Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Bispecific T-Cell Engagers for Small Cell Lung Cancer

Friday, April 11, 2025

6:00 AM – 7:30 AM

Faculty

Anne Chiang, MD, PhD
Elizabeth Krueger, NP
Beth Sandy, MSN, CRNP, FAPO
Erin Schenk, MD, PhD

Moderator

Neil Love, MD

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Dr Chiang — Disclosures

Advisory Committees	Amgen Inc, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Fosun Pharma, Genentech, a member of the Roche Group, Janssen Biotech Inc, Zai Lab
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Ms Krueger — Disclosures

No relevant conflicts of interest to disclose

Ms Sandy — Disclosures

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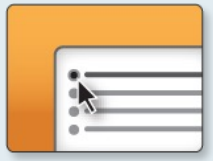
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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Clinicians Attending via Zoom

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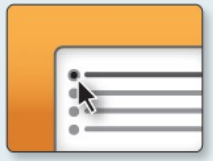

Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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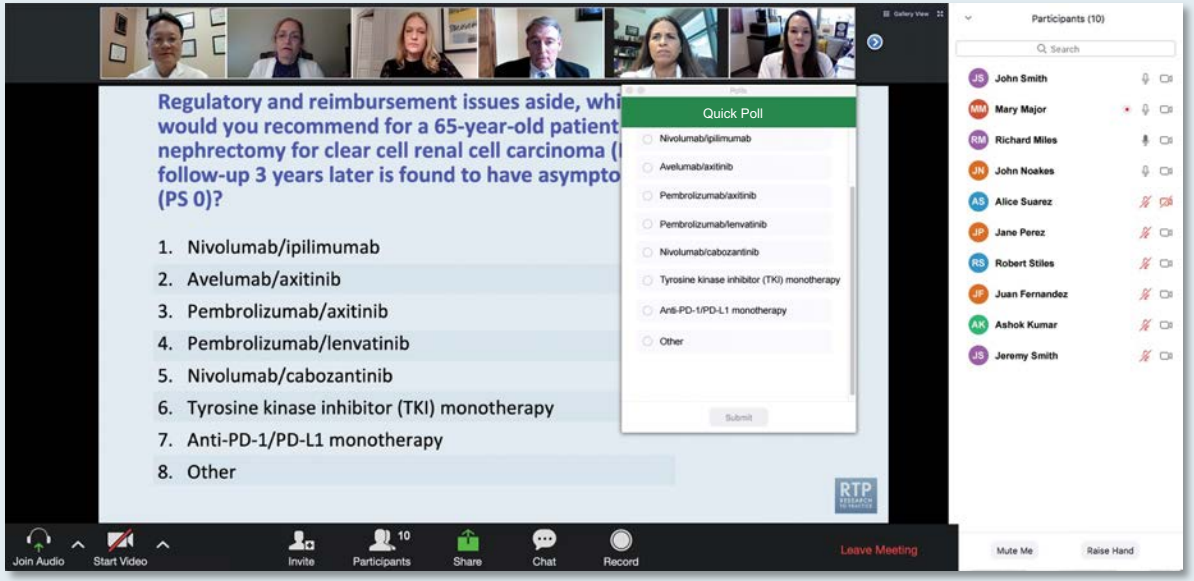
Clinicians, Please Complete the Pre- and Postmeeting Surveys



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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.

- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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ONCOLOGY NURSING UPDATE WITH DR NEIL LOVE

Bispecific Antibodies in Lymphoma Part 1 — An Interview with Ms Robin Klebig for Oncology Nurses

MS ROBIN KLEBIG
MAYO CLINIC

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Spotify

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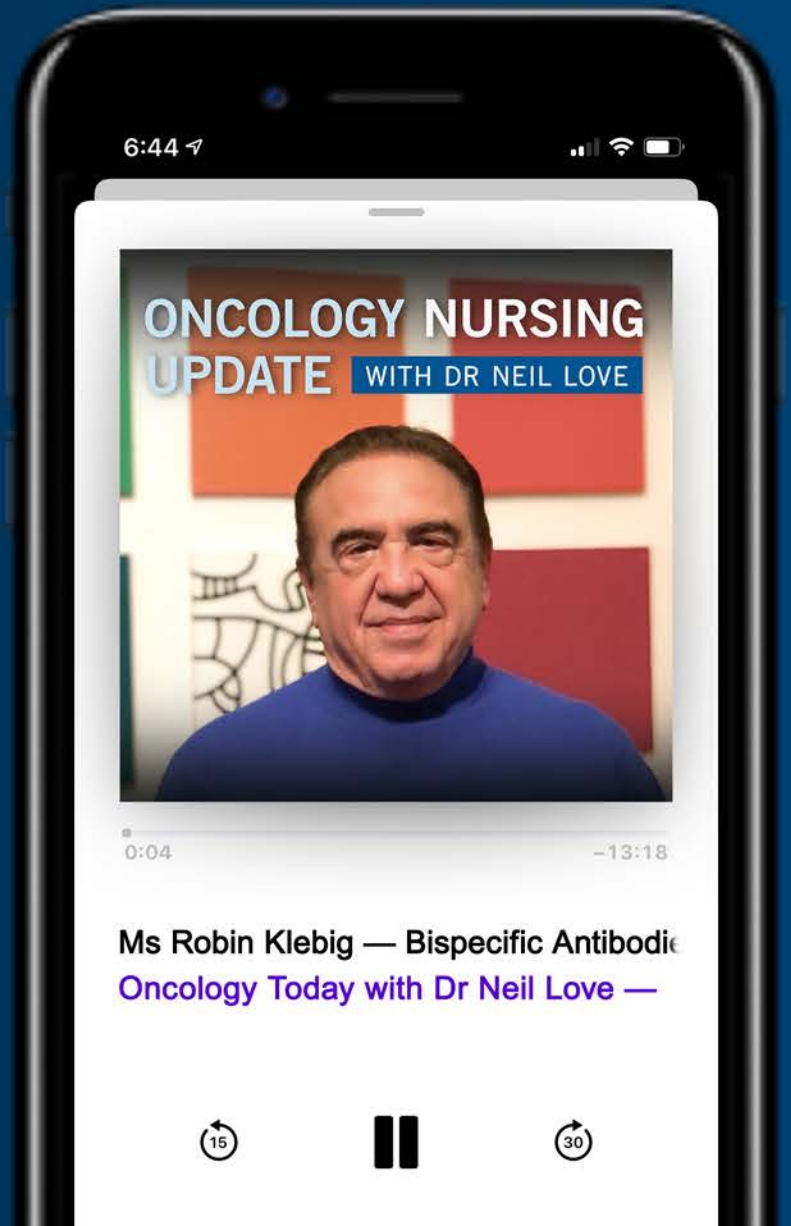
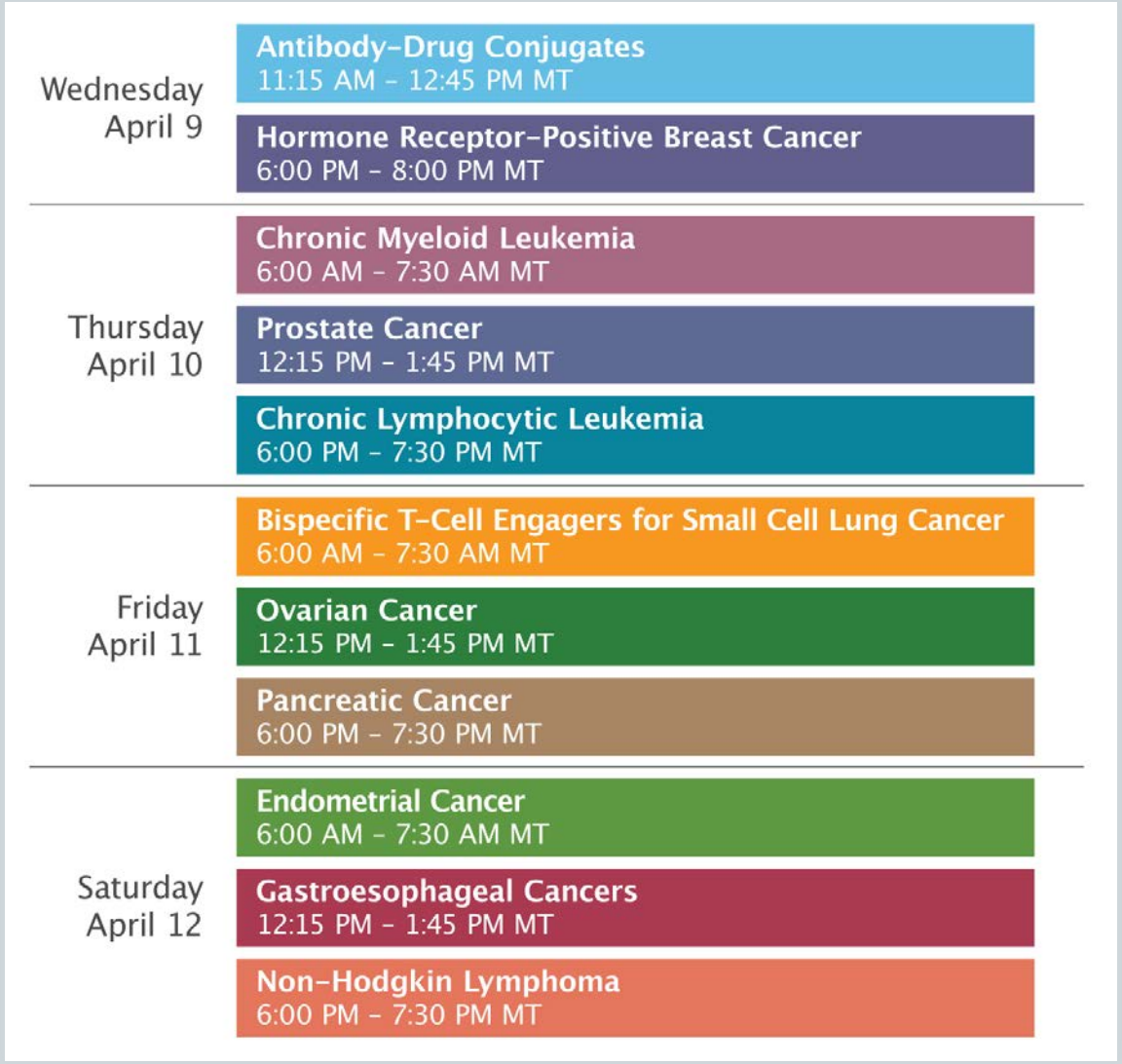


“Understanding the Current Paradigm and New Approaches”
Seventeenth Annual RTP-ONS NCPD Symposium Series



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Understanding the Current Paradigm and New Approaches
RTP Faculty at ONS 2025

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Agenda

Introduction: Overview of Bispecific Antibodies

Module 1: Biology of Small-Cell Lung Cancer (SCLC) and Review of Its Initial Management

Case Presentation: Ms Krueger – 63-year-old man

Module 2: Current Role of Tarlatamab in Therapy for SCLC

Case Presentation: Ms Sandy – 70-year-old woman

Module 3: Future Directions in the Management of SCLC

Case Presentation: Ms Krueger – 81-year-old man

Module 4: Unique Considerations in SCLC Management

Case Presentation: Ms Sandy – 67-year-old woman

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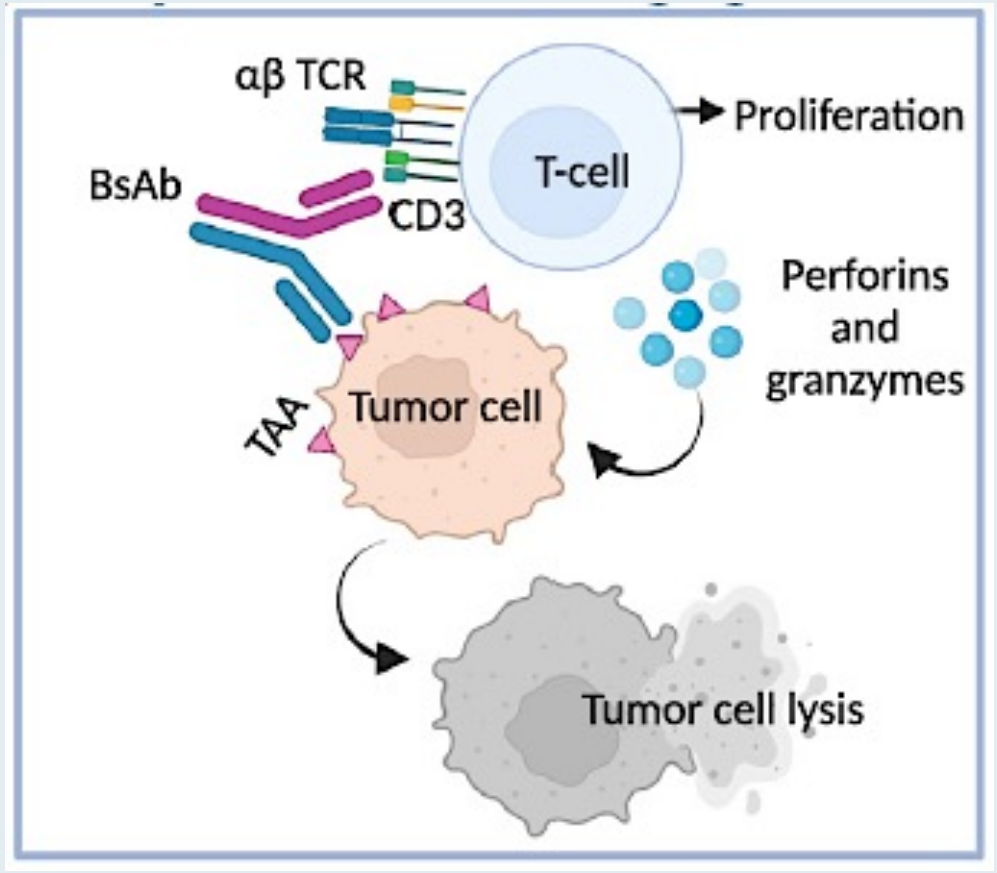
Mechanism of Action of Bispecific Antibodies: T-Cell Engagers



Bispecific antibodies bind the TCR and the selected TAA to facilitate the formation of a synapse between the two cell types; the synapse activates T cells, which can release perforins and granzymes to lyse tumor cells.

Herrera M et al. *Trends Cancer* 2024;10(10):893-919.

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Examples of Bispecific Antibodies with FDA-Approved Indications for Hematologic Cancers

- **Blinatumomab** (CD3 x CD19) for adult and pediatric Philadelphia chromosome-positive acute lymphocytic leukemia
- **Talquetamab** (CD3 x GPRC5D) for multiple myeloma (MM)
- **Teclistamab** (CD3 x BCMA) for MM
- **Elranatamab** (CD3 x BCMA) for MM
- **Glofitamab** (CD3 x CD20) for diffuse large B-cell lymphoma (DLBCL)
- **Epcoritamab** (CD3 x CD20) for follicular lymphoma (FL)
- **Mosunetuzumab** (CD3 x CD20) for DLBCL and FL

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications?randparam=228524.

Examples of Bispecific Antibodies with FDA-Approved Indications for Solid Tumors

- **Amivantamab** (EGFR x c-MET) for EGFR exon20ins non-small cell lung cancer
- **Tarlatamab** (CD3 x DDL3) for extensive-stage SCLC
- **Tebentafusp** (CD3 x gp100-HLAA02:01) for uveal melanoma
- **Zanidatamab** (HER2-ECD2 x HER2-ECD4) for HER2-positive biliary tract cancer

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancerhematologic-malignancies-approval-notifications?randparam=228524.

Patient Education: Cytokine Release Syndrome (CRS)

- CRS is most common after the first two doses, which is why you will be monitored in the hospital for 22-24 hours after treatment on days 1 and 8

- You will receive a “step-up dose”, or a smaller dose on your first day of treatment
  - If your treatment is delayed by more than two weeks, the “step-up dose” and monitoring may be repeated
  - Dexamethasone, a steroid, will be given before the first two doses to help lower the risk of CRS

- With later doses, monitoring will usually happen in infusion for 2-8 hours after treatment

- Notify your team or get medical help right away if you have any signs or symptoms, including:
  - Fever of 100.4 degrees or higher
  - Low blood pressure or dizziness
  - New tiredness or headache
  - Shortness of breath or trouble breathing
  - Nausea and vomiting
  - Confusion, restlessness, or feeling anxious
  - Problems with walking, or loss of balance or coordination
  - Unusual bleeding
  - Weakness or shaking (tremors)
  - Trouble sleeping

Courtesy of Elizabeth Krueger, NP

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Small Cell Lung Cancer: Advances in a Changing Landscape

Yale NewHaven Health
Smilow Cancer Hospital

Yale CANCER CENTER

Anne Chiang MD, PhD, FASCO
Associate Professor, Division of Thoracic Medical Oncology
Yale University School of Medicine
Associate Yale Cancer Center Director, Clinical Initiatives

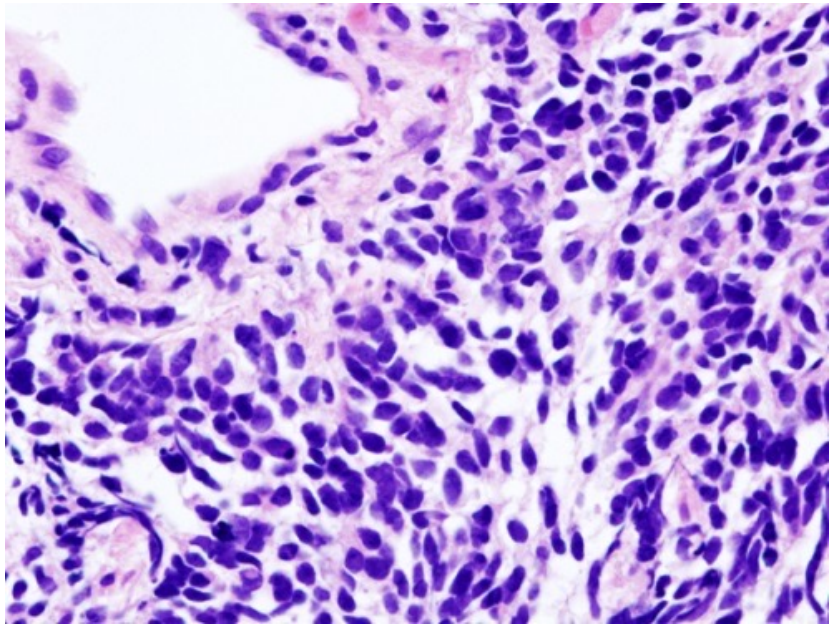
SCLC: Incidence and Risk Factors

- ~14% of lung cancer
- ~ 250,000 new cases and 200,000 deaths globally each year
  - ~16,000 new cases of SCLC in the US in 2024
  - Median age at diagnosis in the US is 69 years
- 95% SCLC patients have history of tobacco use
  - 2.5-13% SCLC patients are never smokers, and may have a better prognosis
  - Rarely, NSCLC patients with driver mutations such as EGFR may undergo histologic transformation to SCLC

Wang Q. *J Thorac Oncol*. 2023;18(1):31.
Rudin CM. *Nat Rev Dis Primers*. 2021 Jan 14;7(1):3
Kim SY, Park H, Chiang AC, JAMA .2025 March 31, doi:10.1001/jama.2025.0569

SCLC: Morphology

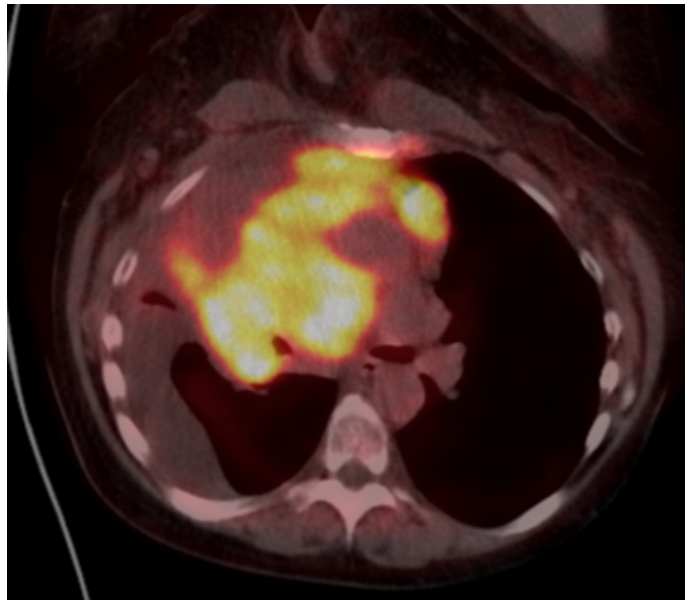
- **Characteristics:**
  - Rapid proliferation time
  - Early development of widespread metastases
  - Increased sensitivity to both chemotherapy and radiation
- **Pathology**
  - High-grade neuroendocrine tumor
  - Small “blue” cells, sparse cytoplasm, nuclear molding
  - 75% with one or more neuroendocrine markers, e.g. chromogranin, synaptophysin, CD56, INSM1



Kim SY, Park H, Chiang AC, JAMA .2025 March 31, doi:10.1001/jama.2025.0569

SCLC: Staging and Prognosis

- Staging:
  - Limited Stage (LS-SCLC): 30%
    - Includes stage I-III in the TNM staging system
    - Typically confined to 1 hemothorax and LNs
    - Can be treated within a radiation field
  - Extensive Stage (ES-SCLC): 70%
    - Distant metastatic disease, such as in brain, liver, bones, adrenals
    - Can include malignant pleural effusion
- Prognosis:
  - Limited Stage: mOS ~4.7 years, 3YOS 56.5%
  - Extensive Stage: mOS ~13 months, 3YOS 17.6%



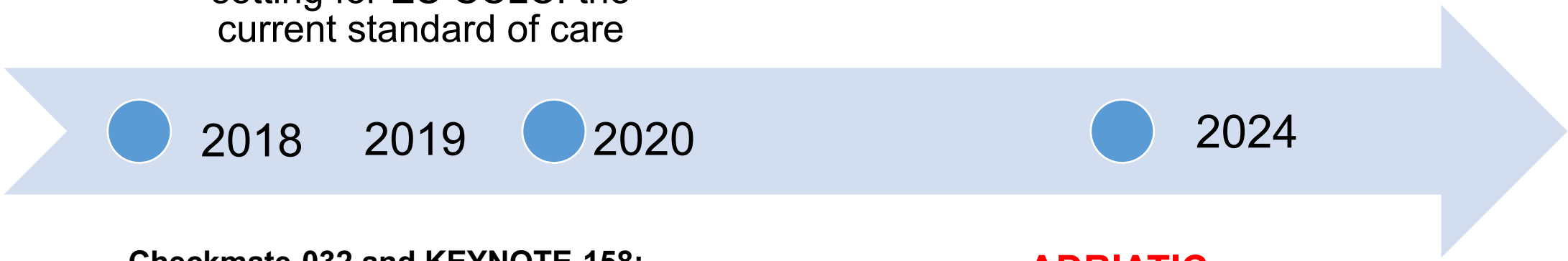
LS-SCLC: Stage IIIC (T4N3N0):
RUL lung mass, mediastinal LAD

Kim SY, Park H, Chiang AC, JAMA .2025 March 31, doi:10.1001/jama.2025.0569

The Current Era of Immunotherapy (IO)

IMpower-133 and CASPIAN:

Using IO in the frontline setting for ES-SCLC: the current standard of care



Checkmate-032 and KEYNOTE-158:
Using IO in 3L setting, subsequently withdrawn due to negative phase III trials but still in NCCN guidelines if no prior IO exposure

ADRIATIC:

Using IO as consolidation in the limited stage setting ASCO 2024, approved by FDA

ADRIATIC study design

Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomization

N=730

R‡

Durvalumab
1500 mg Q4W
N=264

Placebo
Q4W
N=266

Durvalumab + tremelimumab
D 1500 mg Q4W + T 75 mg Q4W for 4 doses, followed by D 1500 mg Q4W
N=200

Stratified by:
Disease stage (I/II vs III)
PCI (yes vs no)

cCRT components
- Four cycles of platinum and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks
- RT must commence no later than end of cycle 2 of CT

Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

Dual primary endpoints:
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

Key secondary endpoints:
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

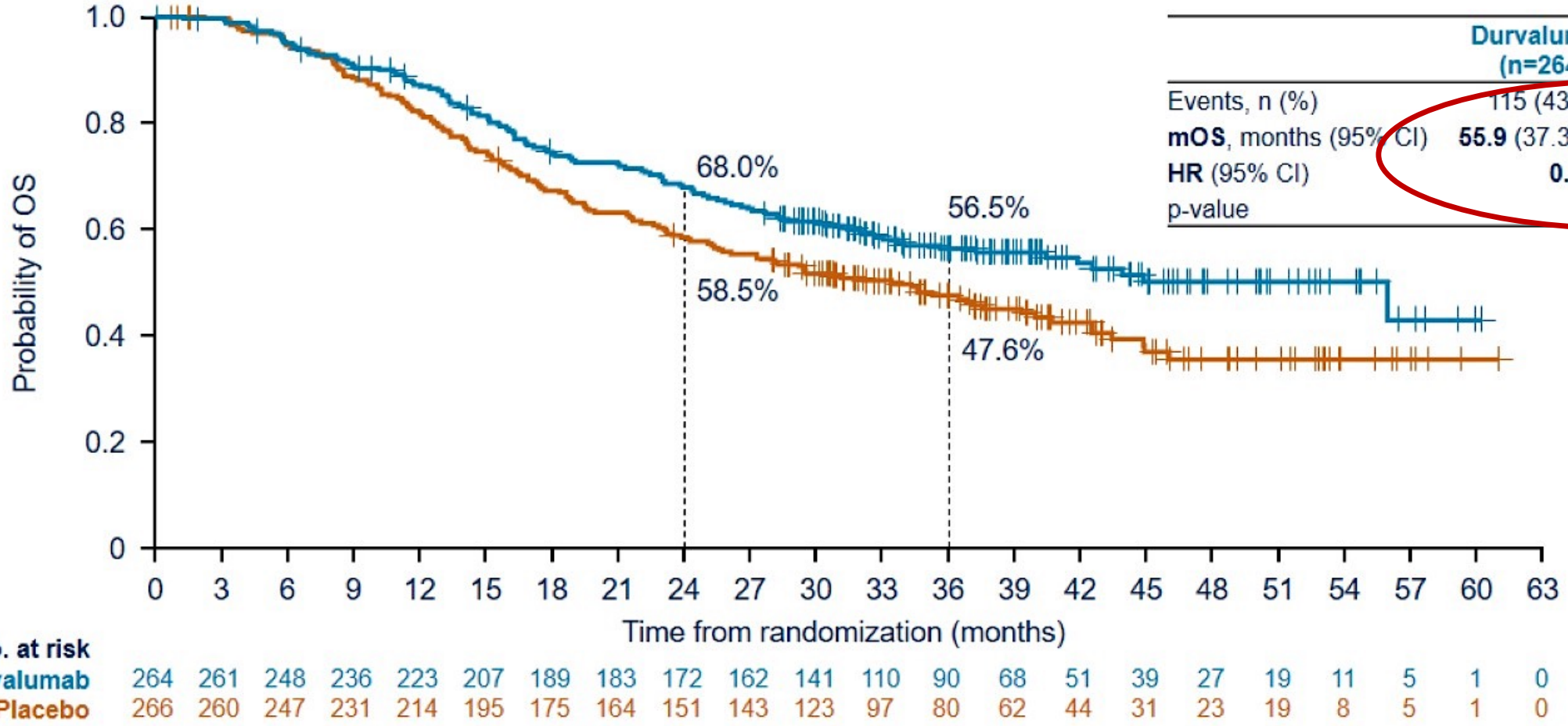
Other secondary endpoints:
- OS/PFS landmarks
- Safety

*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization.
†If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator.
‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization.

Overall survival (dual primary endpoint)

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

No. at risk																					
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

Abstract LBA5

Conclusions

- **Durvalumab as consolidation treatment after cCRT demonstrated statistically significant and clinically meaningful improvement in OS and PFS compared with placebo in patients with LS-SCLC**
  - **OS HR 0.73** (95% CI 0.57–0.93), p=0.0104; mOS 55.9 (95% CI 37.3–NE) vs 33.4 (95% CI 25.5–39.9) months
  - **PFS HR 0.76** (95% CI 0.61–0.95), p=0.0161; mPFS 16.6 (95% CI 10.2–28.2) vs 9.2 (95% CI 7.4–12.9) months
  - Treatment benefit was generally consistent across predefined patient subgroups for both OS and PFS
- **Durvalumab consolidation treatment for up to 2 years was well tolerated, and safety findings were consistent with the known safety profile of durvalumab monotherapy in the post-cCRT setting**

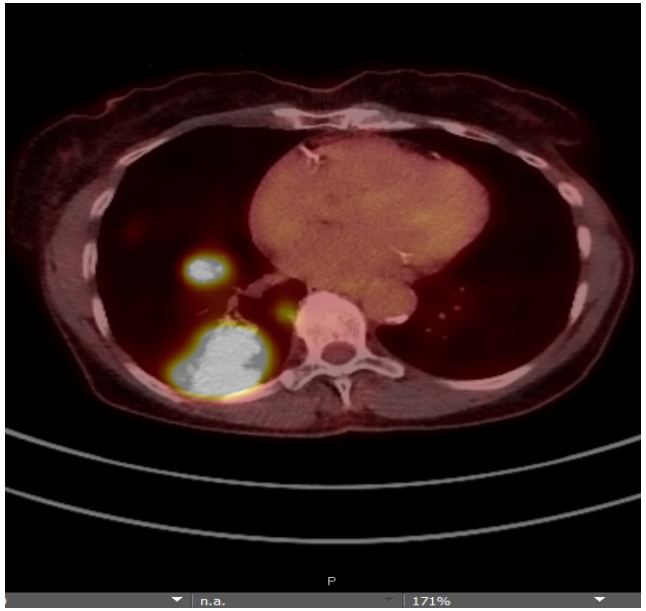
Consolidation durvalumab IS the new standard of care for patients with LS-SCLC who have not progressed after cCRT

Abstract LBA5

Extensive Stage SCLC

- 65-year-old African American female (40 py tobacco history) presented in spring 2020 with worsening SOB on exertion and weight loss over several months.
- PET scan shows 7.2 cm RLL mass, satellite nodules, extensive regional nodal involvement in right hilar, mediastinal, and axillary LNs.
- Brain MRI is negative
- Biopsy of LN reveals small cell carcinoma

She needs systemic treatment!



Treatment options include:

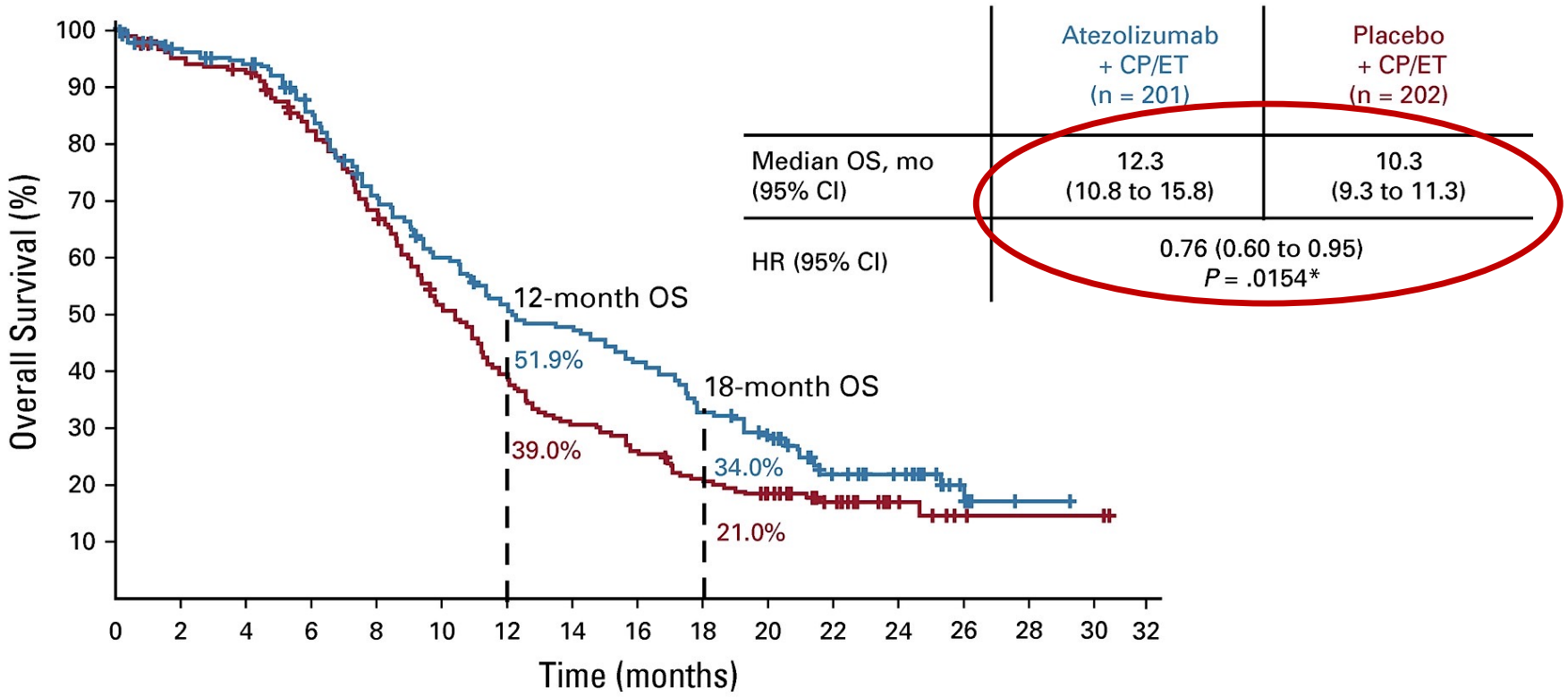
a. Carboplatin/etoposide/atezolizumab x 4 cycles => maintenance atezolizumab (IMpower133)

b. Carboplatin/etoposide/durvalumab x 4 cycles => maintenance durvalumab (CASPIAN)

c. Cisplatin/etoposide/durvalumab x 4 cycles => maintenance durvalumab (CASPIAN)

d. Carboplatin/etoposide

IMpower133: Atezolizumab/Carboplatin/Etoposide



	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

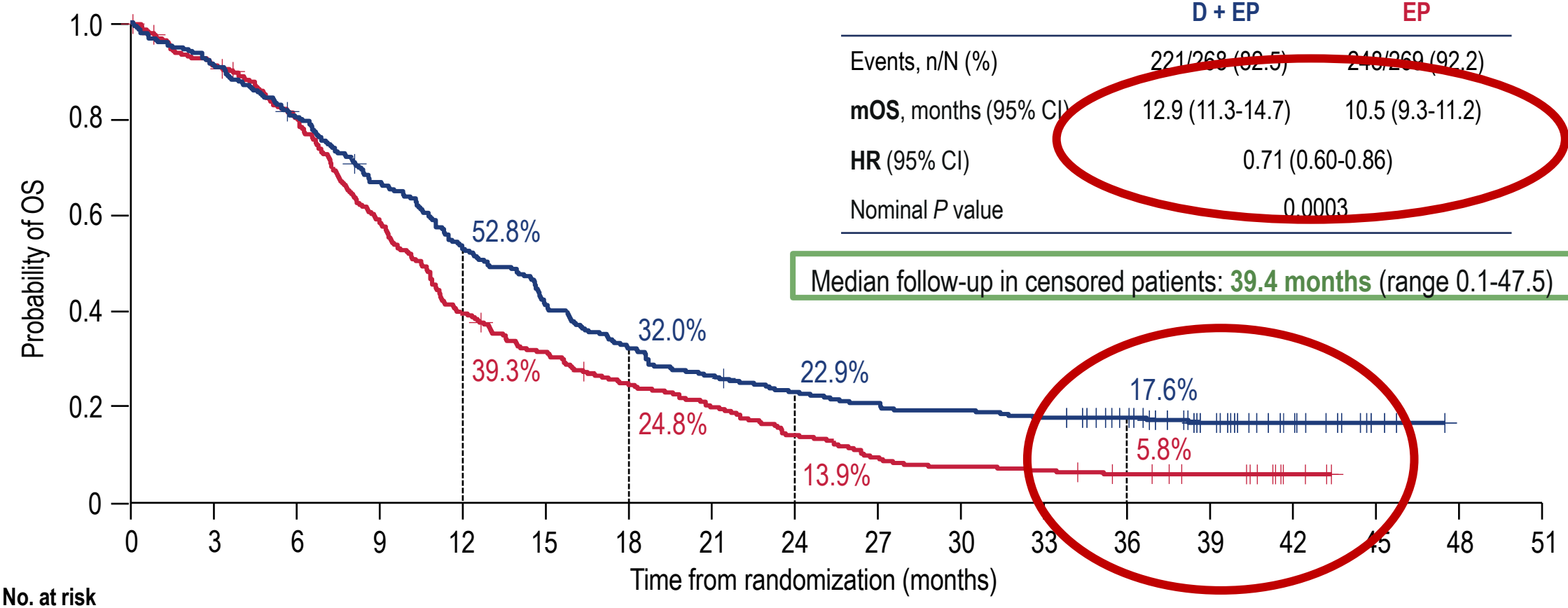
Atezolizumab + CP/ET	201	187	180	159	130	109	93	86	75	61	51	28	21	8	1
Placebo + CP/ET	202	189	183	160	131	97	74	58	49	39	33	20	8	3	2	2

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

CASPIAN: Durvalumab/Platinum/Etoposide

	D + EP	EP
Events, n/N (%)	221/268 (82.5)	249/269 (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

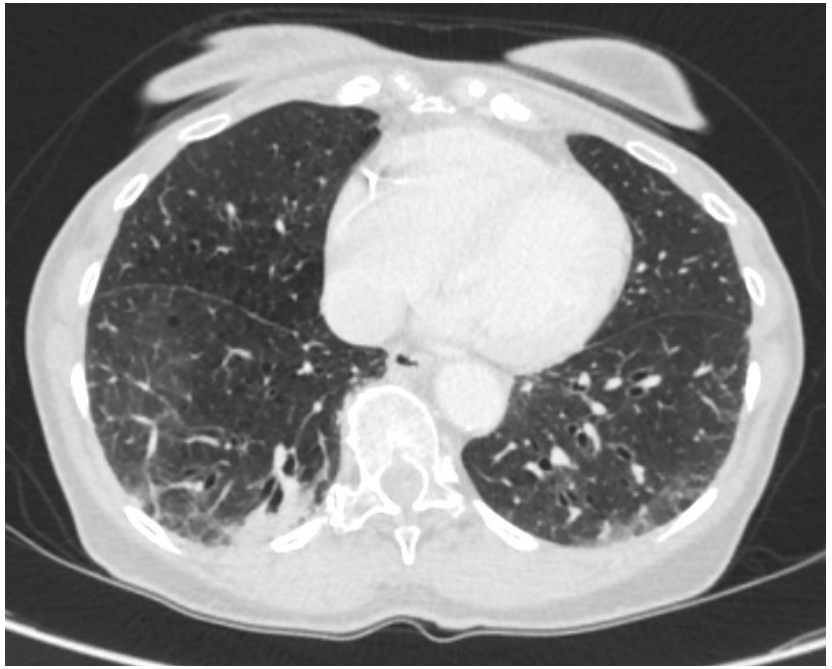
D + EP	268	244	214	177	140	109	85	70	60	54	50	46	39	25	13	3	0	0
EP	269	243	212	156	104	82	64	51	36	24	19	17	13	10	3	0	0	0

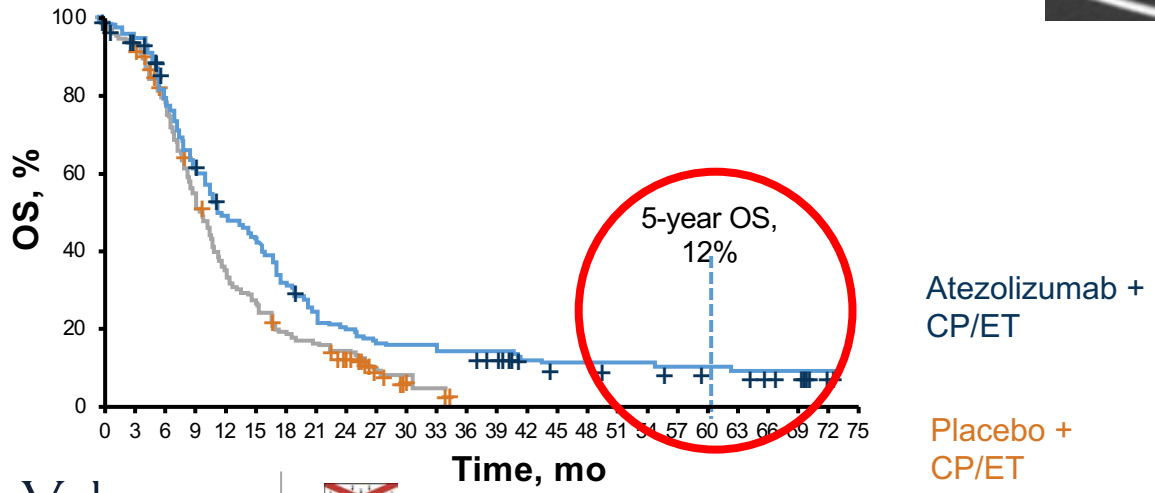
Data cutoff: March 22, 2021.

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

ES-SCLC Clinical Case

- Pt has excellent response to 4 cycles of carboplatin, etoposide and atezolizumab and continues maintenance on monthly atezolizumab
- Atezo tolerated well except lichenoid rash controlled with steroid topical cream
- Pt was on maintenance Atezo for 3 years and is now 2 years off therapy with no evidence of disease!





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Approaches to Improve Long-term Outcomes

- Seek to understand heterogeneity and determinants of response and resistance
- Optimize front line therapy with additional agents
- Add novel agents in the maintenance setting
- Improve support of our patients throughout their journey

Roundtable Discussion

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Mass General Brigham
Mass General Cancer Center

Small-Cell Lung Cancer Case Presentation

Elizabeth Krueger, NP
Nurse Practitioner
Massachusetts General Hospital Center
for Thoracic Cancers
Boston, Massachusetts

Case Presentation: 63-year-old man

63yo male, former smoker with ES-SCLC diagnosed 1/2022 when he presented to local ED with difficulty speaking s/p fall (ultimately thought due to seizure activity)

- Diagnostics:
  - Brain MRI with at least 7 brain metastases including 2.8cm R frontal lesion, 1.5cm R frontal lesion and 2cm L cerebellar lesion.
  - PET CT with 1.5cm RUL nodule and 1.5cm R hilar node.
  - Bronch/EBUS + small cell lung CA (positive TTF-1, INSMI, synaptophysin, chromogranin and negative for Napsin A, p40. P53 overexpressed, RB loss. Molecular diagnostics negative for fusion transcripts).
- Treatment History:
  - Completed HA-WBRT followed by 1L carboplatin/etoposide/atezolizumab x 4 cycles (3/2022-5/2022) followed by maintenance atezolizumab.
    - Fatigue, appetite changes, immune mediated skin toxicity (pruritus, lichenoid plaques, requiring standing hydroxyzine TID).
  - SBRT to enlarging RUL and LUL FDG avid nodules (7/2023) and continued atezolizumab
  - 4/2024 with progression in RUL, R hilum and LUL. Rechallenged with carboplatin/etoposide (and ongoing atezolizumab) x 4 given prior response
  - November 2024 symptomatic, diffuse progression in lungs, nodes and liver. Transitioned to tarlatamab

Case Presentation: 63-year-old man (continued)

- PMH significant for anxiety, depression, osteoarthritis (elbow, hip), GERD

- Treatment course complicated by PE requiring apixaban, T11 compression fracture (not pathologic) requiring kyphoplasty, urinary frequency and nocturia (requiring 3 drug regimen), chronic headaches (thought post-concussive in setting of fall 2021, prior CNS disease and treatment; requires bilateral myofascial trigger point injections), fatigue (requiring stimulant), cognitive and memory changes (requiring neuropsychological testing)

- Co-managed with medical oncology, radiation oncology, neuro oncology, dermatology, urology, social work, palliative care and psychiatry.

- Retired accountant. College graduate. Single/never married, no children. Lives alone currently but has occasionally had roommates. Sold home shortly after diagnosis, financially savvy, self-motivated to optimize community resources. Parents passed of malignancies (possible lymphoma and GI) when older teen/early 20s, raised younger siblings (sister and a brother). Sister splits time between MA and FL. Brother lives locally but “untrustworthy.” Family does not attend appointments but pt has allowed us to call sister at scan review/treatment changes and as his functional status has declined.

Case Presentation: 63-year-old man (continued)

- 12/4/24 C1D1 tarlatamab 1mg – symptomatically tolerated well with mild nausea and diarrhea x 2. Significant distress r/t shared inpatient room, interior bed without window, roommate on comfort measures due to ongoing capacity challenges.
- 12/11/24 C1D8 tarlatamab 10mg. VNA RN paged weekend first responder C1D13 reporting generalized weakness, lightheadedness and multiple falls. Anticoagulated, unclear if head strike/LOC. Pt refused ED and refused clinic evaluations until next scheduled visit 12/18/24. Did invest in Life Alert system. VNA RN daily followup. Vital signs stable.
- 12/18/24 C1D15 held for ongoing weakness, gait instability and pt's preference to avoid worsening toxicity over holidays. Started home PT. Arranged cane/walker.
- 1/8/25 PS improved, noting improvement in pre-treatment constitutional and respiratory complaints. Worsening diffuse pains, starts oxycodone as needed. Due to delays in dosing repeat C1D1 1mg ramp up dosing.
- 1/15/25 Repeat C1D8, given h/o delayed neurotoxicity and concerns would not present to clinic for urgent evaluation is given 10mg IV dexamethasone prior to hospital discharge.
- 1/22/25 Reports good tolerance without recurrent neuro complaints or worsening constitutional complaints. Treated C1D15 and transitions to ambulatory observation per protocol. Using approx. 40mg oxycodone for diffuse pains, add long acting opioids.

Case Presentation: 63-year-old man (continued)

- 2/12/25 C2D1 delayed 1 week as pt forgot about previously scheduled visit. Reports mild nausea, bowel changes, weight loss (10 lbs), worsening pain and new bLE neuropathy. Plan to treat and obtain new restaging scans prior to next visit – CT Chest/Abd/Pelv, MRI Brain and add MRI total spine (CTs previously without bony metastases). Discussed symptoms possibly r/t disease or treatment toxicity.
- Restaging with nice response in liver, stable disease in chest. MRI Brain without new, progressive disease. MRI total spine aborted d/t pain – rescheduled 4/2/25 per patient preference.
- Plan to continue tarlatamab with restaging q2 cycles or as clinically necessary.
- Admitted OSH 3/22-3/24/25 c/o confusion, pain, urinary retention s/p multiple falls (tripped over dog's leash). Polypharmacy likely contributing.
- 3/26/25 Reports fatigue, taste changes, weight loss. C3D15 tarlatamab.
- 4/1/25 Calls to report 2 falls at home, 1 with head strike. Also reports new scant hematuria. Recommend urgent visit vs local ED but pt declines both. Plan daily VNA RN visit and daily medical oncology telephone check-ins.
- 4/2/25 MRI total spine performed – has significant multilevel degenerative joint disease but no evidence of osseous metastases or leptomeningeal disease. His pain is likely due to arthritis and possibly aggravated by tarlatamab.

Patient specific challenges and considerations

Physical

- Enjoyed several years of disease stability and good functional status
- Local progression amenable to targeted interventions (rarely see in SCLC given aggressiveness of disease)
- High healthcare utilizer for comorbid conditions
- Neurological complaints due to disease, prior and current therapy, ? Psychiatric component

Psychological/Social

- Limited supports (partly a decision)
- Cognitive and memory changes requiring frequent reeducation (always in writing) and reinforcement
- ? Undiagnosed personality disorder – splitting and undermining providers; pleasant and cooperative in person vs angry, suspicious in writing. Maintain primary MD/APP, treating RN and shared visits with multidisciplinary providers whenever possible. Have offered to help coordinate 2nd opinions but repeatedly declines.
- "Budgeted" for 1-1.5 yr life expectancy – Increasing financial toxicity. Existential crisis due to good response and inability to plan for future. Increasing financial toxicity.

Operational

- Prefers written communication within electronic medical record over telephone which can cause delays in evaluation and management
- Lives ~2 hours from hospital, relies on ride service so frequently declines urgent visits
- Visiting RN services in place and presents to local ED for symptoms and side effects – care coordination challenging. Finds VNA "intrusive"
- Delays in tarlatamab infusions can result in need to repeat step-up dosing, hospital admissions and create capacity challenges in infusion due to length of observations

Patient Education- Side effect management

- As needed antiemetics and bowel medications
- Encourage fluids (mindful that ES-SCLC may require fluid restriction for SIADH) and small, frequent meals/snacks with emphasis on protein
- Nutrition consultation
- For taste changes use plastic utensils, chew on cardamom, suck on citrus candies
- As needed APAP, NSAIDs or consider complementary supportive care (yoga, reiki, massage, acupuncture) for muscle and joint pains
- Fertility/Sexuality counseling
- Speak to provider before beginning any new medications, herbs or supplements

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Yale NewHaven Health
Smilow Cancer Hospital

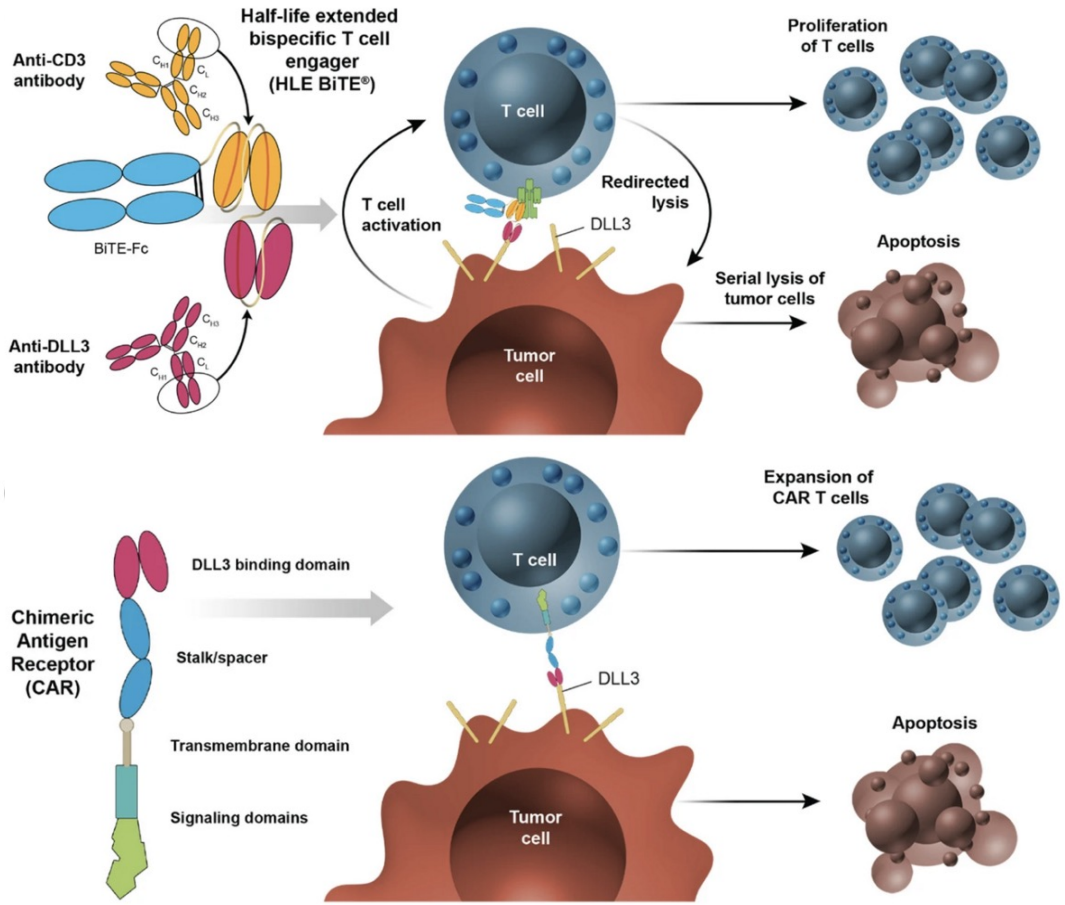
Yale CANCER CENTER

Advances in Treatment of Relapsed SCLC: Tarlatamab

Anne Chiang MD, PhD, FASCO
Associate Professor, Division of Thoracic Medical Oncology
Yale University School of Medicine
Associate Yale Cancer Center Director, Clinical Initiatives

Targeting DLL3 expression to improve the immune response in SCLC

- Tarlatamab is a bispecific T cell engager (BiTE) combining the binding specificities for DLL3 and CD3 genetically fused to the IgG Fc region
- Designed to induce T cell proliferation and tumor cell lysis
- Adoptive cellular therapy using modified T cells to express a CAR targeting DLL3



Owen DH, et al. J Hematol Oncol 2019

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer

M.-J. Ahn, B.C. Cho, E. Felip, I. Korantzis, K. Ohashi, M. Majem, O. Juan-Vidal, S. Handzhiev, H. Izumi, J.-S. Lee, R. Dziadziuszko, J. Wolf, F. Blackhall, M. Reck, J. Bustamante Alvarez, H.-D. Hummel, A.-M.C. Dingemans, J. Sands, H. Akamatsu, T.K. Owonikoko, S.S. Ramalingam, H. Borghaei, M.L. Johnson, S. Huang, S. Mukherjee, M. Minocha, T. Jiang, P. Martinez, E.S. Anderson, and L. Paz-Ares, for the DeLLphi-301 Investigators*

Baseline Characteristics

	Part 1 + 2 Tarlatamab 10 mg (n = 100)	Part 1 Tarlatamab 100 mg (n = 88)	Part 3 Tarlatamab 10 mg (n = 34)
Median age, years (range)	64 (35–82)	62 (34–80)	66 (49–80)
Male, %	72	70	71
Asian / Black or African American / White,* %	41 / 0 / 58	41 / 0 / 58	6 / 3 / 91
Ever smoker / non-smoker, %	92 / 8	94 / 6	97 / 3
ECOG performance status: 0 / 1, %	26 / 74	27 / 73	29 / 71
Prior lines of therapy, median (range)	2 (1–6)	2 (1–8)	2 (2–6)
2 prior lines of therapy, %	65	55	65
≥ 3 prior lines of therapy, %	33	43	35
Prior anti-PD-(L)1 treatment, %	73	70	82
< 90 days to progression after first-line platinum therapy,† %	28	20	21
Brain / liver metastases, %	23 / 39	36 / 34	12 / 35
DLL3 expression (> 0%), n/N evaluable (%)	80/83 (96)	71/74 (96)	N/A‡

Data cutoff, June 27, 2023. Median follow-up was 10.6 months for tarlatamab 10 mg and 10.3 months for tarlatamab 100 mg.
*No patients of American Indian, Alaska Native, Native Hawaiian, or other Pacific Islander race were enrolled.
†Platinum sensitivity was calculated as end of first-line platinum therapy to date of first progression.
‡DLL3 sample analysis from Part 3 in progress.
DLL3, delta-like ligand 3; **ECOG**, Eastern Cooperative Oncology Group; **N/A**, not available; **PD-(L)1**, programmed death 1 / ligand 1.

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Ahn M-J et al. N Engl J Med 2023;389:2063-2075.

Tarlatamab Anti-Tumor Activity

Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Objective response rate, n (%) (97.5% CI)	40 (40.0) (29.1, 51.7)	28 (31.8) (21.1, 44.1)
Complete response	1 (1)	7 (8)
Partial	39 (39)	21 (24)
Disease control rate, n (%) (95% CI)	70 (70.0) (60.0, 78.8)	55 (62.5) (51.5, 72.6)

FDA grants accelerated approval to tarlatamab-dlle for extensive stage small cell lung cancer on May 16, 2024

Tarlatamab 10 mg demonstrated anti-tumor activity in heavily pre-treated SCLC with an objective response rate of 40%

Data cutoff, June 27, 2023. Median follow-up was 10.6 months for tarlatamab 10 mg and 10.3 months for tarlatamab 100 mg. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 188).
Part 3 did not have adequate follow-up for response analysis.
*Not evaluable and no post-baseline scan were considered non-responders for response analysis. **SCLC**, small cell lung cancer.

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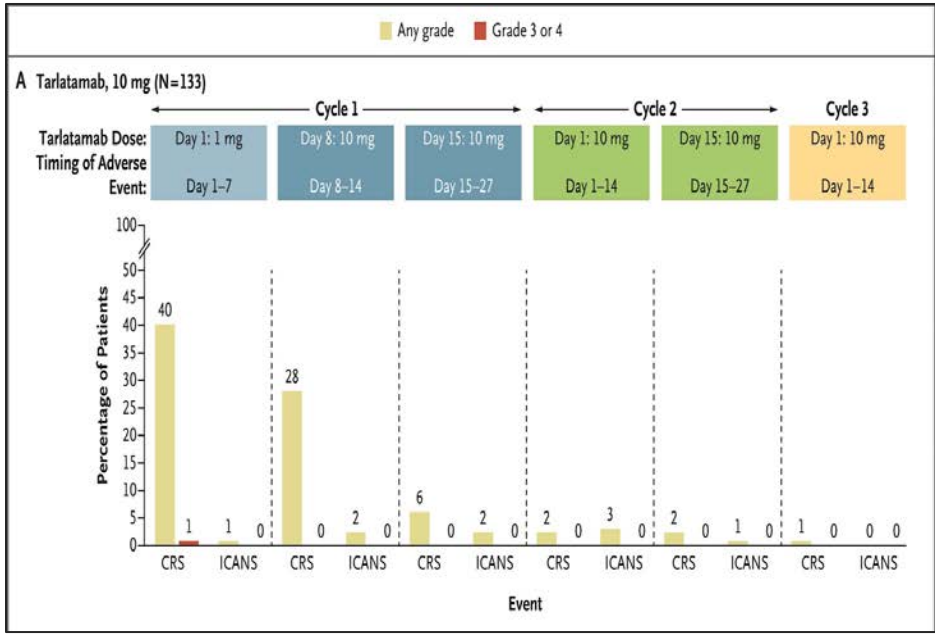
Ahn M-J et al. N Engl J Med 2023;389:2063-2075.

Tarlatamab: Adverse Events

- Cytokine-release syndrome (CRS) is a systemic inflammatory syndrome with sudden release of cytokines presenting as fever +/- hypotension or hypoxia
  - Grade 1/2 CRS seen in 56% patients, Grade 3 CRS seen in 3%
- Immune effector cell-associated neurotoxicity syndrome (ICANS) characterized by confusion, cognitive deficit, weakness
  - Grade 1/2 seen in 12% patients, no Grade 3 ICANS seen
- Other side effects include dysgeusia, decreased appetite, nausea, neutropenia

- CRS mostly managed with acetaminophen, IV hydration, steroids
  - Other interventions at 10 mg dose:
    - Tocilizumab used in 5% patients (7/133)
    - Supplemental Oxygen in 8% pts (11/133)
    - Vasopressor support in 1% pts (1/133)
- ICANS managed with steroids, neuro consult

- Most centers admit patients after C1D1, D8 treatment for 22-24 hrs
  - Need to be within one hour of hospital for subsequent doses
  - Need reliable patients and caregivers



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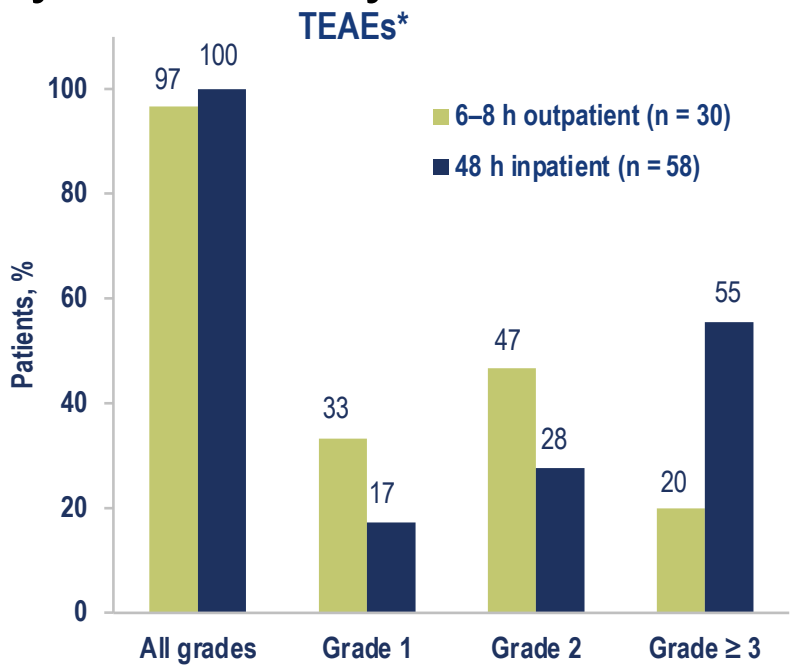
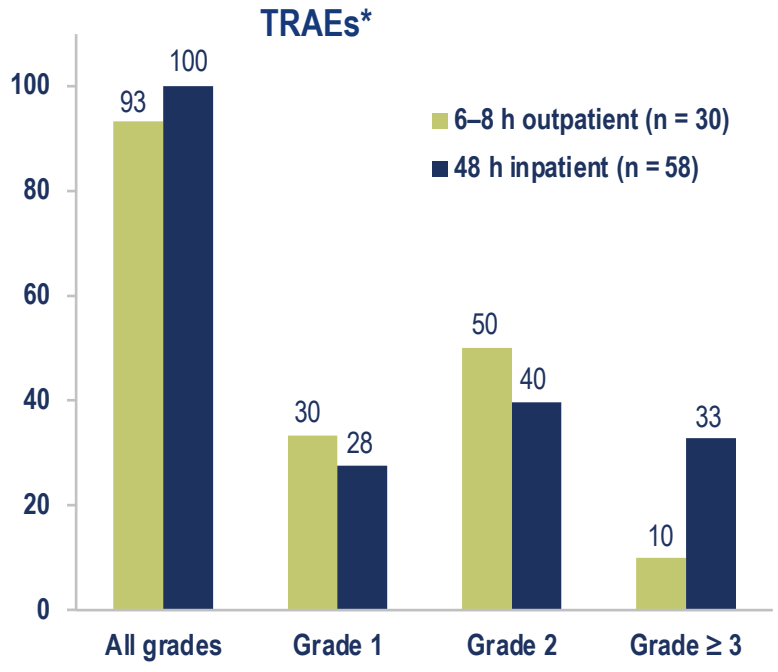
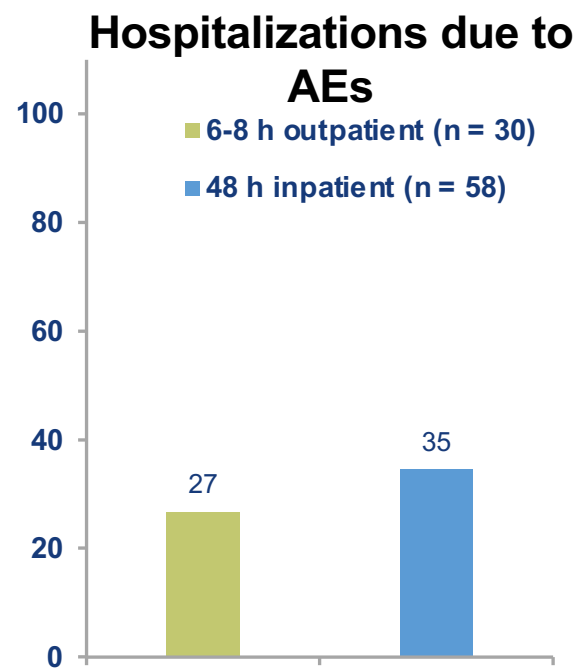
Ahn M-J et al. N Engl J Med 2023;389:2063-2075.

Looking Forward:
6-8h Outpatient vs 48h Inpatient Monitoring

Cycle 1 Safety Profile







The most common TRAEs (≥ 20% either group) within 24 hours post tarlatamab administration on cycle 1 day 1 or cycle 1 day 8 were CRS, nausea, and asthenia.

Chiang et al, ESMO-IO poster 2024
Chiang et al, ESMO Open April 2025, 104538

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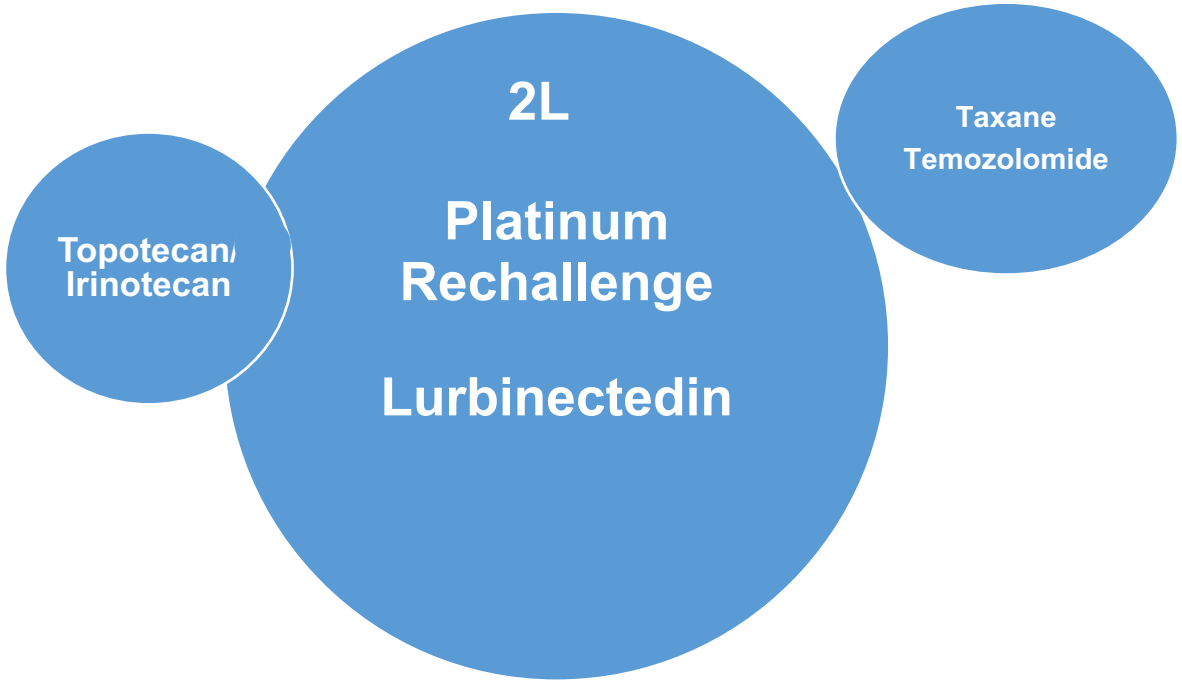
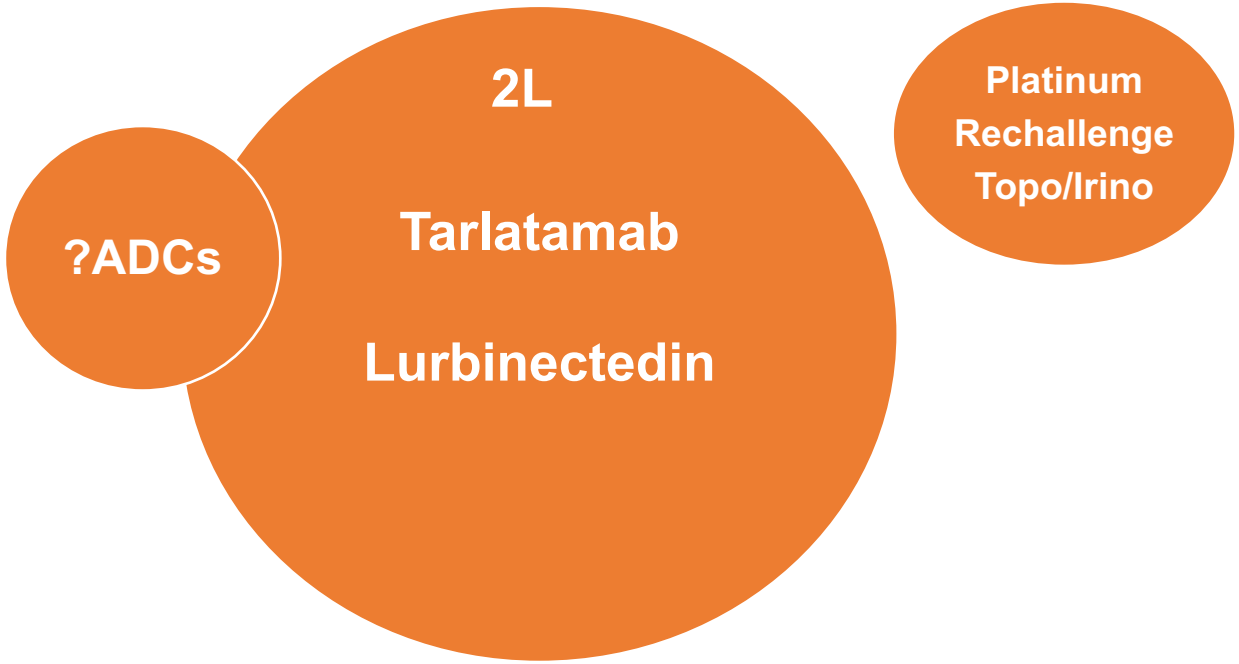
A Changing Landscape for Relapsed SCLC





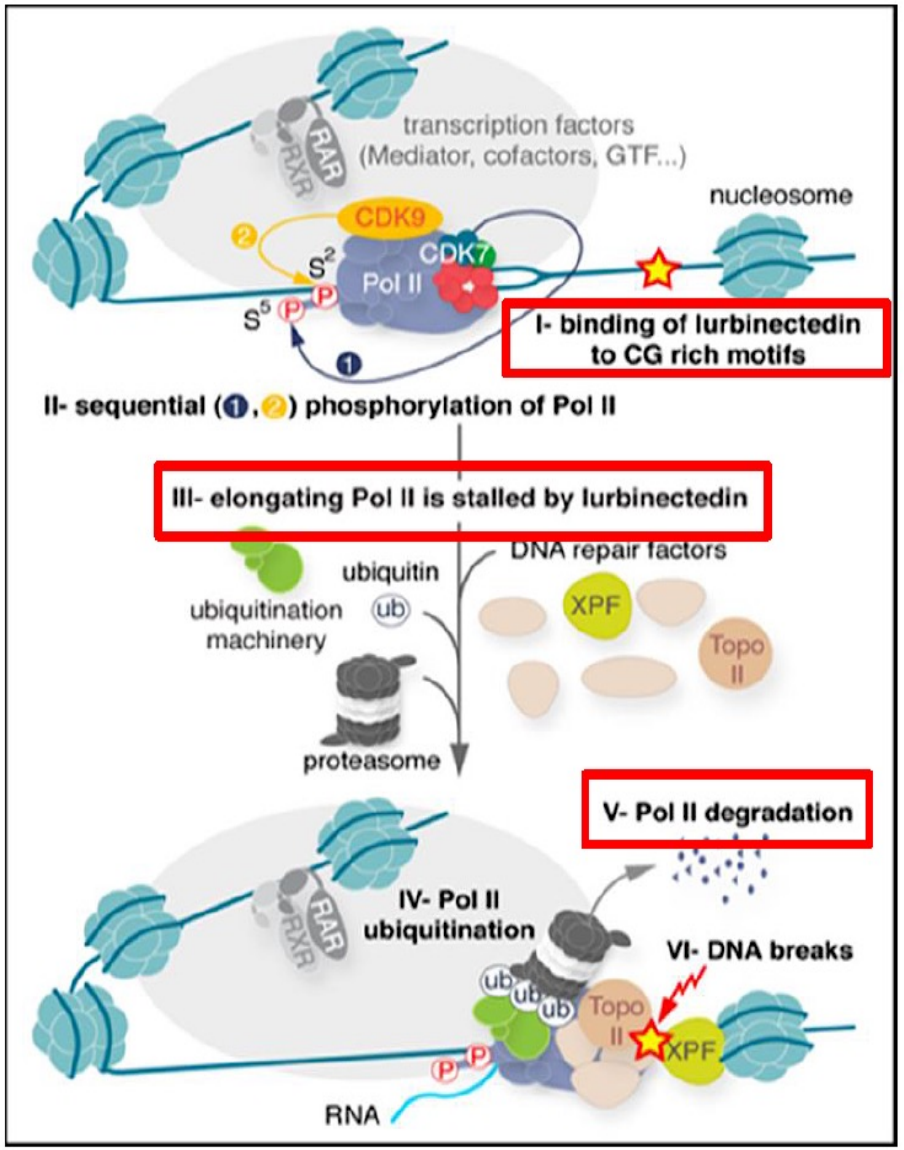
Other: e.g. tri-specifics, CAR-T, Radiopharmaceuticals

2023: pre Tarlatamab approval

2024: post Tarlatamab approval

Lurbinectedin

- Lurbinectedin binds to the minor groove of DNA
- Mechanisms of action:
  - inhibits transcription through stalling and degradation of RNA polymerase II
  - induces DNA double-strand breaks resulting in apoptosis



Lurbinectedin

Selective inhibitor of transcription & TME

Phase 2 single-arm basket trial

105 pts with relapsed SCLC (2 or 3L)

3.2 mg/m^2 dose IV q3weeks

1° endpoint: Overall response rate = **35.2%**

Platinum-response: **45.0%** (S) vs **22.2%** (R)

Confirmatory Phase 3 in SCLC (ongoing)

Accelerated FDA approval (June 2020)

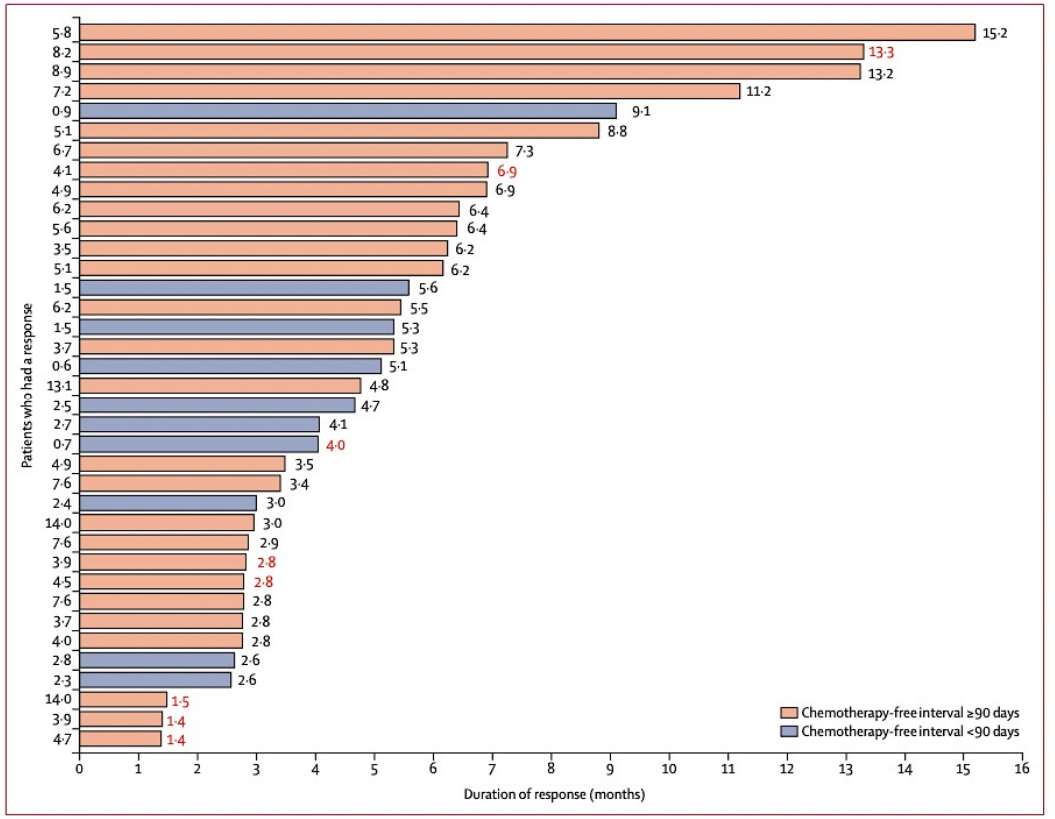


Figure 1: **Duration of response by investigator assessment**
Each bar represents a patient with SCLC who responded to treatment (n=37). Data shown on the left of each bar are the chemotherapy-free interval (months); data shown on the right of each bar are the duration of response (0 is the time of starting response). Data in red font refer to eight patients censored at the cutoff date: seven with no documented progression (under follow-up) and one who discontinued treatment due to an investigator's decision and then received further therapy. SCLC=small-cell lung cancer.

Trigo et al, Lancet Oncol 21:645; Subbiah et al, Lung Cancer 150:90, 2020

Balancing Patient Factors for Treatment

Tarlatamab

- Shorter platinum-free interval (e.g. chemoresistant disease)
- More robust patients with better performance status
- Reliable patient and caregiver
- Live within 1 hour from hospital

Lurbinectedin

- Longer platinum-free interval
- Older, more frail patients
- Patients who live alone or far away (>1h) from hospital
- Need central line

Clinical Cases

- 68 yo female h/o COPD, GERD, Graves disease, SIADH, PE on anticoagulation, ECOG 1
- Diagnosed with LS-SCLC s/p definitive chemoradiation completed in 2/24
- Recurrence 6 months later with metastases to brain, liver, bones, treated with gamma knife radiation followed by carbo/etoposide/durvalumab with response, then maintenance durva
- Progression of disease and started tarlatamab 2/25
- C1D1, D8, doses tolerated well with no CRS, ICANS during hospital observation stay
- C1D15 tolerated well in outpatient clinic

- 79 yo female h/o HTN, DM, COPD on 2L Oxygen for exertion, GERD, PE on anticoagulation, ECOG 1, lives with daughter
- Diagnosed with ES-SCLC treated with carbo/etop/atezolizumab with response after 4 cycles, but progression after 5 cycles of maintenance Atezo
- Treated with lurbinectedin x 2 cycles with progression
- Started tarlatamab in 2/25 with G3 CRS with fever and hypoxemic respiratory failure after C1D1, treated with acetaminophen, Oxygen, steroids
- C1D8 tolerated well with G1 CRS (chills, tachypnea), G1 ICANS (ICE score 8/10) treated with steroids with resolution
- C1D15 tolerated well in outpatient clinic

SCLC: Key Points

- Tarlatamab is an exciting new option to target the SCLC “immune desert”
- Side effects such as CRS and ICANS can be managed, primarily with hospital observation stay after C1D1 and D8
- Lurbinectedin is a useful tool for relapsed SCLC patients
- Stay tuned for other agents including antibody-drug conjugates

Roundtable Discussion

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Case Presentation: Ms Sandy – 70-year-old woman

Module 3: Future Directions in the Management of SCLC

Case Presentation: Ms Krueger – 81-year-old man

Module 4: Unique Considerations in SCLC Management

Case Presentation: Ms Sandy – 67-year-old woman

Small-Cell Lung Cancer Case Presentation

Beth Sandy, MSN, CRNP, FAPO

Case Presentation: 70-year-old woman

- 70 y/o female, who is deaf, presented with chest pain and SOB in 1/2023 with 3.5cm R lung mass and 6cm hilar and mediastinal lymph nodes.
- Bronchoscopy of nodes + SCLC
- 3/28/2023-6/2023 treated with etoposide/carboplatin X 4 cycles and XRT to chest overlapped C3 and C4
- 11/2023 progressive disease in the chest and now 8cm mass in the pelvis
- 11/2023 etoposide/carboplatin/atezolizumab X 4 cycles, followed by maintenance Atezolizumab

Case Presentation: 70-year-old woman (continued)

- 8/2024: disease progression and started on lurbinectedin
- 10/2024: developed brain mets, treated with WBXRT
- 10/2024: radiation to pelvic metastasis
- 11/2024: progression of disease on lurbinectedin
- 1/2025: started on Tarlatamab

Case Presentation: 70-year-old woman (continued)

- Comes with her son. She lives alone.
- They come from Delaware to Philadelphia. Has not been an issue for patient and family
  - They are dedicated to their mom, they want the best treatment
- Need to have sign language interpreter available at visits
  - This was not always arranged, made things difficult
- She has learned to trust me as her NP, reads my lips well
  - Refuses to see another NP…. She changes her schedule if I go on vacation.

Case Presentation: 70-year-old woman (continued)

- Admitted for monitoring of C1, had developed R arm pain. After infusion, sent her for xray of the R humerus which detected a new metastasis
- While admitted for CRS monitoring, in the AM, she got out of bed and fell while walking to the bathroom and fractured her R humerus
- Extended hospital stay, required surgery for rod placement. Had also had some mild, grade 1 CRS which delayed the surgery
- She was discharged 2 weeks after 1st dose of Tarlatamab

Case Presentation: 70-year-old woman (continued)

- Patient concerns:

  #1: because discharged and complications, had to resume 1mg dose again in the step up

Last Dose Given	Time since dose	Action
1mg on Day 1	More than 2 weeks	Must restart step-up
10mg on D8	More than 3 weeks	Must go back to 1mg
10mg on D15 or more	More than 4 weeks	Must go back to 1mg

- Patient concerns:

  #2: Because the patient is deaf will I have a hard time assessing for ICANS?

  Because the patient has had WBXRT, will I have a hard time assessing for ICANS?

Package Insert Tarlatamab 3/2025.

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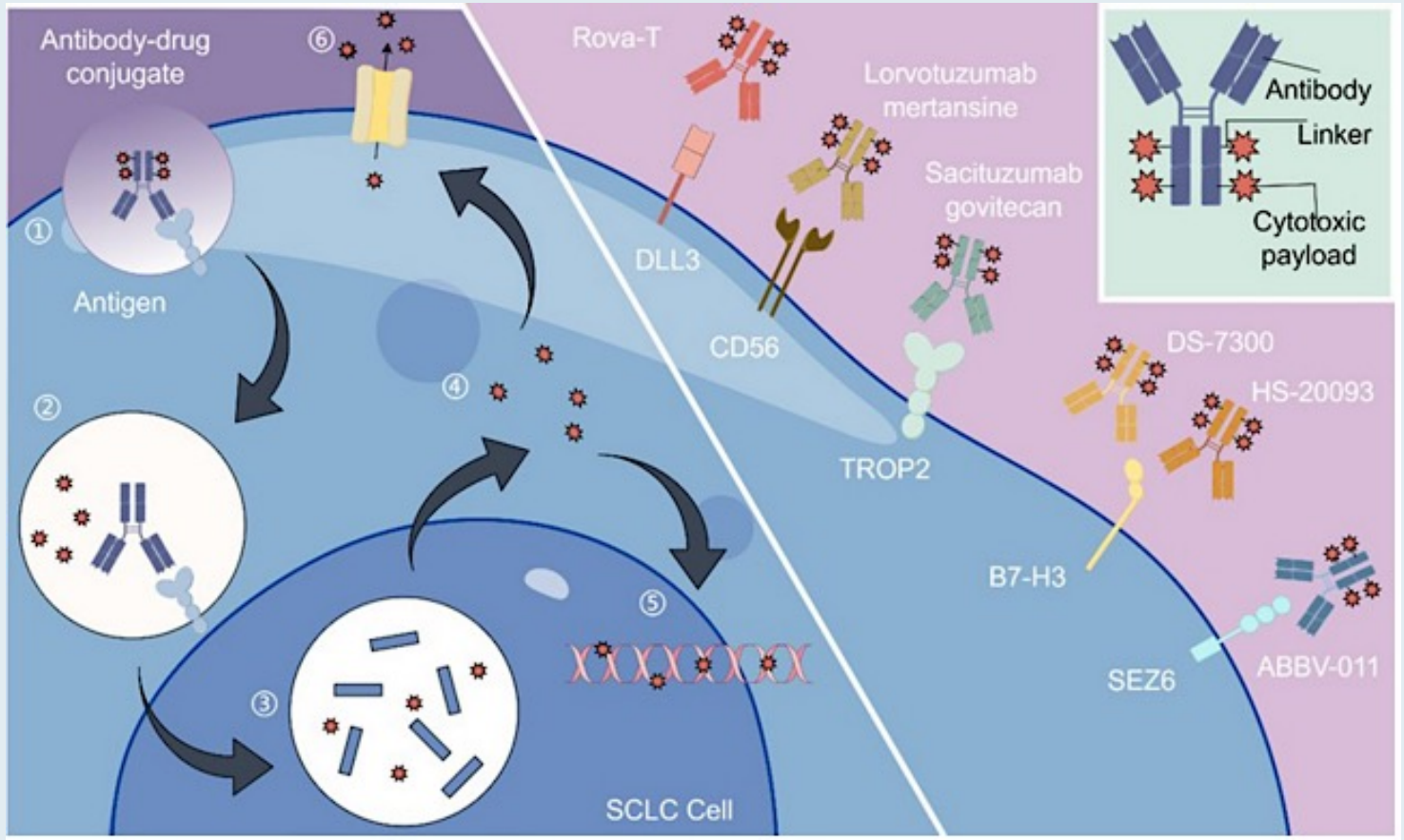
Future Directions in SCLC Management

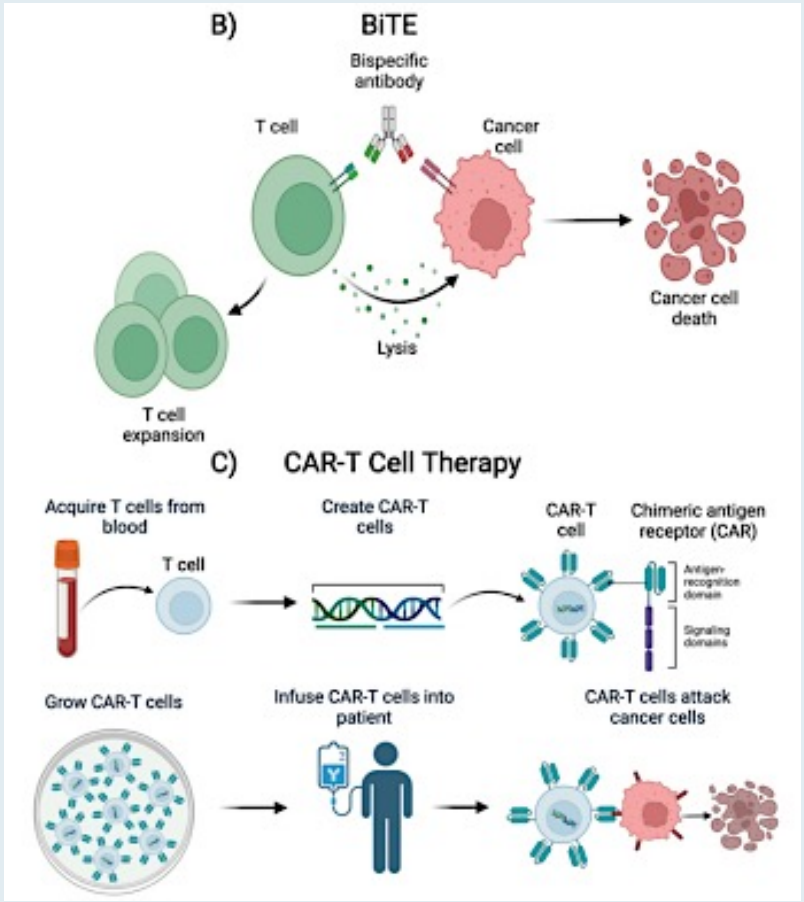
Erin Schenk, MD, PhD
Assistant Professor, Thoracic Oncology
Division of Medical Oncology
Department of Medicine
University of Colorado Anschutz Medical Campus

New and Emerging Targets for SCLC

Antibody-Drug Conjugates



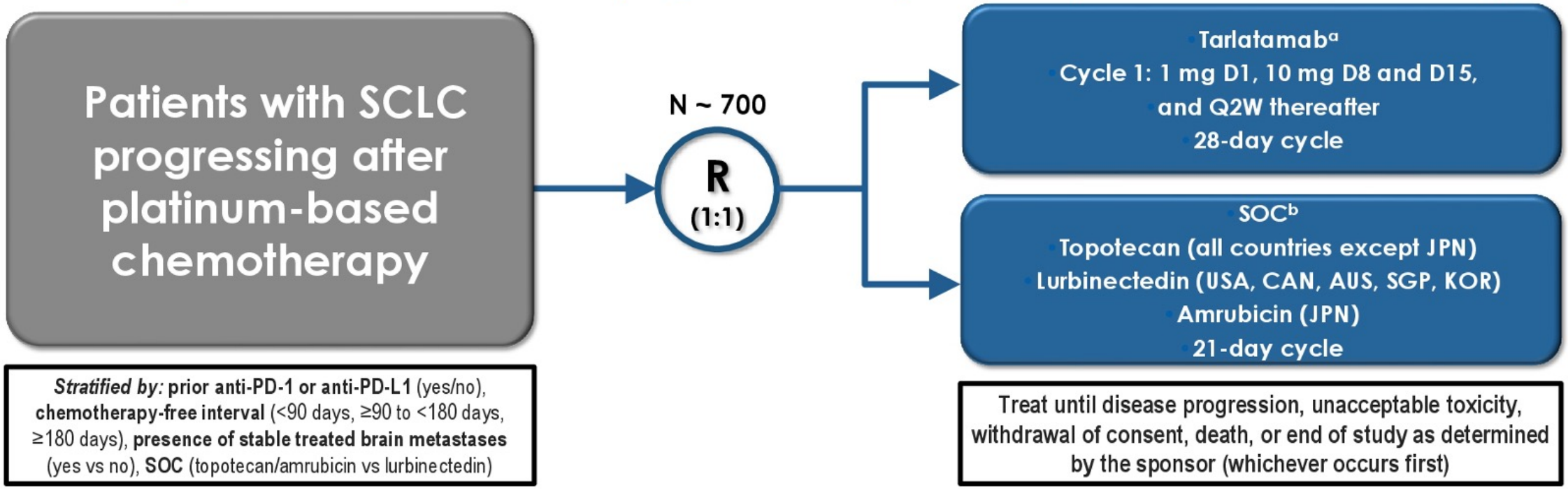
Novel Immune-Based Therapies



Meng Y et al. *Disc Onc* 2024;15:327; Bragasin EI et al. *Explor Target Antitumor Ther* 2025;6:1002302.

DeLLphi-304

Phase 3, open-label, randomized, multi-center study evaluating efficacy and safety of tarlatamab compared with SOC in patients with SCLC who have progressed after 1 prior line of platinum-based chemotherapy



Pre- and post-infusion medication requirements include dexamethasone administered within 1 hour prior to cycle 1 tarlatamab infusion on D1 and D8 and IV hydration following cycle 1 tarlatamab doses on D1, D8, and D15

[a]Tarlatamab will be administered as a 60-minute IV infusion

[b]Standard of care (21-day cycle): Lurbinectedin (USA, Canada, Australia, Singapore, and Korea) will be administered as 3.2 mg/m^2 IV on day 1 every 3 weeks. Topotecan (all countries, except Japan and China) will be administered as IV at 1.5 mg/m^2 or oral at 2.3 mg/m^2/day on days 1, 2, 3, 4, and 5 every 3 weeks. Topotecan (China) will be administered as IV at 1.25 mg/m^2 or oral at 2.3 mg/m^2/day on days 1, 2, 3, 4, and 5 every 3 weeks. Amrubicin (Japan) will be administered as 40 mg/m^2 IV on days 1 to 3 every 3 weeks.

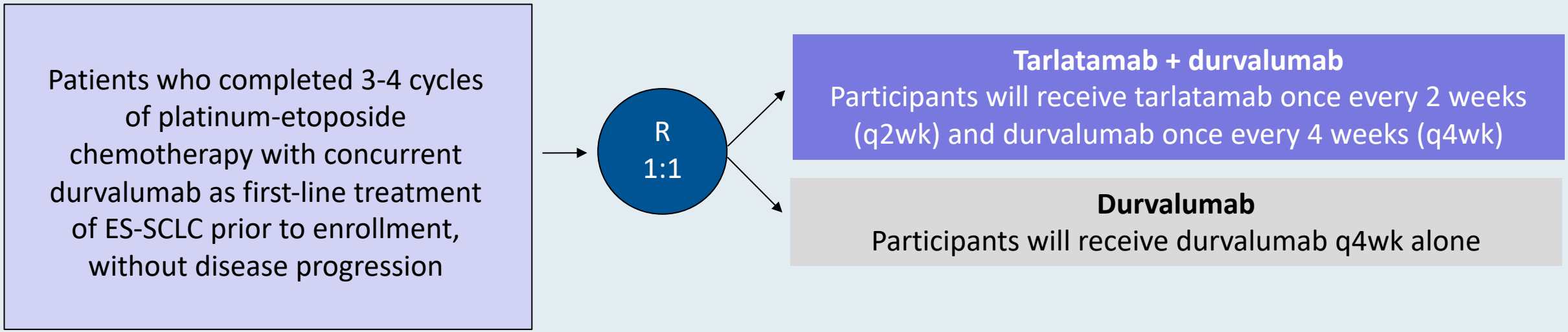
PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; SCLC, small cell lung cancer; SOC, standard of care.

Paz-Ares LG et al. ASCO 2023;Abstract TPS8611.

Courtesy of Melissa Johnson, MD

DeLLphi-305

- **A Phase 3, open-label, multicenter, randomized study of tarlatamab in combination with durvalumab vs durvalumab alone in subjects with ES-SCLC following platinum, etoposide and durvalumab**



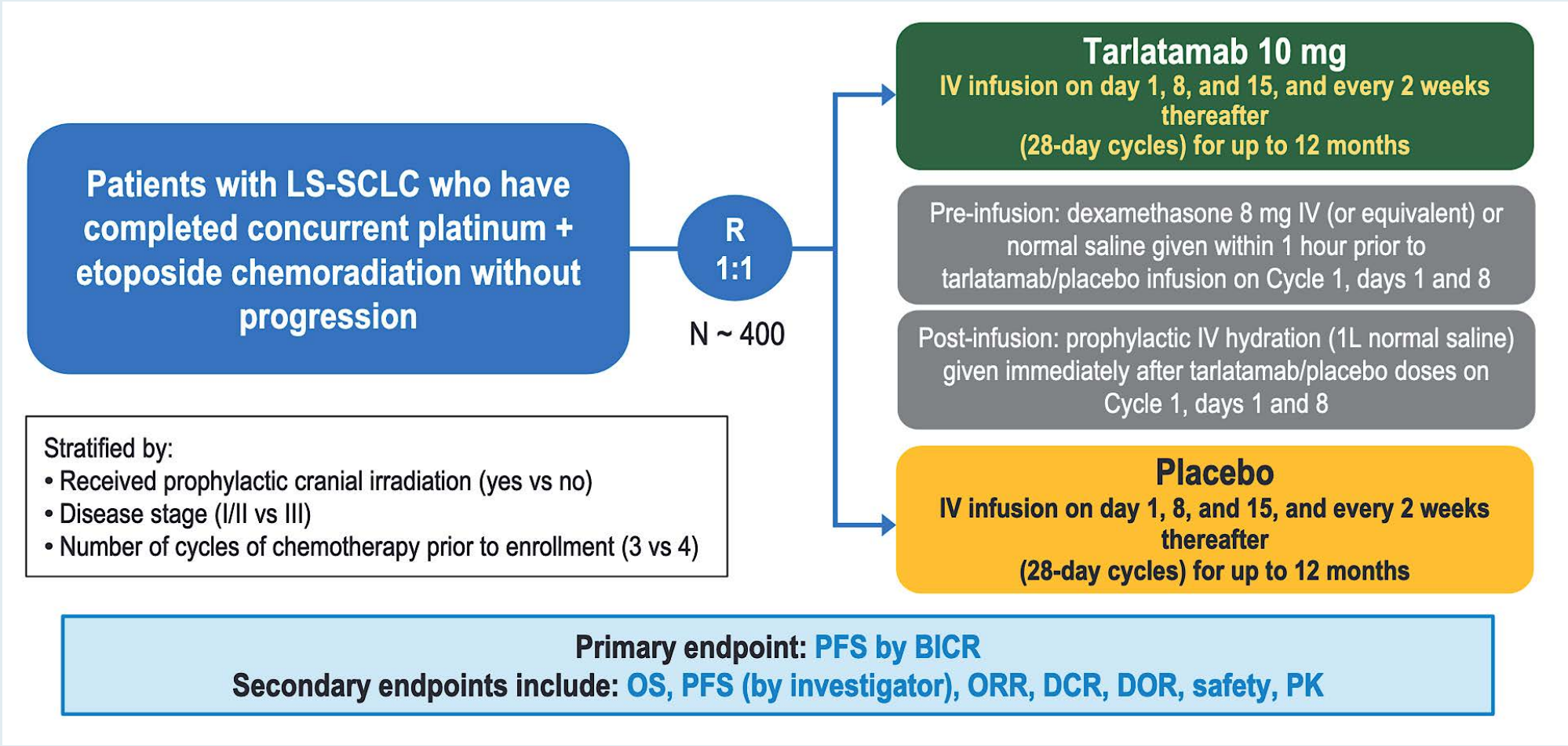
Primary endpoint: OS
Key secondary endpoints: PFS, ORR, DCR, DoR

www.clinicaltrials.gov. NCT06211036. Accessed July 2024.

Courtesy of Melissa Johnson, MD

DeLLphi-306

- A Phase 3, randomized, double-blind, placebo-controlled, multicenter study of tarlatamab therapy in subjects with limited-stage small cell lung cancer (LS-SCLC) who have not progressed following concurrent chemoradiation therapy

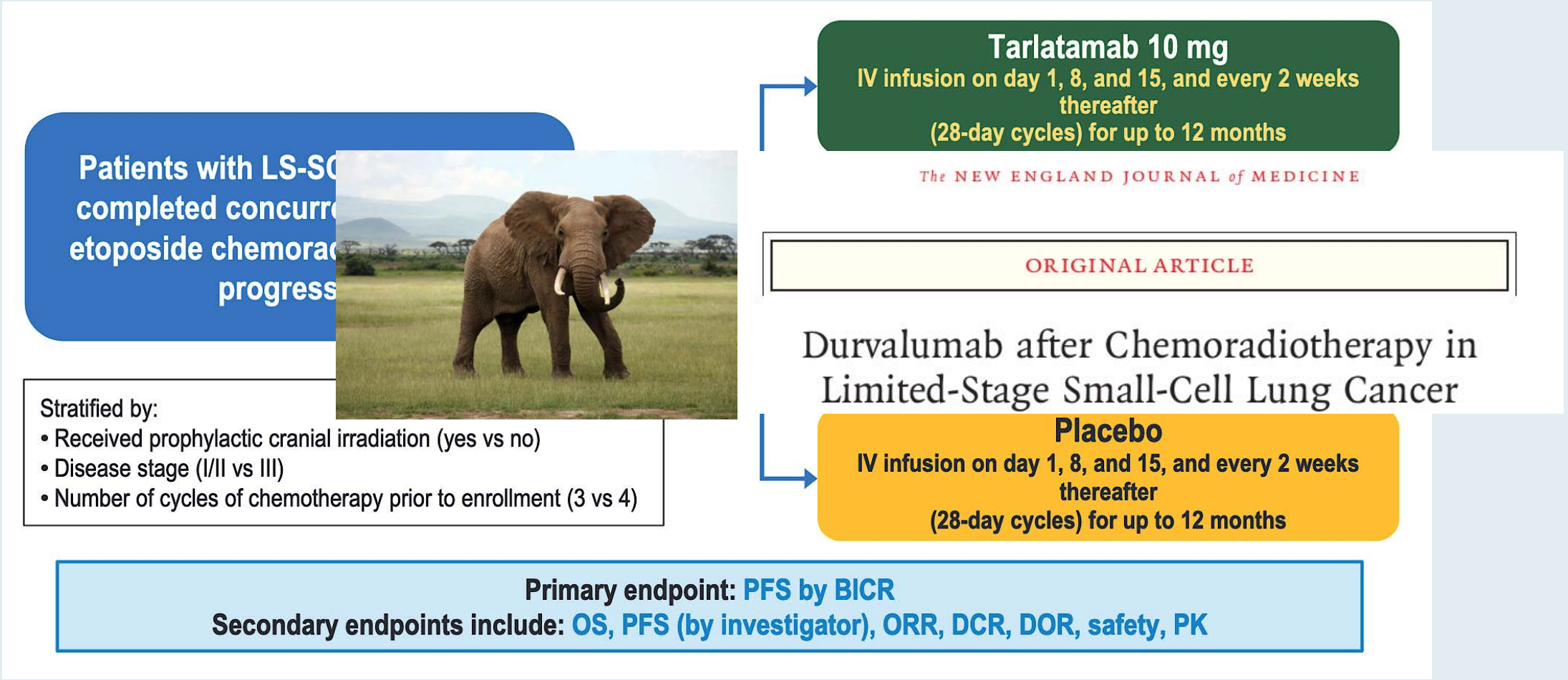


Hummel H et al. European Lung Cancer Congress 2024;Abstract 214TiP.
https://www.britannica.com/animal/African-bush-elephant, Chen Y et al. *NEJM* 2024;391:1313-27.

Courtesy of Melissa Johnson, MD

DeLLphi-306

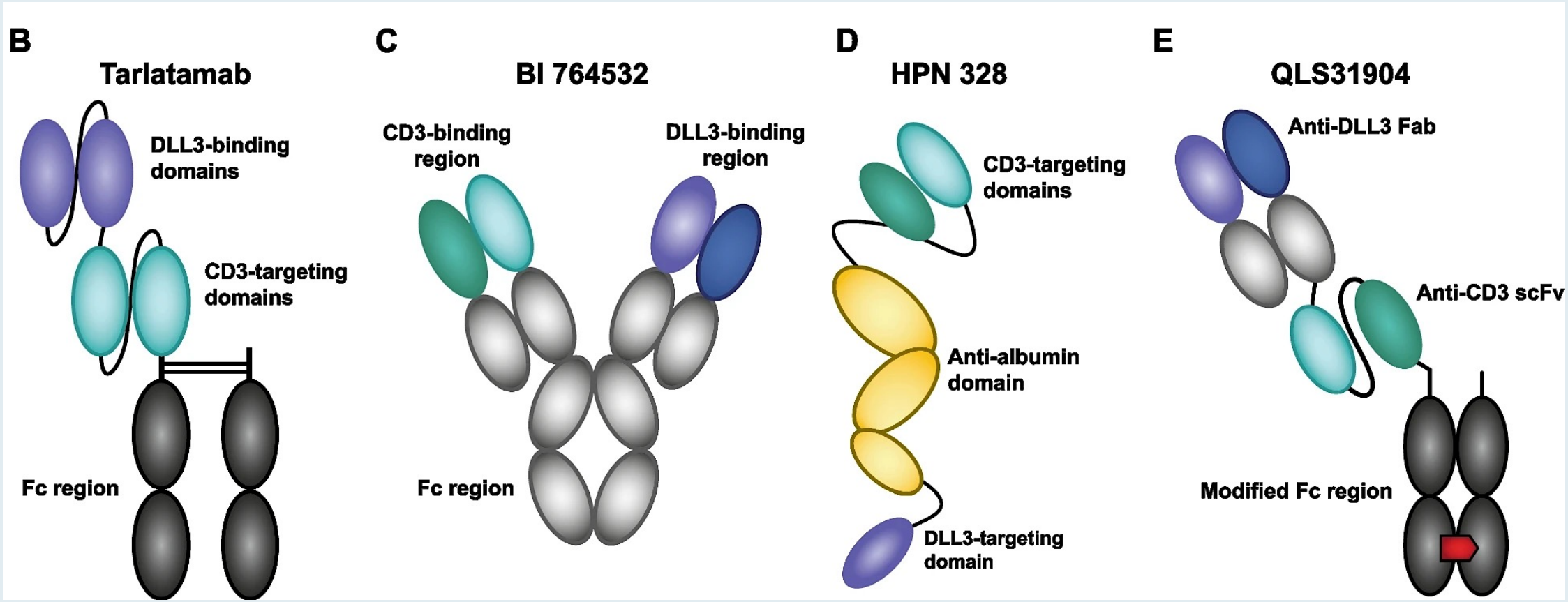
- A Phase 3, randomized, double-blind, placebo-controlled, multicenter study of tarlatamab therapy in subjects with limited-stage small cell lung cancer (LS-SCLC) who have not progressed following concurrent chemoradiation therapy



Hummel H et al. European Lung Cancer Congress 2024;Abstract 214TiP.
https://www.britannica.com/animal/African-bush-elephant, Chen Y et al. *NEJM* 2024;391:1313-27.

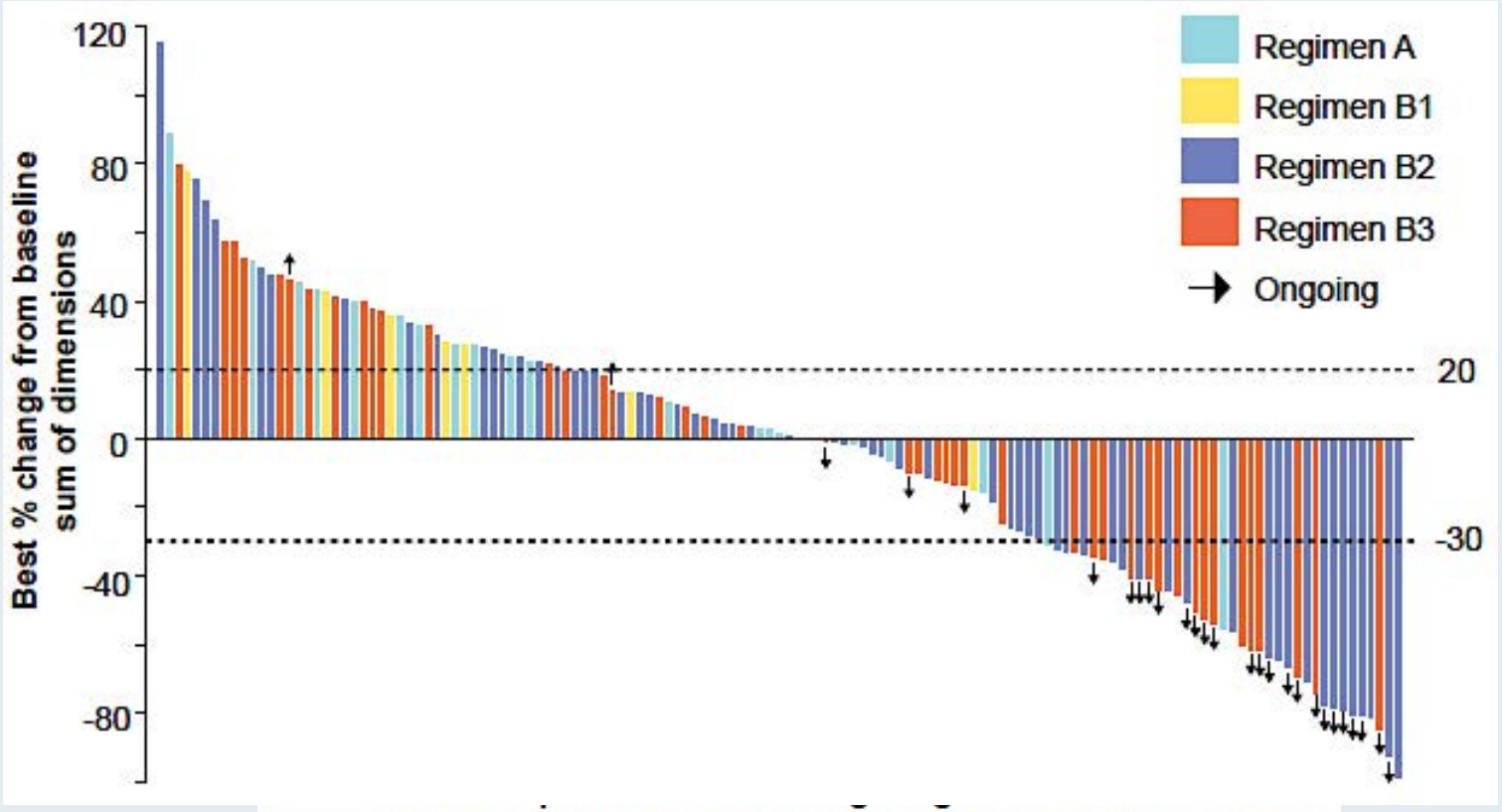
Courtesy of Melissa Johnson, MD

DLL3-CD3 T-Cell Engagers in Development



Rudin CM et al. *J Hema and Onc*;16, 66 (2023)

Updated Analysis of Overall Efficacy of Obrixtamig (BI 764532)



n, (%)**	Regimen A (n=24)	Regimen B1 (n=10)	Regimen B2 (n=79)	Regimen B3 (n=41)	All patients (N=154)††
ORR	1 (4)	0	18 (23)	8 (20)	27 (18)
PR	1 (4)	0	18 (23)	8 (20)	27 (18)
SD	5 (21)	1 (10)	19 (24)	12 (29)	37 (24)
PD	13 (54)	7 (70)	25 (32)	15 (37)	60 (39)
DCR	6 (25)	1 (10)	37 (47)	20 (49)	64 (42)
NE‡‡	5 (21)	2 (20)	17 (22)	6 (15)	30 (20)

Wermke M et al. ESMO 2024;Abstract 670P.

Updated Analysis of Efficacy of Obrixtamig: Dose-Limiting Toxicities and Maximum Tolerated Dose

DLTs[§] during the MTD evaluation period	Dose at DLT onset (µg/kg)	Tumor type
CRS grade 4	B2.3	SCLC
Infusion-related reaction grade 2	B2.3	SCLC
Nervous system disorder grade 3	B2.3	SCLC
CRS grade 3	B2.4	epNEC
ICANS grade 3	B2.6	SCLC
ICANS grade 5	B2.8	epNEC

- Six patients had DLTs, all with regimen B2 and all during the step-in dosing period
- The MTD was not reached

Ongoing Clinical Development

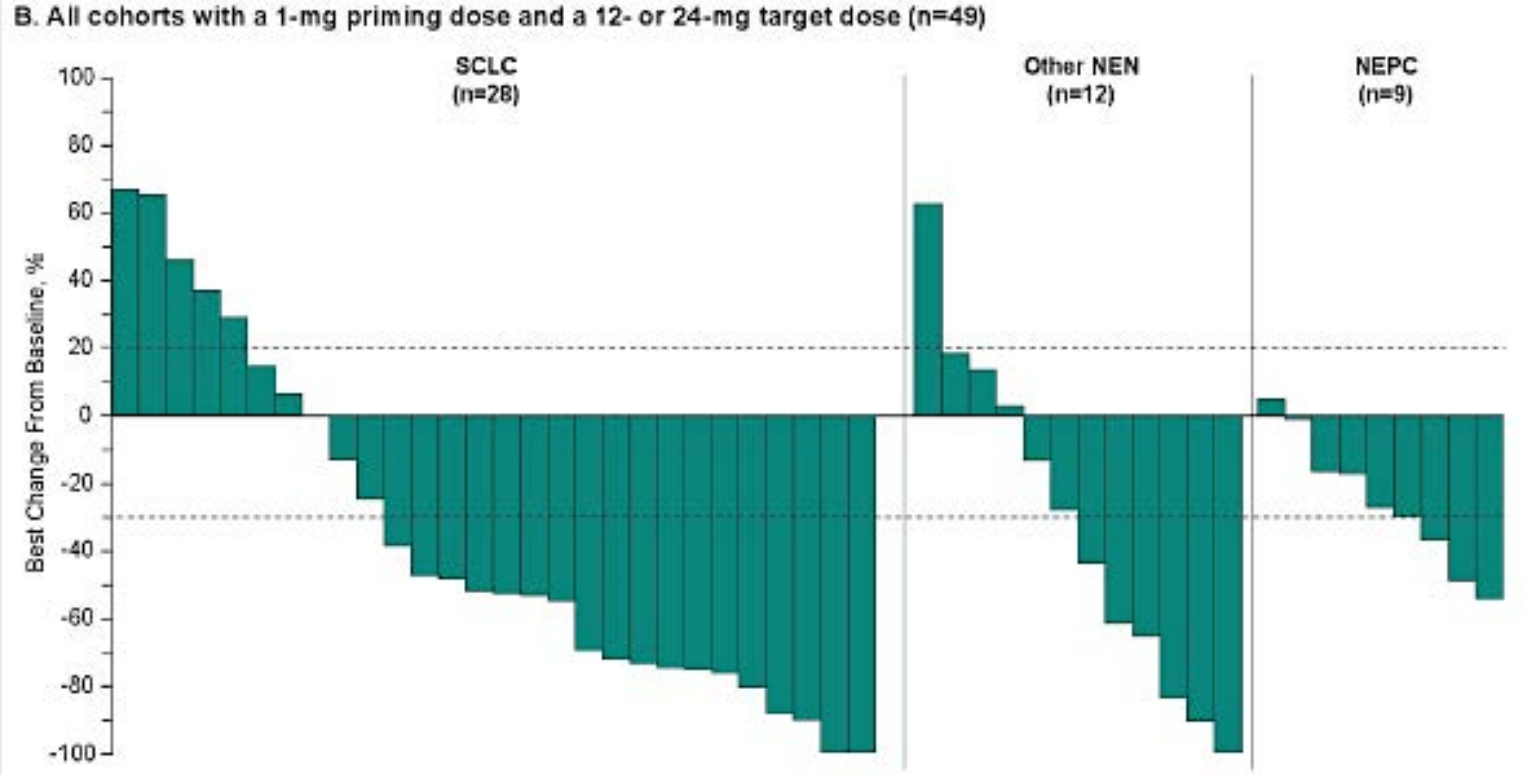
DAREON-5 – Phase 2 SCLC, NEC 3rd line+

DAREON-8 – Phase 1 ES-SCLC 1st line + chemo IO

DAREON-9 – Phase 1 Refractory SCLC + topotecan

Wermke M et al. ESMO 2024;Abstract 670P.

Phase I/II Trial of MK-6070 (HPN328): Response

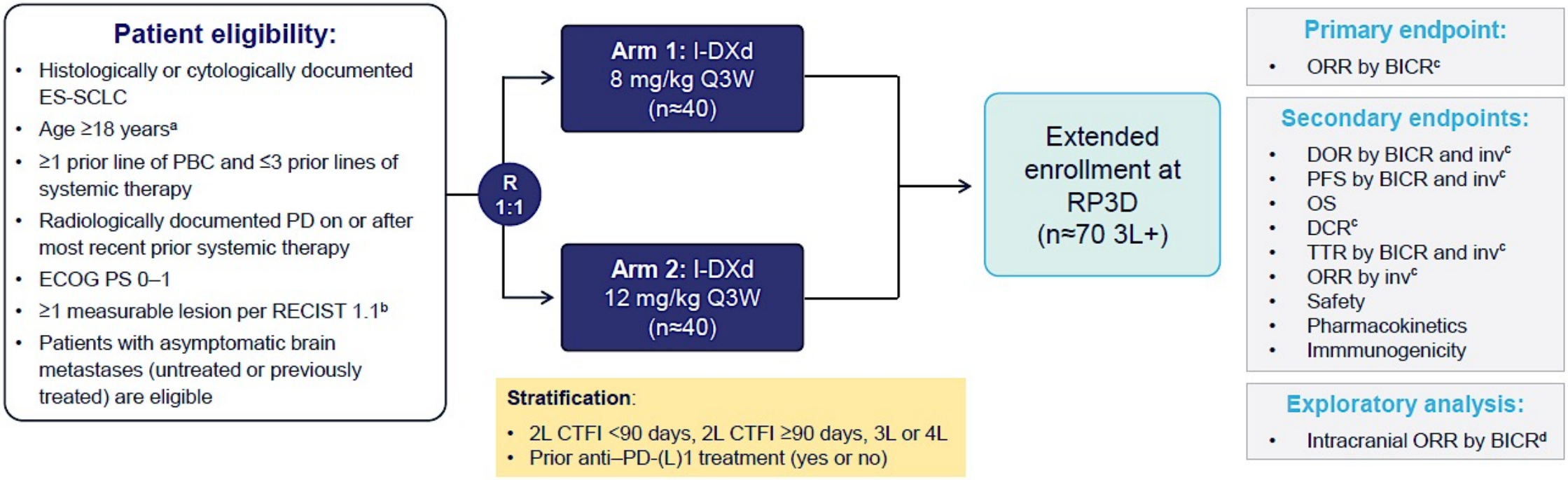


	SCLC n=28	Other NEN[a] n=13
RECIST v1.1		
ORR	11 (39%)	6 (46%)
DCR	20 (71%)	6 (46%)
Extracranial response per RECIST v1.1[b]		
ORR	14 (50%)	6 (46%)
DCR	21 (75%)	6 (46%)

Beltran H et al. ASCO 2024;Abstract 8090.

Ifinatamab Deruxtecan (I-DXd)
B7-H3 Targeting ADC

Phase 2 IDeate-Lung01 study (NCT05280470)

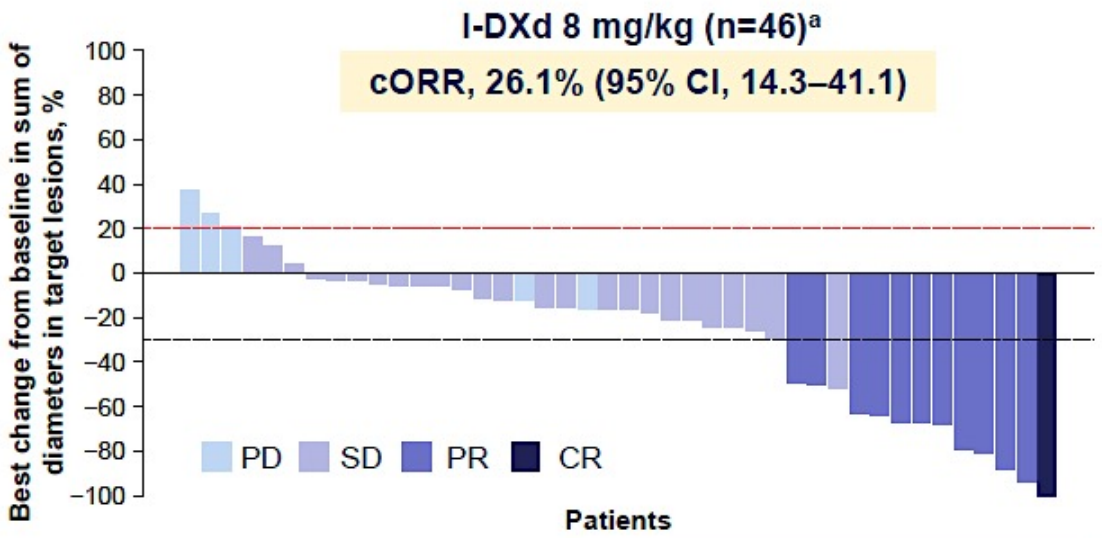


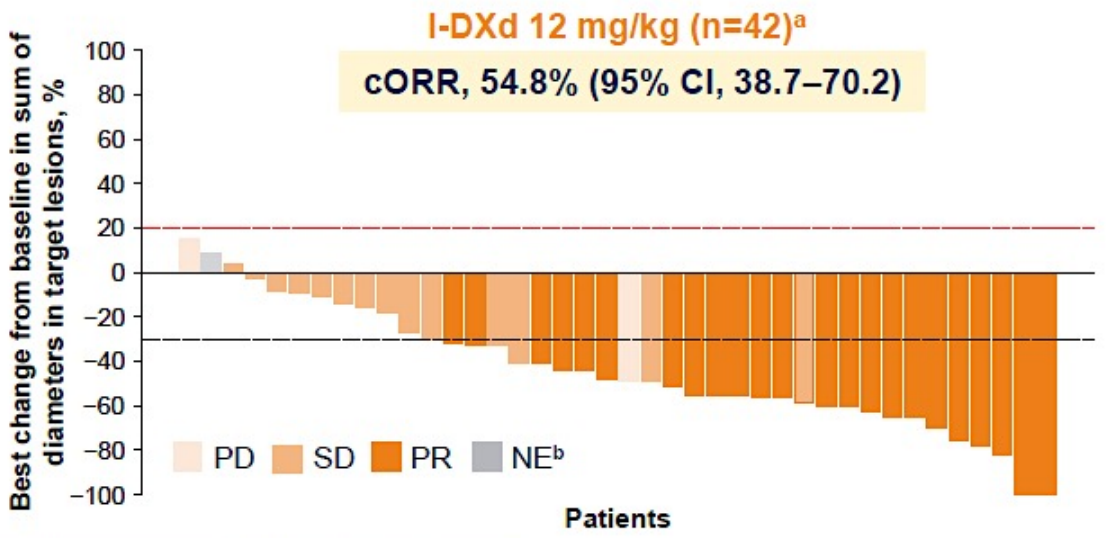
[a]Or local legal age of consent. [b]Patients must also have ≥1 lesion that has not been irradiated and is amenable to biopsy. [c]Per RECIST 1.1. [d]Per CNS RECIST.
2L, second-line; 3L+, third-line and beyond; 4L, fourth-line; BICR, blinded independent central review; CTFI, chemotherapy treatment-free interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; inv, investigator; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PD, progressive disease; PD-(L)1; programmed death (ligand) 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; RP3D, recommended Phase 3 dose; TTR, time to response.

Courtesy of Charles Rudin, MD, PhD, MSKCC

Ifinatamab Deruxtecan (I-DXd) Activity in SCLC 2L+

I-DXd has promising antitumor activity; patients treated with 12 mg/kg had a higher ORR than those treated with 8 mg/kg





Confirmed response by BICR[c]	I-DXd 8 mg/kg n=46	I-DXd 12 mg/kg n=42
ORR, % (95% CI)	26.1 (14.3–41.1)	54.8 (38.7–70.2)
CR, n (%)	1 (2.2)	0
PR, n (%)	11 (23.9)	23 (54.8)
DCR, % (95% CI)	80.4 (66.1–90.6)	90.5 (77.4–97.3)

Data cutoff: April 25, 2024. The median follow-up for 8-mg/kg and 12-mg/kg cohorts was 14.6 months (range, 0.6–17.0) and 15.3 months (range, 0.8–20.3) respectively.

[a]Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan were included in the waterfall plot: in the I-DXd 8-mg/kg cohort, n=42; 2 patients died and 2 patients withdrew consent before the Week 6 assessment; in the 12-mg/kg cohort, n=40; 1 patient died before the Week 6 assessment and 1 patient did not have target lesions at baseline. [b]This patient has a BOR of NE because the only post-baseline tumor scan was conducted outside the designated time window; the timepoint response was SD. [c]Per RECIST 1.1.

BICR, blinded independent central review; BOR, best overall response; cORR, confirmed ORR; CR, complete response; DCR, disease control rate; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease.

Rudin CM et al. WCLC 2024;Abstract OA04.03.

The Future for SCLC Is Already Here

Recruiting

A Study to Evaluate the Safety and Efficacy of Gocatamig (MK-6070) and Ifinatamab Deruxtecan (I-DXd) in Participants With Relapsed/Refractory Extensive-Stage Small Cell Lung Cancer (MK-6070-002)

ClinicalTrials.gov ID NCT06780137

Sponsor Merck Sharp & Dohme LLC

Information provided by Merck Sharp & Dohme LLC (Responsible Party)

Last Update Posted 2025-03-25

Breakthrough Treatment Barriers to Overcome

- **For several DLL3 T-cell engager therapies, treatment initiation requires hospitalization due to CRS AEs**
  - **Ongoing efforts to reduce duration of hospitalization and implement outpatient monitoring strategies**
- **Dosing frequency**
  - **Q1week / Q2week → Q3week**
- **Long-term AEs**
  - **Dysguesia can impact QoL**

Barriers to Clinical Trial Participation

Efficacy vs Patient Burden

- Hospitalization requirement
- Dosing frequency
  - MK-6070 Q2week + I-DXd Q3week
- Potential for increased AEs with dual agents
- Travel / Lodging / Parking at a tertiary referral center

Roundtable Discussion

RTP
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Agenda

Introduction: Overview of Bispecific Antibodies

Module 1: Biology of Small-Cell Lung Cancer (SCLC) and Review of Its Initial Management

Case Presentation: Ms Krueger – 63-year-old man

Module 2: Current Role of Tarlatamab in Therapy for SCLC

Case Presentation: Ms Sandy – 70-year-old woman

Module 3: Future Directions in the Management of SCLC

Case Presentation: Ms Krueger – 81-year-old man

Module 4: Unique Considerations in SCLC Management

Case Presentation: Ms Sandy – 67-year-old woman

Mass General Brigham
Mass General Cancer Center

Small-Cell Lung Cancer Case Presentation

Elizabeth Krueger, NP
Nurse Practitioner
Massachusetts General Hospital Center
for Thoracic Cancers
Boston, Massachusetts

Case Presentation: 81-year-old man

81 yo, male former smoker with a history of prostate cancer s/p prostatectomy, type 2 DM, HTN, and hyperlipidemia. He presented to a local hospital in January 2024 after a mechanical fall in the context of a 20 lb unintentional weight loss and cough. LFT elevations noted on admission (AST 84, ALT 35).

- **Diagnostics:**
  - CT C/A/P – LLL lung mass w/ adjacent satellite subpleural nodules; left lower perihilar masslike opacity; diffuse subpleural disease; numerous bilobar hepatic lesions
  - IR-guided liver biopsy – small cell carcinoma (IHC positive for synaptophysin, chromogranin and TTF1; Ki67+)

- **Treatment:**
  - 2/2024 C1D1 Carboplatin/Etoposide/Atezolizumab x 4 cycles
  - 5/10/2024 CT C/A/P after 4 cycles demonstrates disease progression in chest and liver
  - 5/25/2024 Starts second-line lurbinectedin
  - 6/29/24: CT C/A/P - worsening hepatic disease, MRI brain with new punctate lesions
  - 7/20/24 C1D1 tarlatamab

Case Presentation: 81-year-old man (continued)

C1D1 tarlatamab 1 mg step up dosing

- Administered in outpatient clinic with plan for direct admission for 22-24H of CRS/ICANS monitoring.
- Labs notable for AST 159, ALT 141 due to extensive hepatic disease
- Complicated by grade 2 CRS treated with dexamethasone and tocilizumab
  - Fever 104.3 occurred around the 13H mark after drug administration
    - Symptomatic management with acetaminophen, ibuprofen and meperidine for rigors.
  - Asymptomatic HoTN SBP 70s, IVF x2L did not require pressure support
  - 0.5-2L new oxygen requirement
    - Tocilizumab 8mg/kg infused over 1 hour in a single dose (not to exceed 800mg)
    - Tocilizumab is preferred first rescue medication with CRS
    - Dexamethasone is preferred rescue medication with ICANS but can also be used with CRS
  - Symptoms resolved and he was monitored for an additional 12H prior to discharge
  - Strict return/call criteria reviewed- fever >100.4, low blood pressure, significant fatigue, breathing issues, restlessness, confusion, feeling anxious, dizziness, HA, tremor/seizure, trouble speaking, memory problems.

Recommended management for CRS

Grade[a]	Presenting symptoms	Actions
Grade 1	**Symptoms require symptomatic treatment only (e.g., fever ≥ 100.4°F without hypotension or hypoxia).**	**Withhold TCE until CRS resolves.** **Administer symptomatic treatment.** Administer pretreatment medications prior to next dose of TCE.
Grade 2	**Temperature ≥100.4 °F (38 °C) with either:** **• Hypotension responsive to fluid and not requiring vasopressors, and/or** **• Oxygen requirement of low-flow nasal cannula[d] or blow-by**	**Withhold TCE until CRS resolves.** **Administer symptomatic treatment.** **Consider dexamethasone 8 mg IV (or equivalent) and/or tocilizumab.** Monitor patients for 22-24 hour hospitalization following next dose of TCE. Instruct patients to remain within proximity of a healthcare facility for an additional 24 hours after discharge.
Grade 3 (1st occurrence)	**Temperature ≥100.4 °F (38 °C) with either:** **• Hypotension requiring one vasopressor with or without vasopressin, and/or** **• Oxygen requirement of high-flow nasal cannula[c], facemask, non-rebreather mask, or Venturi mask**	**Withhold TCE until CRS resolves.** **Administer dexamethasone 8 mg IV (or equivalent) every 8 hours for up to 3 doses.** **Recommend tocilizumab 8 mg/kg (dose capped at 800 mg).** **Provide supportive therapy, which may include intensive care.** Monitor patients for 22-24 hour hospitalization following next dose of TCE. Instruct patients to remain within proximity of a healthcare facility for an additional 24 hours after discharge. Administer pretreatment dexamethasone prior to next dose of TCE.
Grade 3 (recurrent)	Temperature ≥100.4 °F (38 °C) with either: • Hypotension requiring one vasopressor with or without vasopressin, and/or • Oxygen requirement of high-flow nasal cannula[c], facemask, non-rebreather mask, or Venturi mask	Permanently discontinue therapy with TCE. Provide supportive therapy, which may include intensive care, as above.
Grade 4	**Temperature ≥100.4 °F (38 °C) with either:** **• Hypotension requiring multiple vasopressors (excluding vasopressin), and/or** **• Oxygen requirement of positive pressure (e.g., continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, and mechanical ventilation)**	Permanently discontinue therapy with TCE. **Provide supportive therapy, which may include intensive care, as per grade 3.**

What is Tocilizumab?

Monoclonal antibody that blocks the inflammatory protein IL-6

Treats CRS without affecting anti-tumor activity

8mg/kg for one dose infused over 1 hour, dose not to exceed 800mg

Case Presentation: 81-year-old man (continued)

C1D8 tarlatamab 10mg step up dosing

- No changes to treatment plan.
- Continued pain at tumor sites during observation period.
- Tolerated D8 without incident and was discharged within 22 hours.

C1D15 tarlatamab 10mg transitioned to outpatient observation.

- New grade 1 thrombocytopenia, likely due to treatment effect or marrow involvement.
- Was able to treat through this and remained stable.

Imaging

- SCANS after 2 cycles demonstrate response in the CNS (new punctate lesions are no longer observed) and hepatic disease has responded.
- Over the course of 6 months dominant liver lesion in segment 7 went from 54mm->25mm, segment 8 lesion 36mm->19mm.

Case Presentation: 81-year-old man (continued)

Physical

- Management of co-morbid conditions- DM2 on multiple agents, weight loss and hypoglycemia

Psychological/Social

- Code status: ES-SCLC; was considering DNR/I though given potential for severe CRS/ICANS, he elected to stay FULL CODE
- Health care proxy- changed frequently due to strained interpersonal relationships
- Primary caretaker for his 17 yo great granddaughter with high functioning ASD. No formal guardianship plan in place after he passes
- Arranged for home based palliative care

Operational

- How can we improve home monitoring? Blood pressure cuff, sat probe, home thermometer
- Delinked visits so he can be home for school drop off/pick up
- Discharge with a x1 dose of dexamethasone in hand?

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Unique Considerations in SCLC Management

Erin Schenk, MD, PhD
Assistant Professor, Thoracic Oncology
Division of Medical Oncology
Department of Medicine
University of Colorado Anschutz Medical Campus

Overview of Small Cell Lung Cancer

Cell of origin

- Neuroendocrine

Initial presentation

- Smoking history/comorbidities
- Hilar and mediastinal nodes/symptomatic
- Brain metastases, high growth rate
- Superior vena cava (SVC) syndrome

Clinical issues

- Paraneoplastic syndromes (SIADH, neurologic)
- SVC syndrome
- Brain metastases

Paraneoplastic Syndromes

- Inappropriate production of hormones/bioactive substances or expression of shared antigens that generate an autoimmune response (T or B cell mediated)
- Neuroendocrine cells/SCLC has a predisposition to secrete substances and express shared antigens

Syndrome	Presentation	Lab findings	Treatment options
SIADH	Falls, headache, nausea, fatigue, muscle cramps, seizures, lethargy, tremors, depressed mood	Hyponatremia	Fluid restriction <1,000 mL/day with adequate protein and sodium intake
		Increased urine osmolality	Demeclocycline, conivaptan, Tolvaptan
			Hypertonic saline
Cushing Syndrome	Muscle weakness, peripheral edema, hypertension, weight gain	Hypokalemia, elevated ACTH not suppressed with dexamethasone	Ketoconazole, octreotide, metyrapone, mitotane, etomidate, mifepristone

SIADH, syndrome of inappropriate antidiuretic hormone; ACTH, adrenocorticotropic hormone.

Soomro Z et al. *J Thorac Disease* 2020;12(10):6253-63.

RTP RESEARCH TO PRACTICE

Patient Case – A Rapid Response

- 65F slow recovery from COVID
  - Cough and dyspnea
  - ~2-3 months nausea, vomiting
- Imaging showed LUL mass with mediastinal adenopathy and pleural metastases
- Diagnosis: Extensive-stage (ES) SCLC
- Therapy start: no more nausea

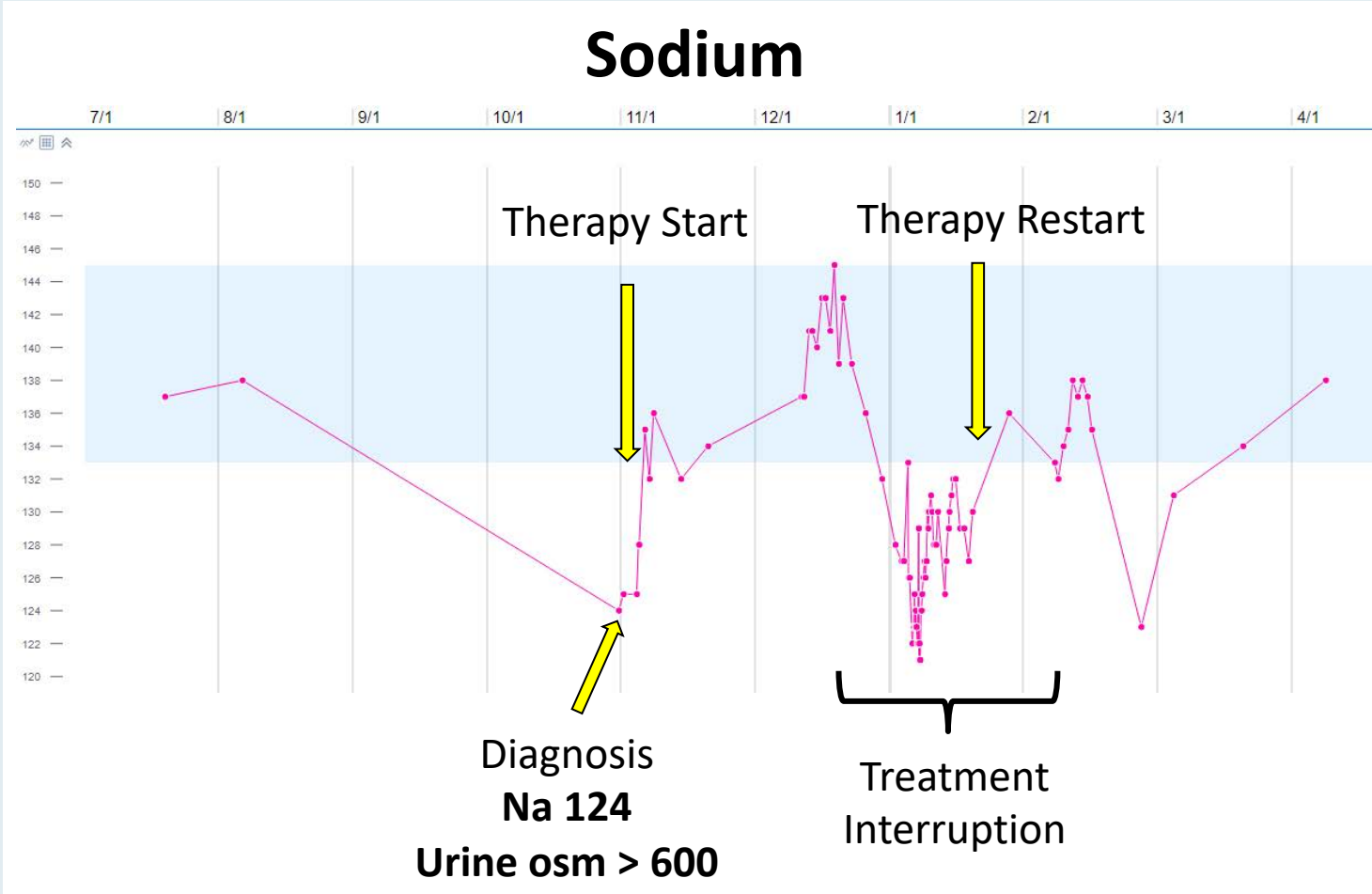


Image courtesy of Erin Schenk, MD, PhD, University of Colorado

Superior Vena Cava Syndrome

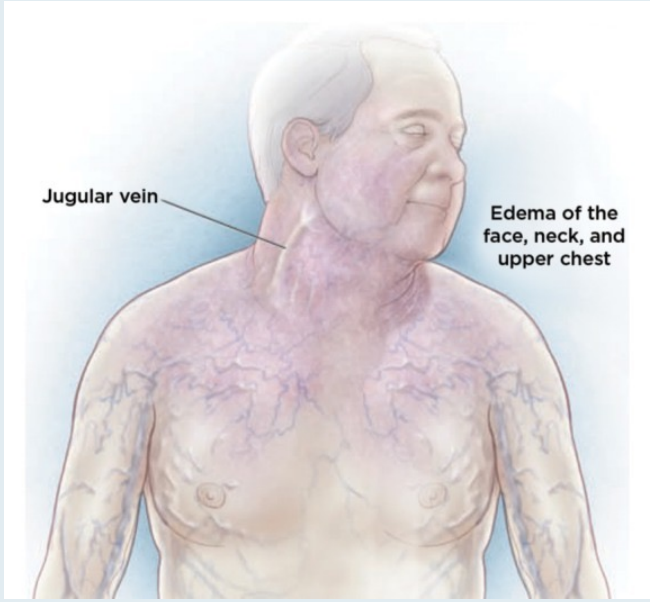
NSCLC (50%), SCLC (22%) and lymphoma (12%) are the most common malignant etiologies

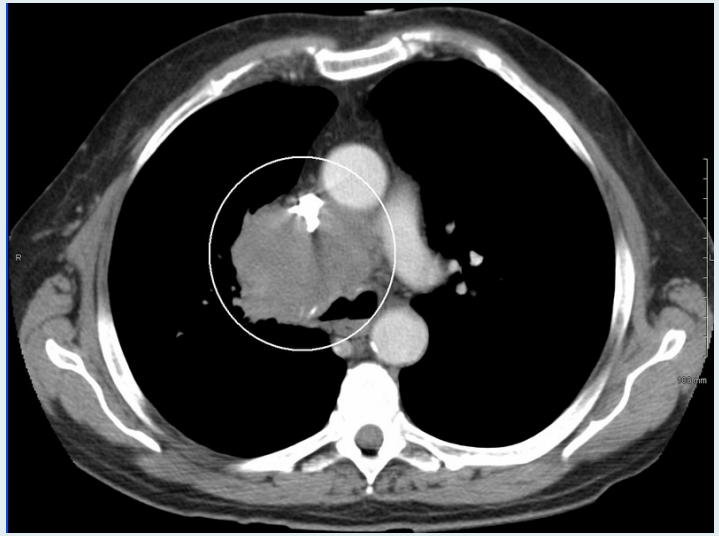
Clinical presentation

- Patient may report feeling fullness in the head, facial edema, and dyspnea
- Physical exam:
  - Venous distension in neck or chest wall, facial and UE edema

Management/treatment

- Manage underlying disease
- Radiation, chemotherapy, corticosteroids, procedures

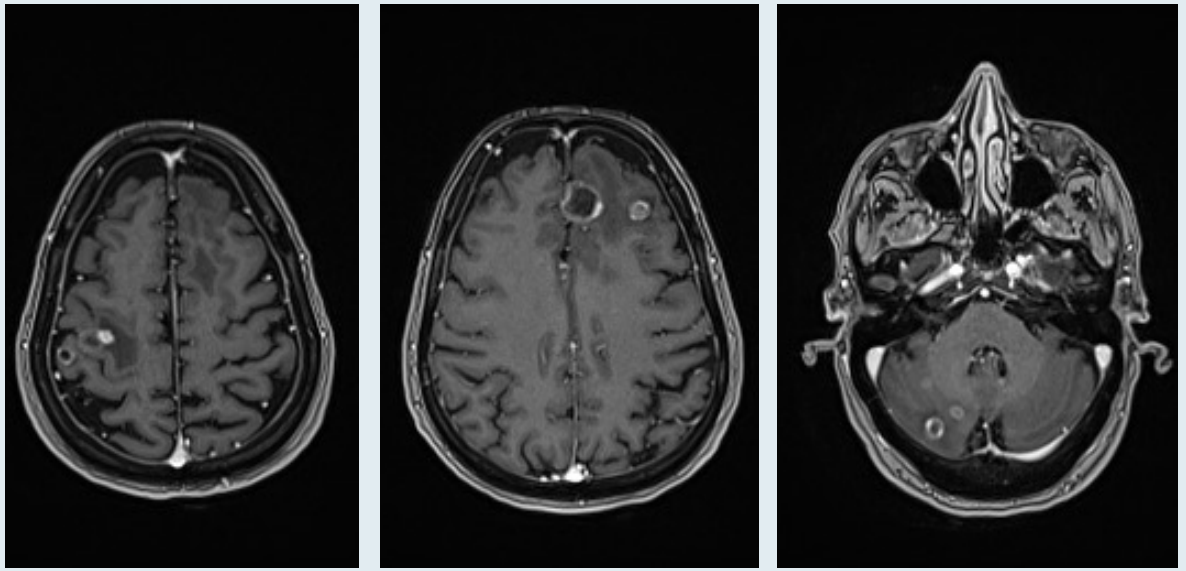




Chow R et al. *Ann Palliat Med* 2024;13(3):620-26, *J Adv Prac in Onc*, 01 September 2018, 9(6):677-9; https://commons.wikimedia.org/wiki/File:SVCCT.PNG

Patient Case – Heartbreak, Delayed

- **Feb 2023**: 60F LUL nodule on CT lung cancer screening
  - PET LUL + bone metastases – ES SCLC
  - MRI brain negative
  - 1st line carbo/etop/atezo (April 2023)
- **Oct 2023**: LUL lesion recurrence
  - Starts DLL3/CD3 T-cell engager trial
- **Oct 2024**: LUL progression. Undergoes resection
- Follow-up surveillance – NED
- **Mar 2025:** ED for left sided weakness and confusion



- **Mar 2025**: SRS to 9 lesions

Images courtesy of Erin Schenk, MD, PhD, University of Colorado

Brain Metastases and SCLC

- >10% of patients have BM at initial diagnosis
- **>50% will develop BM within 2 years**

Clinical presentation

- Risk factors for BM in SCLC not clear, but BM incidence appears to be higher in younger patients
- SCLC more likely associated with multiple BM as opposed to single BM
- Parenchymal and leptomeningeal metastases

Lukas RV et al. *Oncotarget* 2017;8(41):71223-33; Zeng H et al. *Front Oncol* 2022;12:889161; UpToDate 2025.

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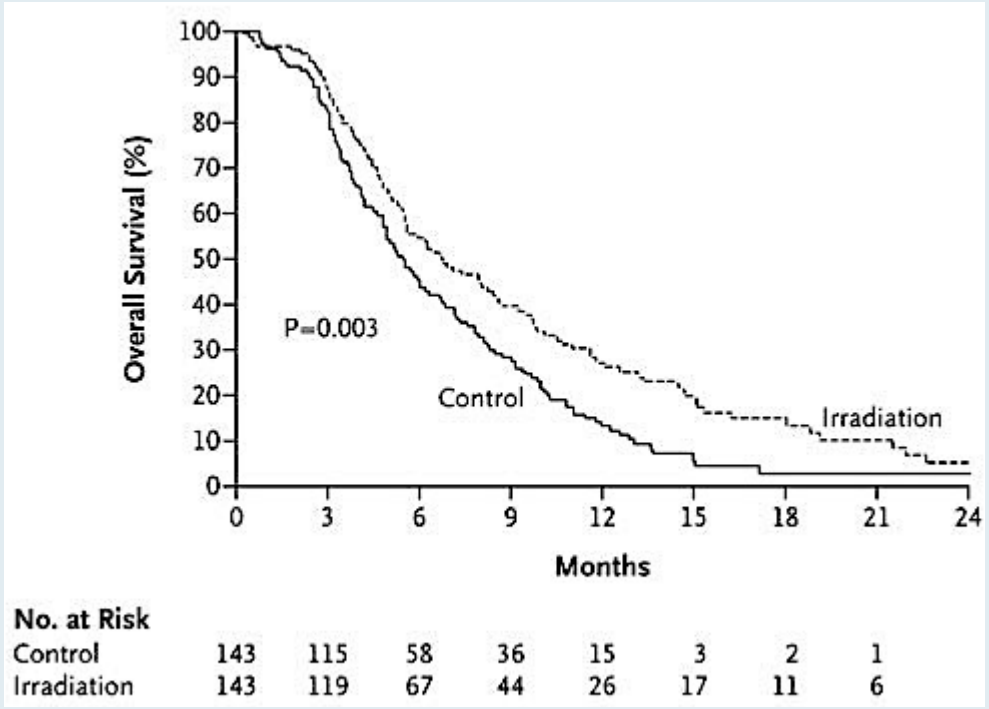
Management/treatment



PCI in ES-SCLC

- No confirmation of absence of brain metastases

Lukas RV et al. *Oncotarget* 2017;8(41):71223-33; Zeng H et al. *Front Oncol* 2022;12:889161; UpToDate 2025. Slotman B et al. *NEJM* 2007;357:664-72.

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Management/treatment

- MAVERICK (SWOG-1827) PCI vs MRI surveillance
- No systemic therapy with clear CNS disease control benefit
- Radiation approaches
  - WBRT +/- hippocampal sparing
  - Practice shifting toward SRS when possible

Lukas RV et al. *Oncotarget* 2017;8(41):71223-33; Zeng H et al. *Front Oncol* 2022;12:889161; UpToDate 2025. Slotman B et al. *NEJM* 2007;357:664-72.

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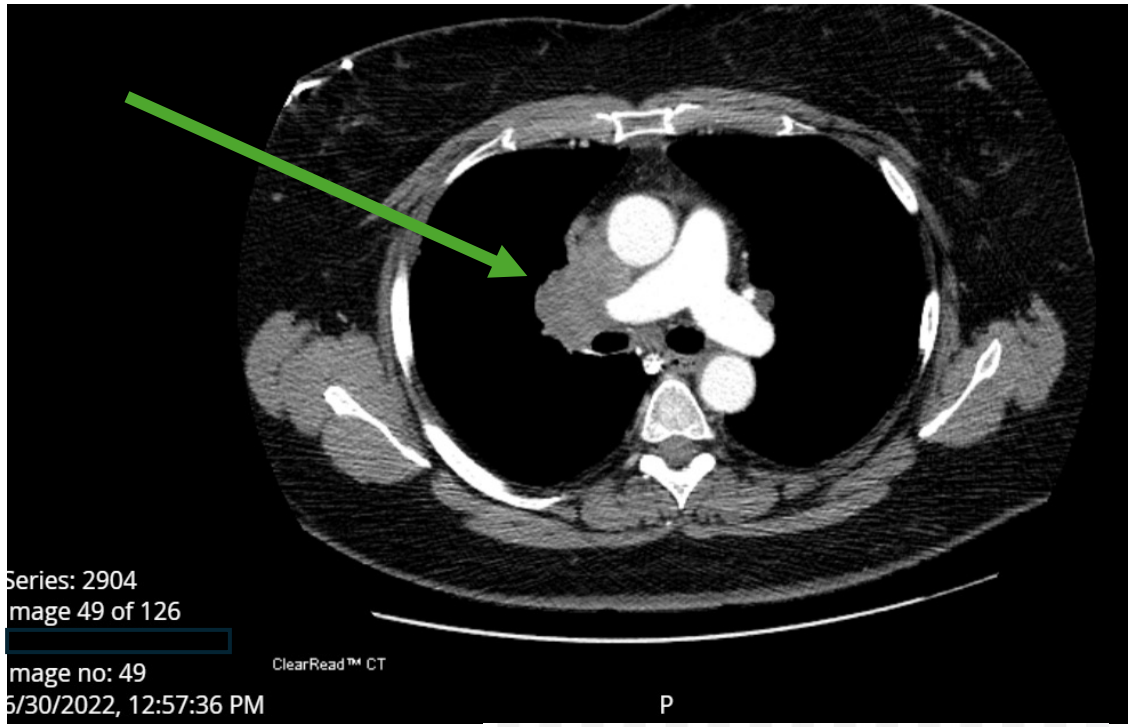
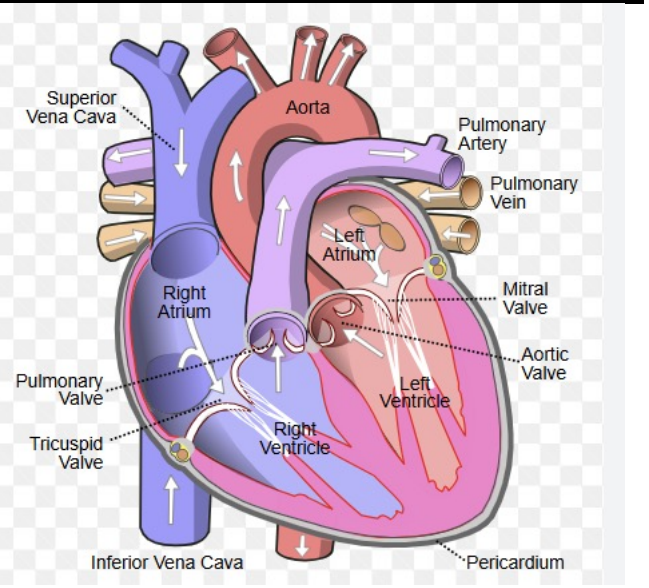
Small-Cell Lung Cancer Case Presentation

Beth Sandy, MSN, CRNP, FAPO

Case Presentation:
67-year-old woman

- 67 y/o female diagnosed with extensive stage SCLC in 6/2022
- Presentation: Facial swelling (and cough that was not out of the ordinary necessarily)
- Bronch + SCLC
- Found to have SVC syndrome: palliative XRT X 3 fractions
- Found to have brain mets at diagnosis as well and had SRS (cyberknife) to 3 lesions





Case presentation: 67-year-old woman (continued)

- 9/2022: Carboplatin/Etoposide/Atezolizumab followed by Atezolizumab maintenance until 6/2023
- 6/2023: progressive disease in the R hilum, as well as one new brain met 4mm R occipital lobe
- 6/2023: started lurbinectedin chemotherapy
- 10/2023 imaging shows response to lurbinectedin and resolution of brain met (no radiation)
- 2/2024: progression, 4 more cycles of etoposide/carboplatin/durvalumab
- 8/2024: progressive brain mets, WBXRT
- 10/2024: progression in the chest and new liver met
- 12/2024: Started Tarlatamab

Case presentation: 67-year-old woman (continued)

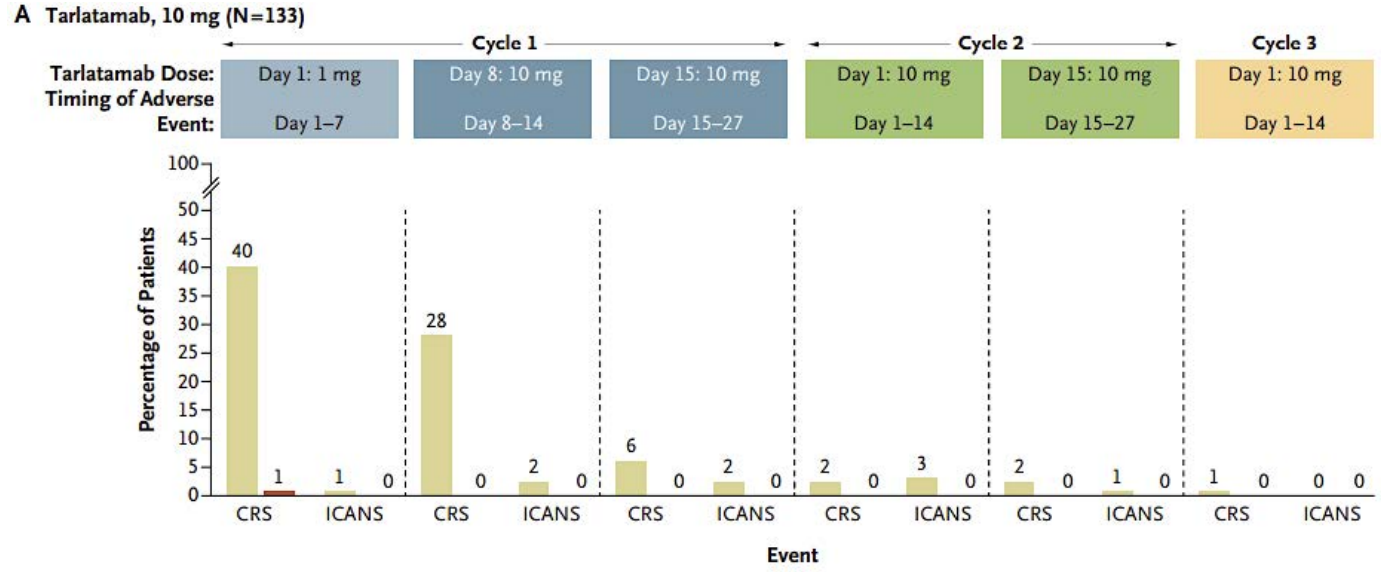
- We reviewed CRS and ICANS
- CRS: overview, reassured most commonly occurs in first 2 doses and will be inpatient
- ICANS:
  - I didn’t voice this out loud, however, as a provider I had concerns on ability to evaluate this
  - Patient had SRS to brain followed by WBXRT
  - At baseline, her cognition was off….

Case presentation: 67-year-old woman (continued)

- 12/10/2024: treatment #1 tolerated well, no real s/e
- 12/17/2024: treatment #2, developed CRS while admitted for overnight monitoring
  - Fever, complicated by hypotension
  - Developed lethargy
  - Though admitted, was worrisome to patient's daughter who was with her
  - Was treated with acetaminophen, dexamethasone, IV fluids
  - Quickly improved in 24-48 hours and was discharged after 48 hours
- 12/24/2024: treatment #3 tolerated well

CRS with Tarlatamab

- Step up dosing due to CRS
- 1mg on D1 and 10mg D8 and on
- Majority happens in treatment #1 and treatment #2
- Occurred in 51% of patients
- Majority was grade 1 or 2



Grade 1= Fever only

Grade 2= Fever + a complicating factor:

- hypotension*, hypoxia*, tachycardia, lethargy, nausea/vomiting

*Hypotension responsive to fluids, not requiring vasopressors

*Hypoxia requiring low-flow nasal cannula

Ahn M-J, et al. N Engl J Med 2023;389:2063-75

Roundtable Discussion

RTP
RESEARCH
TO PRACTICE

Understanding the Current Paradigm and New Approaches in the Care of Patients with Cancer

A Complimentary NCPD Hybrid Symposium Series Held During the 50th Annual ONS Congress

Ovarian Cancer

Friday, April 11, 2025

12:15 PM – 1:45 PM

Faculty

Courtney Arn, CNP
Jennifer Filipi, MSN, NP
David M O'Malley, MD
Shannon N Westin, MD, MPH, FASCO, FACOG

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

To Claim NCPD Credit

In-person attendees: Please refer to the program syllabus for the NCPD credit link or QR code.

Virtual attendees: The NCPD credit link is posted in the chat room.

NCPD/ONCC credit information will be emailed to each participant within 1 to 2 business days.

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