Key Considerations in the Management of Patients with Small Cell Lung Cancer

A CME/MOC-Accredited Virtual Event

Thursday, November 4, 2021
5:00 PM – 6:00 PM ET

Faculty

Anne Chiang, MD, PhD
David R Spigel, MD

Moderator

Neil Love, MD

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Faculty

Anne Chiang, MD, PhD
Associate Professor
Yale University School of Medicine
Deputy Chief Medical Officer
Chief Integration Officer
Smilow Cancer Hospital
New Haven, Connecticut

David R Spigel, MD
Chief Scientific Officer
Thoracic Oncology
Sarah Cannon Research Institute
Nashville, Tennessee

Moderator

Neil Love, MD
Research To Practice
Miami, Florida

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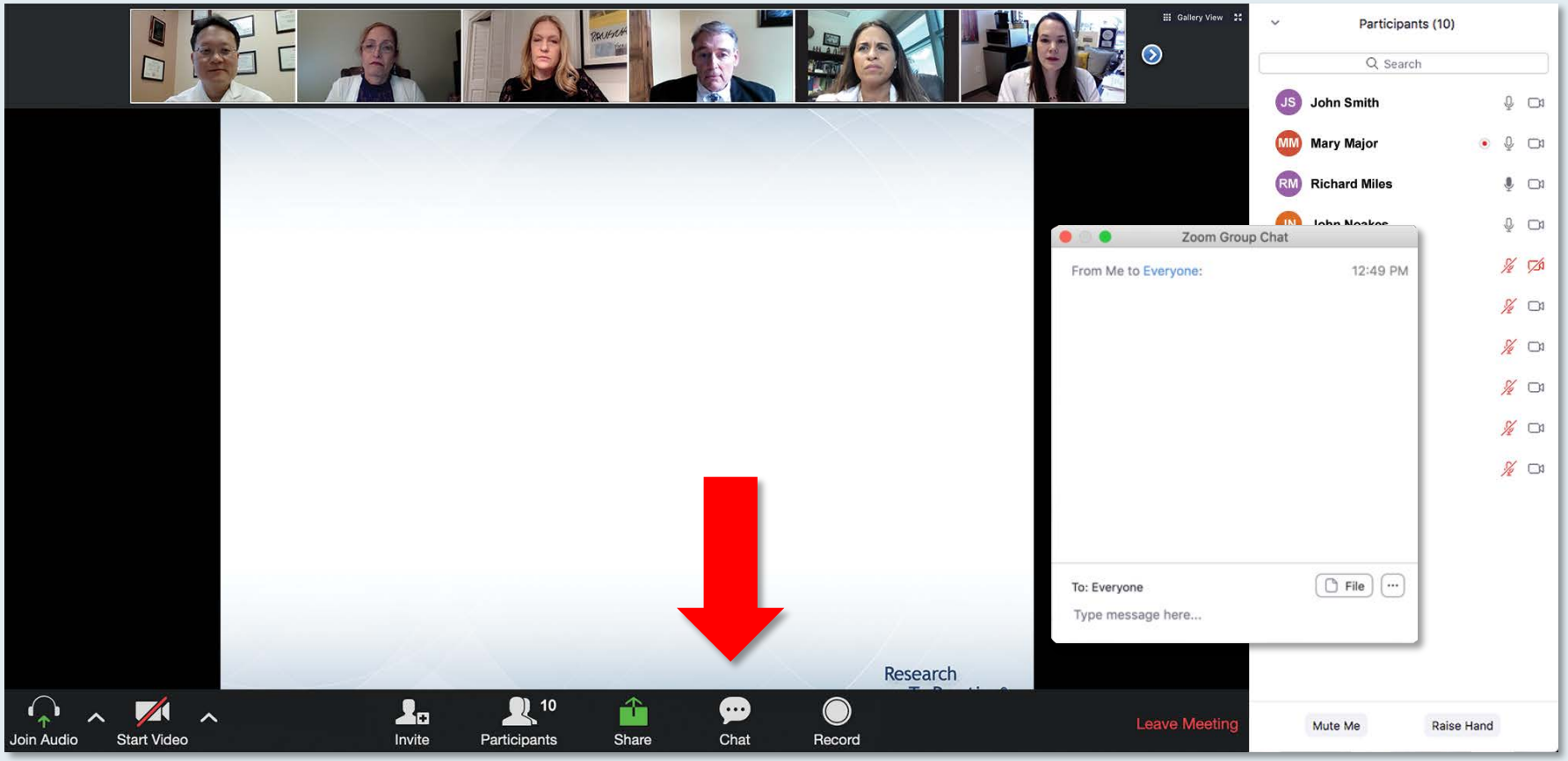

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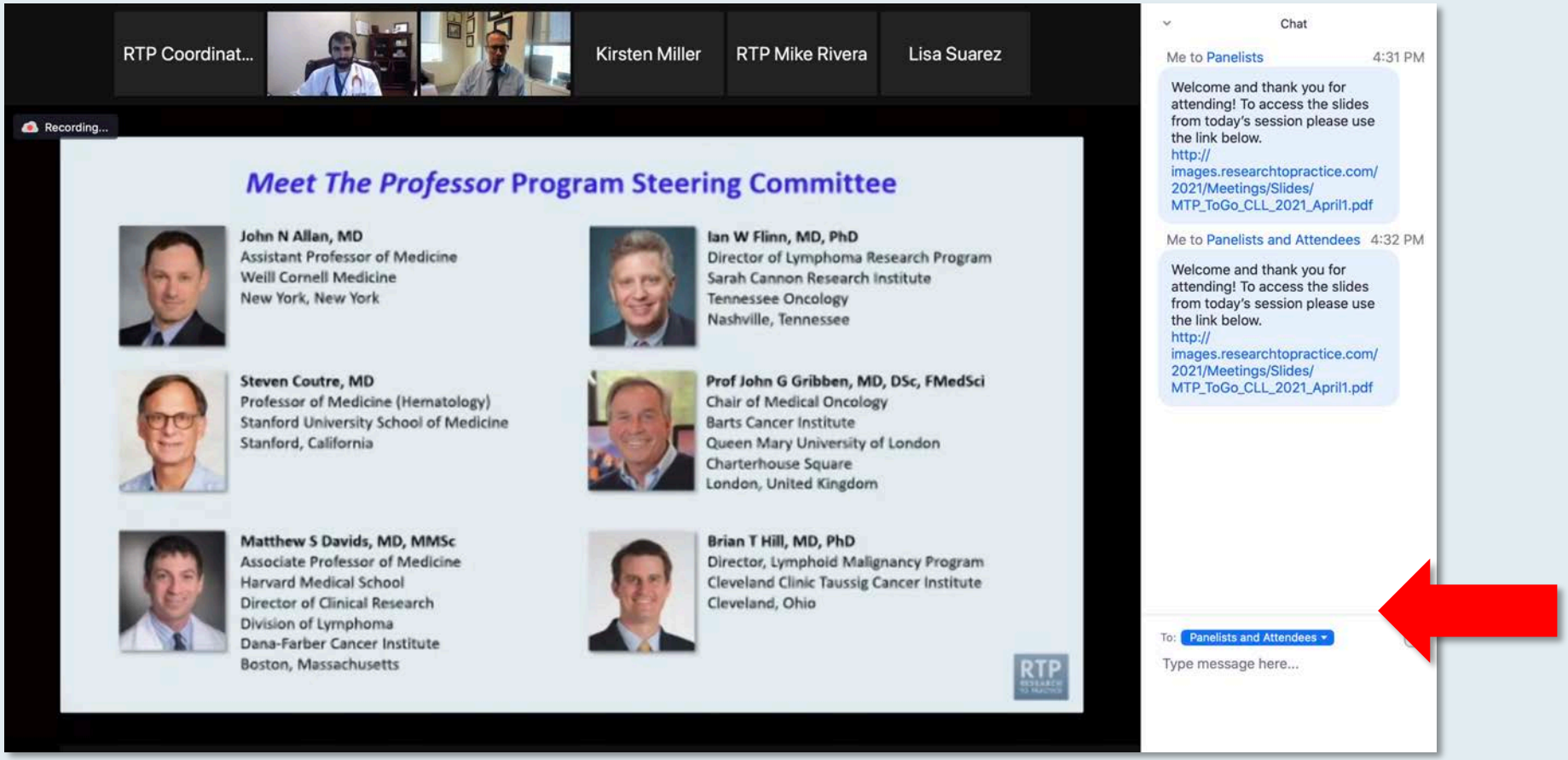

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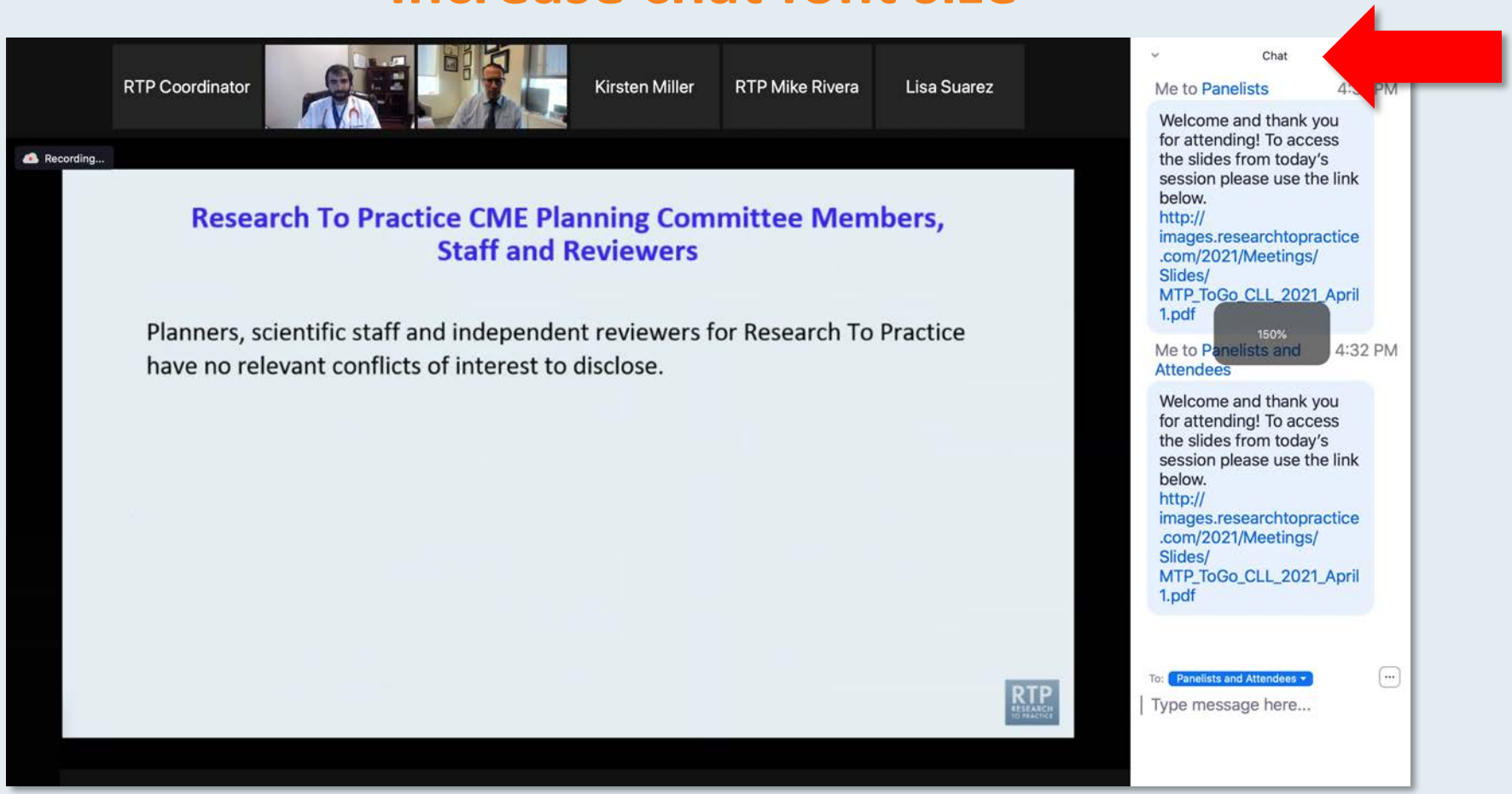

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Key Presentations on Lung Cancer from the 2021 ASCO Annual Meeting

DR JOEL NEAL

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Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Monday, November 8, 2021
5:00 PM – 6:00 PM ET

Faculty
Keith W Pratz, MD

Moderator
Neil Love, MD

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Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Tuesday, November 9, 2021
5:00 PM – 6:00 PM ET

Faculty

Simon Chowdhury, MD, PhD

Moderator

Neil Love, MD

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VIRTUAL MOLECULAR TUMOR BOARD
Optimizing Biomarker-Based Decision-Making for Patients with Non-Small Cell Lung Cancer with EGFR Mutations or with Other Oncogene-Addicted Lung Cancers

A 2-Part CME/MOC-Accredited Webinar Series

Thursday, November 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Marc Ladanyi, MD
Andrew J McKenzie, PhD
Helena Yu, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

Monday, November 15, 2021
5:00 PM – 6:00 PM ET

Faculty

Christopher R Flowers, MD, MS

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Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with ER-Positive Breast Cancer

Wednesday, November 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Kevin Kalinsky, MD, MS

Moderator

Neil Love, MD

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Meet The Professor

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

Thursday, November 18, 2021
5:00 PM – 6:00 PM ET

Faculty

Stephen V Liu, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

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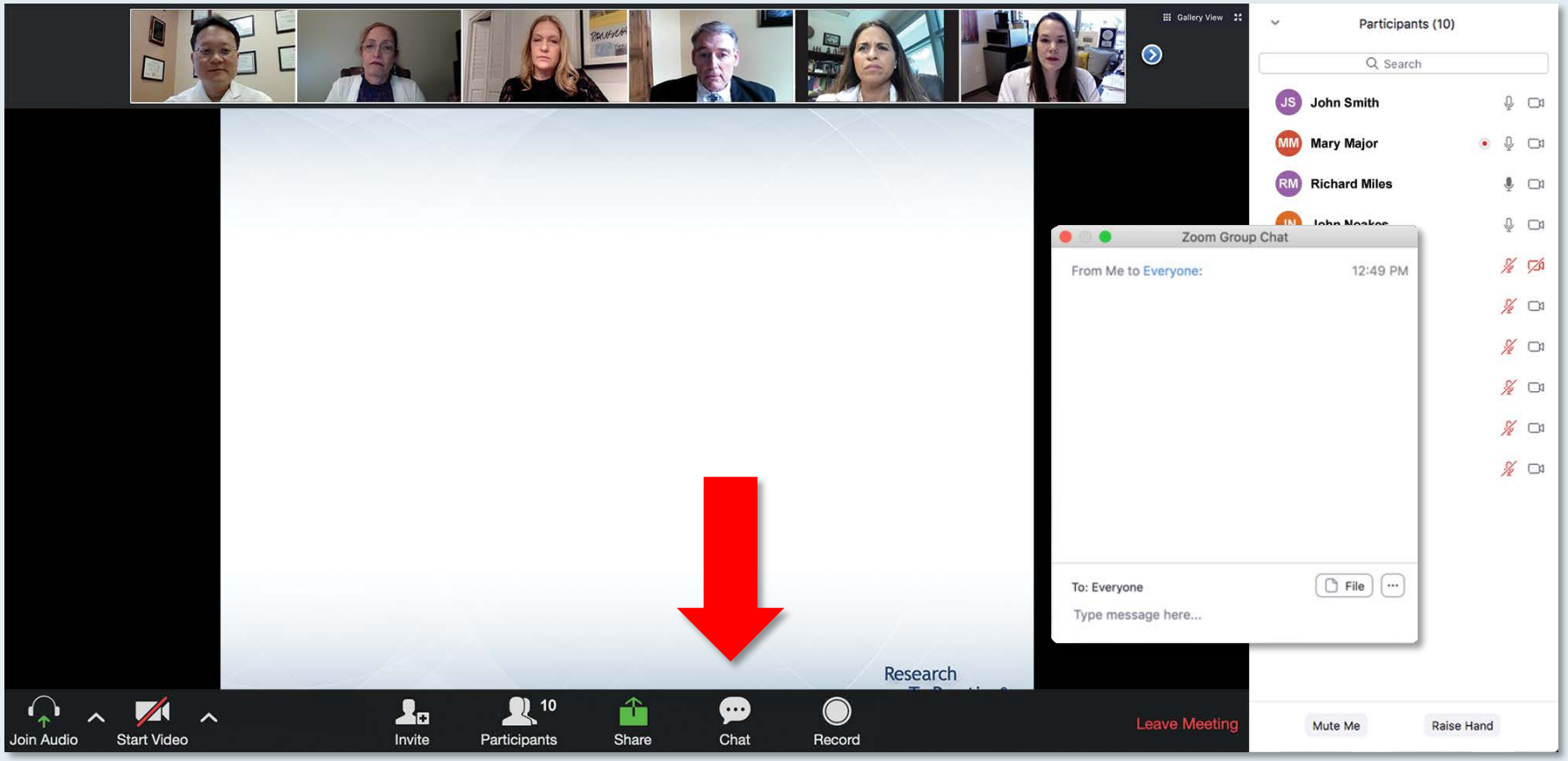

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Agenda

Case – Dr Chiang: An 83-year-old woman with newly diagnosed extensive-stage small cell lung cancer (ES-SCLC)

Case – Dr Spigel: A 63-year-old man with progressive SCLC who received lurbinectedin

Case – Dr Chiang: A 67-year-old man with newly diagnosed ES-SCLC with brain metastases

Case – Dr Spigel: A 61-year-old man with progressive SCLC

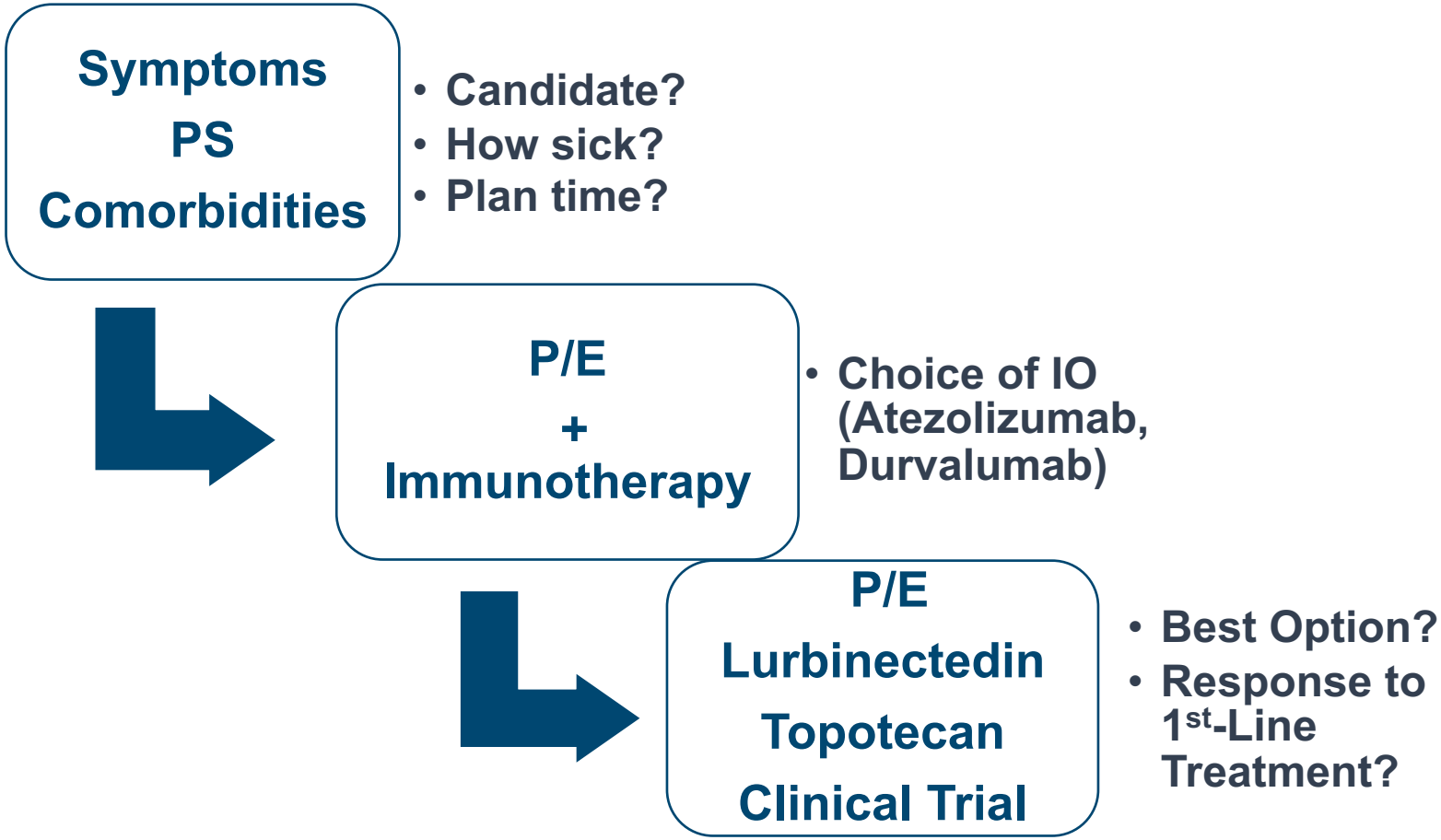
Case – Dr Spigel: A 67-year-old man with progressive SCLC treated with an anti-PD-1/anti-LAG3 antibody on a clinical trial

I know you have a special interest in small cell bladder cancers - I have had a bunch of small cell bladder cases - 6 in last 3 yrs.

I have an Asian pt nonsmoker with small cell bladder ca - locally advanced –
had 4 cycles of carboplatin etoposide as pt was cisplatin ineligible.
Was found to progress in 6 wks post chemo and was not able to get cystectomy due to local progression.
Pt is now getting palliative radiation given hematuria and obstruction.
NGS pending
What would be your next option?
His sister also had small cell of the lung ca — is there a familial component?
Sister is a nonsmoker.

Dr. Ashish Khot

SCLC Decision Making



Courtesy of David R Spigel, MD

Agenda

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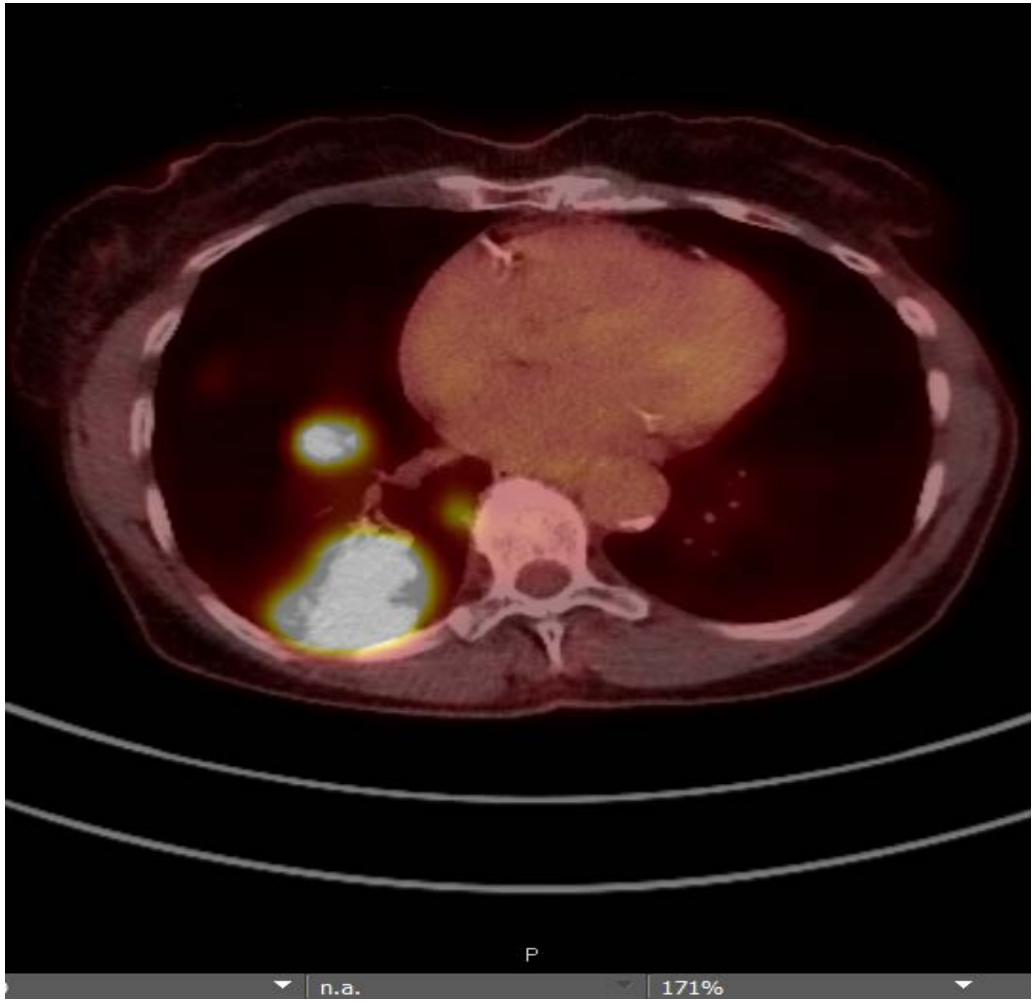
Case Presentation – Dr Chiang: An 83-year-old woman with newly diagnosed ES-SCLC

- 83-year-old African American female (40 py tobacco history) presented in spring 2020 with 30 lb weight loss over several months, worsening SOB on exertion, abdominal discomfort
- PMH: CAD, s/p MI, PVD, s/p femoral artery stent, lupus with rash, DM, hypothyroidism, asthma
- Physical exam reveals shotty neck adenopathy, right axillary LAD
- PET scan shows 6.2 cm RLL mass inseparable from costal pleura, additional tumor nodules in RLL, extensive regional nodal involvement in right hilar, right level 1-5, 7, 8, and right axillary LNs
- Brain MRI is negative
- Biopsy of LN reveals small cell carcinoma, positive for synaptophysin, Ki-67 is 90%

How would you treat this patient?



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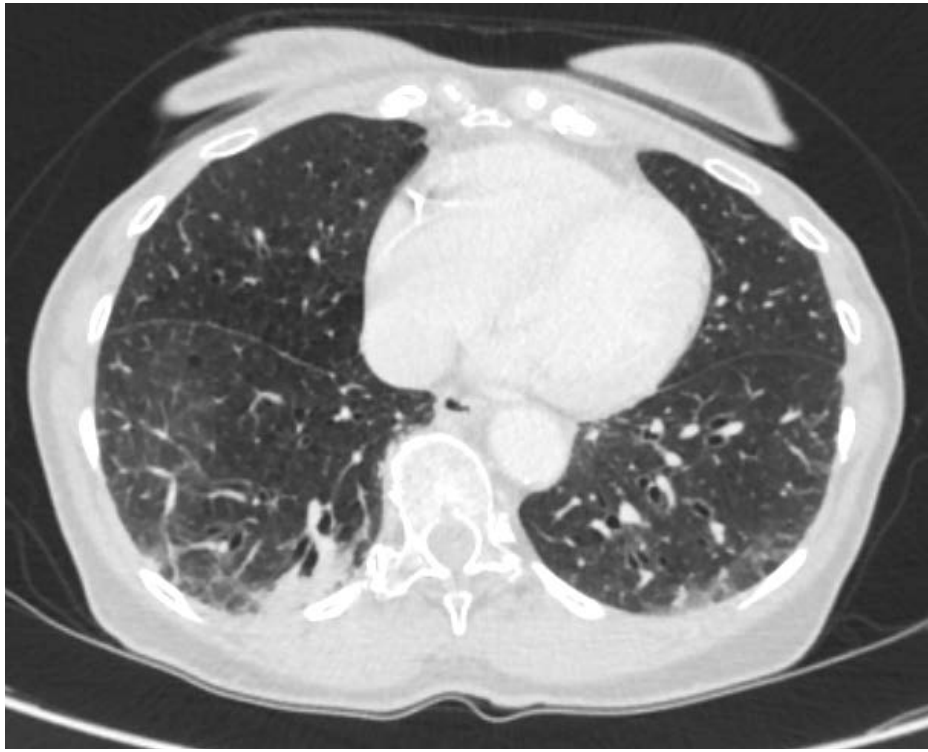
Courtesy of Anne Chiang, MD, PhD

Case Presentation – Dr Chiang: An 83-year-old woman with newly diagnosed ES-SCLC (cont)

- Pt has excellent response to 4 cycles of carboplatin, etoposide and atezolizumab and continues maintenance on monthly atezolizumab
- Atezo tolerated well except immunotherapy-induced lichenoid rash controlled with steroid topical cream
- Pt is on cycle 9 of maintenance Atezo

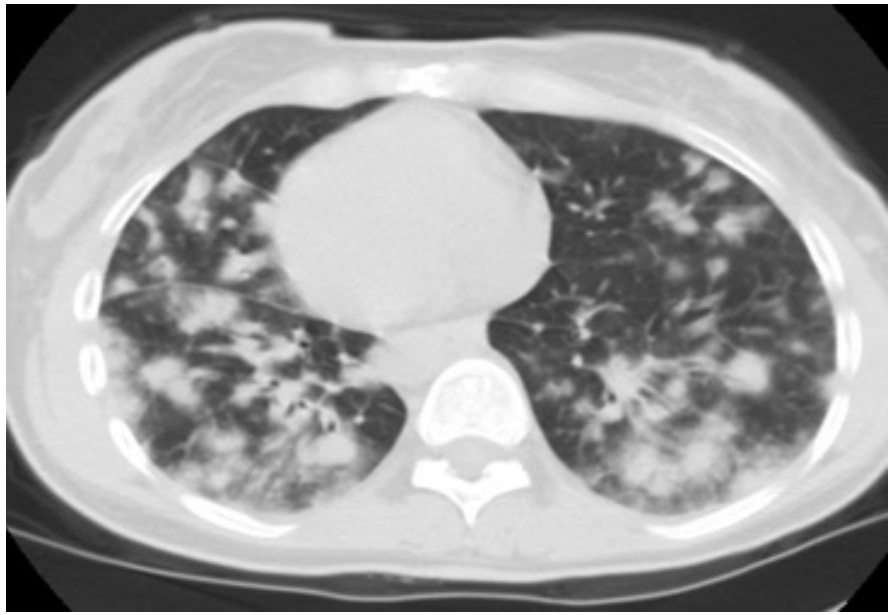
How long do you continue maintenance immunotherapy?



Courtesy of Anne Chiang, MD, PhD

Case Presentation – Dr Chiang: An 83-year-old woman with newly diagnosed ES-SCLC (cont)

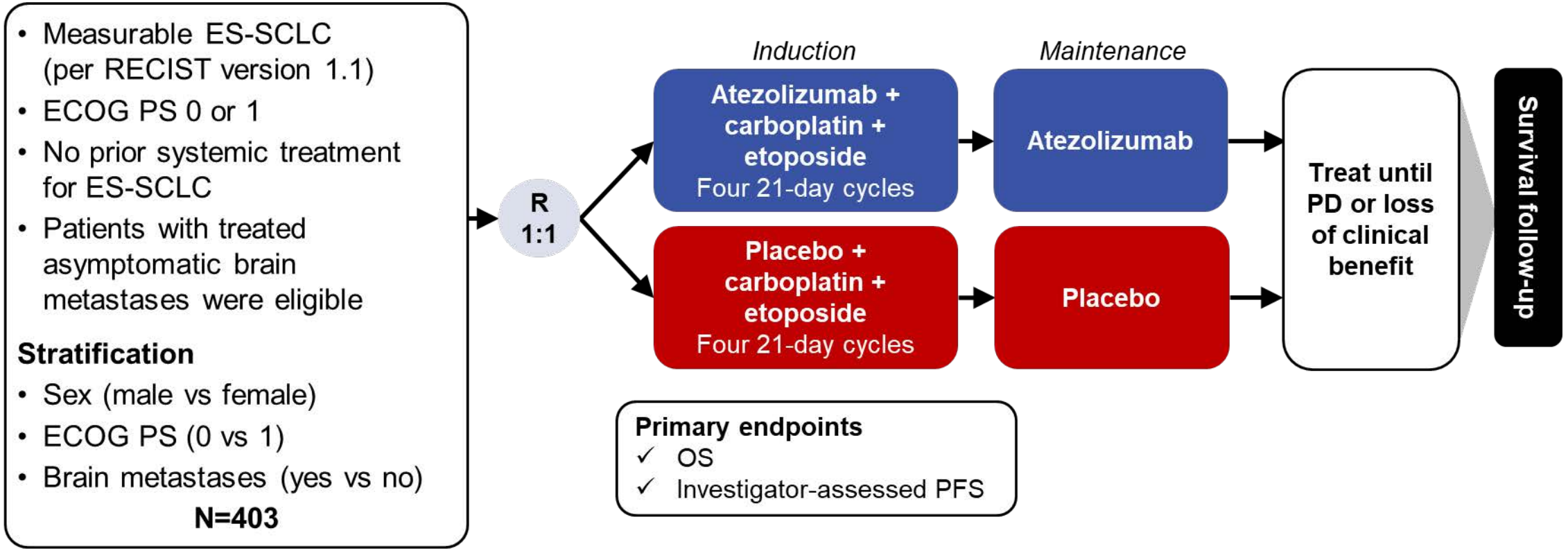
- Pt developed acute SOB, dry cough for several days and was evaluated in the ER, where she was hypoxic to 92%, hemodynamically stable
- CTA showed no PE but bilateral ground glass opacities
- Treated with high dose steroids, with taper over 6 weeks



Do you consider rechallenge with IO?

Courtesy of Anne Chiang, MD, PhD

IMpower133: First-Line Atezolizumab/Carboplatin/Etoposide



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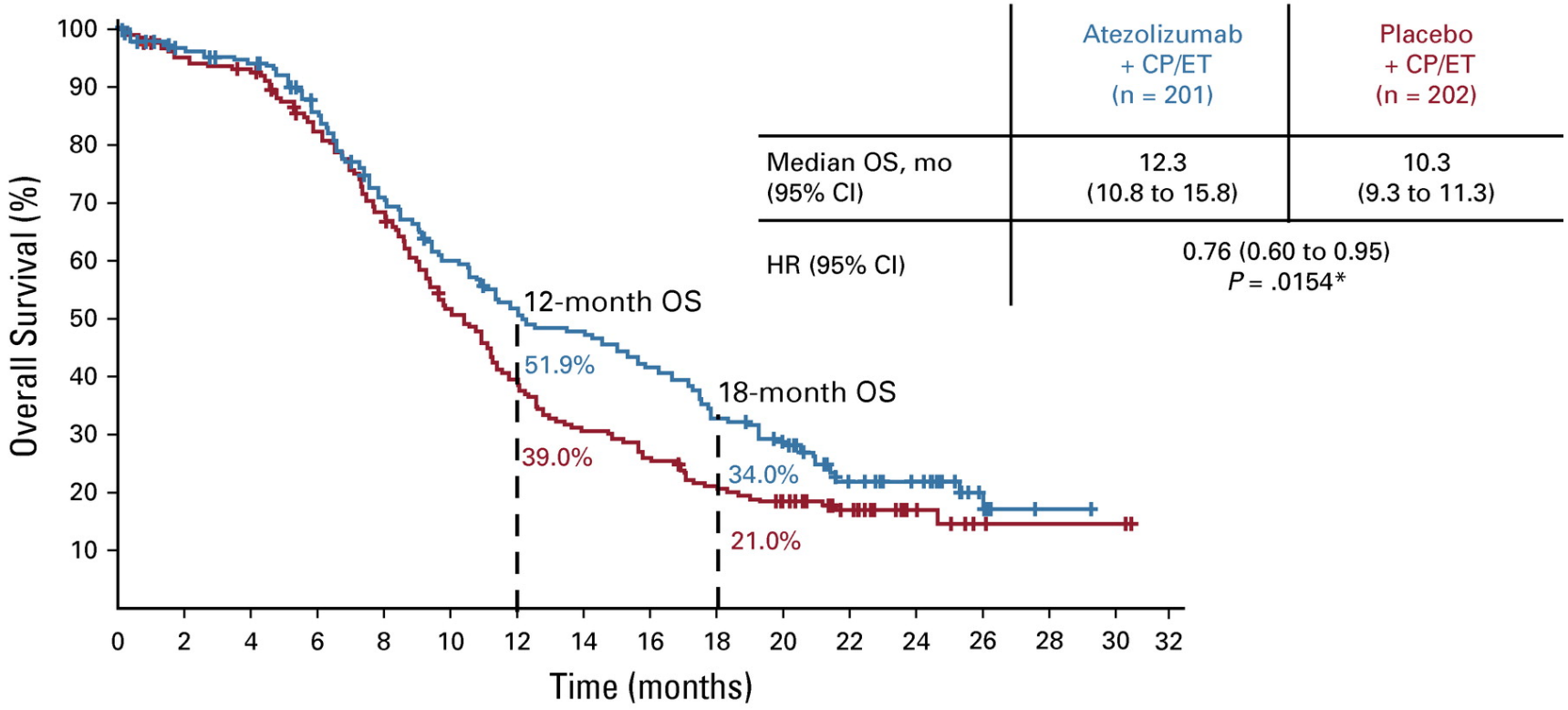
Courtesy of Anne Chiang, MD, PhD

IMpower133: Overall Survival

A



	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*	

No. of Patients at Risk

Atezolizumab + CP/ET	201	187	180	159	130	109	93	86	75	61	51	28	21	8	1
Placebo + CP/ET	202	189	183	160	131	97	74	58	49	39	33	20	8	3	2	2

Stephen V. Liu; Martin Reck; et al, *Journal of Clinical Oncology* 2021 39619-630. Median Follow up 22.9 months

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Courtesy of Anne Chiang, MD, PhD

Atezolizumab Immune-Related Adverse Events

irAE	Atezolizumab group (n=198)		Placebo group (n=196)	
	All grades	Grades 3-4	All grades	Grades 3-4
Rash	37 (18.7%)	4 (2.0%)	20 (10.2%)	0
Hypothyroidism	25 (12.6%)	0	1 (0.5%)	0
Hepatitis	14 (7.1%)	3 (1.5%)	9 (4.6%)	0
Infusion-related reaction	11 (5.6%)	4 (2.0%)	10 (5.1%)	1 (0.5%)
Hyperthyroidism	11 (5.6%)	0	5 (2.6%)	0
Pneumonitis	4 (2.0%)	1 (0.5%)	5 (2.6%)	2 (1.0%)
Colitis	3 (1.5%)	2 (1.0%)	0	0
Pancreatitis	1 (0.5%)	1 (0.5%)	2 (1.0%)	2 (1.0%)
Severe cutaneous reaction	2 (1.0%)	0	0	0
Adrenal insufficiency	0	0	2 (1.0%)	0
Rhabdomyolysis	2 (1.0%)	1 (0.5%)	0	0
Nephritis	1 (0.5%)	1 (0.5%)	1 (0.5%)	0
Hypophysitis	1 (0.5%)	0	0	0
Vasculitis	0	0	1 (0.5%)	0
Diabetes mellitus	1 (0.5%)	0	0	0
Guillain-Barre Syndrome	1 (0.5%)	1 (0.5%)	0	0

Horn et al, NEJM 2018.

Courtesy of Anne Chiang, MD, PhD

CASPIAN Study Design

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

- Treatment-naive 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)

1:1:1 R

Stratified by planned platinum (carboplatin vs cisplatin)

Durvalumab + EP[a] Q3W for 4 cycles	**Durvalumab** Q4W until PD
Durvalumab + tremelimumab + EP[a] Q3W for 4 cycles	**Durvalumab[c]** Q4W until PD
EP[a] Q3W for up to 6 cycles[b]	**Optional PCI[b]**

Primary endpoint

- OS

Secondary endpoints

- PFS[d]
- ORR[d]
- Safety & tolerability
- PROs

- Updated analysis of OS after median follow-up of approximately 3 years was a planned exploratory analysis
  - PFS and ORR data were not collected since the previous data cutoff
  - Serious AEs (including deaths) were analyzed, but other safety data were not collected

[a]EP consists of etoposide 80-100 mg/m^2 with either carboplatin AUC 5-6 or cisplatin 75-80 mg/m^2, durvalumab dosed at 1500 mg, tremelimumab dosed at 75 mg. [b]Patients could receive an additional 2 cycles of EP (up to 6 cycles total) and PCI at the investigator's discretion. [c]Patients received an additional dose of tremelimumab post EP.

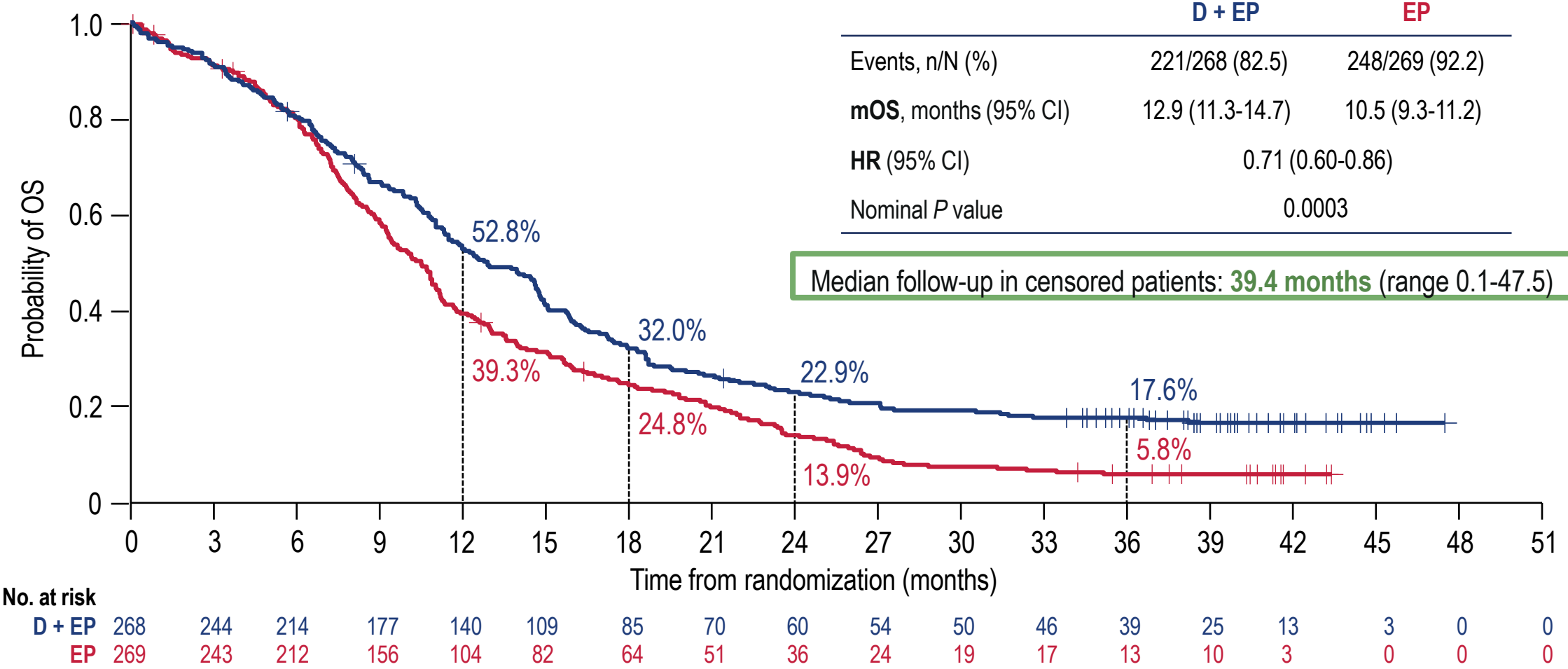
Paz-Ares LG, et al. *Ann Oncol*. 2021;32(suppl 5):S1283-S1346.

Courtesy of Anne Chiang, MD, PhD

CASPIAN: 3-Year OS Update with 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: March 22, 2021. Paz-Ares LG, et al. *Ann Oncol*. 2021;32(suppl 5):S1283-S1346.

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Courtesy of Anne Chiang, MD, PhD

FDA approvals for 1L ES-SCLC

	IMpower133 updated analysis	CASPIAN updated analysis
Median follow up	22.9 mo	39.4 mo
mOS	12.3 vs 10.3 mo	12.9 vs 10.5 mon
HR	0.76, p=0.0154	0.71, p=0.0003
1YOS	51.9 vs 39%	52.8 vs 39.3%
2YOS	22 vs 17%	22.9 vs 13.9%
3YOS		17.6 vs 5.8%
Eligibility	Treated brain mets only	Asymptomatic brain mets allowed
Chemo	Carboplatin	Cis or carboplatin
New Technology Add-on Payments (NTAP)	yes	yes

Courtesy of Anne Chiang, MD, PhD

Immune Therapy Rechallenge

(NCCN Guidelines V3.2021)

Organ	Rechallenge (Grade <1)	Do NOT rechallenge
Skin	Rash, pruritis	Grade 3-4 severe, life-threatening bullous disease
GI	Grade 2/3 PD-1/PD-L1 colitis[a]	Grade 4 colitis
Liver	Grade 2 transaminitis without elevated bilirubin[a]	Grade 3-4 hepatitis
Pancreatitis	Symptomatic grade 2	Grade 3-4 pancreatitis
Endocrine	After hormone repletion	Symptomatic pituitary inflammation
Lung	Grade 1-2, off steroids	Grade 3-4 pneumonitis
Renal	Grade 1-2[a]	Grade 3-4 proteinuria
Ocular	Grade 2	Grade 3-4 uveitis, grade >2 episcleritis
Neurologic	Grade 2 myasthenic gravis, grade 1-2 peripheral neuropathy	GBS, encephalitis, transverse myelitis, grade 3-4 myasthenia gravis
Cardiovascular	Grade 1 myocarditis	Grade >2 myocarditis
Musculoskeletal	Resume after stabilization, management	Severe inflammatory arthritis that impairs ADLs

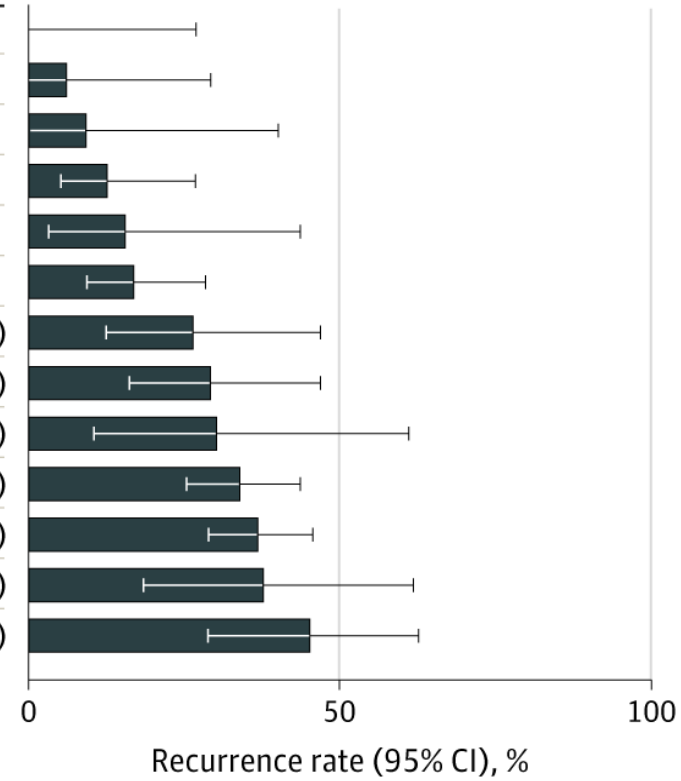
[a]may resume once patient on < Prednisone 10 mg daily.

Courtesy of Anne Chiang, MD, PhD

Rate of Recurrence According to Initial irAE

- 28.8% (130/452) recurrence of initial irAE upon rechallenge
- Higher rechallenge recurrence for the following:
  - Colitis (OR 1.77; CI: 1.14-2.75; *P* =0.01)
  - Hepatitis (OR 3.38; CI: 1.31-8.74; *P* =0.01)
  - Pneumonitis (OR 2.26; CI: 1.18-4.32; *P* =0.01)

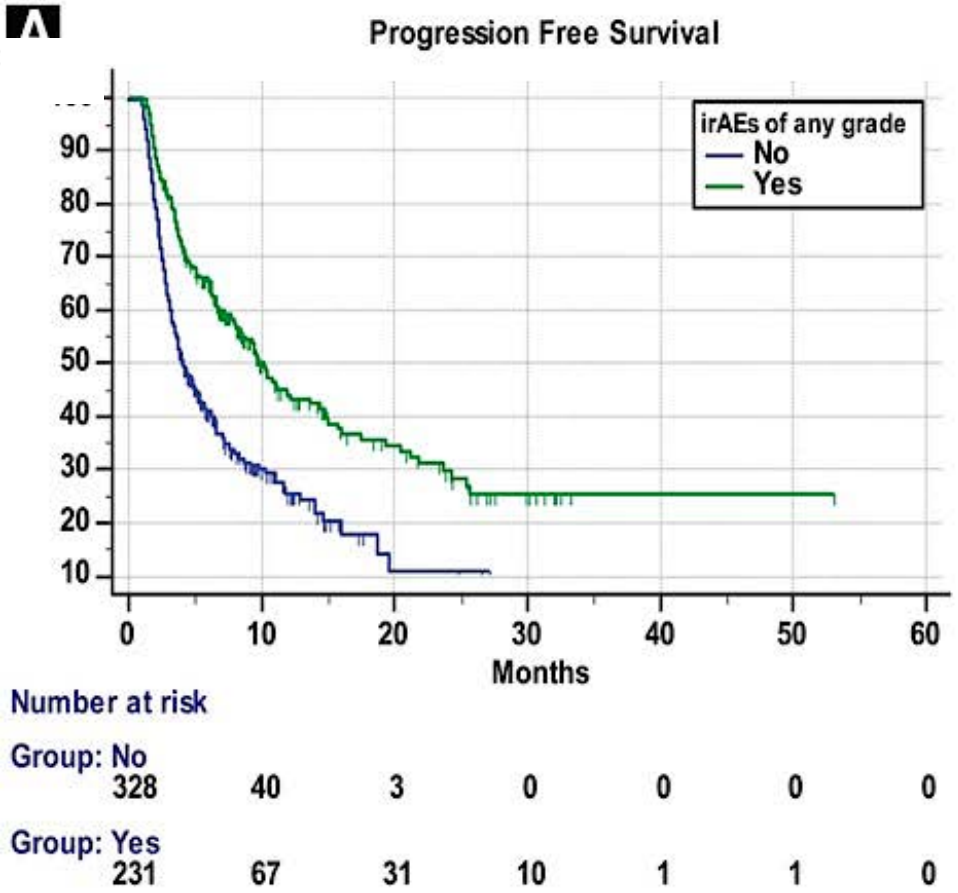
Adverse drug reaction	No. of cases	Recurrence rate (95% CI), %
Diabetes	13	0 (0-27)
Neurologic	17	6 (0-29)
Uveitis	11	9 (0-40)
Adrenal	40	12 (5-27)
Pancreatitis	13	15 (3-43)
Thyroiditis	60	17 (9-28)
Hypophysitis	23	26 (12-47)
Hepatitis	31	29 (16-47)
Hematologic	10	30 (10-61)
Pneumonitis	101	34 (25-43)
Colitis	123	37 (29-45)
Skin	16	38 (18-61)
Arthritis	29	45 (28-62)

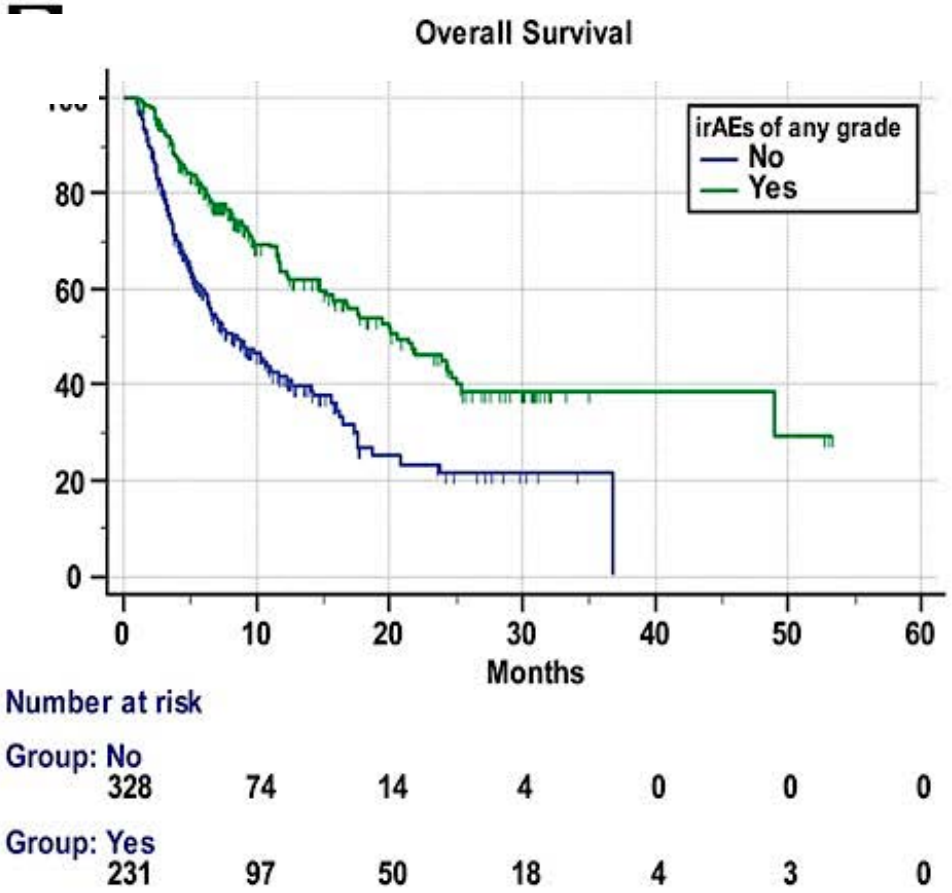


OR = odds ratio.

Dolladille et al, JAMA Oncol 2020.

Better PFS and OS in Patients With irAEs





Cortellini et al, Clinical Lung Cancer 2019.

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A Comprehensive Cancer Center Designated by the National Cancer Institute

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Courtesy of Anne Chiang, MD, PhD

FDA Approves Trilaciclib to Reduce Bone Marrow Suppression Caused by Chemotherapy

Press Release: February 12, 2021

"Today, the US Food and Drug Administration approved trilaciclib as the first therapy in its class to reduce the frequency of chemotherapy-induced bone marrow suppression in adults receiving certain types of chemotherapy for extensive-stage (when the cancer has spread beyond the lungs) small cell lung cancer. Trilaciclib may help protect bone marrow cells from damage caused by chemotherapy by inhibiting cyclin-dependent kinase 4/6, a type of enzyme.

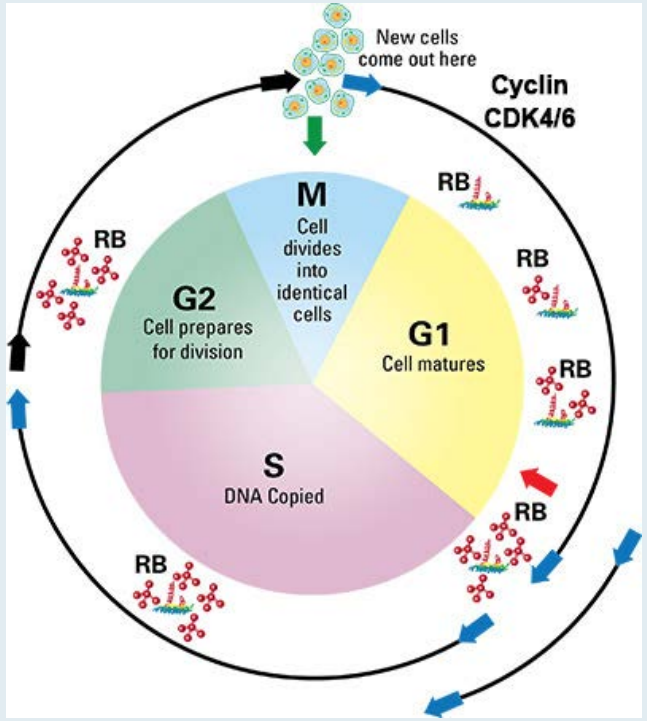
The effectiveness of trilaciclib was evaluated in three randomized, double-blind, placebo-controlled studies in patients with extensive-stage small cell lung cancer. Combined, these studies randomly assigned 245 patients to receive either an infusion of trilaciclib in their veins or a placebo before chemotherapy. The studies then compared the two groups for the proportion of patients with severe neutropenia (a very low count of white blood cells called neutrophils) and the duration of severe neutropenia in the first cycle of chemotherapy. In all three studies, patients who received trilaciclib had a lower chance of having severe neutropenia compared to patients who received a placebo. Among those who had severe neutropenia, patients who received trilaciclib, on average, had it for a shorter time than patients who received a placebo."

https://www.fda.gov/news-events/press-announcements/fda-approves-drug-reduce-bone-marrow-suppression-caused-chemotherapy

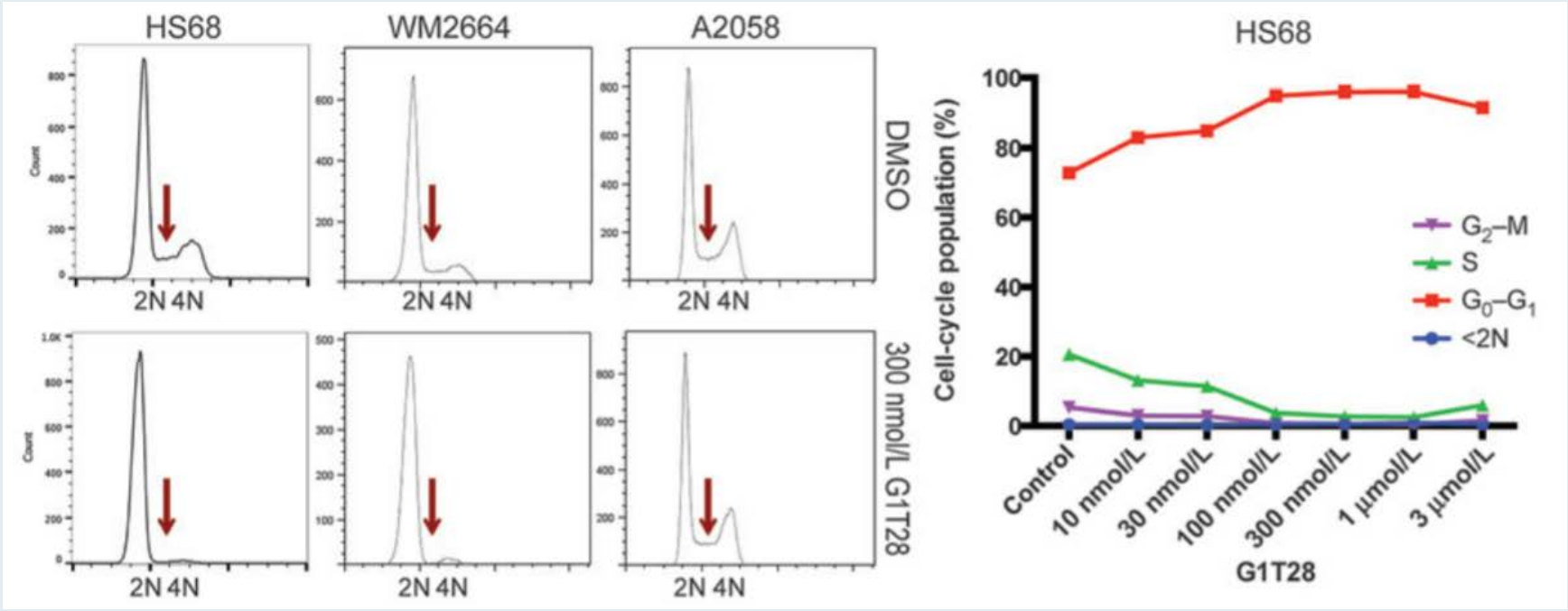
RTP RESEARCH TO PRACTICE

Trilaciclib to Prevent Myelosuppression in SCLC

CDK4/6 inhibitors (G1T28) transiently maintain G1 cell cycle arrest of hematopoietic stem and progenitor cells.



CDK4/6-dependent cell lines

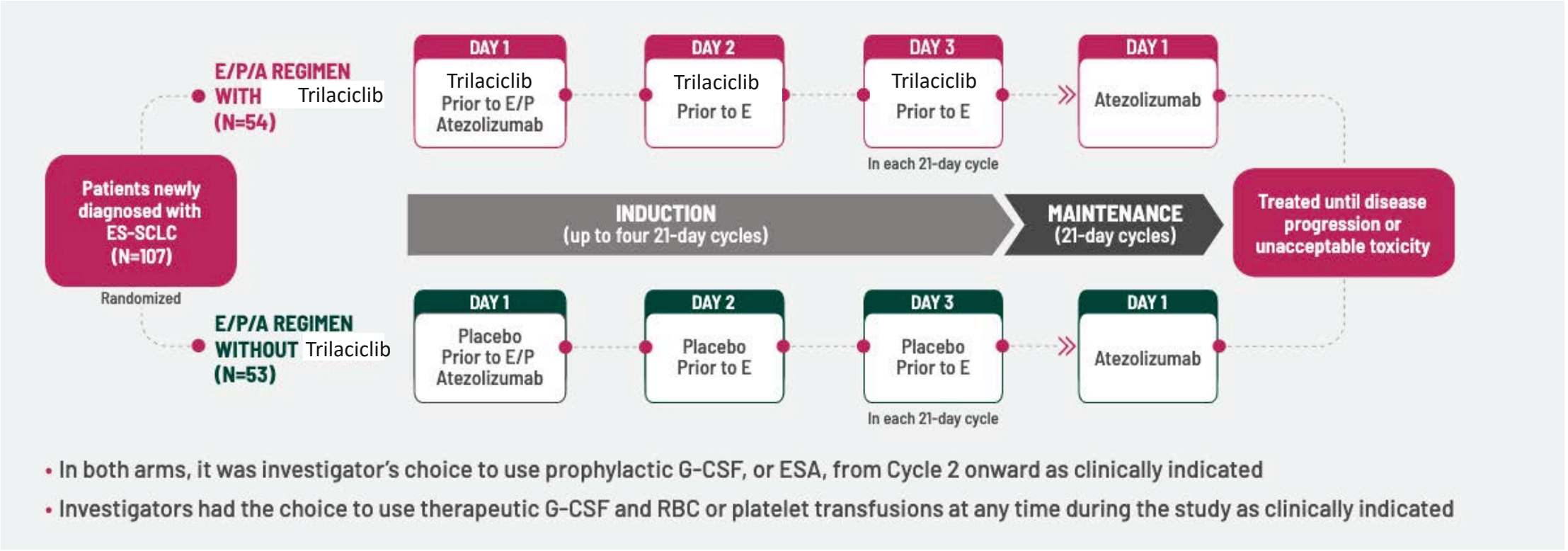


https://www.dana-farber.org/newsroom/publications/paths-of-progress-2019/wrench-in-the-works/

Bisi JE et al. *Mol Cancer Ther* 2016;15(5):783-93.

RTP RESEARCH TO PRACTICE

Trilaciclib: Randomized Phase II in 1st-Line ES-SCLC

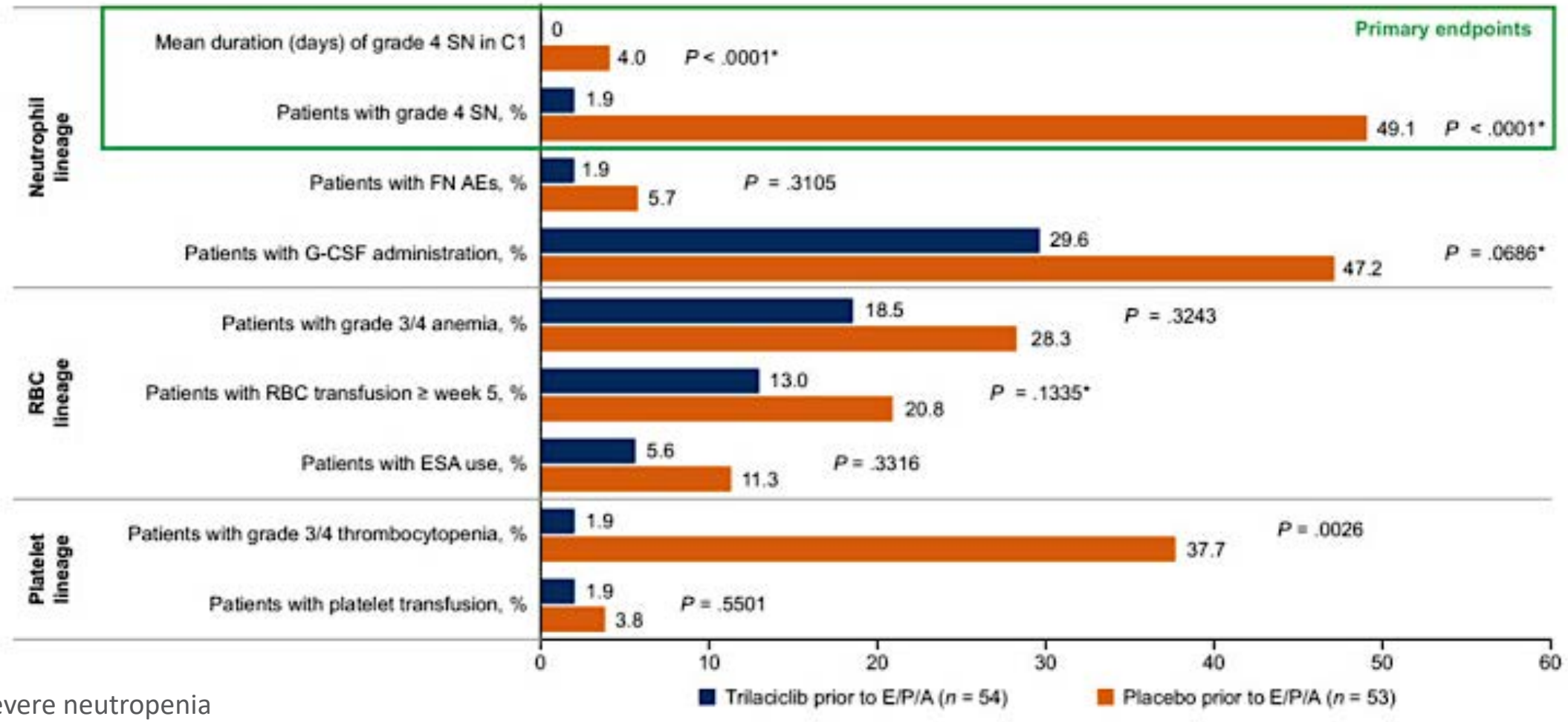


- In both arms, it was investigator's choice to use prophylactic G-CSF, or ESA, from Cycle 2 onward as clinically indicated
- Investigators had the choice to use therapeutic G-CSF and RBC or platelet transfusions at any time during the study as clinically indicated

Daniel, Int J of Cancer, 2020

Courtesy of David R Spigel, MD

Trilaciclib: Randomized Phase II in 1st-Line ES-SCLC

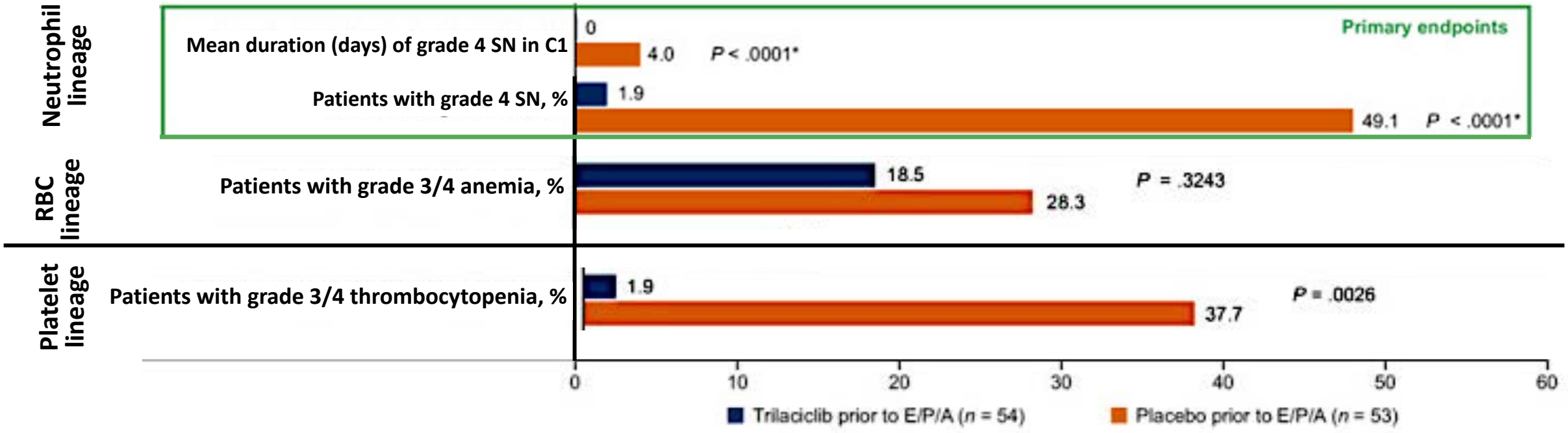


SN = severe neutropenia

Daniel, Int J of Cancer, 2020

Courtesy of David R Spigel, MD

Trilaciclib: Randomized Phase II in 1st-Line ES-SCLC



SN = severe neutropenia

Daniel, Int J of Cancer, 2020

Courtesy of David R Spigel, MD

Concerning FDA approval of trilaciclib (Cosela) in extensive-stage small-cell lung cancer

Kerrington Powell [a], V Prasad [b,*]

[a] *College of Medicine, Texas A&M Health Science Center, College Station, TX 77843, United States*
[b] *Department of Epidemiology and Biostatistics, University of California San Francisco, 550 16th St, 2nd Fl, San Francisco, CA 94158, United States*

Transl Oncol **2021;14(11):101206.**

RTP RESEARCH TO PRACTICE

Potential Role and Impact of Trilaciclib in Clinical Practice

"Based on the current phase II data, trilaciclib appears to be an intervention that may make a positive impact by preventing CIM, maintaining immune system function, and minimizing cytotoxic AEs, although many of these outcomes remain unclear. Using this drug may augment chemotherapy and ICI regimens, but whether or not trilaciclib helps patients live longer or live better is a matter of continuing debate and uncertainty.

Trilaciclib has elements of bioplausibility, but molecular determinants of CDK4/6-independence and dependence are complex, and the therapy must prove itself with empirical validation. Phase III trials testing survival, anti-tumor efficacy, and quality of life outcomes are the only way forward. By doing so, we can safely implement this therapy to provide a clinical benefit to patients."

Powell K, Prasad V. *Transl Oncol* 2021;14(11):101206.

Agenda

Case – Dr Chiang: An 83-year-old woman with newly diagnosed extensive-stage small cell lung cancer (ES-SCLC)

Case – Dr Spigel: A 63-year-old man with progressive SCLC who received lurbinectedin

Case – Dr Chiang: A 67-year-old man with newly diagnosed ES-SCLC with brain metastases

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Case Presentation – Dr Spigel: A 63-year-old man with progressive SCLC who received lurbinectedin

HPI

A 63yo gentleman who presented 1/2020 with w/ lung lesions and extensive bone involvement. Bronchoscopy confirmed SCLC – a sacral biopsy was negative. He received carboplatin/etoposide/atezolizumab (and zoledronic acid) 2/2020 for suspected ES-SCLC.

PMH

COPD

Psoriatic arthritis

HTN

SH

Single

Retired

1 PPD x 46yrs

Case Presentation – Dr Spigel: A 63-year-old man with progressive SCLC who received lurbinectedin (cont)

Course:

Received 4 cycles of carboplatin/etoposide/atezolizumab 2/2020 – 5/2020

Complete response in lungs

PSA 19 – Prostate biopsy: 3+4=7, Leuprolide given; PSA responded

Thoracic RT given 3000Gy – ending 6/2020

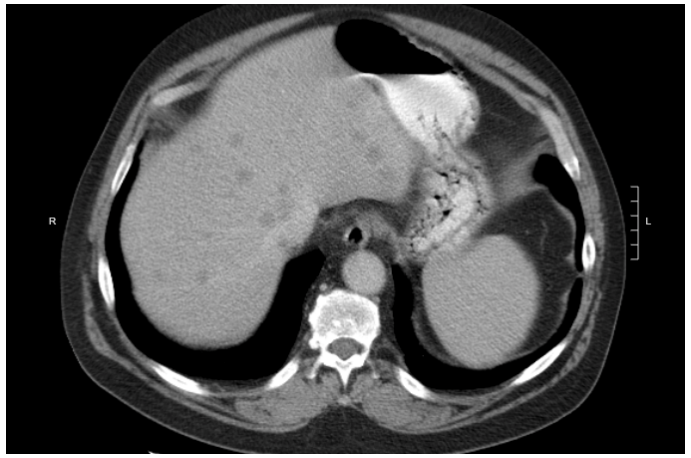
9/2020 new liver lesions on surveillance imaging

Sensitive Relapsed Treatment:

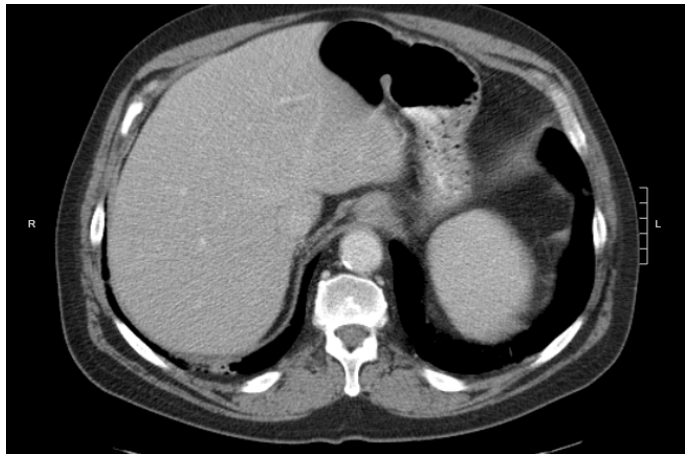
Lurbinectedin initiated 9/2020

Visit 10/2021 – CR – 17 cycles

No toxicity

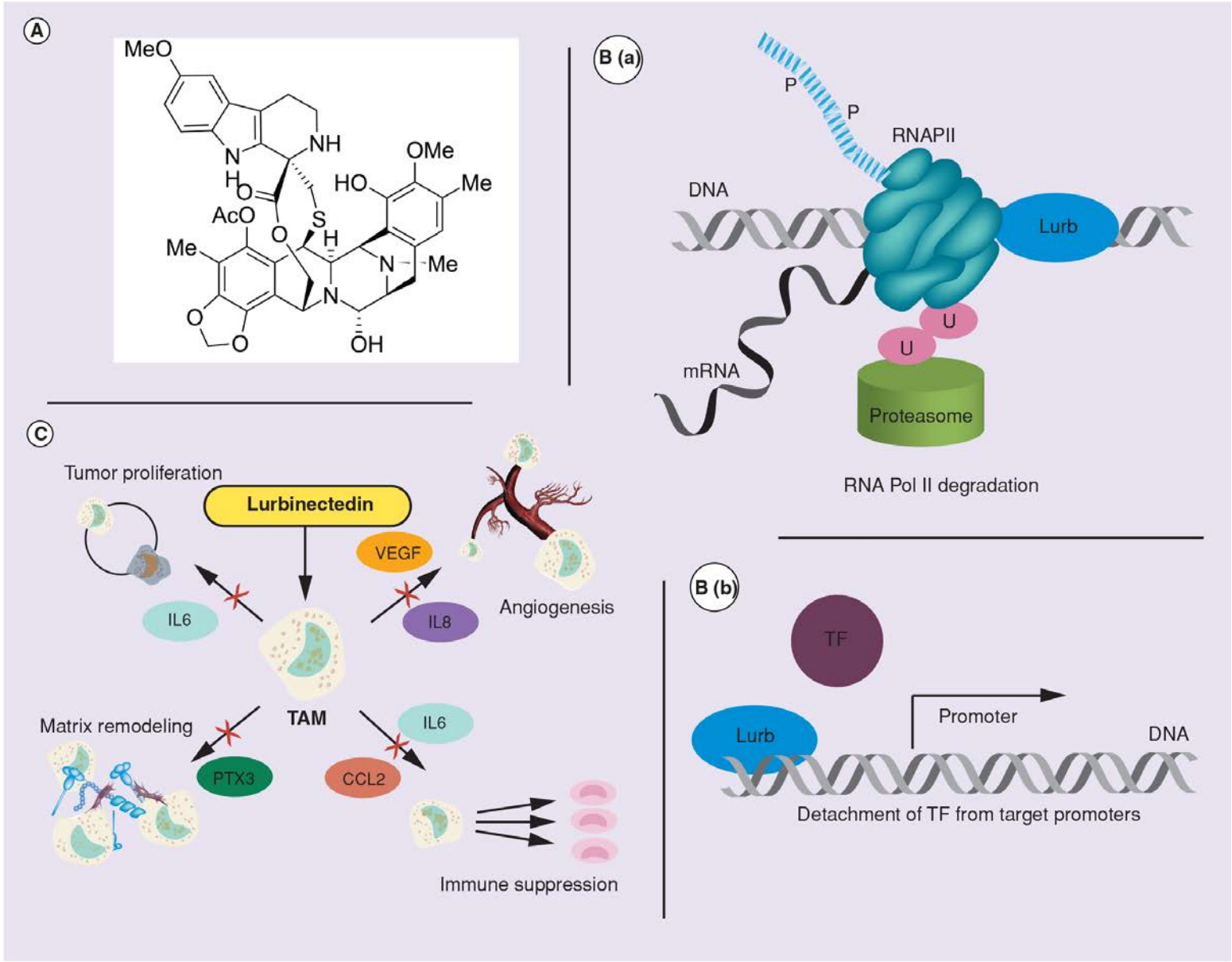


9/2020



10/2020

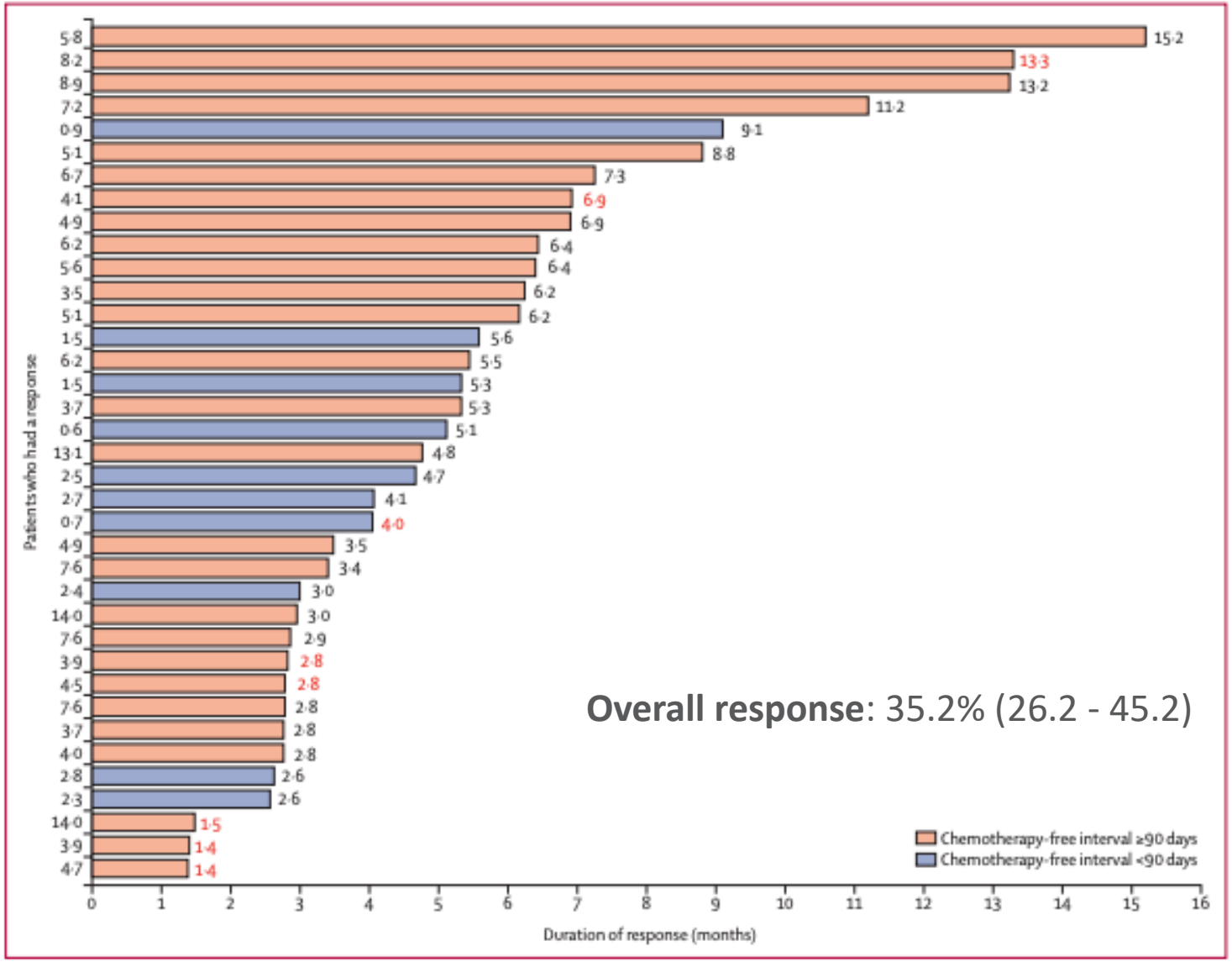
Lurbinectedin



Farago, Fut Onc 2019

Courtesy of David R Spigel, MD

Lurbinectedin Phase II DOR

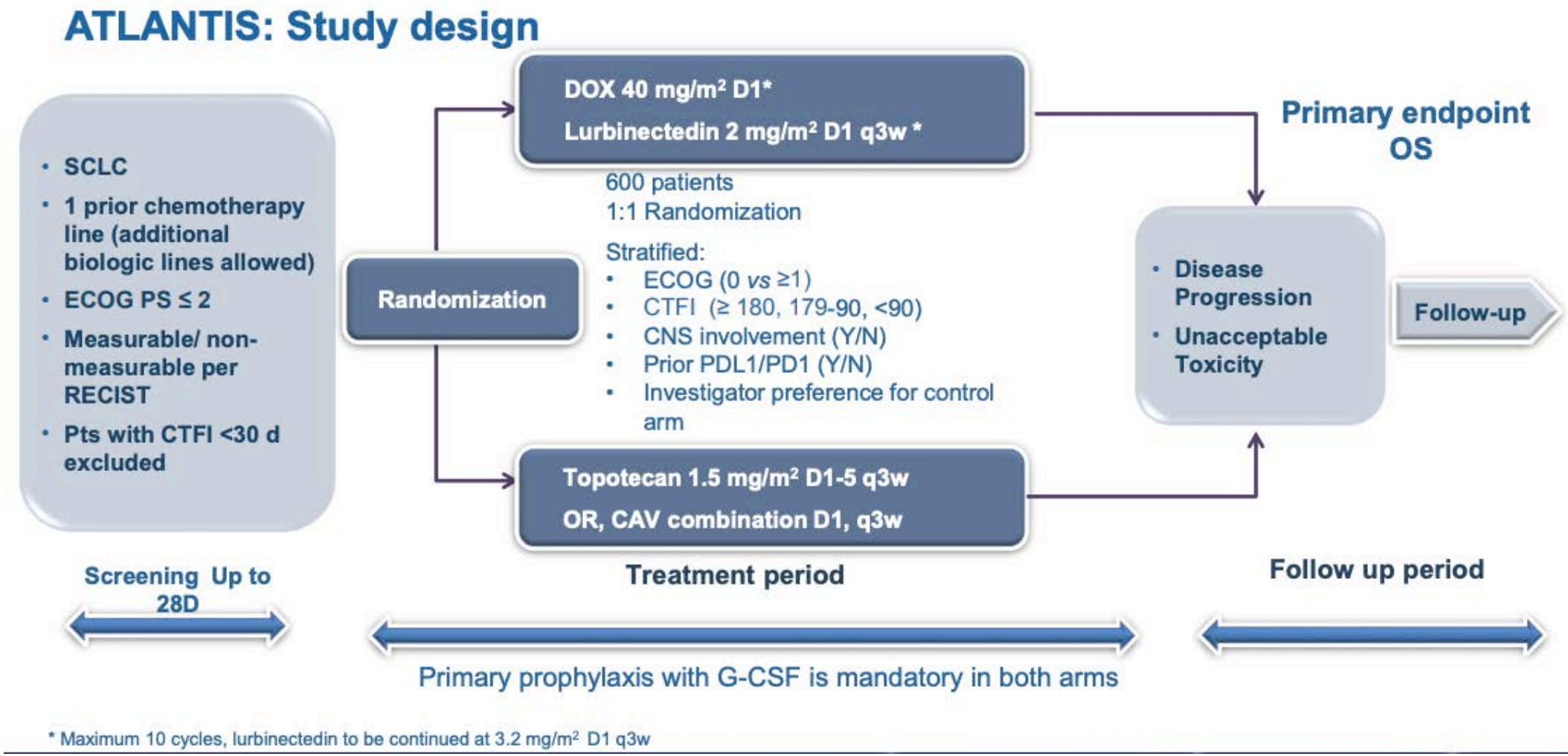


Overall response: 35.2% (26.2 - 45.2)

Trigo, Lancet Onc 2020

Courtesy of David R Spigel, MD

Lurbinectedin Ph III: ATLANTIS

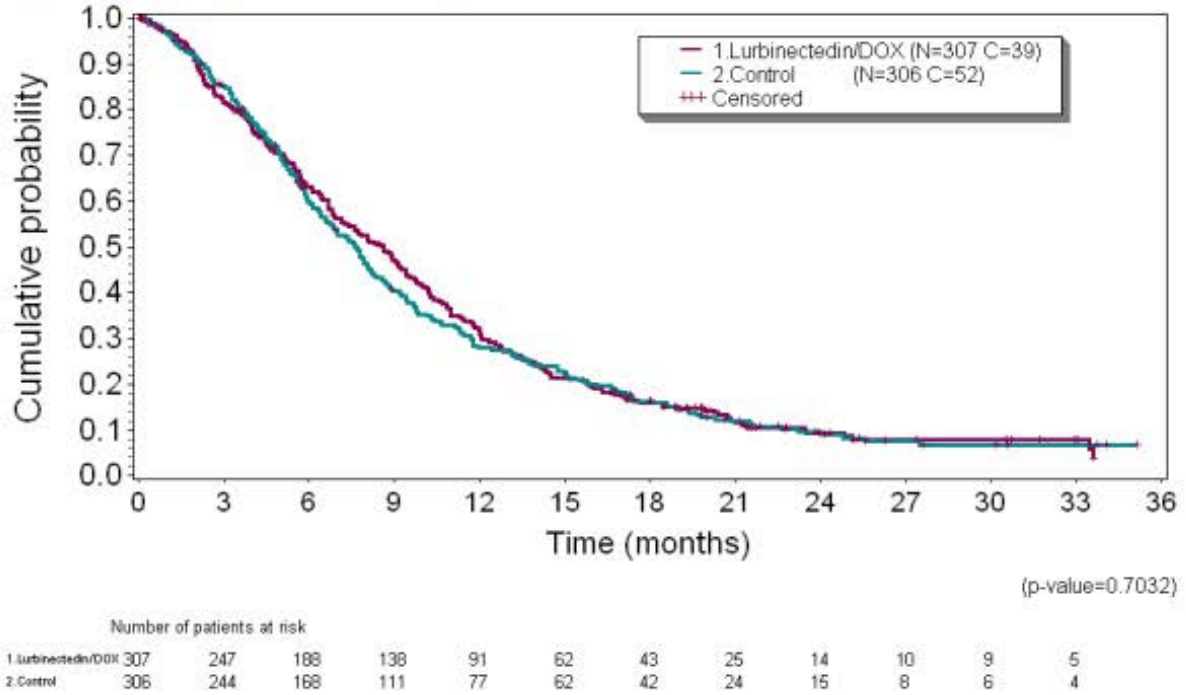


Paz-Ares, WCLC 2021

Courtesy of David R Spigel, MD

Lurbinectedin Ph III: ATLANTIS

Overall Survival (ITT population)



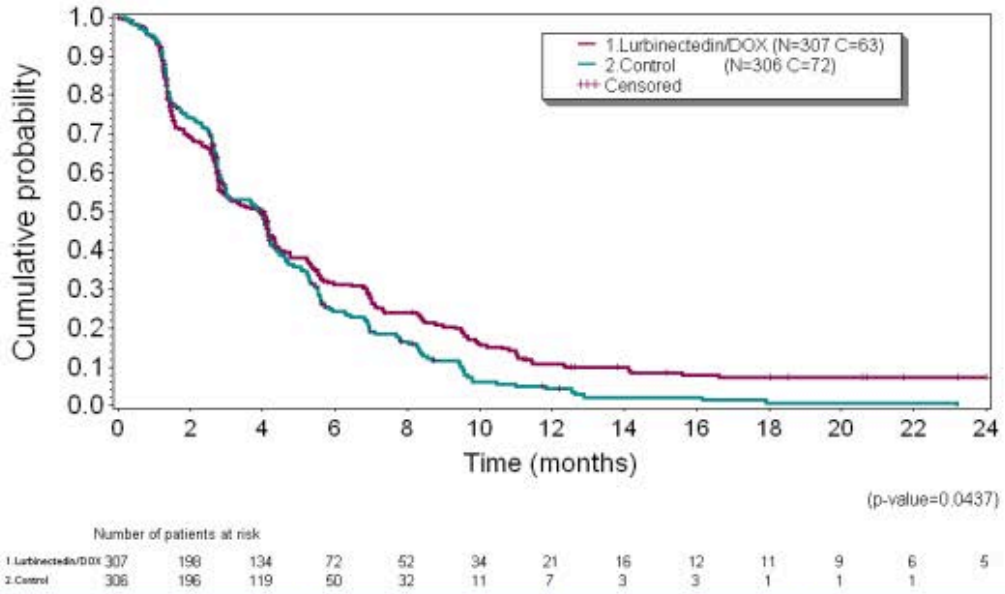
	Lurbinectedin+DOX (N=307)	Control (N=306)	Parameter	p-value
Events, n (%)	268 (87.3)	254 (83.0)		
Censored, n (%)	39 (12.7)	52 (17.0)		
Median OS (95% CI), months	**8.6 (7.1, 9.4)**	**7.6 (6.6, 8.2)**	**HR : 0.967 (0.815, 1.148)**	**0.7032**
Mean OS, months	10.6	9.9		

Paz-Ares, WCLC 2021

Courtesy of David R Spigel, MD

Lurbinectedin Ph III: ATLANTIS

PFS by Independent Review Committee: Lurbinectedin/Doxo vs Control



	Lurbinectedin+DOX (N=307)	Control (N=306)	Parameter	p-value
Events, n (%)	244 (79.5)	234 (76.5)		
Censored, n (%)	63 (20.5)	72 (23.5)		
Median PFS (95% CI), months	**4.0 (2.8, 4.2)**	**4.0 (3.0, 4.1)**	**HR: 0.831 (0.693, 0.996)**	**0.0437**
Mean PFS, months	5.9	4.6		
PFS (%) at 6 months (95% CI)	31.3 (25.8, 36.9)	24.4 (19.1, 30.1)		0.0851
PFS (%) at 12 months (95% CI)	10.8 (7.1, 15.3)	4.4 (2.1, 8.1)		0.0129

Paz-Ares, WCLC 2021

Courtesy of David R Spigel, MD

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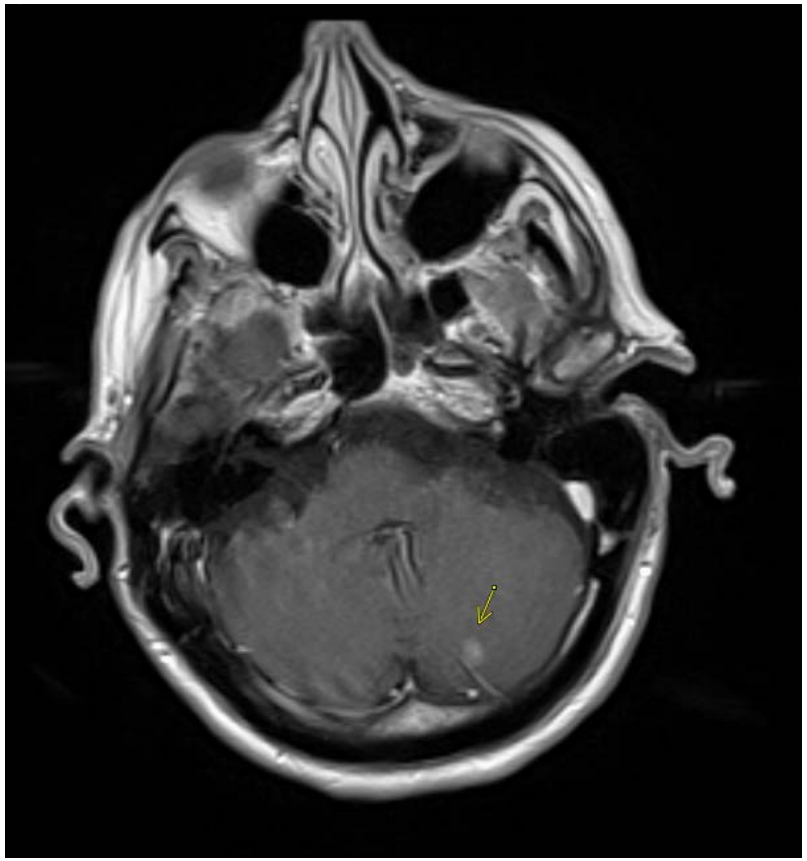
Case – Dr Spigel: A 67-year-old man with progressive SCLC treated with an anti-PD-1/anti-LAG3 antibody on a clinical trial

Case Presentation – Dr Chiang: A 67-year-old man with newly diagnosed ES-SCLC with brain metastases

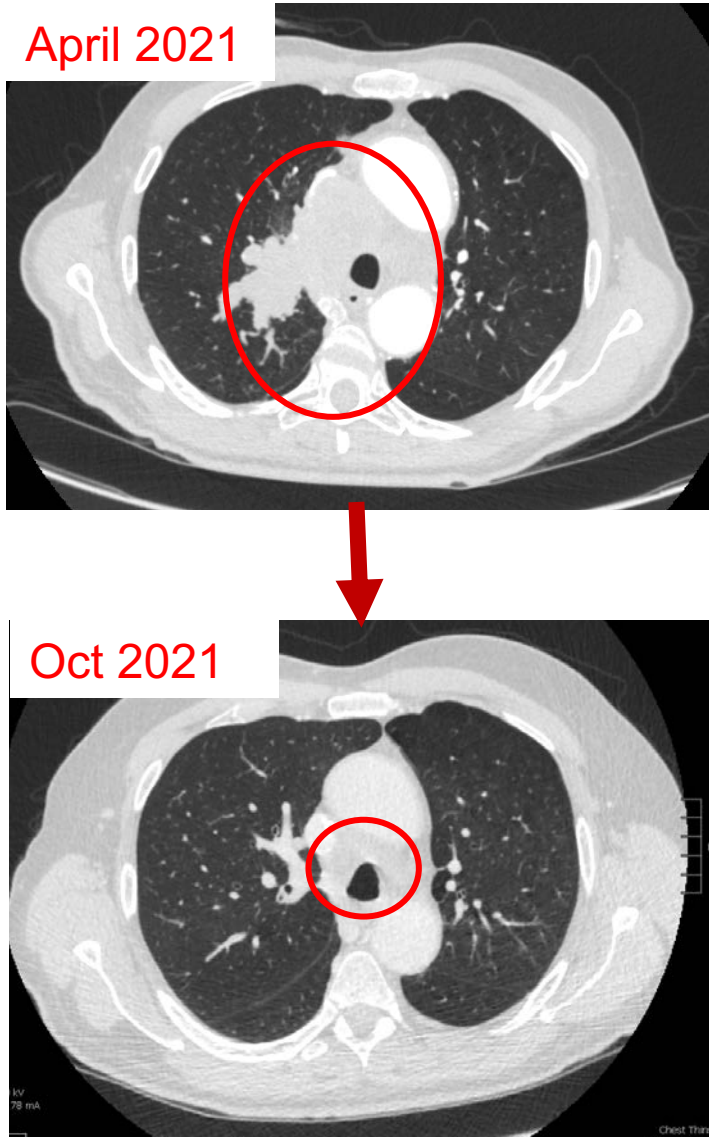
- 67-year-old white male (50 py tobacco history) presented in spring 2021 with 40 lb weight loss over several months, dysphagia, worsening SOB on exertion, weakness
- PMH: CAD, CVA, HTN
- CT scan shows 6.2 x 3.6 cm mediastinal mass extending into the SVC with mass effect on the right pulmonary artery, RUL bronchus, also bulky right hilar mass, multiple satellite solid nodules throughout the right lung
- Brain MRI shows numerous subcentimeter supra- and infratentorial lesions
- EBUS/Biopsy of RUL lung, 4R and 4L LN reveals small cell carcinoma, positive for TTF1, INSM1



What is the next step in treatment?

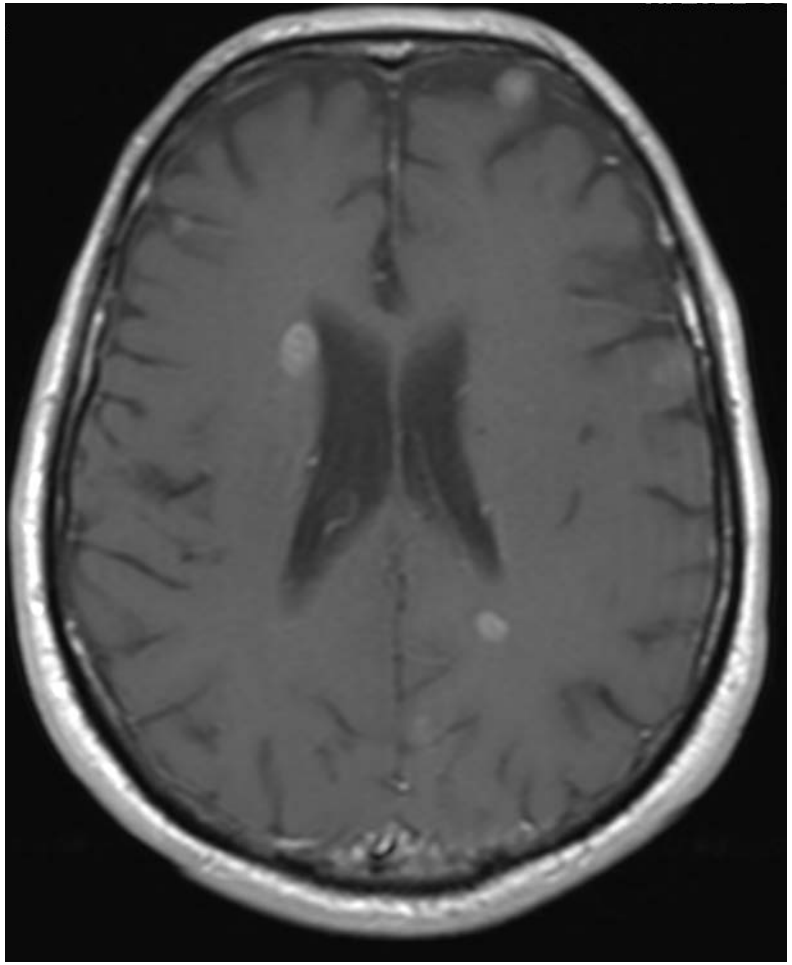
Case Presentation – Dr Chiang: A 67-year-old man with newly diagnosed ES-SCLC with brain metastases (cont)

- Pt is treated as inpatient with carbo/etoposide and discharged
- Pt presents with acute left leg swelling and found to have DVT, started on anticoagulation after repeat MRI brain improved
- Durvalumab added to cycle 3 carbo/etop
- Dose reduction of carbo and etop due to cytopenias, pegfilgrastim added. Pt continues on maintenance durvalumab after 4 cycles of chemo
- Overall response is excellent



Case Presentation – Dr Chiang: A 67-year-old man with newly diagnosed ES-SCLC with brain metastases (cont)

- MRI brain shows POD with greater than 15 lesions
- Restaging CT scans show continued response in mediastinal and right hilar lymphadenopathy, with all disease in the 1-1.5 cm range
- Pt undergoing WBRT



Clinical question:

After definitive WBRT and continued systemic response, do you continue durvalumab or switch to 2nd line therapy?

Brain Metastases: Local vs systemic treatment

- Factors favoring systemic treatment:
  - asymptomatic brain metastatic disease
  - High burden of disease elsewhere requiring systemic therapy
  - Need for quick response
  - Avoid side effects of WBRT, e.g. cognitive defects

- Factors favoring local treatment, e.g. radiation or surgery
  - Contraindications to chemotherapy
  - Need for emergent stabilization, e.g. herniation
  - Relapsed, chemo-refractory disease
  - Eligibility for clinical trial

Courtesy of Anne Chiang, MD, PhD

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Case Presentation – Dr Spigel: A 61-year-old man with progressive SCLC

HPI

A 61yo gentleman who presented 10/2017 with hemoptysis and a large mediastinal/R-lung mass – path confirmed SCLC. He received WBRT (for lesions) 10/2017, carboplatin/etoposide ending 1/2018, chest RT 3/2018 – and presented to me 8/2018 with PD in the adrenal glands.

PMH

HTN

SH

Married

3 children

IT Manager

2 PPD x 40 years

Case Presentation – Dr Spigel: A 61-year-old man with progressive SCLC (cont)

Sensitive Relapsed Treatment:

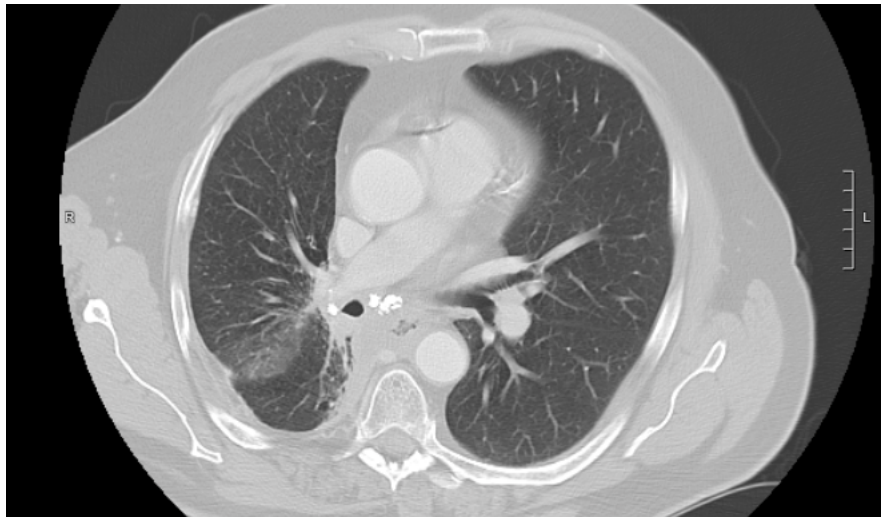
Screened for clinical trials

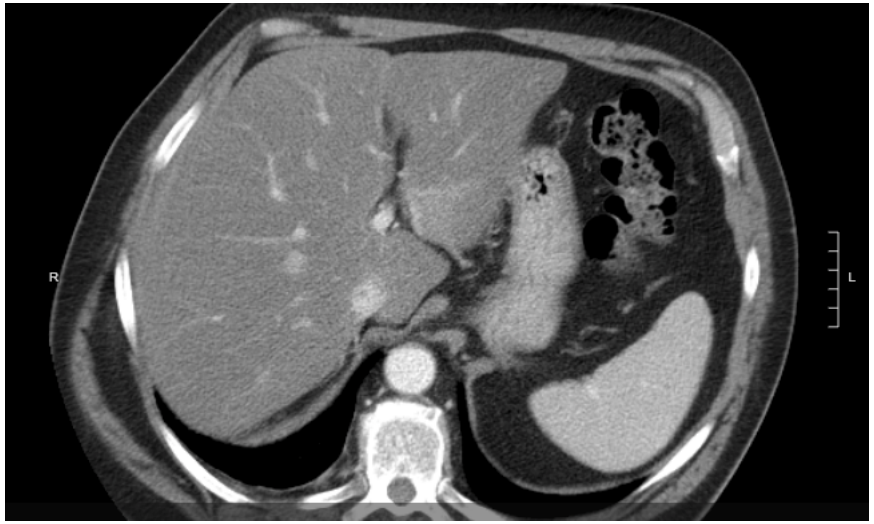
Nivolumab/Ipilimumab initiated 8/2018 – Adrenal lesions resolved 10/2018

Treated with 5 x 6wk cycles of Ipilimumab

Monthly Nivolumab has continued

Visit 10/2/2021 – Complete remission - no toxicity





Oct 2021

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Case Presentation – Dr Spigel: A 67-year-old man with progressive SCLC treated with an anti-PD-1/anti-LAG3 antibody on a clinical trial

HPI

A 67yo who presented with LS-SCLC – s/p carboplatin/etoposide/RT ending 11/2017. Recurrent disease was confirmed in the liver by biopsy 11/2018.

PMH

Unremarkable

SH

Married – 4 children

Greenskeeper

1.5 PPD x 45yrs

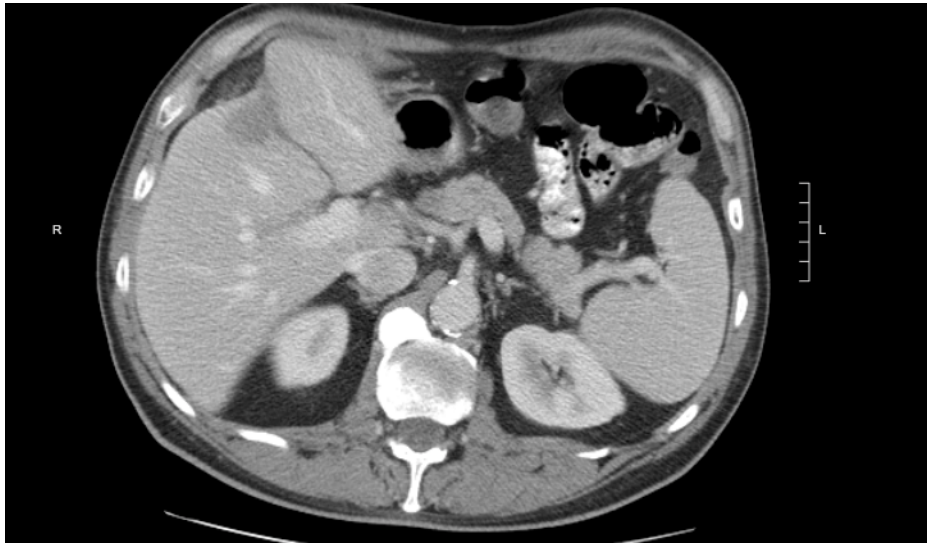
Case Presentation – Dr Spigel: A 67-year-old man with progressive SCLC treated with an anti-PD-1/anti-LAG3 antibody on a clinical trial (cont)

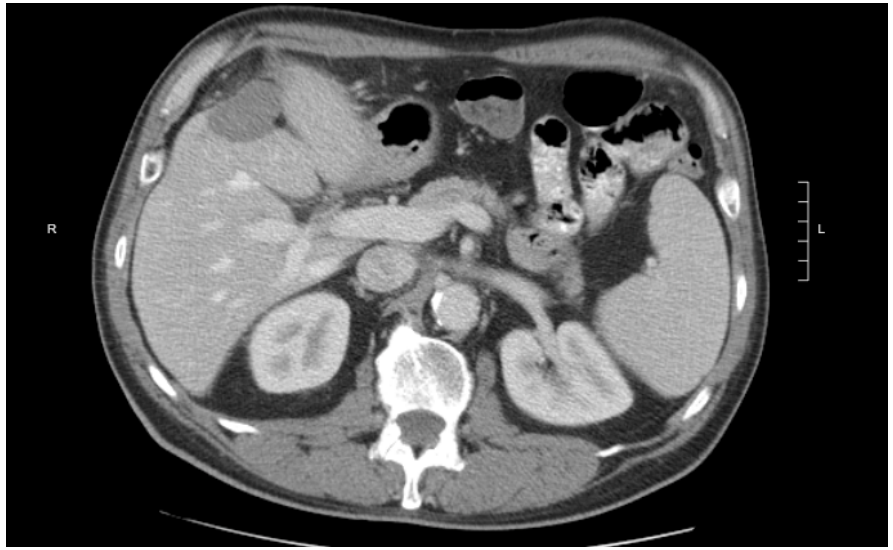
Sensitive Relapsed Treatment:

11/2018 Carboplatin/Etoposide x 4

2/2019 RF ablation of liver lesion f/b Atezolizumab

8/2019 Progressive disease in liver and regional LAN





8/2019

Case Presentation – Dr Spigel: A 67-year-old man with progressive SCLC treated with an anti-PD-1/anti-LAG3 antibody on a clinical trial (cont)

3rd-Line Treatment:

8/2019 Anti-PD-1/Anti-LAG3 on trial

Developed hypothyroidism – managed with levothyroxine

Remained on therapy until 10/2021 – stopped due to recurrent bilateral pleural effusions (and pericardial effusion)

-s/p bilateral thoracenteses (x2), pericardial window

-on steroids

-NED

Limited Stage SCLC trials

Trial	Agent	Setting	Trial ID
NRG-LU005	Atezolizumab	During chemoradiation in limited SCLC	NCT03811002
CLOVER	Durvalumab	During chemoradiation in solid tumors	NCT03509012
ADRIATIC	Durvalumab	After chemoradiation in nonprogressors	NCT03703297
STIMULI	Nivolumab/ ipilimumab	After chemoradiation in limited SCLC	NCT02046733

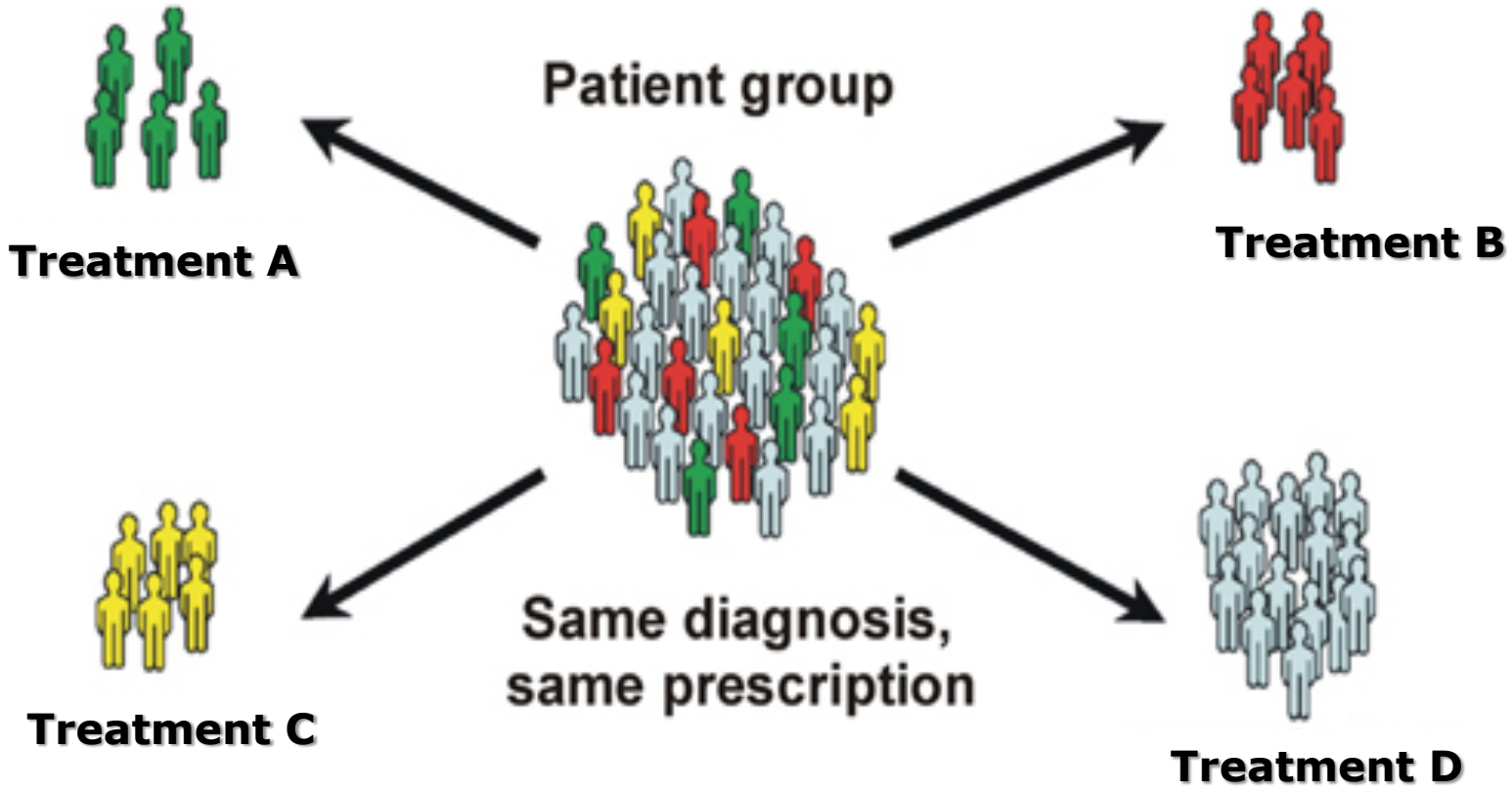
Courtesy of Anne Chiang, MD, PhD

Novel Agents and Strategies in SCLC

- LS-SCLC: Durvalumab
- First-Line ES-SCLC: Tiragolumab (Anti-TIGIT)
  Venetoclax
- Relapsed SCLC: Liposomal Irinotecan
  SC-011 (ADC)
  AMG 757 (Anti-DLL3/CD3 Bispecific Ab)

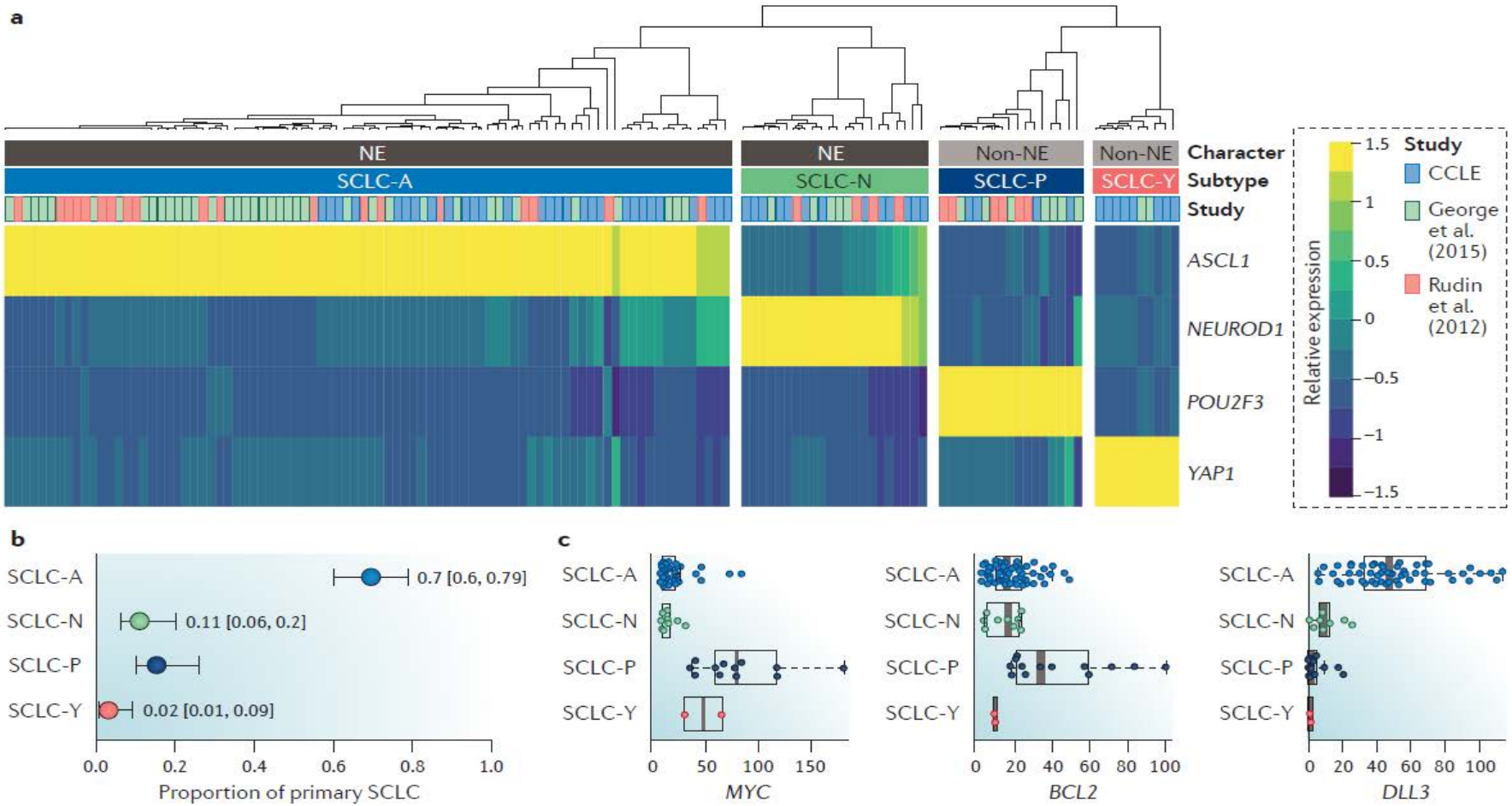
Courtesy of David R Spigel, MD

The Promise of Genotype-directed Therapy



Courtesy of Anne Chiang, MD, PhD

SCLC Biology: Molecular Subtypes by Expression of Key Transcriptional Regulators



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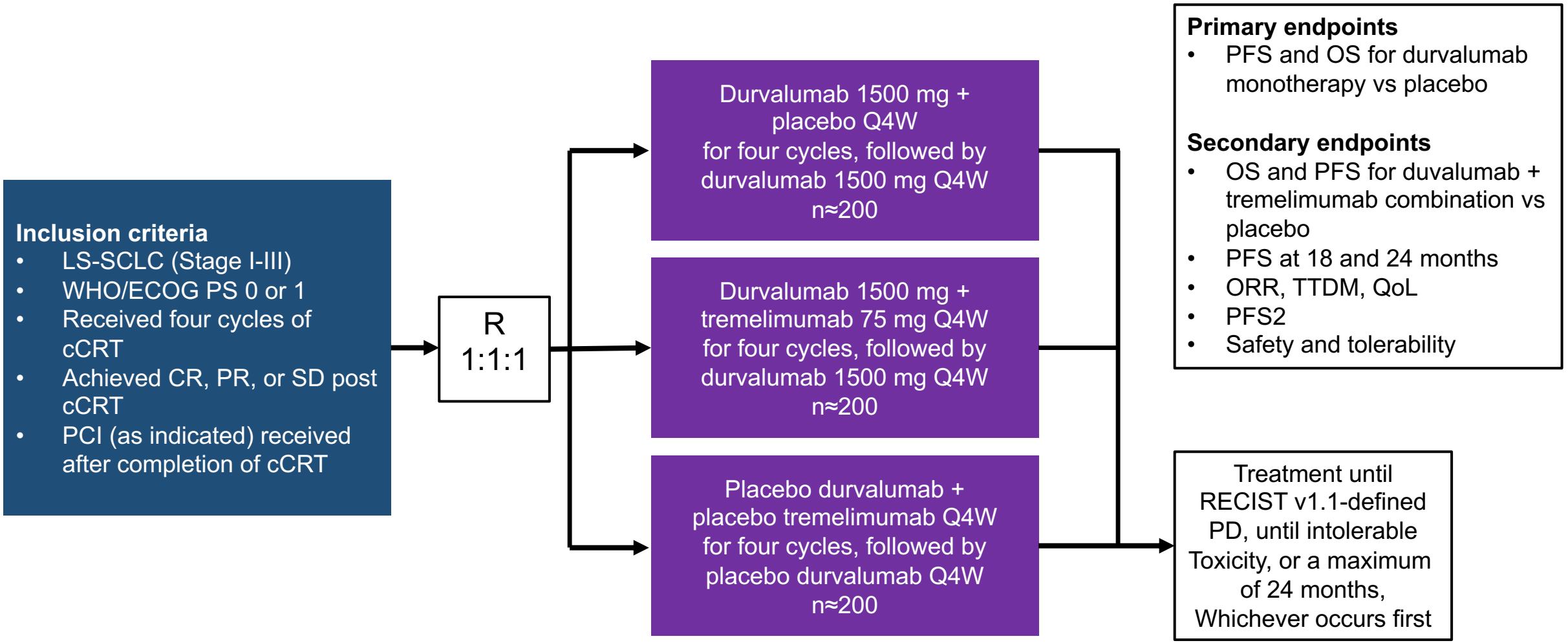
A Comprehensive Cancer Center Designated by the National Cancer Institute

Yale SCHOOL OF MEDICINE

Rudin C et al, Nature Reviews Cancer 2019:19;289-297

Courtesy of Anne Chiang, MD, PhD

ADRIATIC Study Design



Courtesy of Anne Chiang, MD, PhD

Select Ongoing Trials for Small Cell Lung Cancer

Radiation therapy

PRIMALung: PRophylactic cerebral Irradiation or active MAgnetic resonance imaging surveillance in small-cell lung cancer patients

Efficacy and safety of prophylactic cranial irradiation versus MRI surveillance in patients with limited-stage small cell lung cancer who achieved remission after first-line chemoradiotherapy

PCI for patients with ES-SCLC after RCT: A prospective randomized study

Simultaneous integrated boost vs routine IMRT in limited-stage small-cell lung cancer

SWOG S1827 (MAVERICK): Testing whether the use of brain scans alone instead of brain scans plus preventive brain radiation affects lifespan in patients with small cell lung cancer

Hypo-fractionated versus conventionally fractionated radiotherapy for patients with LS-SCLC

Select Ongoing Trials for Small Cell Lung Cancer (Continued)

Chemotherapy

Phase 3 study evaluating efficacy, safety and pharmacokinetics of trilaciclib in extensive-stage small cell lung cancer patients receiving carboplatin combined with etoposide or topotecan

IMforte: A Phase III, open-label study of maintenance lurbinectedin in combination with atezolizumab compared with atezolizumab in participants with extensive-stage small-cell lung cancer

EMERGE 402 Phase 4 observational study: Safety and outcomes in patients with SCLC receiving treatment with lurbinectedin

RESILIENT: Study of irinotecan liposome injection in patients with small cell lung cancer

Immunotherapy

ADRIATIC: Study of durvalumab + tremelimumab, durvalumab, and placebo in limited stage small-cell lung cancer in patients who have not progressed following concurrent chemoradiation therapy

SKYSCRAPER-02: A study of atezolizumab plus carboplatin and etoposide with or without tiragolumab in patients with untreated extensive-stage small cell lung cancer

Select Ongoing Trials for Small Cell Lung Cancer (Continued)

Immunotherapy (continued)

Toripalimab in combination with platinum plus etoposide in patients with extensive-stage small cell lung cancer

A randomized, double-blind, placebo controlled Phase III study to investigate efficacy and safety of HLX10 + chemotherapy (carboplatin-etoposide) in patients with extensive stage small cell lung cancer (ES-SCLC)

Study of platinum plus etoposide with or without BGB-A317 in participants with untreated extensive-stage small cell lung cancer

MK 7339-013/KEYLYNK-013: Placebo-controlled study of concurrent chemoradiation therapy with pembrolizumab followed by pembrolizumab and olaparib in newly diagnosed treatment-naïve limited-stage small cell lung cancer (LS-SCLC)

ETER701: A study of TQB2450 or placebo combined with anlotinib, etoposide and carboplatin versus etoposide and carboplatin in subjects with extensive small cell lung cancer

LUMINANCE: Study of durvalumab in combination with platinum and etoposide for the first line treatment of patients with extensive-stage small cell lung cancer

Select Ongoing Trials for Small Cell Lung Cancer (Continued)

Immunotherapy (continued)

Camrelizumab combined with apatinib, etoposide and cisplatin to treat small-cell lung cancer

SKYSCRAPER-02C: Study of atezolizumab plus carboplatin and etoposide with or without tiragolumab in participants with untreated extensive-stage small cell lung cancer

A study of carboplatin plus etoposide with or without ZKAB001 (anti-PD-L1 antibody) in patients with ES-SCLC

Chemoradiation with or without atezolizumab in treating patients with limited stage small cell lung cancer

CheckMate 451: An investigational immuno-therapy study of nivolumab, or nivolumab in combination with ipilimumab, or placebo in patients with extensive-stage disease small cell lung cancer (ED-SCLC) after completion of platinum-based chemotherapy

MAURIS: Atezolizumab (ATZ) in combination with carboplatin (Cb) and etoposide (Eto) in the treatment of patients with previously untreated extensive-stage small cell lung cancer (ES-SCLC): A multicenter, phase IIIb, single arm, safety study

Select Ongoing Trials for Small Cell Lung Cancer (Continued)

Novel agents/other

Tazemetostat in combination with a PARP inhibitor or checkpoint inhibitor in patients (Pts) with solid tumors

The Canadian Small Cell Lung Cancer Database (CASCaDe): A multi-institutional real-world evidence collaboration

Phase Ib study of AMG 757, a half-life extended bispecific T-cell engager immuno-oncology therapy, combined with AMG 404, an anti-PD-1 antibody, in patients with small cell lung cancer (SCLC)

Case Presentation – Dr Naidoo: A 76-year-old man with ES-SCLC and a heavy smoking history – Part 1

Dr Jarushka Naidoo

- Presents with hemoptysis → 10-cm mediastinal mass and bilateral lung lesions
- Biopsy: Small cell lung carcinoma

Questions

- What is the optimal first-line treatment for this patient?

RTP RESEARCH TO PRACTICE

Treatment Options

1. Carboplatin/etoposide/atezolizumab
2. Carboplatin/etoposide/durvalumab
3. Carboplatin/etoposide
4. Carboplatin/etoposide and thoracic radiation therapy

Case Presentation – Dr Naidoo: A 76-year-old man with ES-SCLC and a heavy smoking history – Part 2

Dr Jarushka Naidoo

- Presents with hemoptysis → 10-cm mediastinal mass and bilateral lung lesions
- Biopsy: Small cell lung carcinoma
- ***Carboplatin/etoposide/atezolizumab***
- ***MRI after completion of treatment: No brain metastases***

Question

- ***What are the optimal treatment options moving forward?***

RTP RESEARCH TO PRACTICE

Treatment Options

1. Observation alone
2. Prophylactic cranial irradiation
3. A 3-monthly CT scan of the brain
4. A 3-monthly MRI scan of the brain

Case Presentation – Dr Naidoo: A 76-year-old man with ES-SCLC and a heavy smoking history – Part 3

Dr Jarushka Naidoo

- Presents with hemoptysis → 10-cm mediastinal mass and bilateral lung lesions
- Biopsy: Small cell lung carcinoma
- Carboplatin/etoposide/atezolizumab
- MRI brain after completion of treatment: No brain metastases
- ***Three months after completion of treatment: Profound weakness, confusion, headaches***
- ***MRI brain: Uptake on the surface of the brain***
- ***CSF studies suspicious for autoimmune process***

Question

- ***What is the diagnosis and consequent recommended management?***

Treatment Options

1. Paraneoplastic syndrome, which can be treated with observation only
2. Progressive disease treated with whole-brain radiation therapy
3. An immune-related encephalitis treated with high-dose corticosteroids
4. A viral encephalitis treated with antivirals

Meet The Professor

Optimizing the Management of Acute Myeloid Leukemia

Monday, November 8, 2021
5:00 PM – 6:00 PM ET

Faculty
Keith W Pratz, MD

Moderator
Neil Love, MD

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