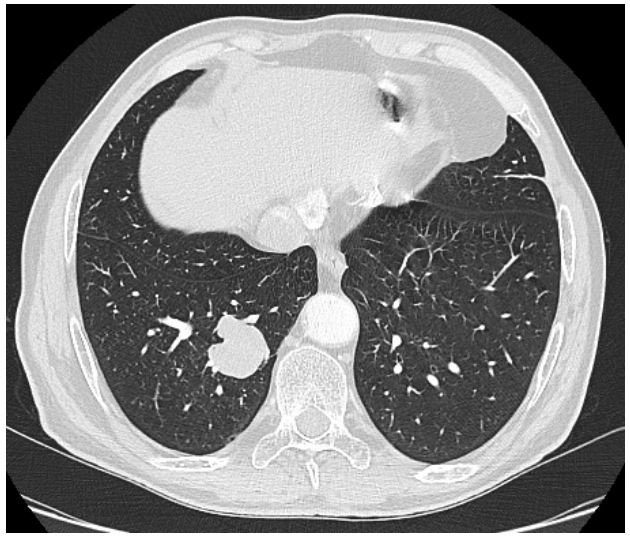
- Jan 2018:
  - Cervical pain (2 months)
  - Stage IV SCLC of the RLL with spinal cord compression (C6)
  - Local hospital: **Radiation therapy (10 x 300 cGy)**
- Feb 2018:
  - Second opinion at Hospital Universitario12 de Octubre
  - **What would be your recommendation?**

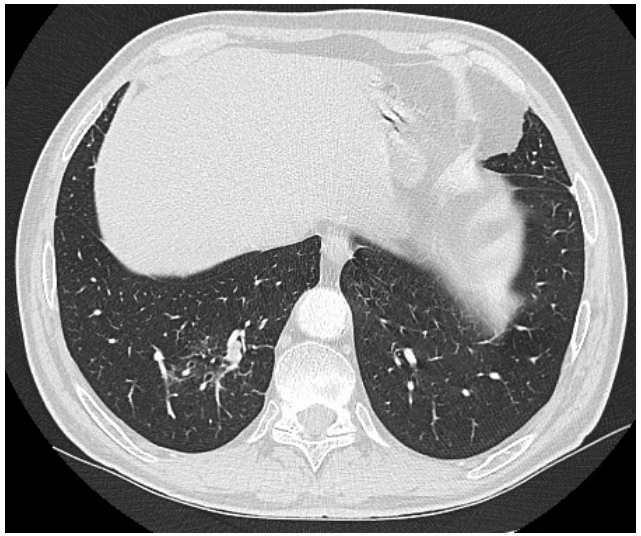
Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)



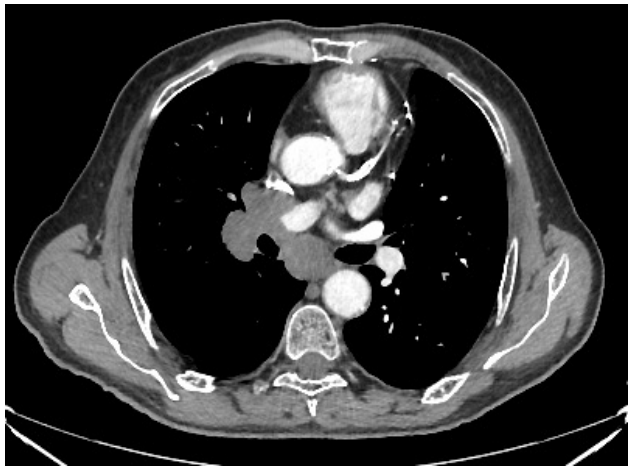
Feb 2018

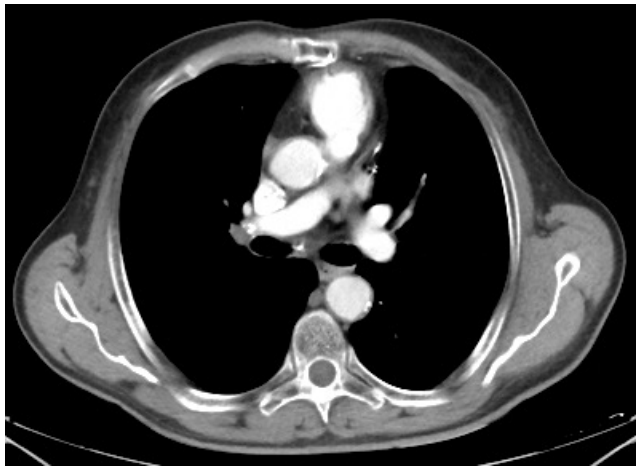
Carbo
Etoposide
Durva

2 courses

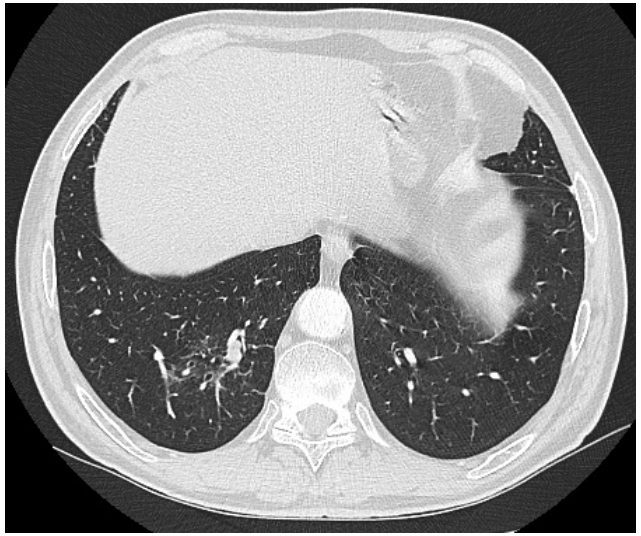


April 2018

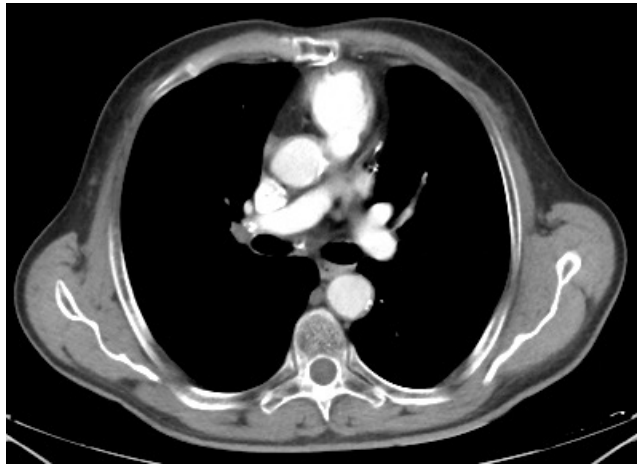




Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)

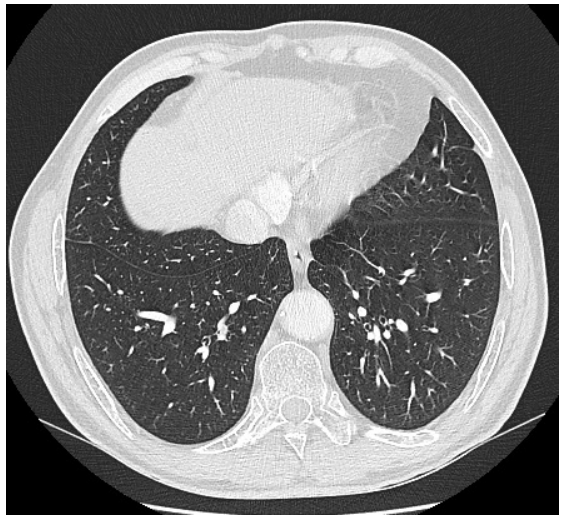


April 2018

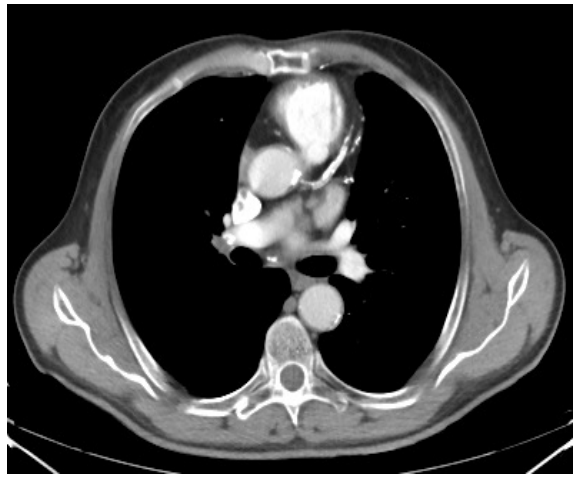


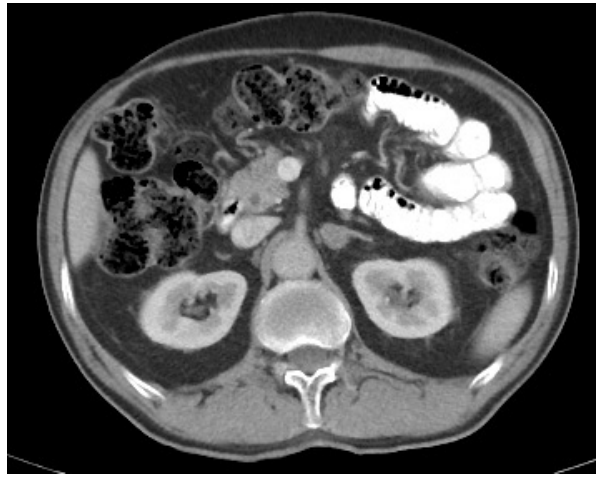
Carbo
Etoposide
Durva

14 courses

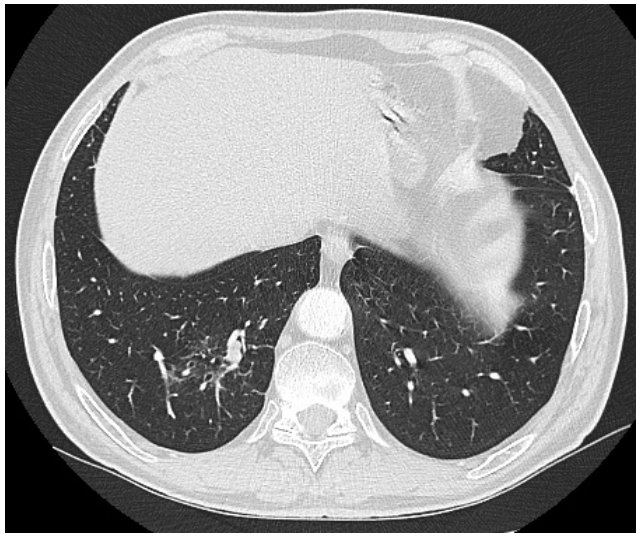


Feb 2019

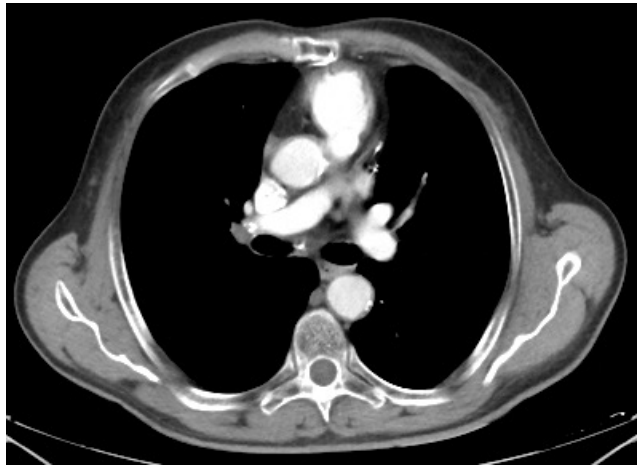




Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)

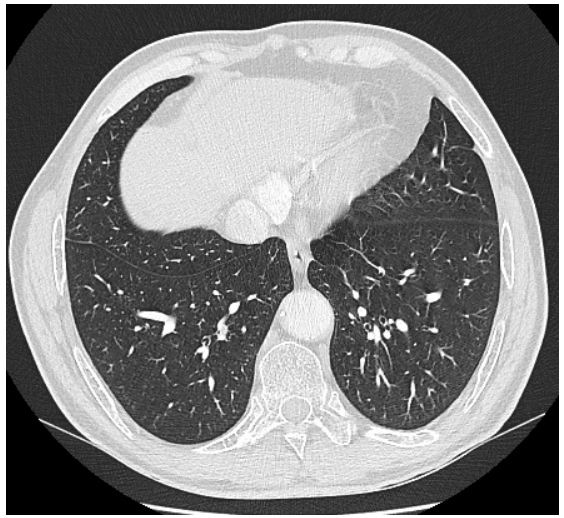


April 2018

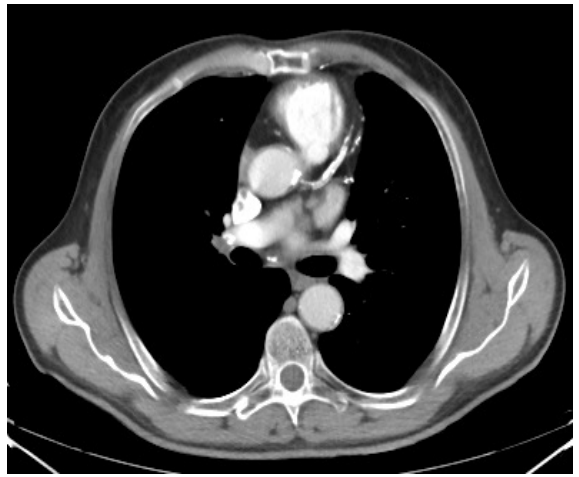


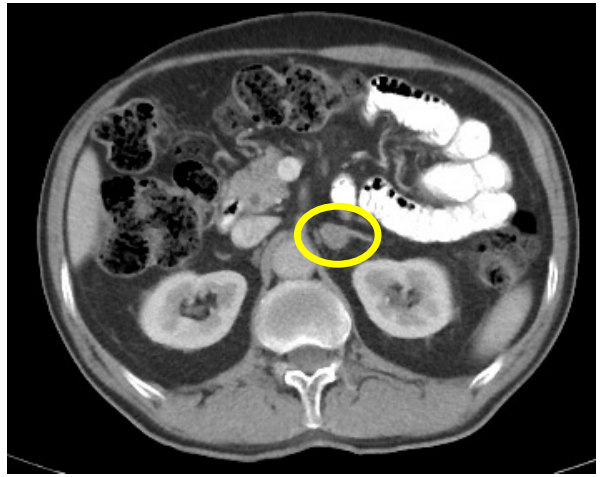
Carbo
Etoposide
Durva

2 courses



Feb 2019





PFS = 12 months

Case Presentation – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression (continued)

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- Jan 2018: Stage IV SCLC of the RLL with SCC
- Jan 2018: Local hospital: **Radiation therapy** (10 x 300 cGy)
- Feb 2018 – Feb 2019: **CASPIAN regimen x 14**
- March 2019 – June 2019: **Cb/VP-16 x 4**
- October 2019 – Jan 2022: **Lurbinectedin-Irinotecan x 36**

Response – PFS

PR - 12 m

SD - 4 m

PR - 27 m+

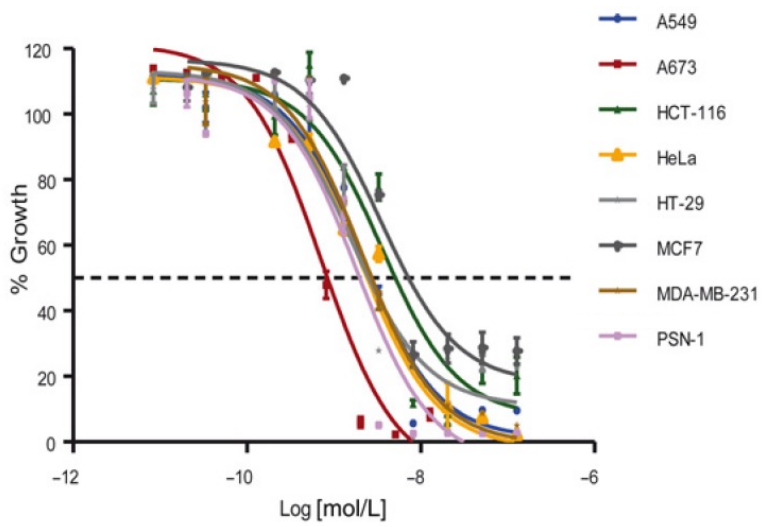
SURVIVAL: 46+ months

Key Relevant Data Sets

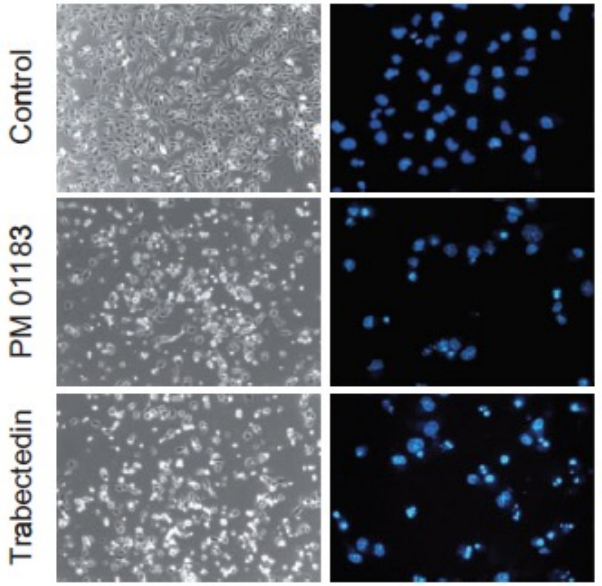
Lurbinectedin - Preclinical Antitumor Activity

Antitumor activity of lurbinectedin (PM01183) has been proven in several preclinical tumor models

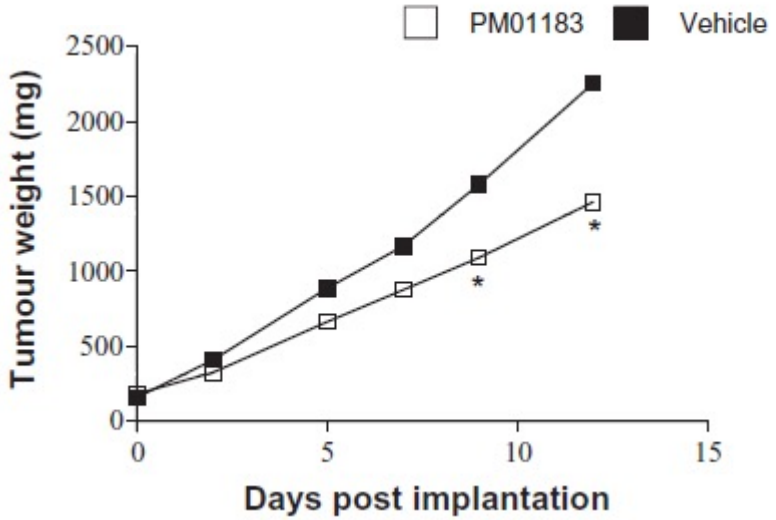
Lurbinectedin showed antiproliferative activity with IC_{50} values in the low nanomolar range in human lung (A549), Ewing sarcoma (A673), colon (HCT-116, HT-29), breast (MCF7, MDA-MB-231), cervix (HeLa), and pancreas (PSN-1) cancer cell lines[1]



Exposure of A549 lung cancer cells to 150 nM lurbinectedin for 24 hours induced cell death by apoptosis[2]



Lurbinectedin (0.18 mg/kg in 3 consecutive weekly doses) showed statistically significant inhibition of tumor growth *in vivo* in an NCI-H460 lung xenograft model compared with vehicle-treated animals[2]



1. Santamaría Nuñez G, et al. Mol Cancer Ther. 2016;15(10):2399-2412.

2. Leal JF, et al. Br J Pharmacol. 2010;161(5):1099-1110.

Courtesy of Luis Paz-Ares, MD, PhD

BASKET Trial - Lurbinectedin monotherapy Efficacy in Patients With SCLC

	All patients (n=105)	Chemotherapy-free interval <90 days (n=45)	Chemotherapy-free interval ≥90 days (n=60)
RECIST responses, %			
CR / PR / SD,* %	0 / 35 / 33	0 / 22 / 29	0 / 45 / 37
PD, %	27	40	17
Not evaluable,‡ %	5	9	2
Overall response, %	35.2	22.2	45.0
Disease control, %□	68.6	51.1	81.7
Duration of response			
Median DoR, months (95% CI)	5.3 (4.1–6.4)	4.7 (2.6–5.6)	6.2 (3.5–7.3)
Progression-free survival			
Median PFS, months (95% CI)	3.5 (2.6–4.3)	2.6 (1.3–3.9)	4.6 (2.8–6.5)
4-month PFS rate, %	46.6	29.1	59.9
6-month PFS rate, %	32.9	18.8	43.5
Overall survival			
Median OS, months (95% CI)	9.3 (6.3–11.8)	5.0 (4.1–6.3)	11.9 (9.7–16.2)
6-month OS rate, %	67.1	45.8	83.6
12 month OS rate, %	34.2	15.9	48.3

**Includes five patients with partial response not confirmed; ‡ five patients were not evaluable because they had no radiological assessment during treatment due to early death from malignant disease (n=2), symptomatic deterioration because of disease progression (n=2), and patient refusal (n=1); □ partial response or stable disease*

Median follow-up of 17.1 months (as of data cut-off January 15, 2019)

Courtesy of Luis Paz-Ares, MD, PhD

Trigo et al. Lancet Oncol 2020

BASKET Trial | Treatment-Related Adverse Events

	Grade 1–2	Grade 3	Grade 4
Haematological abnormalities (regardless of relation to study drug)*			
Anaemia	91 (87%)	9 (9%)	0
Leucopenia	53 (50%)	20 (19%)	10 (10%)
Neutropenia	27 (26%)	22 (21%)	26 (25%)
Thrombocytopenia	39 (37%)	3 (3%)	4 (4%)
Biochemical abnormalities (regardless of relation to study drug)*			
Creatinine†	86/104 (83%)	0	0
Alanine aminotransferase	69/103 (67%)	5/103 (5%)	0
γ-glutamyl transferase	52/103 (50%)	13/103 (13%)	2/103 (2%)
Aspartate aminotransferase	44/103 (43%)	2/103 (2%)	0
Alkaline phosphatase	31/103 (30%)	3/103 (3%)	0

Treatment-related adverse events			
Fatigue	54 (51%)	7 (7%)	0
Nausea	34 (32%)	0	0
Decreased appetite	22 (21%)	0	0
Vomiting	19 (18%)	0	0
Diarrhoea	13 (14%)	1 (1%)	0
Febrile neutropenia	0	2 (2%)	3 (3%)
Pneumonia	0	2 (2%)	0
Skin ulcer	0	1 (1%)	0

Data are n (%) of patients. NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. *Based on all patients with laboratory data available. †Version 4.0 of NCI-CTCAE grades any creatinine increases from baseline as abnormalities, even if creatinine values remain within the normal range.

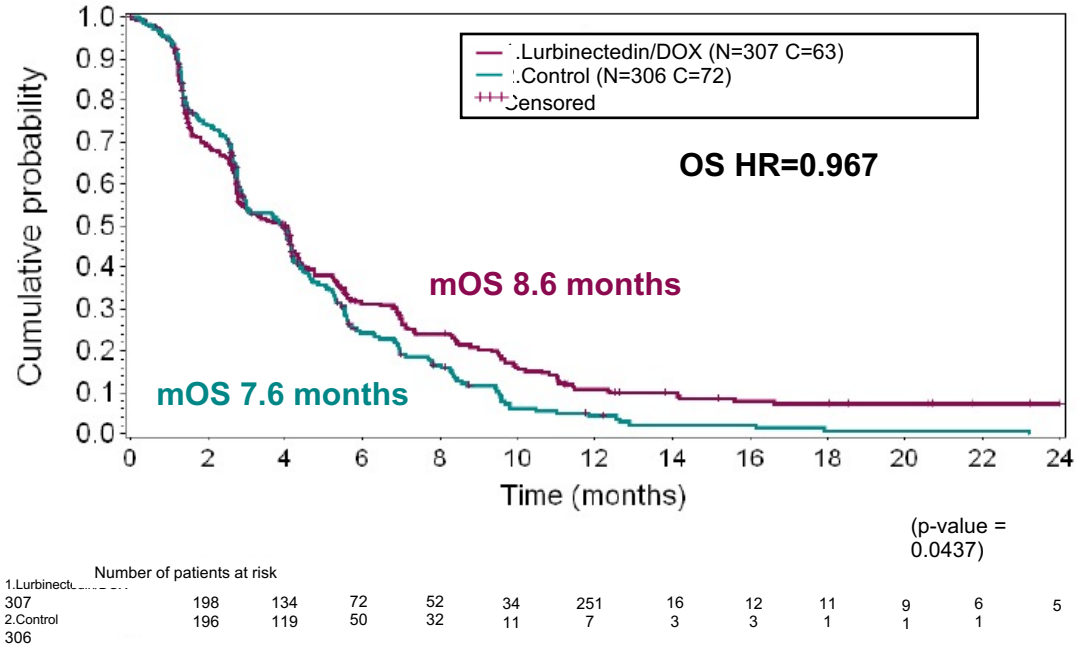
***Table 3:* Most common NCI-CTCAE laboratory abnormalities and treatment-related adverse events**

Trigo J, et al. Lancet Oncol. 2020;21(5):645-654

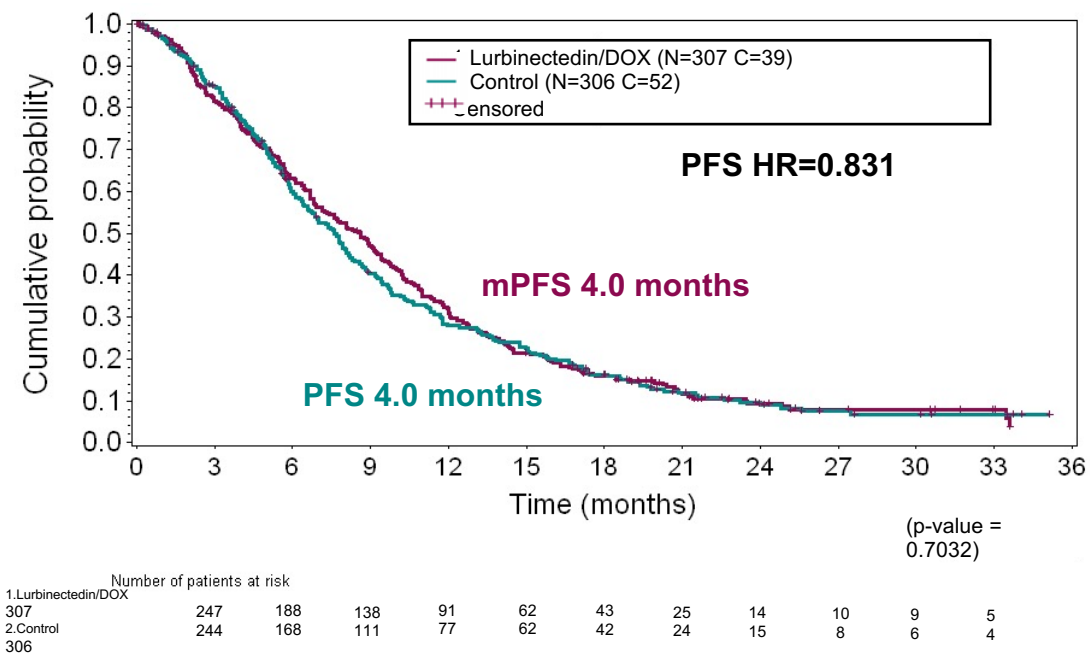
Courtesy of Luis Paz-Ares, MD, PhD

ATLANTIS Trial | Lurbinectedin + Doxorubicin
Overall Survival and Progression-free Survival

Overall Survival



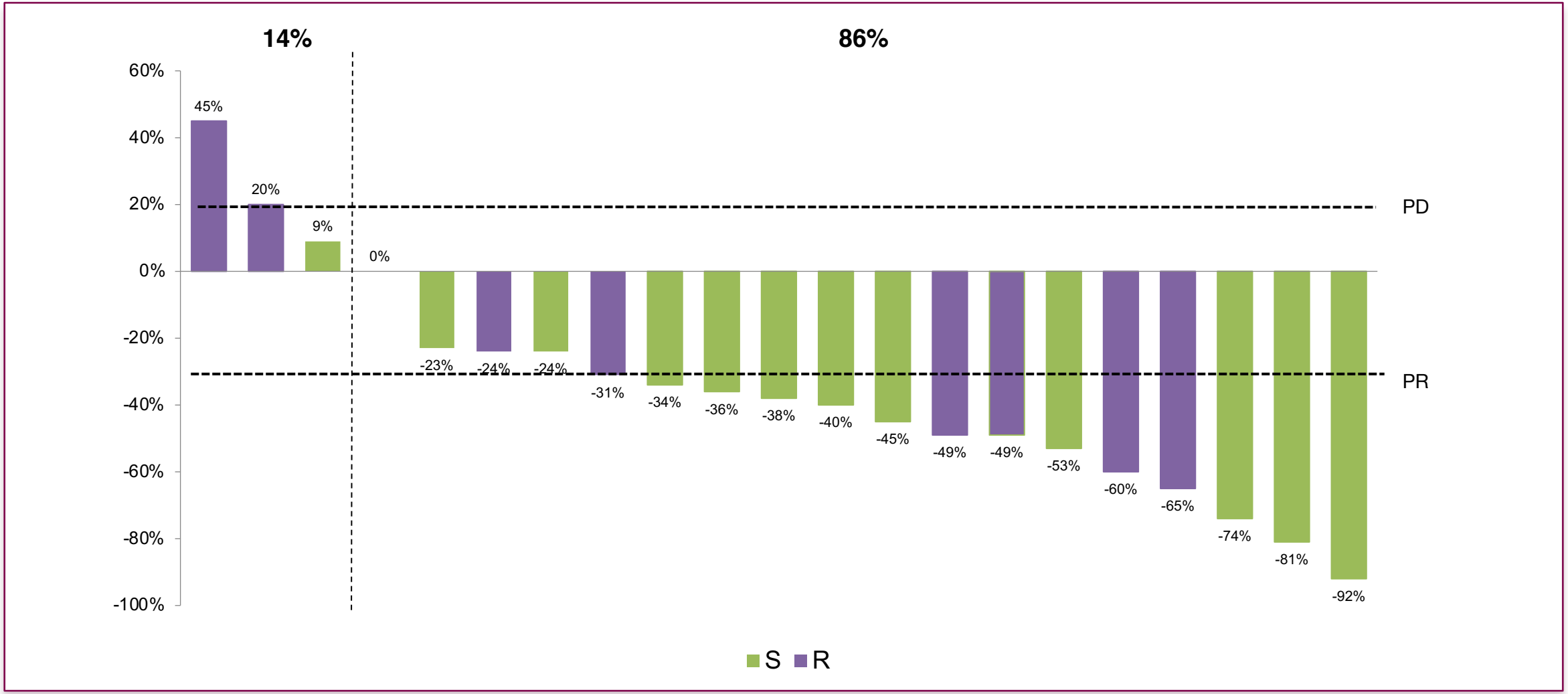
Progression-free Survival



- *Paz-Ares et al. WCLC 2021 (PL02.03)*

Courtesy of Luis Paz-Ares, MD, PhD

Phase 1b/2 Trial | Lurbinectedin + Irinotecan Efficacy in the SCLC Cohort

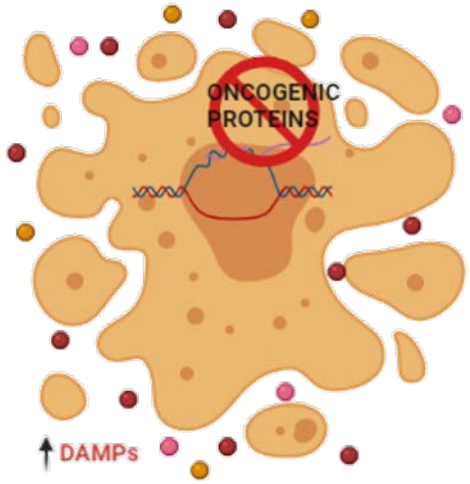


1. Ponce-Aix S. Presented at WCLC 2020. Oral OA11.04.

- *SCLC, small-cell lung cancer; CTFI, chemotherapy-free interval; CNS, central nervous system; PR, partial response; SD, stable disease; DOR, duration of response; CI, confidence interval; PFS, progression-free survival.*

Courtesy of Luis Paz-Ares, MD, PhD

Synergistic action of LUR + αPD-1/PD-L1: Rationale



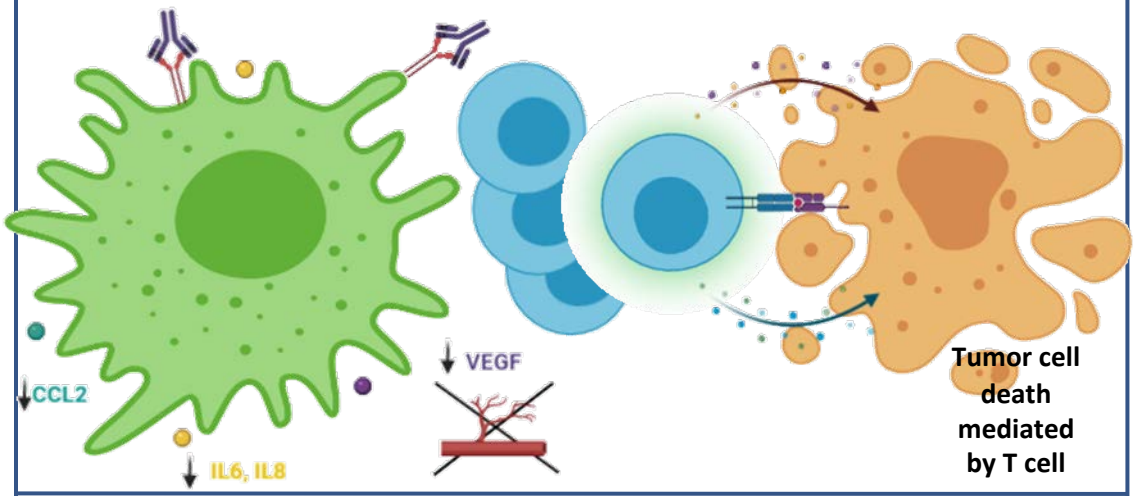
Tumor cell death mediated by LUR

Tumor cells ↓ Tumor cells

- Lurbinectedin inhibits production of oncogenic proteins and kills the tumor cell

Tumor cells ↓ Immune cells

- Lurbinectedin produces immunogenic tumor cell death and decreases the number of TAMs within the tumor



Immune cells ↓ Tumor cells

- Lurbinectedin inhibits the production of tumorigenic and immuno-suppressive chemokines by TAMs

Immune cells ↓ Immune cells

- αPD-1/PD-L1 block causes the T-cells to remain active and kill the tumor cells

Tumor Cell Death and Immune Response

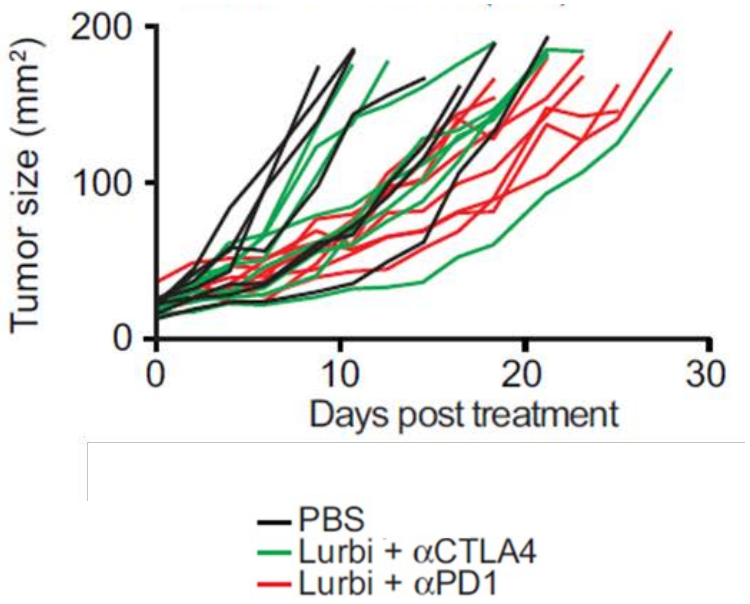
Santamaría *et al*., Mol Cancer Ther. 2016
Belgiovine *et al*., Br J Can 2017
Xie W *et al*., Oncoimmunology. 2019

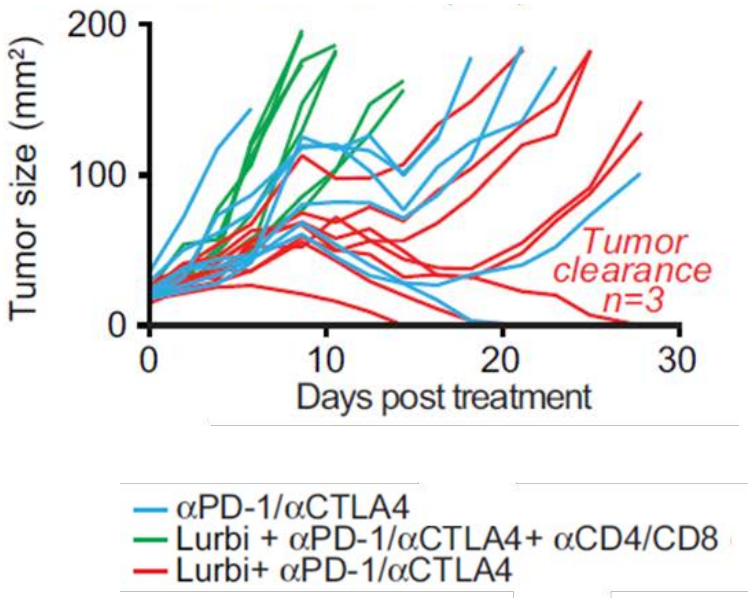
Germano *et al*., Cancer Res 2010
Germano *et al*., Cancer Cell 2013
Povo-Retana *et al*., Cancers. 2020

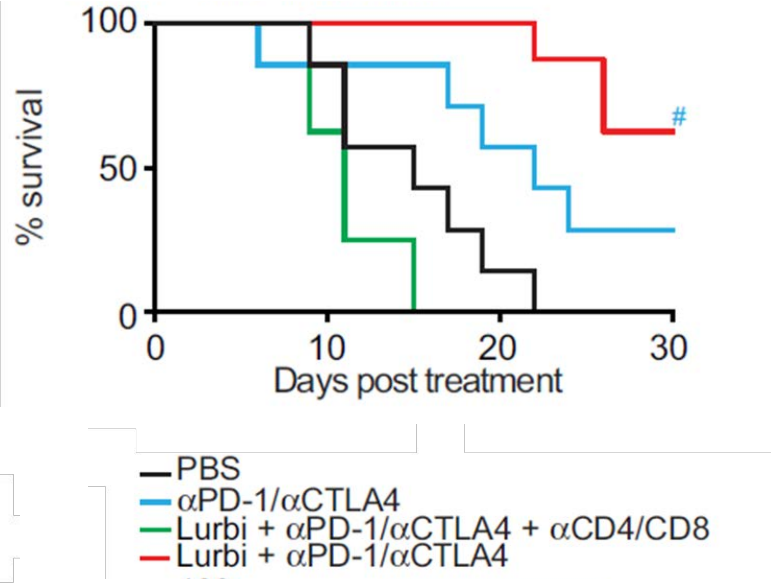
Courtesy of Luis Paz-Ares, MD, PhD

Lurbinectedin and anti-PD1 Demonstrated Synergism *in vivo*

- Lurbinectedin sensitizes cancers to therapy with immune checkpoint blockers targeting CTLA4 or PD1
- The combination of lurbinectedin with aPD1 or aCTLA4 in tumor bearing animals significantly extended life expectancy and led to tumor clearance







Xie W *et al*., Oncoimmunology. 2019 Sep 5;8(11):e1656502

Courtesy of Luis Paz-Ares, MD, PhD

2SMALL Phase I/II trial: Lurbinectedin plus Atezolizumab

Objective responses (ORR) were observed in 15 pts (57.7%), including complete responses (CR) in 2 pts (7.7%), partial response (PR) in 13 pts (50%). Stable disease (SD) was observed in 7 pts (26.9%) and 3 pts (11.54%) were in progressive disease (PD). Disease control rate (DC) was 84.61%,

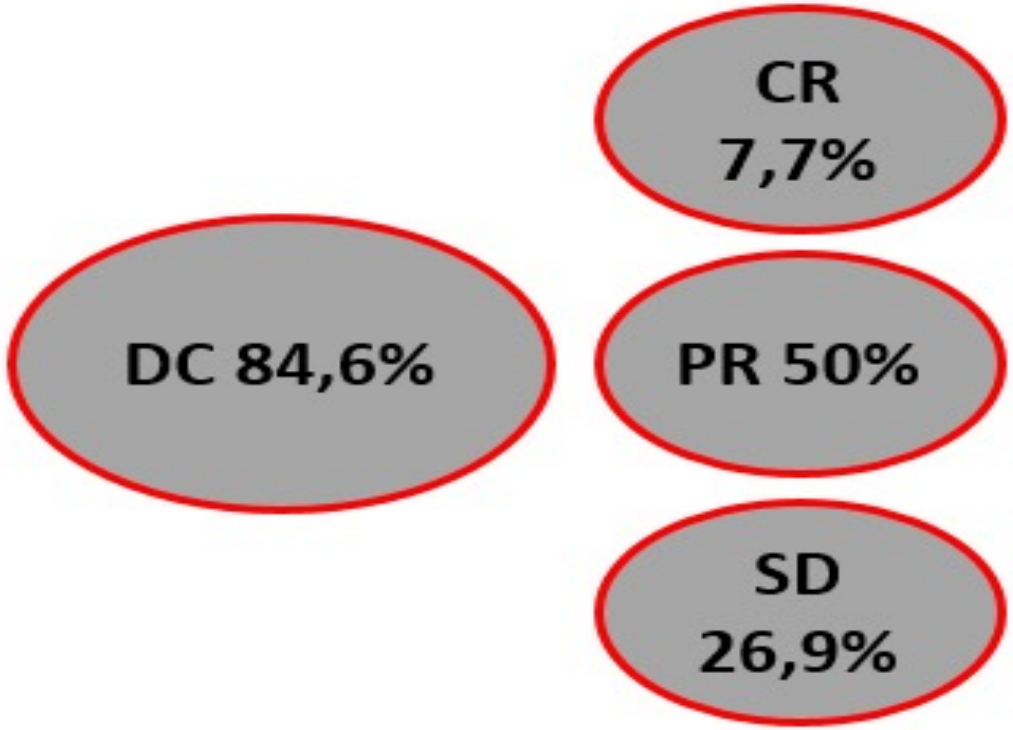


FIGURE 1 Disease Control Rate and ORR

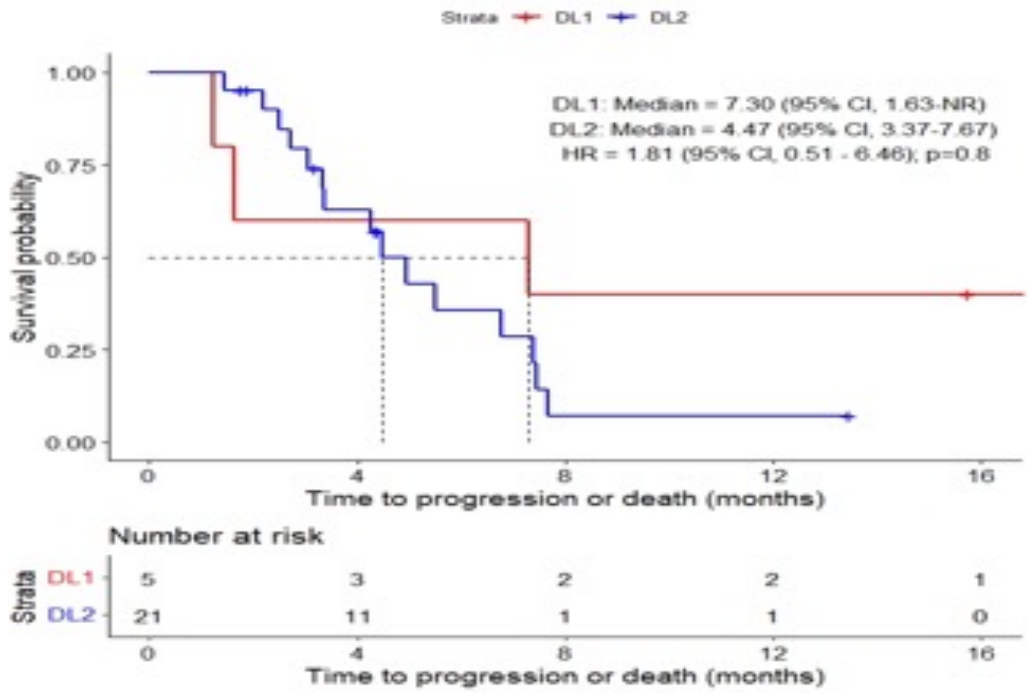
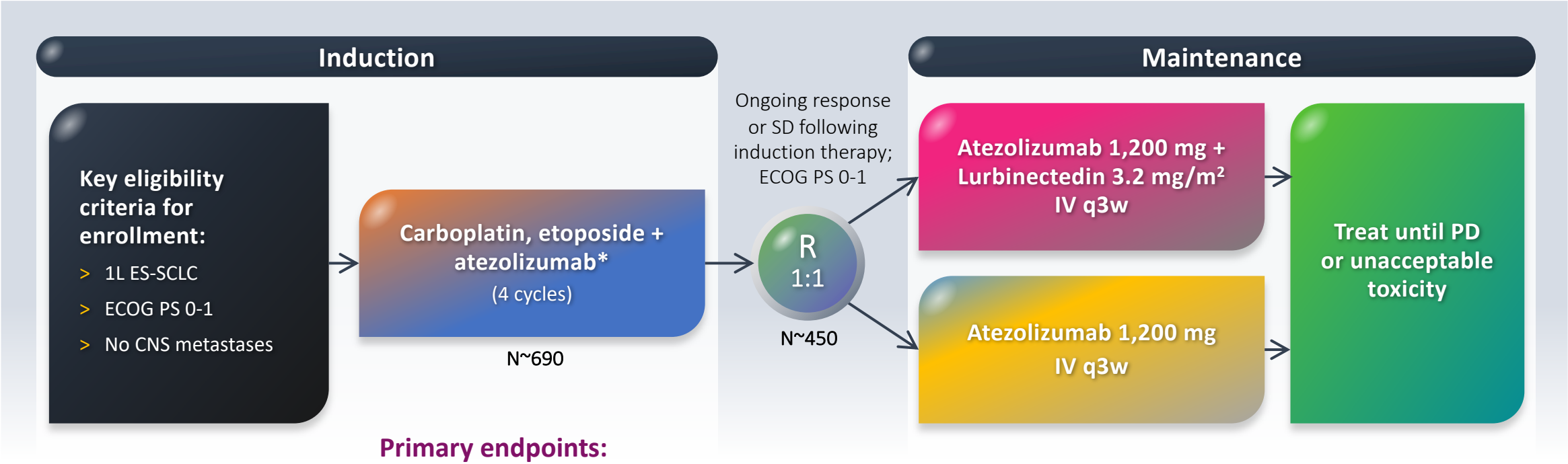


FIGURE 2 **Progression-free Survival** curve for DL1 and DL2 dosing limiting toxicity patients.

Courtesy of Luis Paz-Ares, MD, PhD

IMforte trial design



Primary endpoints:

> IRF-assessed PFS and OS

Secondary endpoints:

> Inv-assessed PFS, ORR, DOR, landmark PFS & OS, safety

- *PCI allowed following induction treatment*
- ***DOR**, duration of response; **Inv**, investigator; **IRF**, independent review facility; **ORR**, objective response rate; **OS**, overall survival; **PCI**, prophylactic cranial irradiation; **PD**, disease progression; **PFS**, progression-free survival; **SD**, stable disease*

Courtesy of Luis Paz-Ares, MD, PhD

Agenda

Case – Dr Paz-Ares: A 69-year-old woman with newly diagnosed extensive-stage small-cell lung cancer (ES-SCLC) who receives carboplatin/etoposide/atezolizumab

Case – Dr Weiss: A 46-year-old woman with newly diagnosed ES-SCLC who receives carboplatin/etoposide/durvalumab

Case – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression

Case – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin

Case – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression

Case Presentation – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin

- A 70 year old man was previously treated with CbP/VP16/atezolizumab with PR, but PD after 8 months while on atezolizumab maintenance therapy.
- Repeat platinum-doublet vs. lurbinectedin were discussed and the patient chose lurbinectedin.
- Patient returns on day 10 with fever and a cough productive of green sputum. O2 sat 90% (baseline 94%), RR15, no increased WOB.
- Chest Xray is ambiguous, with opacities difficult to specify. CT obtained demonstrated PNA. There is no cancer growth, perhaps diminution. CBC notable for WBC 1, ANC 200, Hgb 7 (baseline 12 pre-chemo) and plt 50.

Courtesy of Jared Weiss, MD

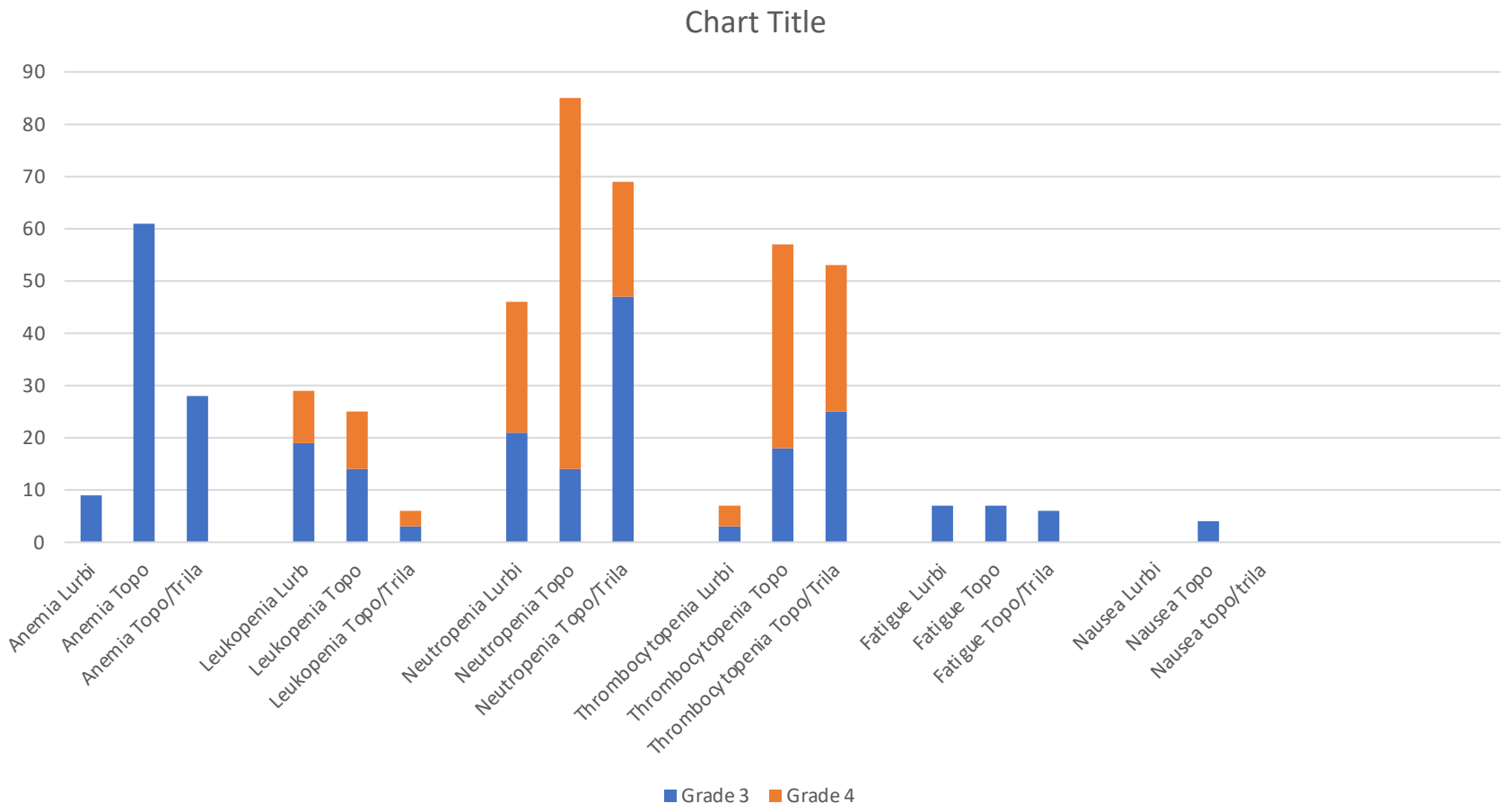
What is the incidence of NTP w/Lurbi?

	Grade 1/2, n (%)	Grade 3, n (%)	Grade 4, n (%)
Hematological abnormalities (regardless of relation to study drug)[a]			
Anemia	91 (87)	9 (9)	0
Leukopenia	53 (50)	20 (19)	10 (10)
Neutropenia	27 (26)	22 (21)	26 (25)
Thrombocytopenia	39 (37)	3 (3)	4 (4)
Biochemical abnormalities (regardless of relation to study drug)[a]			
Creatinine[b]	86/104 (83)	0	0
Alanine aminotransferase	69/103 (67)	5/103 (5)	0
Aspartate aminotransferase	52/103 (50)	13/103 (13)	2/103 (2)
Y-glutamyl transferase	44/103 (43)	2/103 (2)	0
Alkaline phosphatase	31/103 (30)	3/103 (3)	0
Treatment-related adverse events			
Fatigue	54 (51)	7 (7)	0
Nausea	34 (32)	0	0
Decreased appetite	22 (21)	0	0
Vomiting	19 (18)	0	0
Diarrhea	13 (14)	1 (1)	0
Febrile neutropenia	0	2 (2)	3 (3)
Pneumonia	0	2 (2)	0
Skin ulcer	0	1 (1)	0

Trigo, Lancet Oncology 2020

Courtesy of Jared Weiss, MD

G3-4 Heme AEs; NB: This is cross-trial comparison, not randomized data



Hart, Adv. Ther, 2021
Trigo, Lancet Oncol 2020

Courtesy of Jared Weiss, MD

More Cross Trial Comparison; stuff people feel (NB: any grade, prior was G3-4)

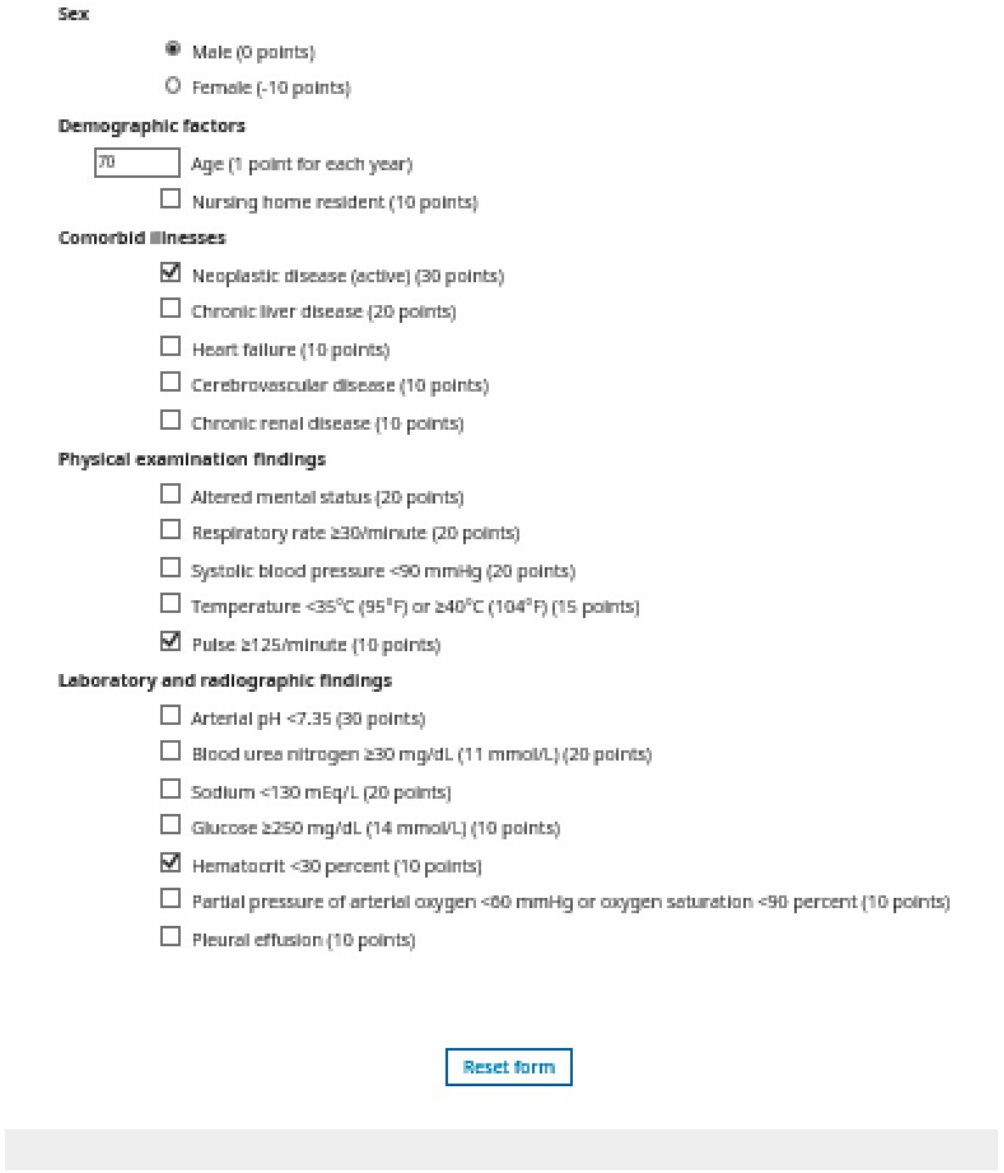
	Lurbinectedin	Topotecan	Topotecan/Trilaciclib
Fatigue	58	41	36
Nausea	32	50	28
Decreased appetite	21	18	21
Vomiting	18	32	6
Diarrhea	15	29	16

Hart, Adv. Ther, 2021
Trigo, Lancet Oncol 2020

Courtesy of Jared Weiss, MD

Management

- Patient did not want to be admitted and asked if he could be managed at home.
- After recommendation for admission, he declined.



Sex

- (•) Male (0 points)
- ( ) Female (-10 points)

Demographic factors

- [70] Age (1 point for each year)
- [ ] Nursing home resident (10 points)

Comorbid illnesses

- [x] Neoplastic disease (active) (30 points)
- [ ] Chronic liver disease (20 points)
- [ ] Heart failure (10 points)
- [ ] Cerebrovascular disease (10 points)
- [ ] Chronic renal disease (10 points)

Physical examination findings

- [ ] Altered mental status (20 points)
- [ ] Respiratory rate ≥30/minute (20 points)
- [ ] Systolic blood pressure <90 mmHg (20 points)
- [ ] Temperature <35°C (95°F) or ≥40°C (104°F) (15 points)
- [x] Pulse ≥125/minute (10 points)

Laboratory and radiographic findings

- [ ] Arterial pH <7.35 (30 points)
- [ ] Blood urea nitrogen ≥30 mg/dL (11 mmol/L) (20 points)
- [ ] Sodium <130 mEq/L (20 points)
- [ ] Glucose ≥250 mg/dL (14 mmol/L) (10 points)
- [x] Hematocrit <30 percent (10 points)
- [ ] Partial pressure of arterial oxygen <60 mmHg or oxygen saturation <90 percent (10 points)
- [ ] Pleural effusion (10 points)

Reset form

	Class I 0.1% mortality (see note below)
0 to 70 points:	Class II 0.6% mortality
71 to 90 points:	Class III 0.9% mortality
91 to 130 points:	Class IV 9.3% mortality
131 to 405 points:	Class V 27.0% mortality

PORT/PSI
Fine, NEJM 1997
(Accessed on uptodate)

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin (continued)

Followup

- Patient was treated with levofloxacin.
- His daughter stayed with him for two weeks.
- His nurse navigator called him daily.
- He returned to clinic for C2.
- CBC: WBC 3, ANC 1100, Hgb 10, Plt 150

Courtesy of Jared Weiss, MD

Poll Question

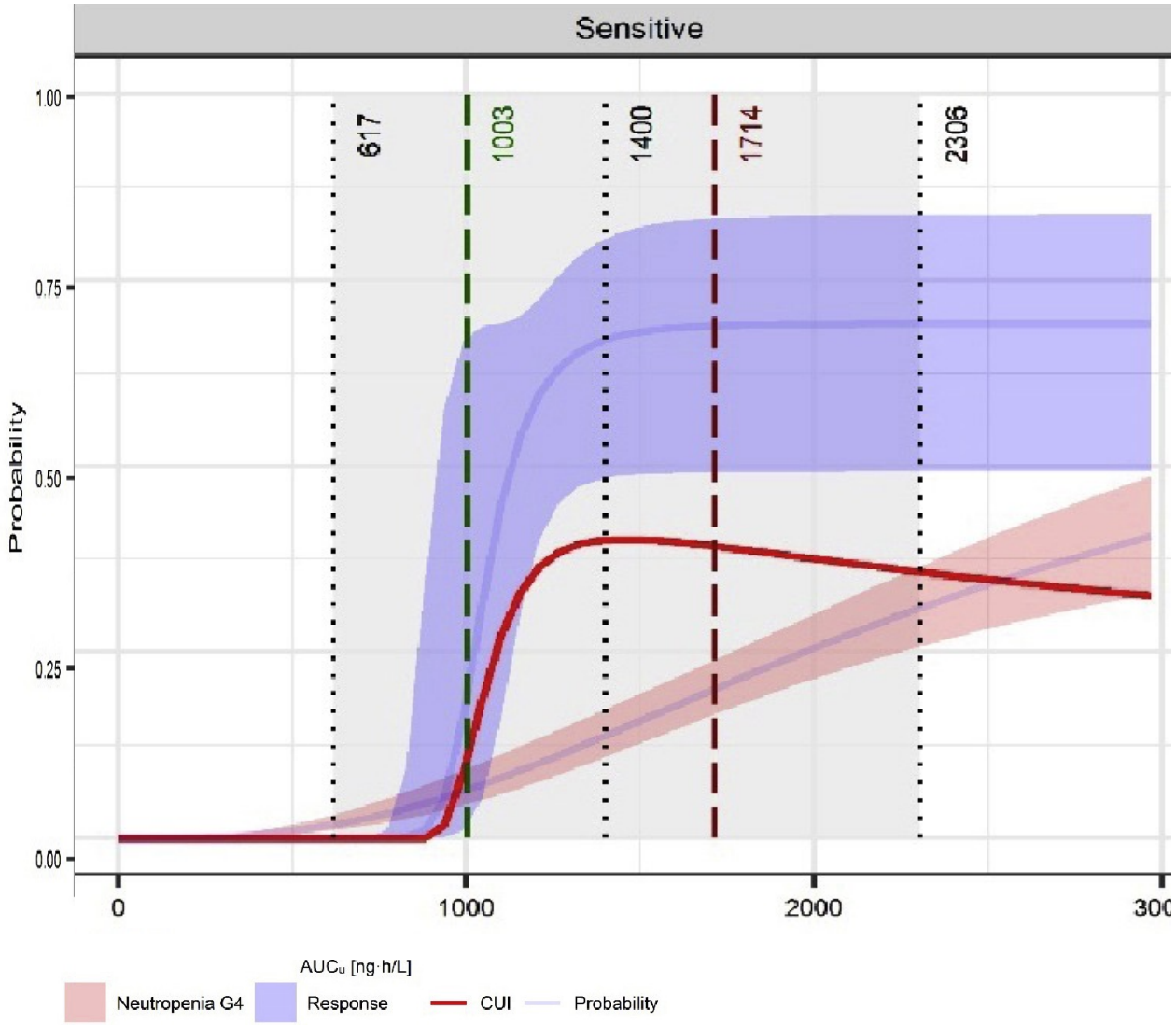
Should the dose of the next cycle be reduced?

Yes

No

Courtesy of Jared Weiss, MD

Why Lurbinectedin was not dose-reduced



Exposure in AUC (X axis) vs. Probability of response and G4 NTP (Y axis)

Teruel, JTO supplement 2021

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin (continued)

Followup

- Pegfilgrastim given as secondary PPx.
- C2 went well.
- Imaging after two cycles showed PD.
- Options of hospice, topotecan (preceded by trilaciclib) or a phase I clinical trial discussed.
- The patient chose hospice.
- Major comfort complaint was SOB; this was effectively palliated with a fan and morphine.

Courtesy of Jared Weiss, MD

Agenda

Case – Dr Paz-Ares: A 69-year-old woman with newly diagnosed extensive-stage small-cell lung cancer (ES-SCLC) who receives carboplatin/etoposide/atezolizumab

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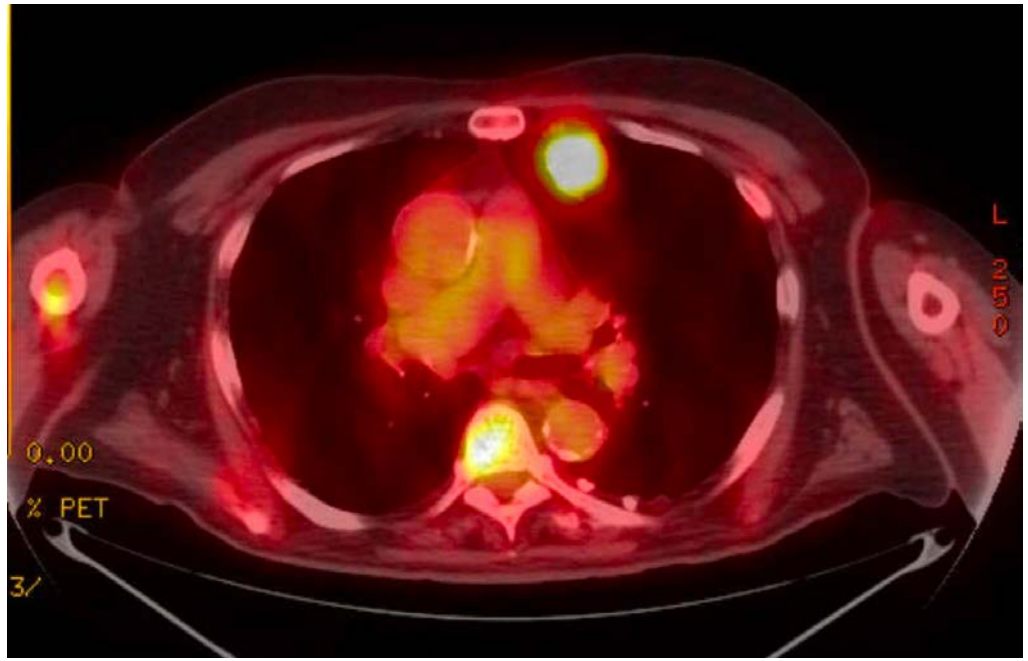
Case – Dr Paz-Ares: A 63-year-old man with ES-SCLC who receives carboplatin/etoposide/durvalumab and then experiences disease progression

Case – Dr Weiss: A 70-year-old man with progressive SCLC who receives lurbinectedin

Case – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression

Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression

- An 82-year-old man presented to his cardiologist with increased DOE.
- CXR showed LUL mass, mediastinal LAD leading to CT then PET.
- PET showed left upper mass with mediastinal and upper abdominal nodal metastases and diffuse osseous metastases.
- MRI brain clear.
- Biopsy showed SCLC.



Courtesy of Jared Weiss, MD

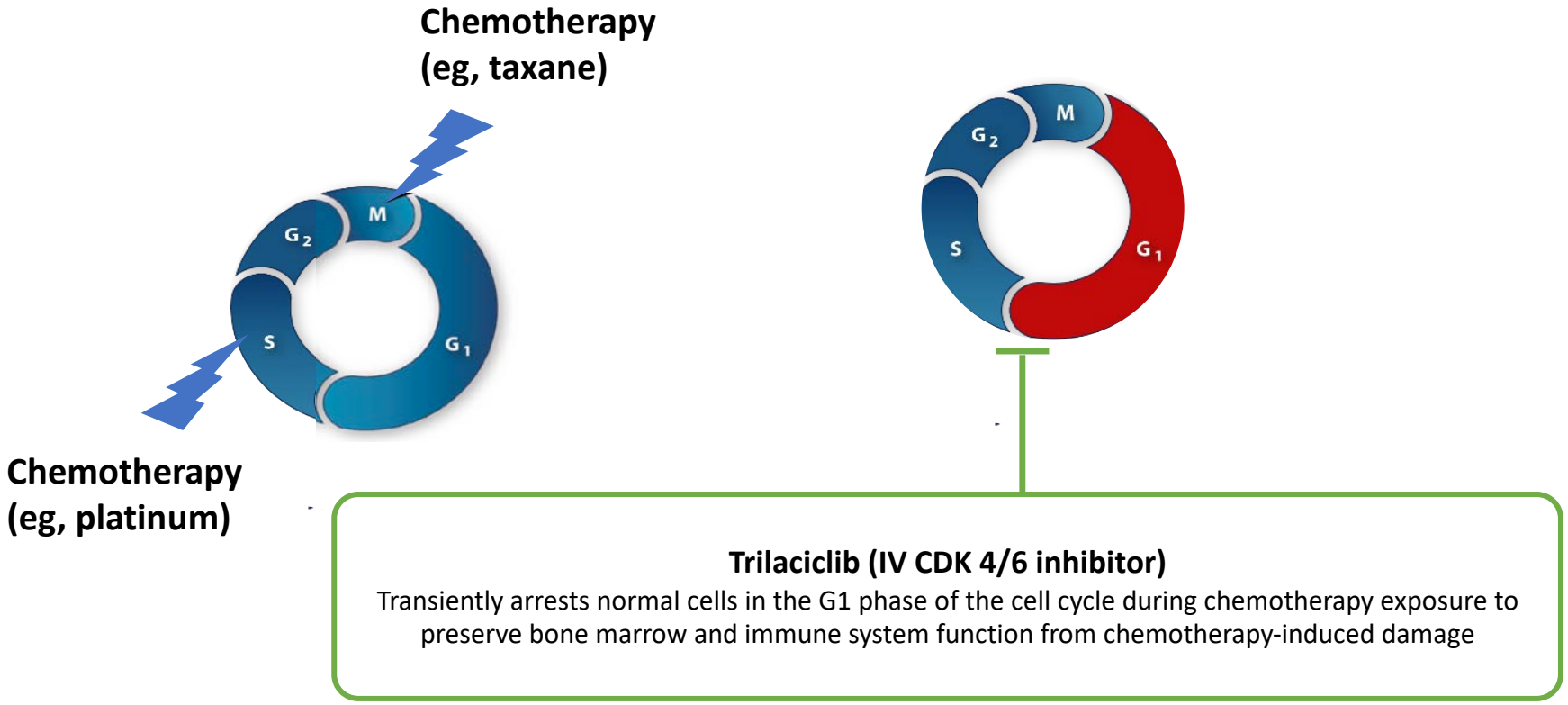
Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression (cont)

Fitness

- MMP: CAD with h/o MI, DM, CHF.
- PS: Bad side of ECOG 1 pre-cancer, now good side of 2. Spends roughly ½ of day in bed or some recumbent position.
- Basic GA: Fully intact in ADLs, dependent on very supportive wife for IADLs. Get up and go 10 seconds.
- Values: Enjoys life and wants to live more. He is particularly motivated to see his grandchildren grow older and to play golf (can't play 9 holes and needs a cart, but is very proud of his game).
- Baseline labs: WBC 7.4, Hgb 14.7, Plt 154; Creat 0.67 (GFR>60).
- Patient enrolls on a clinical trial, G128-02: CbP/VP16 +/- Trilaciclib

Courtesy of Jared Weiss, MD

Trilaciclib Mechanism of Action



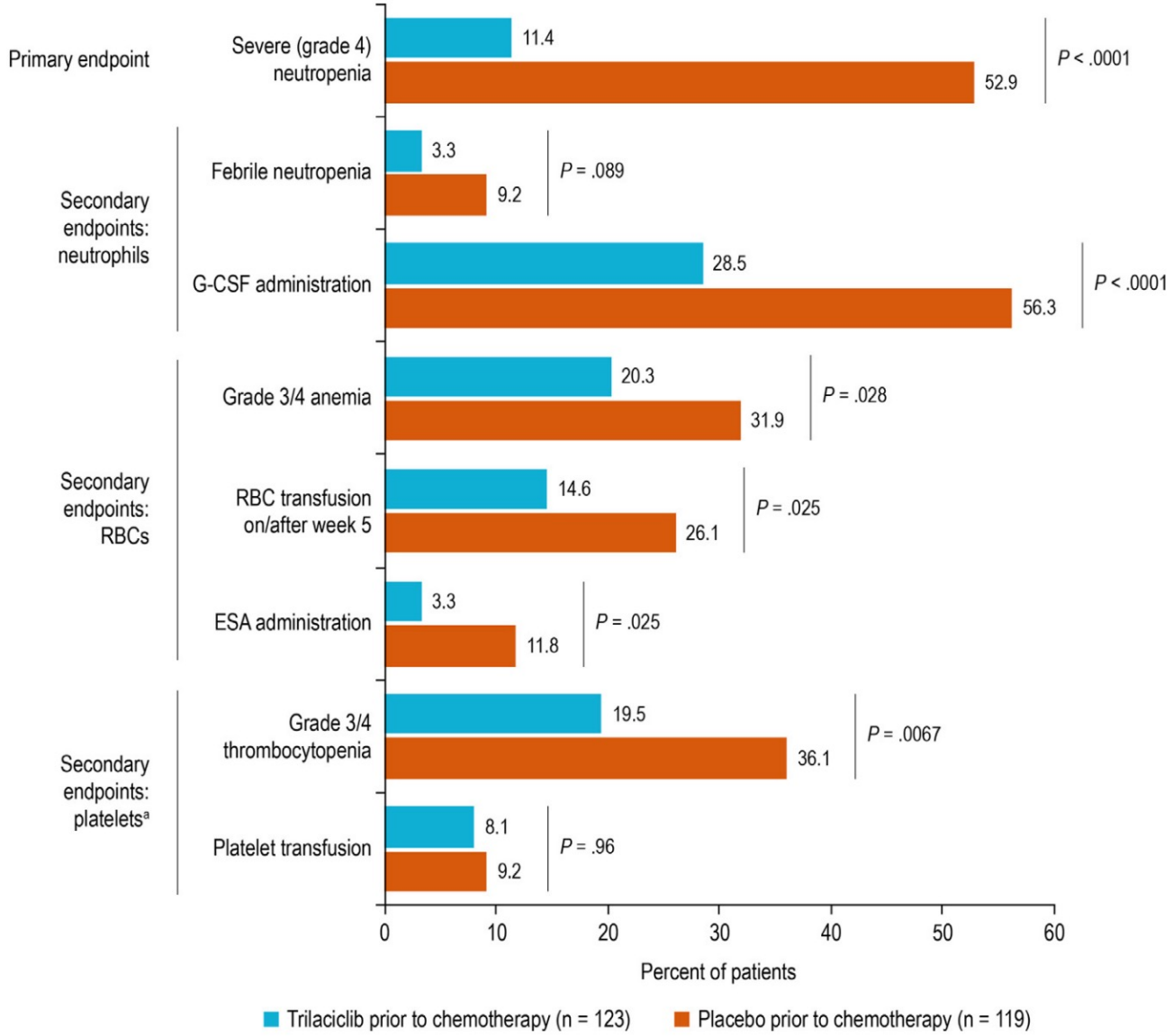
Courtesy of Jared Weiss, MD

G1T28-02

Study	Patient Population	Treatment Schedule
G1T28-05 (NCT03041311)	Newly diagnosed (first-line) ES-SCLC	Trilaciclib 240 mg/m^2 IV QD prior to chemotherapy on days 1-3 of each 21-day E/P/A IV cycle[a] for up to four cycles followed by atezolizumab monotherapy (without trilaciclib) Q21D Placebo IV QD prior to chemotherapy on days 1-3 of each 21-day E/P/A IV cycle for up to four cycles followed by atezolizumab monotherapy (without placebo) Q21D
G1T28-02 (NCT02499770)	Newly diagnosed (first-line) ES-SCLC	Trilaciclib 240 mg/m^2 IV QD prior to chemotherapy on days 1-3 of each 21-day E/P IV cycle[b] Placebo IV QD prior to chemotherapy on days 1-3 of each 21-day E/P IV cycle
G1T28-03 (NCT02514447)	Previously treated (second-/third-line) ES-SCLC	Trilaciclib 240 mg/m^2 IV QD prior to topotecan 1.5 mg/m^2 IV QD on days 1-5 of each 21-day cycle Placebo IV QD prior to topotecan 1.5 mg/m^2 IV QD on days 1-5 of each 21-day cycle

Courtesy of Jared Weiss, MD

Pooled Data

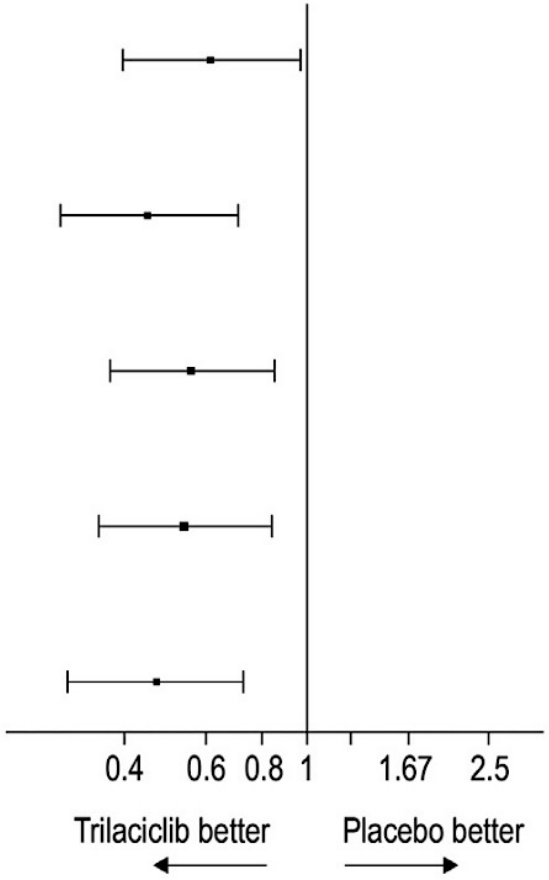


Weiss, Clinical Lung Cancer, 2021

Courtesy of Jared Weiss, MD

PROs

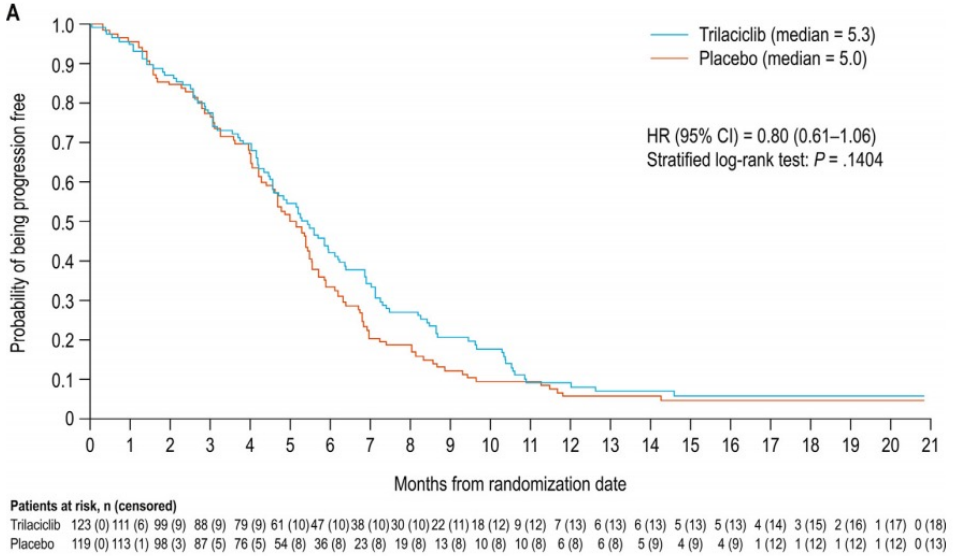
Domain	Events, n Trilaciclib/placebo	TTCD, months Trilaciclib/placebo	Hazard ratio (95% CI)
Physical wellbeing	32/51	NYR/5.16	0.62 (0.40–0.97)
Functional wellbeing	31/55	7.62/3.78	0.45 (0.29–0.71)
Fatigue	39/61	7.03/2.33	0.56 (0.37–0.85)
Anemia trial outcome index	33/55	7.20/3.78	0.54 (0.35–0.84)
FACT-An total	31/58	NYR/3.48	0.47 (0.30–0.73)

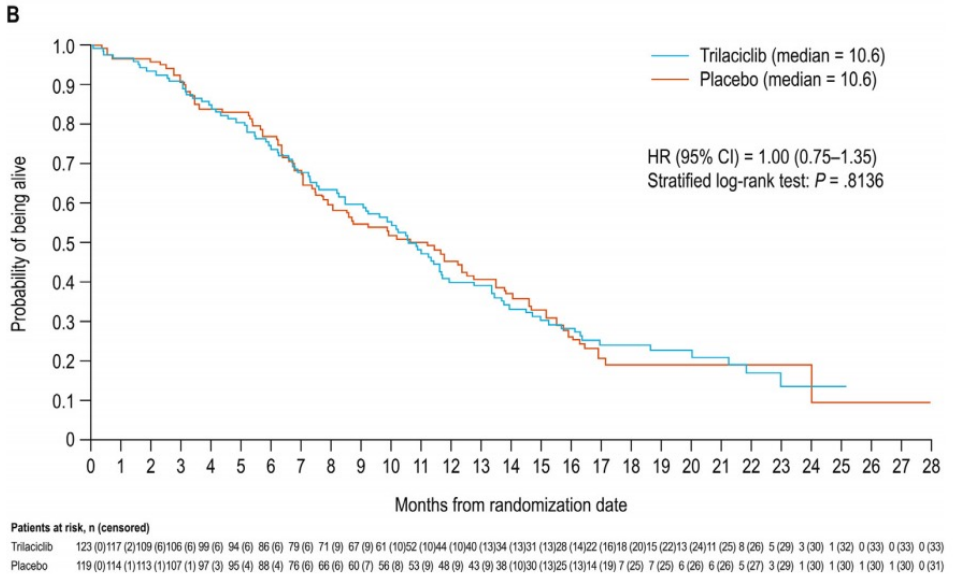


Weiss, Clinical Lung Cancer, 2021

Courtesy of Jared Weiss, MD

No impact on PFS or OS





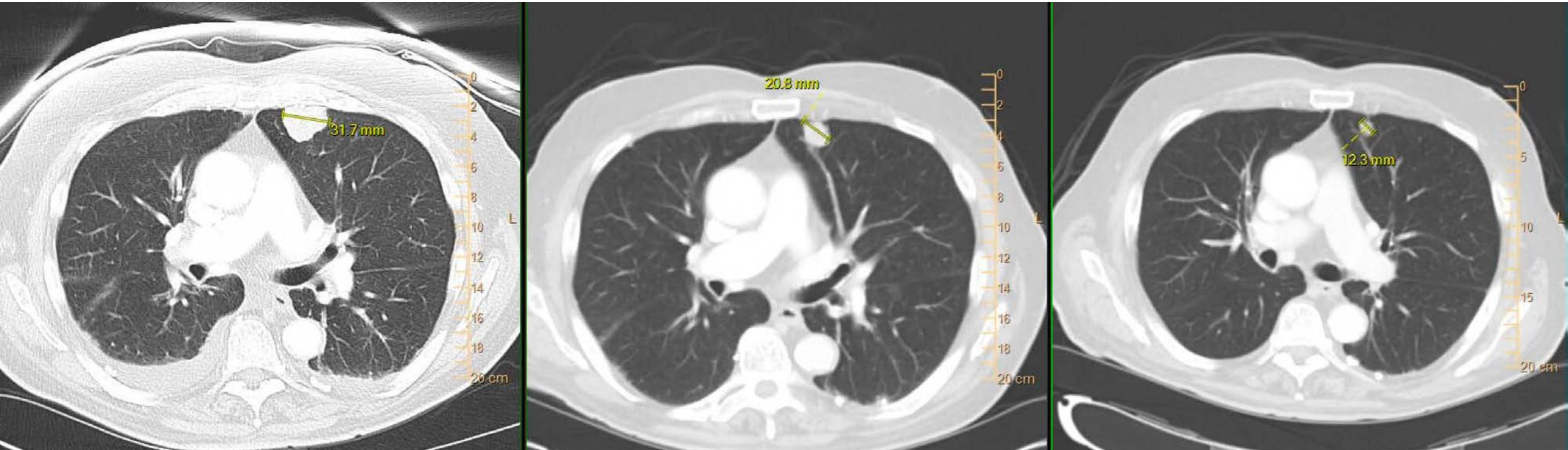
Weiss, Clinical Lung Cancer, 2021

Courtesy of Jared Weiss, MD

Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression (cont)

Progress

	Pre C1	Pre C3	Post C4
WBC	7.4	4.8	3.3
Hgb	14.7	13.2	12.6
Plt	154	246	199



Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression (cont)

- 2 month FU scan showed additional diminution of cancer.
- There was no evidence of progression for nearly 3 years on serial imaging.
- His other medical problems were active, most notably CHF and cholecystitis, culminating in an admission for sepsis.
- Workup for cholecystectomy reveals recurrent lung mass.
- Oncology discusses GOC. Patient strongly wishes to try to continue to live, citing desire for more time with his wife and grandchildren.
- Oncology recommends cholecystectomy prior to chemotherapy, citing risk of recurrent infections and high risk of death if given chemotherapy without it.
- Local surgeon declines to operate, citing multiple comorbidities and high risk. Academic surgeon reviews the case carefully and concurs.
- Oncology recommends strong consideration of hospice. The patient voices understanding of high risk of infection and death, but strongly requests additional therapy for the chance that he could live longer.

Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression (cont)

- In the interim, atezolizumab has been approved in 1L (Lurbi has not yet been).
- Trilaciclib is not yet FDA approved and is not available.
- Chemo: CbP/VP16/Atezo; cytotoxics DR 10%.
- Premeds:
  - Antiemetics: Fosaprepitant, ondansetron, dexamethasone
  - Pegfilgrastim post chemo
  - Levofloxacin post chemo
- Pre C1: WBC 3, Hgb 11.1, Plt 348
- Pre C2: WBC 1.7, Hgb 8.2, Plt 7; had petechia, no active bleed.
- Got 1U PRBC inpatient.
- 1 week later: WBC 7.8, Hgb 9.2, Plt 121.
- Patient wanted chemo. MD concerned. Compromise on atezo alone, RTC 1w.
- Following week, WBC 8.5, Hgb 9.7, Plt 200; after discussion of GOC, C2 given w/further DR (CbP AUC 3.5, VP16 60mg/m^2).

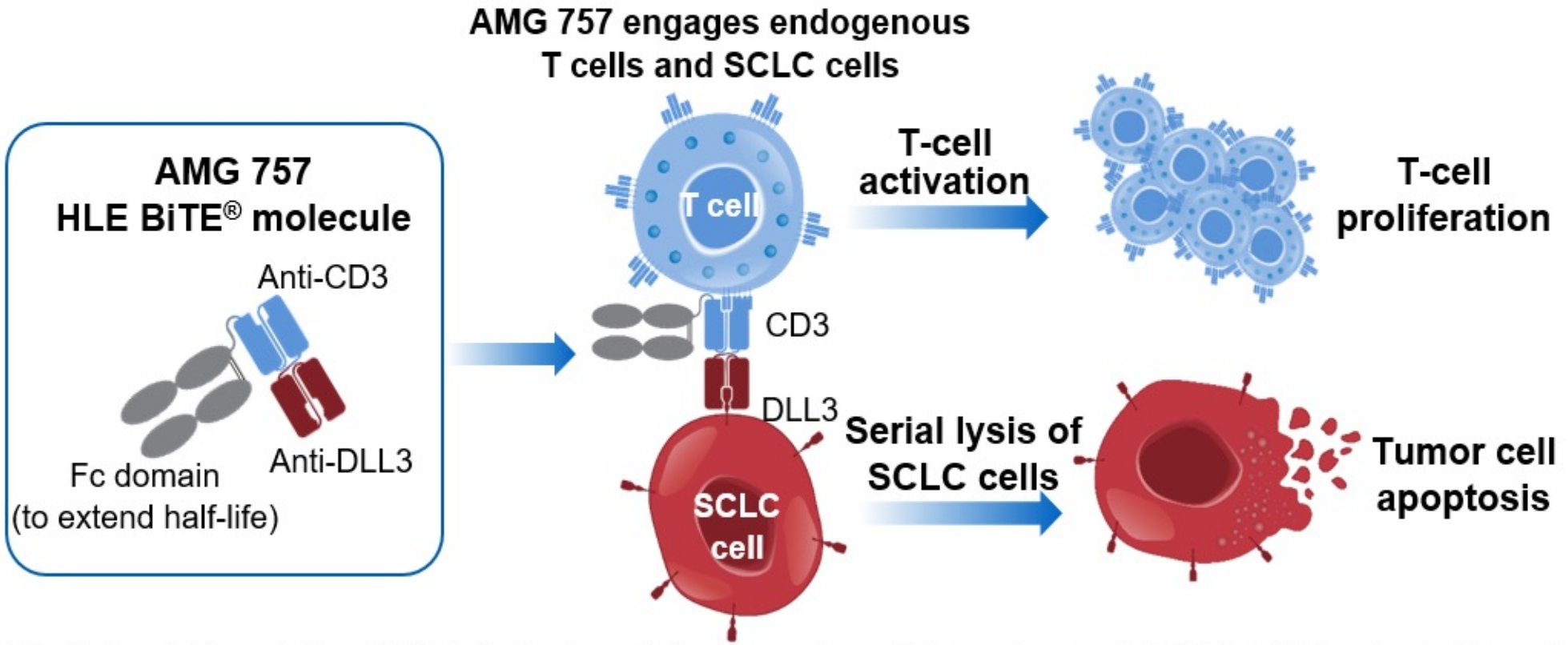
Case Presentation – Dr Weiss: An 82-year-old man with SCLC who experiences disease progression (cont)

Followup

- Patient admitted locally with cholecystitis with sepsis.
- Family meeting held via video and decision made for DNR/DNI and hospice care.
- Patient died comfortably, surrounded by family.

Novel Agents and Strategies

AMG 757: A Half-life Extended BiTE® (bispecific T-cell engager) Immuno-oncology Therapy Targeting DLL3 for SCLC



CD, cluster of differentiation; DLL3, delta-like ligand 3; Fc, fragment crystallizable domain; HLE BiTE, half-life extended bispecific T-cell engager; SCLC, small cell lung cancer.

- BiTE molecules engage a patient's own T cells to attack and eradicate cancer cells[1–3]

1.Stieglmaier J, et al. *Expert Opin Biol Ther*. 2015;15:1093-1099. 2. Einsele H, et al. *Cancer.* 2020;126:3192-3201. 3. Bargou R, et al. *Science.* 2008;321:974-977. 4.

Courtesy of Luis Paz-Ares, MD, PhD

Safety profile

Treatment-related AEs	Patients (N = 66)	
	All Grades, n (%)	Grade ≥ 3, n (%)*
Any treatment-related AE	56 (85)	18 (27)
Treatment-related AEs in ≥ 10% of patients		
CRS	29† (44)	1 (2)
Pyrexia	17 (26)	2 (3)
Fatigue	11 (17)	0 (0)
Asthenia	7 (11)	1 (2)
Dysgeusia	7 (11)	0 (0)
Nausea	7 (11)	0 (0)

- Treatment-related AEs resulted in discontinuation in 3 (5%) patients
  - DLT: grade 5 pneumonitis (1 [2%] patient; 0.3 mg); grade 3 encephalopathy (1 [2%] patient; 100 mg)
- CRS was typically reversible, manageable, and associated with fever, tachycardia, nausea, fatigue, and hypotension‡
  - One CRS event led to treatment discontinuation
  - CRS typically occurred in cycle 1 and did not recur in subsequent cycles
  - CRS management could include supportive care, corticosteroids, and/or anti-IL-6R

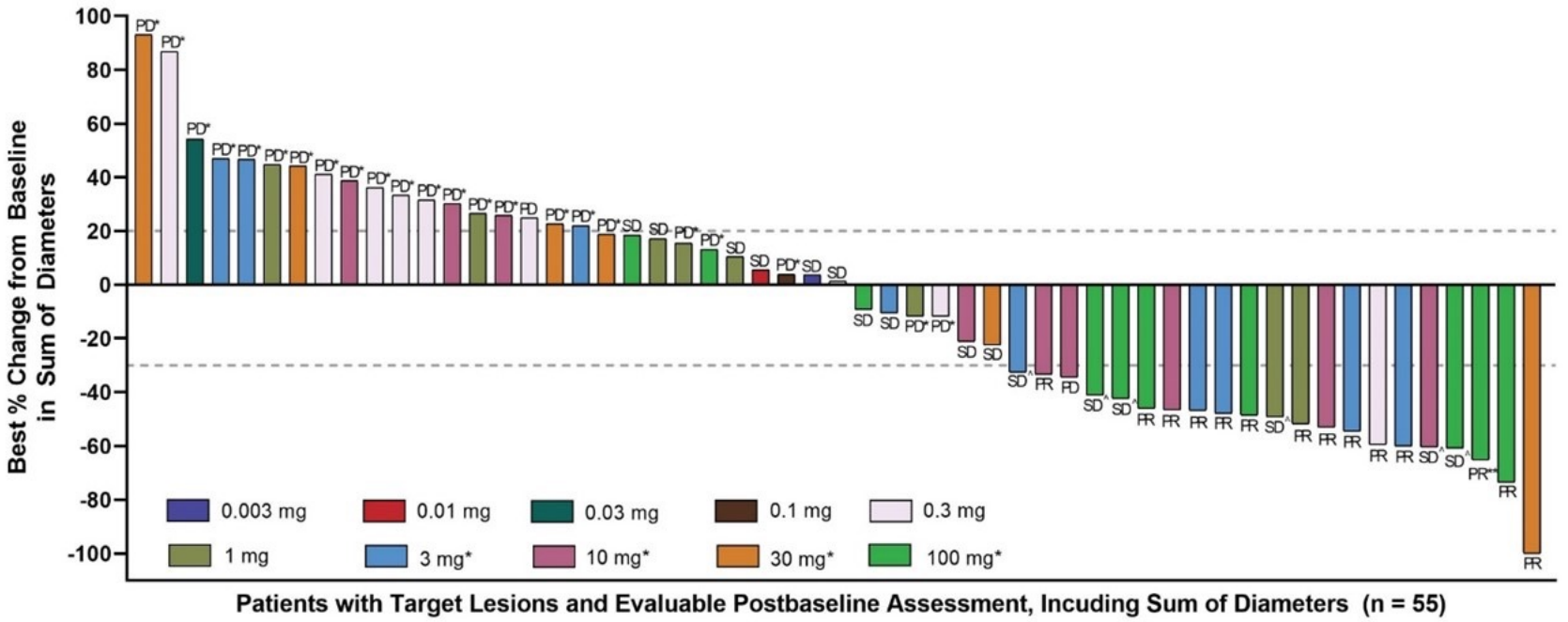
*Includes one patient with grade 5 pneumonitis. †Of the 29 patients, 21 had grade 1, 7 had grade 2, and 1 had grade 3 CRS. ‡Lee 2014 grading. AE, adverse event; CRS, cytokine release syndrome; DLT, dose limiting toxicity.

Tarlatamab monotherapy demonstrated a favorable safety profile

Courtesy of Luis Paz-Ares, MD, PhD

Owonikoko et al., ASCO 2021

Antitumor activity



PD* indicates PD in post baseline scan and came oft study without further confirmation scan. PR** indicates the PR is unconfirmed. SD^ indicates patients who had an initial PR, but did not have confirmation of PR on the subsequent scan. *Step dosing. †Includes patients who received ≥ 1 dose of tarlatamab and had at least 8 weeks follow-up.
PD, progressive disease; PR, partial response; SD, stable disease.

Modified RECIST 1.1 Response, n (%)	Patients† (N = 64)
PR, confirmed	13 (20)
0.3 mg target dose	1/12 (8)
1 mg target dose	1/8 (13)
3 mg target dose	4/11 (36)
10 mg target dose	3/10 (30)
30 mg target dose	1/8 (13)
100 mg target dose	3/11 (27)
PR, unconfirmed	1 (2)
100 mg target dose	1/11 (9)
SD	17 (27)
Disease control rate, %	30 (47)

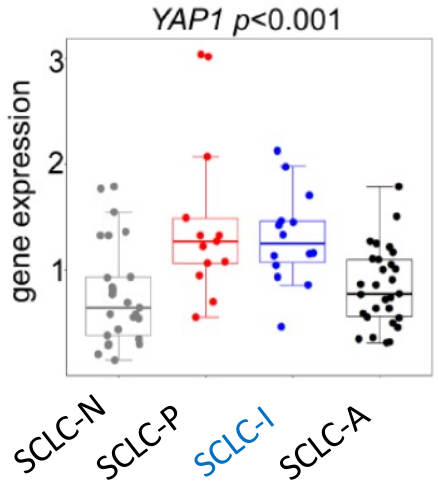
Tumor shrinkage is observed across a range of tarlatamab doses

Courtesy of Luis Paz-Ares, MD, PhD

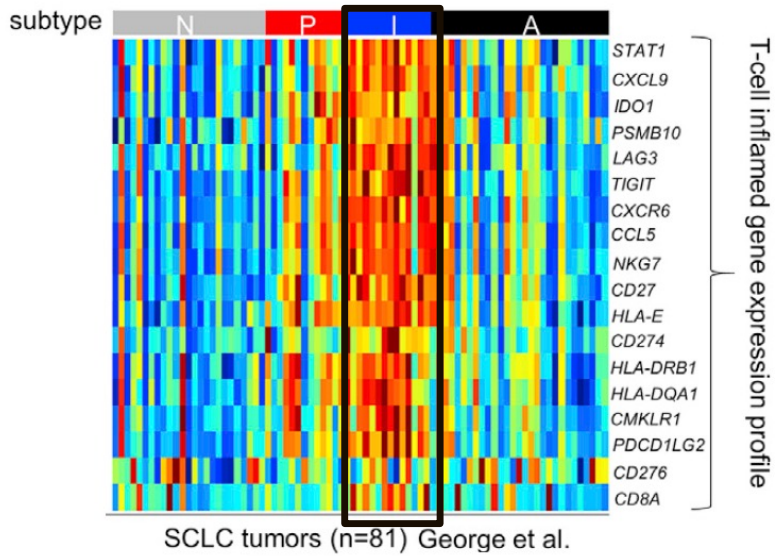
Owonikoko et al., ASCO 2021

SCLC-I: a new subtype with therapeutical implications?

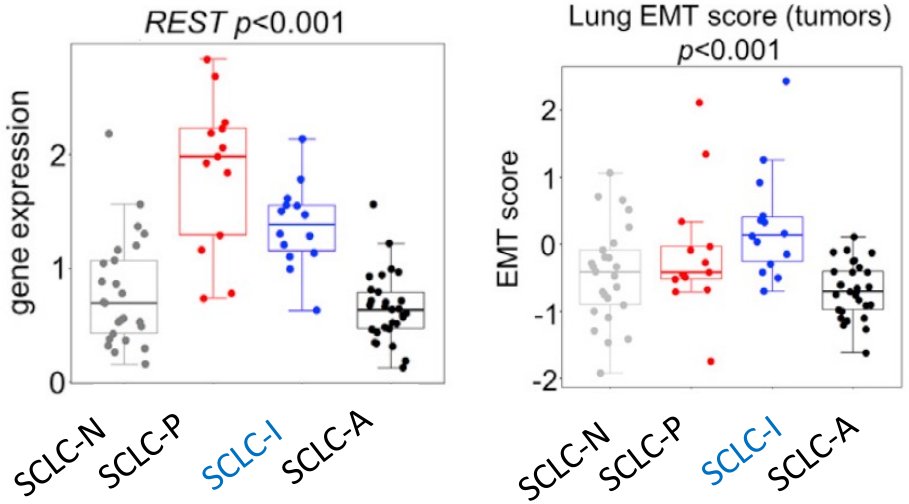
YAP1 expression does not define a particular subtype



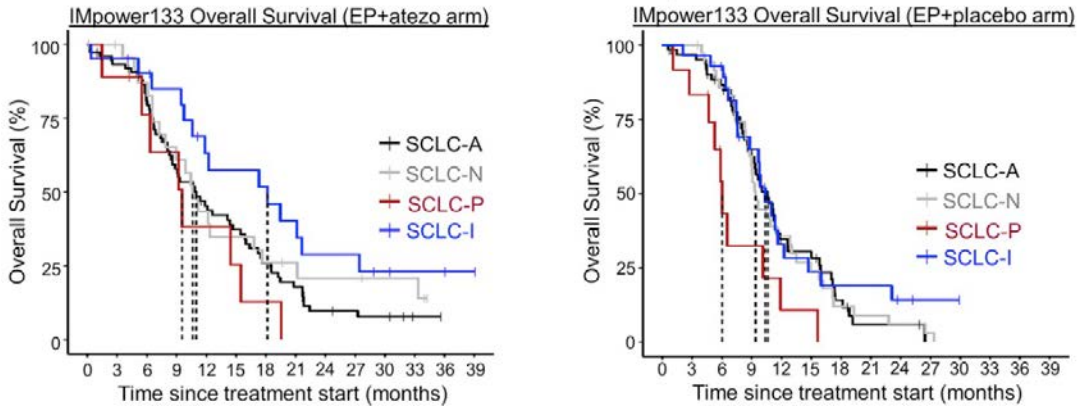
SCLC-I shows an ¨*immune hot*¨ phenotype…



SCLC-I subtype shows Notch activation and an EMT phenotype



…correlating with better response to immunotherapy



Courtesy of Luis Paz-Ares, MD, PhD

Gay et al., *Cancer Cell 2021*

Recent Advances and Real-World Implications in Medical Oncology: A Daylong Multitumor Educational Symposium in Partnership with the North Carolina Oncology Association and the South Carolina Oncology Society

Saturday, February 12, 2022
8:30 AM – 4:00 PM ET

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Recent Advances and Real-World Implications in Medical Oncology: Agenda

Module 1	**Chronic Lymphocytic Leukemia and Lymphomas** 8:35 AM
Module 2	**Multiple Myeloma** 9:40 AM
Module 3	**Genitourinary Cancers** 10:45 AM
Module 4	**Breast Cancer** 12:30 PM
Module 5	**Gastrointestinal Cancers** 1:35 PM
Module 6	**Lung Cancer** 2:40 PM

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Thank you for joining us!

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

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