Small Cell Lung Cancer: Updates and “Targeted” Therapy Approaches

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Clinical Initiatives

Overview

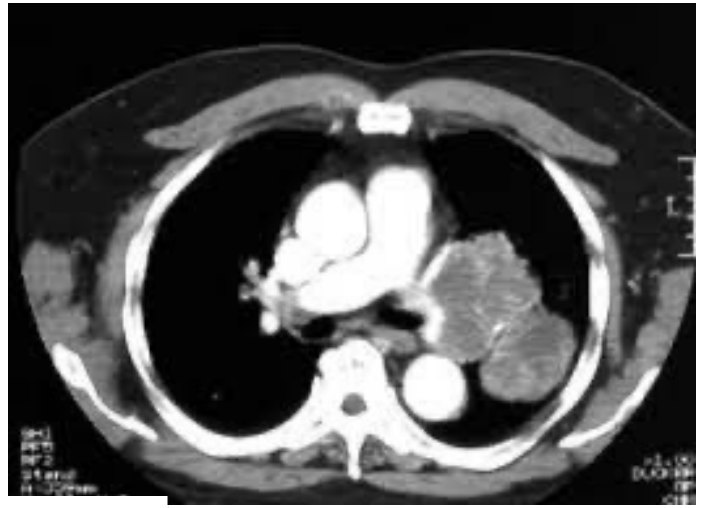
- Debunking SCLC Myths
- The Era of Immunotherapy
  - Limited Stage
  - Extensive Stage
- Using “Targeted” Approaches to Improve Outcomes
  - Maintenance
  - Relapsed SCLC
- Remembering Patient Perspectives

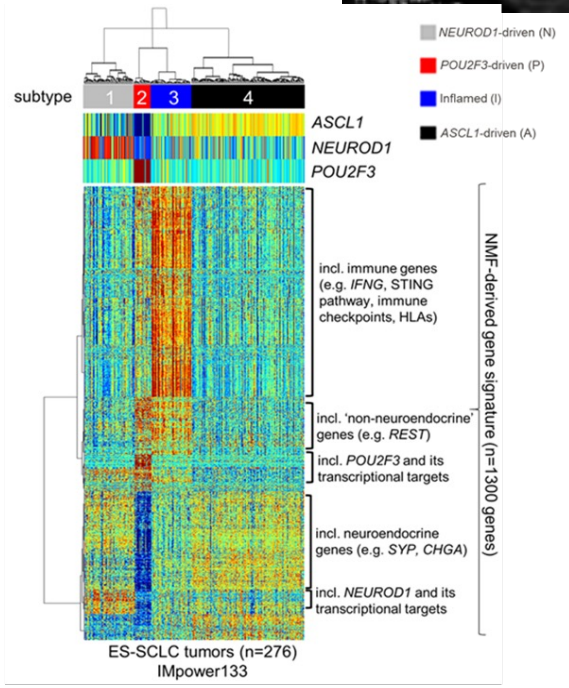
Top 3 SCLC Myths

1. It is difficult to obtain tumor tissue from SCLC pts

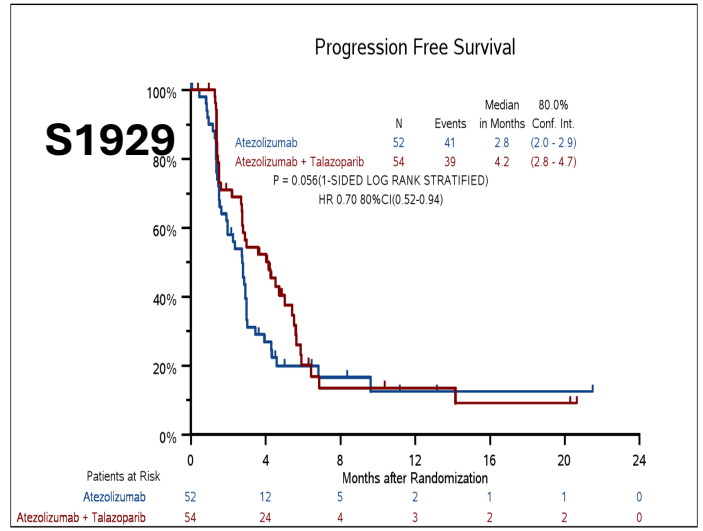
2. “One size fits all” homogenous approach

3. SCLC patients are not ideal clinical trial candidates





Gay et al., *Cancer Cell*, 2021



Karim et al., ASCO, 2023

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Using IO in 3L setting, subsequently withdrawn due to negative phase III trials but still in NCCN guidelines if no prior IO exposure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, likely to be approved by FDA

Immunotherapy Trials in Limited Stage

TABLE 1. Ongoing ICI Trials in Limited-Stage Small Cell Lung Cancer

Trial	No.	Type	ICI	Setting	Estimated Completion Date
DOLPHIN	NCT04602533	Phase II, Germany	Durvalumab	Frontline with CCRT	September 2023
Huang et					
ADRIATIC					
NRG-LU0(					
SURPASS					
ACHILES					
KEYLYNK-013	NCT04624204	Phase III, multinational	Pembrolizumab	Frontline with CCRT, then with olaparib	October 2027

Abbreviations: CCRT, concurrent chemoradiotherapy; ICI, immune checkpoint inhibitor; XRT, radiotherapy.

Durvalumab significantly improved overall survival and progression-free survival for patients with LS-SCLC in ADRIATIC Phase III Trial- ASCO 2024

Wang X, Chiang A, ASCO Ed Book 2024

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)

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

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

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)

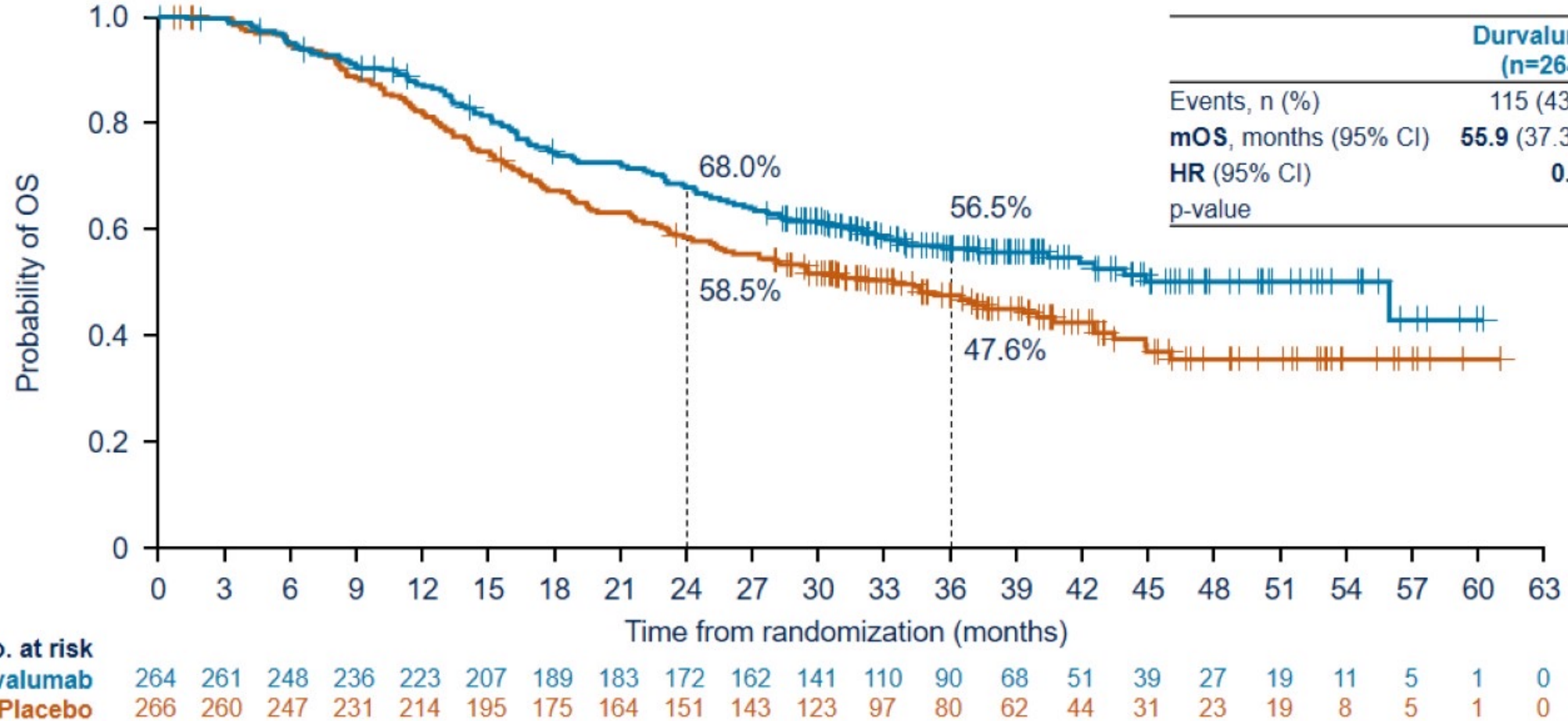
Other secondary endpoints:
- OS/PFS landmarks
- Safety

*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

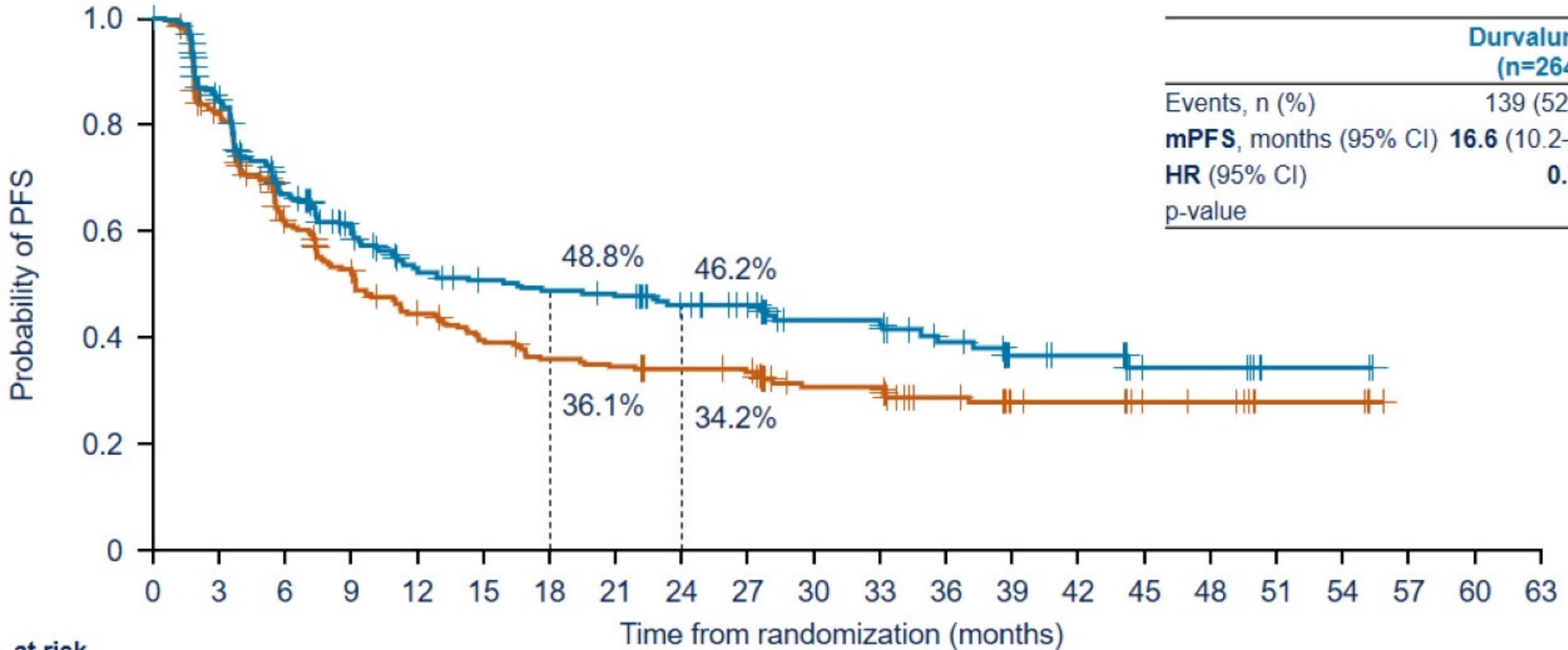
OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

PRESENTED BY: Dr David R. Spigel

CI, confidence interval; mOS, median OS; NE, not estimable.

Progression-free survival* (dual primary endpoint)

- Median duration of follow up in censored patients: 27.6 months (range 0.0–55.8)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

No. at risk																						
Durvalumab	264	212	161	135	113	105	101	98	84	78	51	51	33	21	19	10	10	4	4	0	0	0
Placebo	266	208	146	122	100	88	79	76	71	69	47	47	34	23	22	15	14	5	5	0	0	0

*By BICR per RECIST v1.1.

PFS was analyzed using a stratified log-rank test adjusted for disease stage (I/II vs III) and receipt of PCI (yes vs no). The significance level for testing PFS at this interim analysis was 0.00184 (2-sided) at the 0.5% level, and 0.02805 (2-sided) at the overall 5% level. Statistical significance for PFS was achieved through the recycling multiple testing procedure framework and testing at the 5% (2-sided) alpha level (adjusted for an interim and final analysis).

PRESENTED BY: Dr David R. Spigel

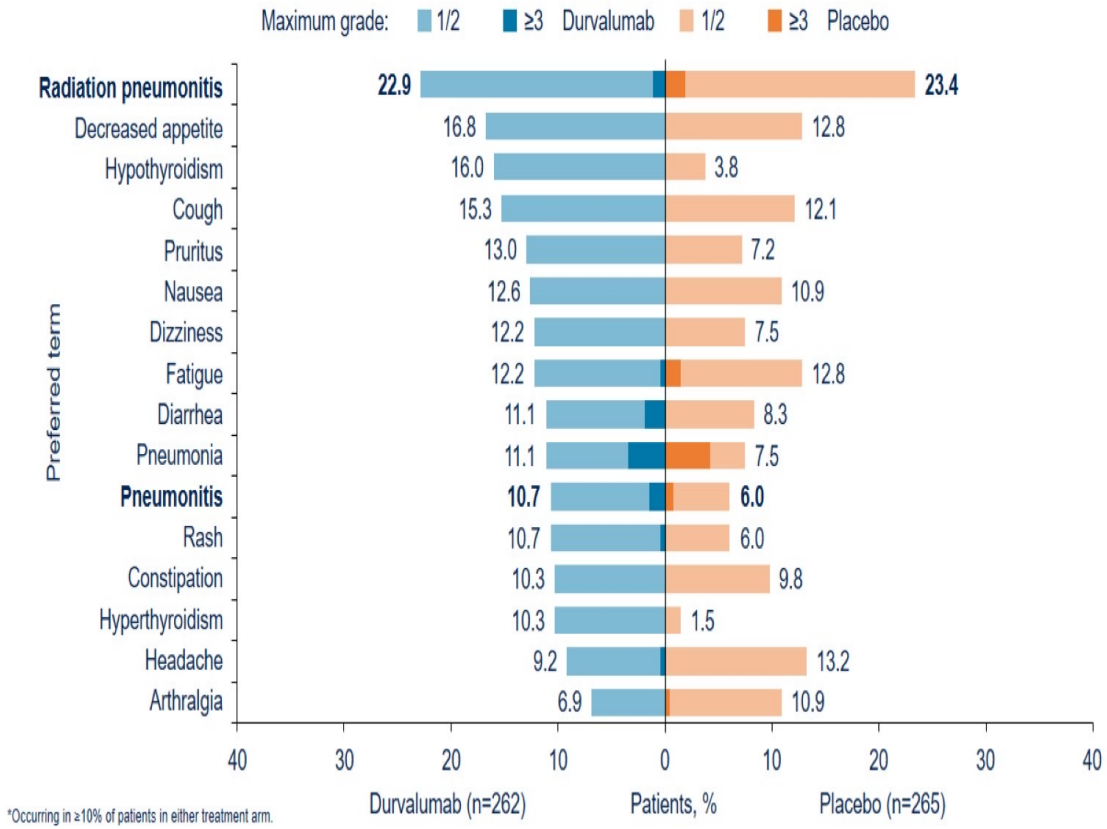
mPFS, median PFS.

Exposure and safety summary

		Durvalumab (n=262)	Placebo (n=265)
Number of durvalumab or placebo doses	Median (range)	9.0 (1–26)	9.0 (1–26)
	Mean (standard deviation)	12.9 (9.6)	11.8 (9.2)
Any-grade all-cause AEs, n (%)		247 (94.3)	234 (88.3)
Maximum grade 3/4 AEs		64 (24.4)	64 (24.2)
Serious AEs		78 (29.8)	64 (24.2)
AEs leading to treatment discontinuation		43 (16.4)	28 (10.6)
AEs leading to death		7 (2.7)	5 (1.9)
Treatment-related* AEs leading to death		2 (0.8)‡	0
Any-grade immune-mediated AEs†		84 (32.1)	27 (10.2)
Maximum grade 3/4 immune-mediated AEs		14 (5.3)	4 (1.5)

Includes AEs with an onset date following first dose of study treatment, or pre-treatment AEs that increased in severity following first dose of study treatment, through to 90 days after last dose or until start of the first subsequent systemic anticancer therapy (whichever occurred first).
*Assessed by investigator. †Defined as an AE of special interest (excluding infusion related/hypersensitivity/anaphylactic reaction) that is consistent with an immune-mediated mechanism that required treatment with systemic corticosteroids, other immunosuppressants, or endocrine therapy. ‡Causes of death were encephalopathy and pneumonitis.

Most frequent AEs*



*Occurring in ≥10% of patients in either treatment arm.

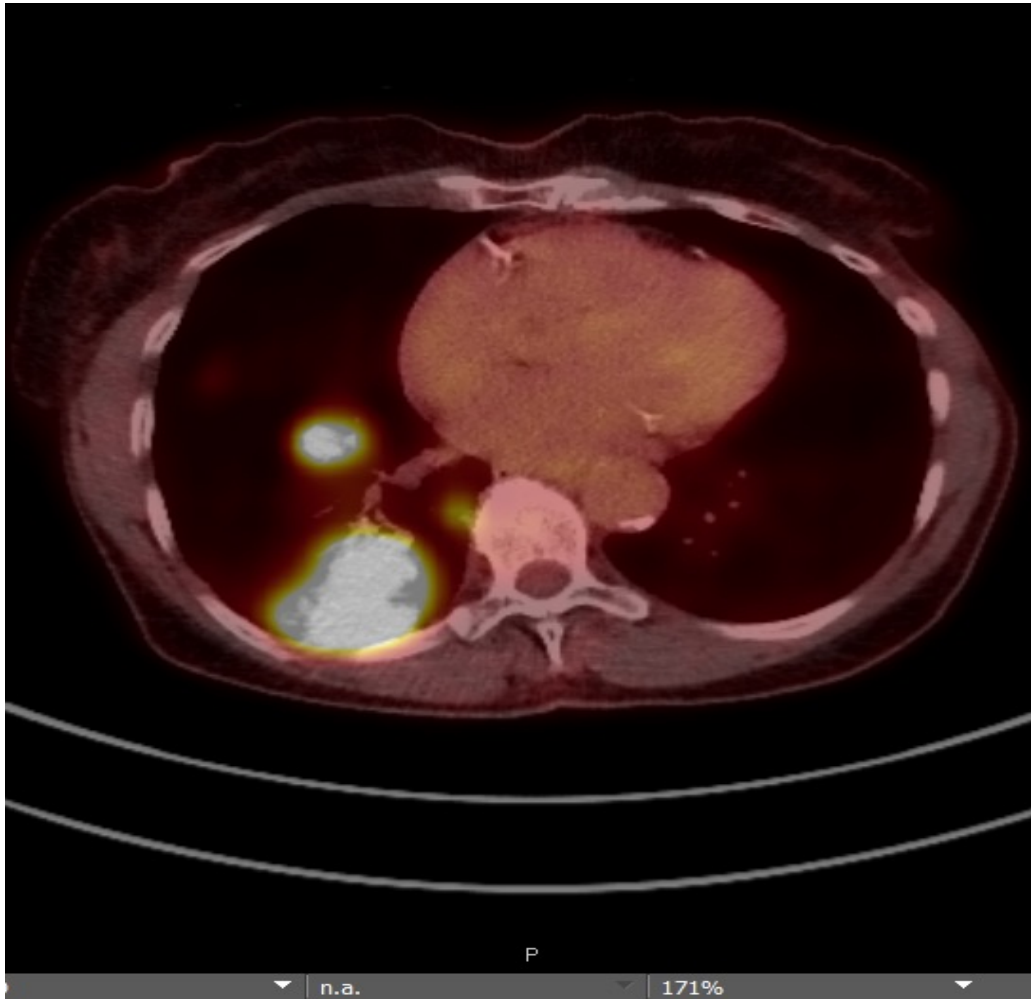
Conclusions

- **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 will become the new standard of care for patients with LS-SCLC who have not progressed after cCRT

Case 1: An “Exceptional Responder”

- 82-year-old African American female (40 py tobacco history) presented in spring 2020 with weight loss over several months, worsening SOB on exertion
- PET scan shows 7.2 cm RLL mass, additional satellite tumor nodules, extensive nodal involvement in right hilar, mediastinal, and 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?

Case 1

All are correct

➔ What regimen do you use?

a. Carbo/etoposide

b. Carbo/etoposide/atezolizumab

c. Carbo/etoposide/durvalumab

d. Cis/etoposide/durvalumab

In the future....

e. Carbo/etoposide/anti-PD1 Ab?

f. Carbo/etoposide/anti-PD(L)1/other agents (e.g. bispecifics, anti-angiogenic Abs?

g. (Carbo)/Antibody-drug conjugate/immunotherapy?

PRIMARY THERAPY FOR EXTENSIVE-STAGE SCLC:

Four cycles of therapy are recommended, but some patients may receive up to 6 cycles based on

Preferred Regimens

- Carboplatin AUC 5 day 1 and etoposide 100 mg/m² days 1, 2, 3 and atezolizumab 1,200 mg day 1 e maintenance atezolizumab 1,200 mg day 1, every 21 days (category 1 for all)[b,5]
- Carboplatin AUC 5 day 1 and etoposide 100 mg/m² days 1, 2, 3 and atezolizumab 1,200 mg day 1 e maintenance atezolizumab 1,680 mg day 1, every 28 days[b]
- Carboplatin AUC 5–6 day 1 and etoposide 80–100 mg/m² days 1, 2, 3 and durvalumab 1,500 mg da maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)[b,6]
- Cisplatin 75–80 mg/m² day 1 and etoposide 80–100 mg/m² days 1, 2, 3 and durvalumab 1,500 mg d maintenance durvalumab 1,500 mg day 1 every 28 days (category 1 for all)[b,6]

Other Recommended Regimens

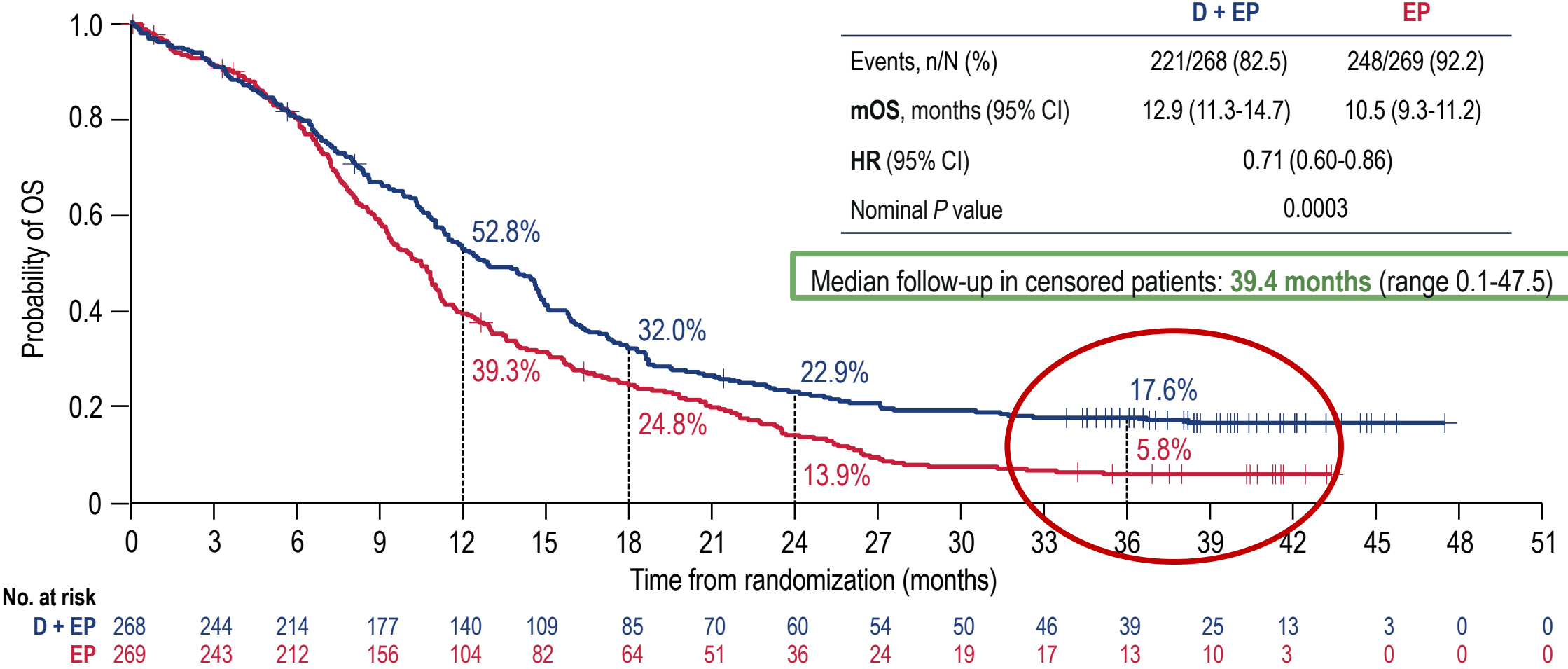
- Carboplatin AUC 5–6 day 1 and etoposide 100 mg/m² days 1, 2, 3[7]
- Cisplatin 75 mg/m² day 1 and etoposide 100 mg/m² days 1, 2, 3[8]
- Cisplatin 80 mg/m² day 1 and etoposide 80 mg/m² days 1, 2, 3[9]
- Cisplatin 25 mg/m² days 1, 2, 3 and etoposide 100 mg/m² days 1, 2, 3[10]

Useful In Certain Circumstances

- Carboplatin AUC 5 day 1 and irinotecan 50 mg/m² days 1, 8, 15[11]
- Cisplatin 60 mg/m² day 1 and irinotecan 60 mg/m² days 1, 8, 15[12]
- Cisplatin 30 mg/m² days 1, 8 and irinotecan 65 mg/m² days 1, 8[13]

carbo = carboplatin; cis = cisplatin; WBRT = whole brain radiotherapy.

CASPIAN 3-Year OS Update: Durvalumab/EP vs EP



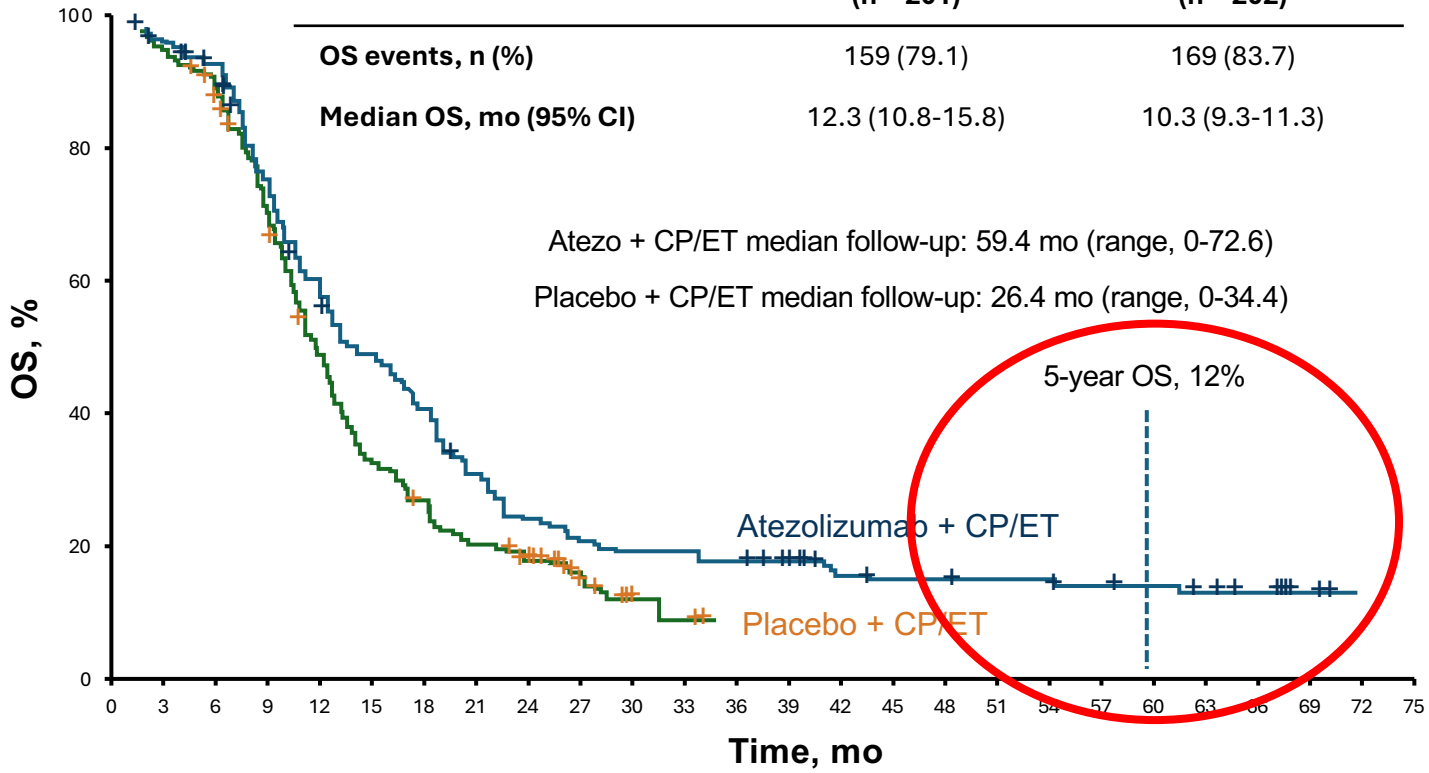
	D + EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3-14.7)	10.5 (9.3-11.2)
HR (95% CI)	0.71 (0.60-0.86)	
Nominal *P* value	0.0003	

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

Data cutoff: March 22, 2021. Paz-Ares LG, et al. *Ann Oncol*. 2021;32(suppl 5):S1283-S1346.

IMpower133 and IMbrella A: Long-Term OS

	Atezo + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
OS events, n (%)	159 (79.1)	169 (83.7)
Median OS, mo (95% CI)	12.3 (10.8-15.8)	10.3 (9.3-11.3)



No. at Risk																								
Atezo + CP/ET	201	182	159	121	93	81	61	48	38	33	30	30	28	26	17	15	15	14	14	12	11	10	8	7	2
Placebo + CP/ET	202	186	160	114	74	55	39	34	25	11	3	2													

OS Rate, y	IMpower133 & IMbrella A: Atezo + CP/ET, % (95% CI) (n = 201)	IMpower133 Only: Placebo + CP/ET, % (95% CI) (n = 202)
1	52 (45-59)	39 (32-46)
2	22 (16-28)	16 (11-21)
3	16 (11-21)	NE[a]
4	13 (8-18)	NE[a]
5	12 (7-17)	NE[a]

Clinical cutoff date: 16 Mar 2023.

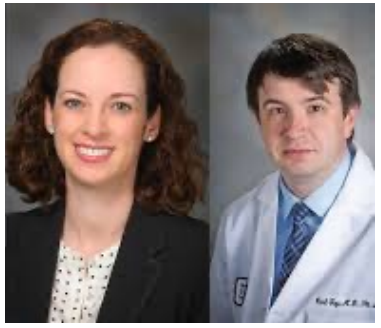
[a] OS rates were NE in the control arm as rollover to IMbrella A was not permitted.

1. Liu S et al. WCLC 2023. Oral presentation.

Using a “Targeted” Approach to Improve Outcomes

- Optimize front line therapy with additional agents
- Seek to understand heterogeneity and determinants of response and resistance
- Add “targeted” agents in the maintenance setting
- Utilize “targeted” agents in the relapsed setting

S2409-PRISM: A Multicohort **PR**ec**I**sion **S**CLC Subtype **M**aintenance Phase II Trial of Immunotherapy Versus Biomarker-Directed Novel Agents in Combination with Immunotherapy in Extensive Stage Small Cell Lung Cancer (ES-SCLC)



Study PI: Anne Chiang, MD PHD

Institute Affiliation: Yale Cancer Center

Study Co-PI: Alberto Chiappori, MD

Institute Affiliation: Moffit Cancer Center

Statistician(s): Mary Redman, PHD, Jieling Miao, MS, Yingqi Zhao, PHD

Translational Medicine PI(s): Carl Gay, MD PHD, Lauren Byers, MD PHD

Cohort Lead(s): Nan Sethakorn, MD PHD, So Yeon Kim, MD

Project Manager: Justine Trevino, Patient Advocate: Judy Johnson

Lung Committee Chair: Jhanelle E. Gray, MD, Sr. Advisor: David Gandara, MD

Targeting SCLC Subtypes: Background

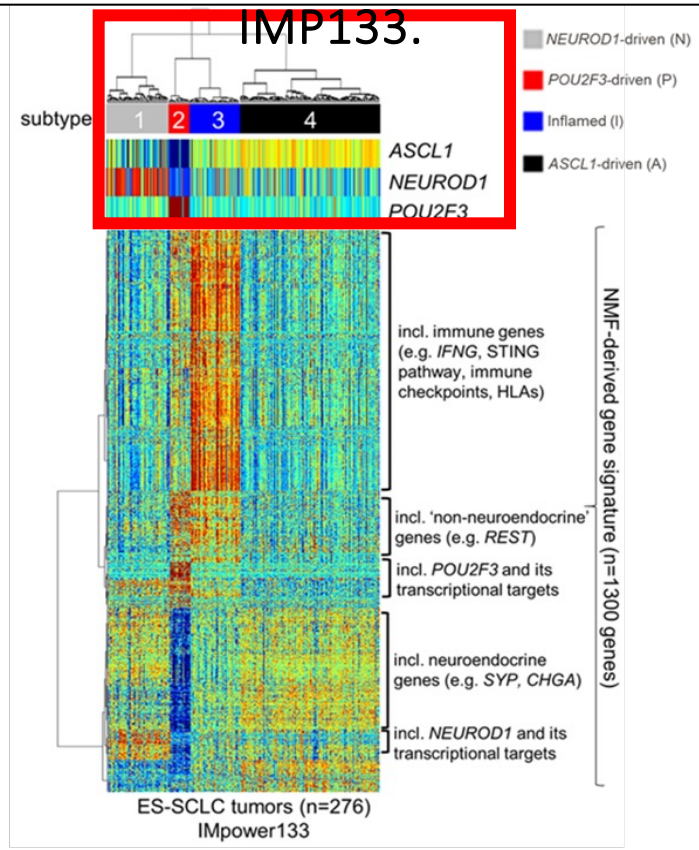
- **Unmet Clinical Need**
  - median OS for ES-SCLC patients is 13 months, despite adding immunotherapy to frontline chemotherapy (IMpower133, CASPIAN trials)
  - Second line treatment lurbinectedin shows ORR 35% and mPFS of 3.5 mo

- **Window for Intervention**
  - Virtually all SCLC patients recur during maintenance immunotherapy within 3 months of completing chemotherapy
  - S1929 is a maintenance trial showing feasibility and benefit of biomarker (SLFN11+) directed, targeted therapy (PARPi) in combination with immunotherapy

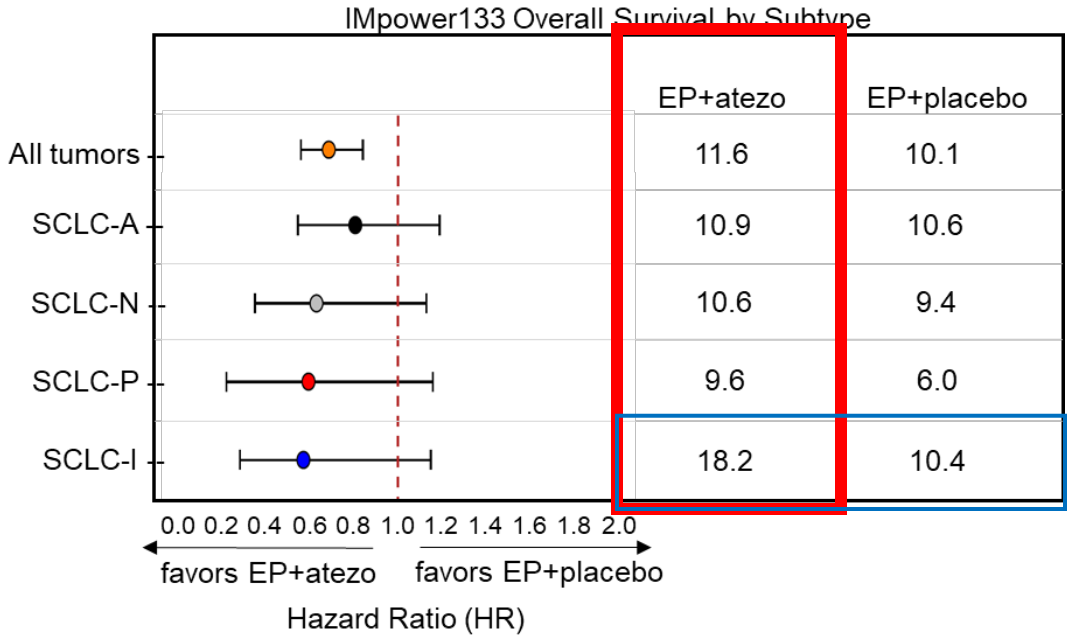
- **Leverage Paradigm Shift**
  - Target selective therapeutic vulnerabilities of discrete molecular subtypes e.g. SCLC-A, SCLC-N, SCLC-P and SCLC-I
  - Gay et al showed SCLC-I group shows greater OS benefit with atezolizumab than other subgroups in IMpower133

SCLC Subtypes Experience Variable Benefit From Frontline Chemoimmunotherapy

Four subtypes defined by expression of transcription factors and inflammatory signature in IMP133.



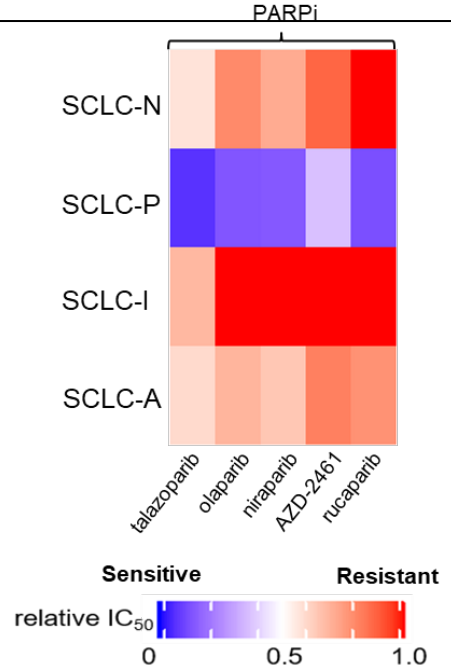
Variable OS in IMP133 EP+atezo arm on subtype-by-subtype basis.



Gay et al., *Cancer Cell*, 2021

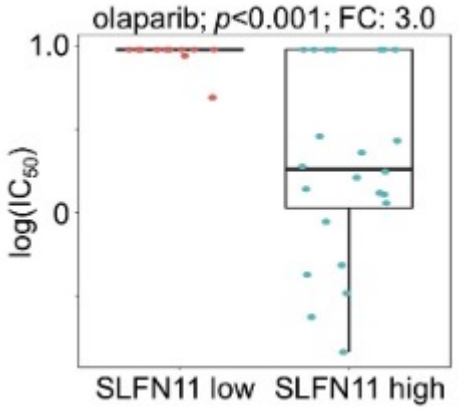
Subtype-specific Vulnerabilities (SCLC-P/A/N)

SCLC-P models are sensitive to PARP inhibitors independent of SLFN11 status.

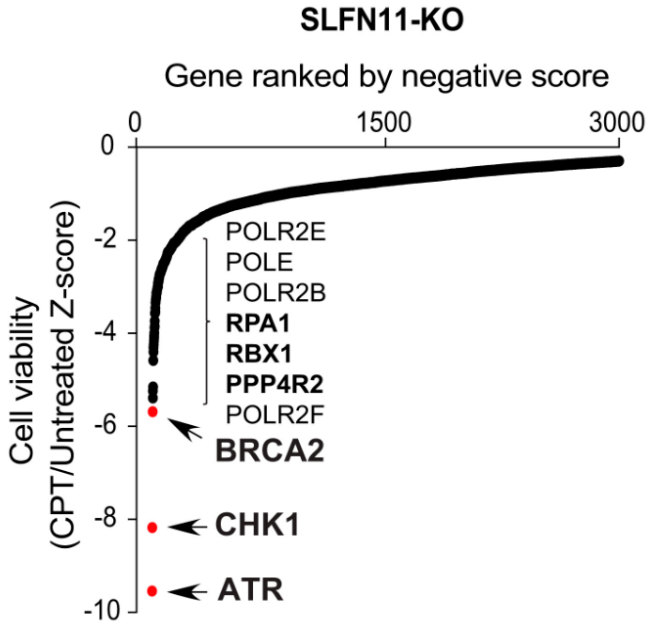


Gay et al., *Cancer Cell,* 2021

SCLC-A/N models are only sensitive to PARP inhibitors if SLFN11- positive.



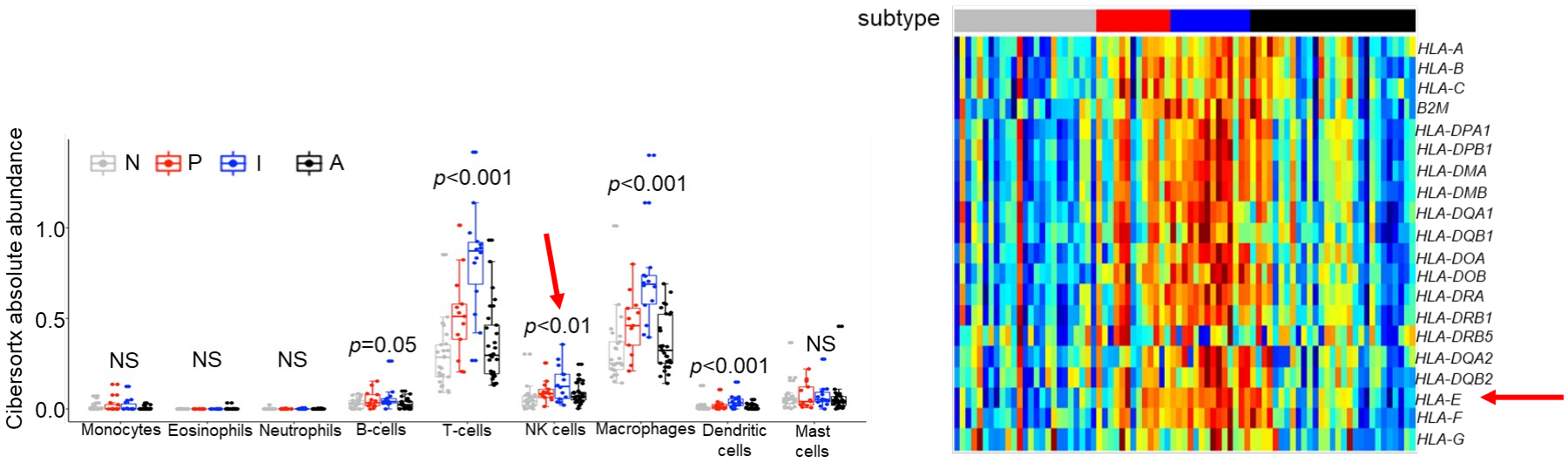
In SLFN11-negative models, loss of ATR is synthetic lethal.



Jo et al., *PNAS,* 2021

Subtype-specific vulnerabilities (SCLC-I)

NK cells and the NKG2A ligand HLA-E are highest in SCLC-I



SCLC tumors (n=81)
George et al.

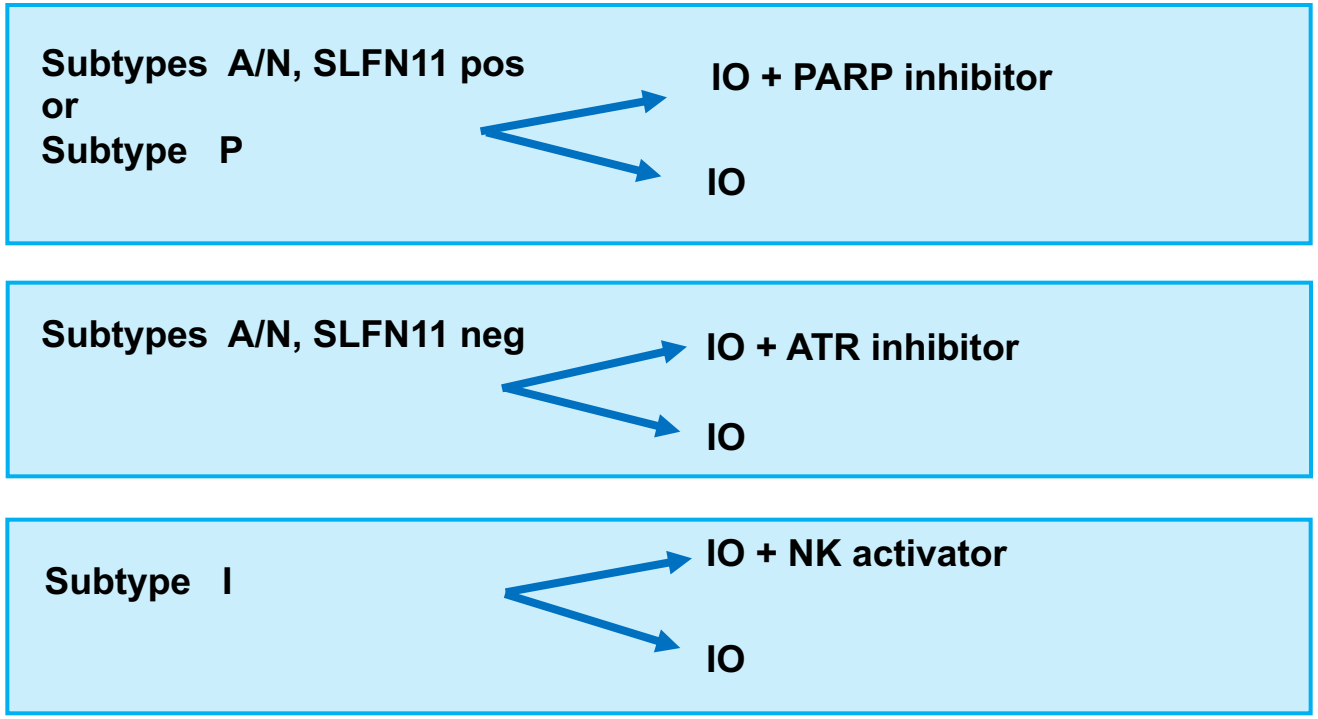
Gay et al., *Cancer Cell,* 2021

S2409-PRISM: A Multicohort **PR**ec**I**sion **S**CLC Subtype **M**aintenance Phase II Trial of Immunotherapy (IO) Versus Biomarker-Directed Novel Agents in Combination with IO in Extensive Stage Small Cell Lung Cancer

Step 1: Screening N=838

- **ES-SCLC Screening**
- **Tissue available for testing**
- **Asymptomatic or Stable Treated Brain Lesions**
- **Allows consent after initial cycle for tissue screening**

Step 2: Randomization N=312



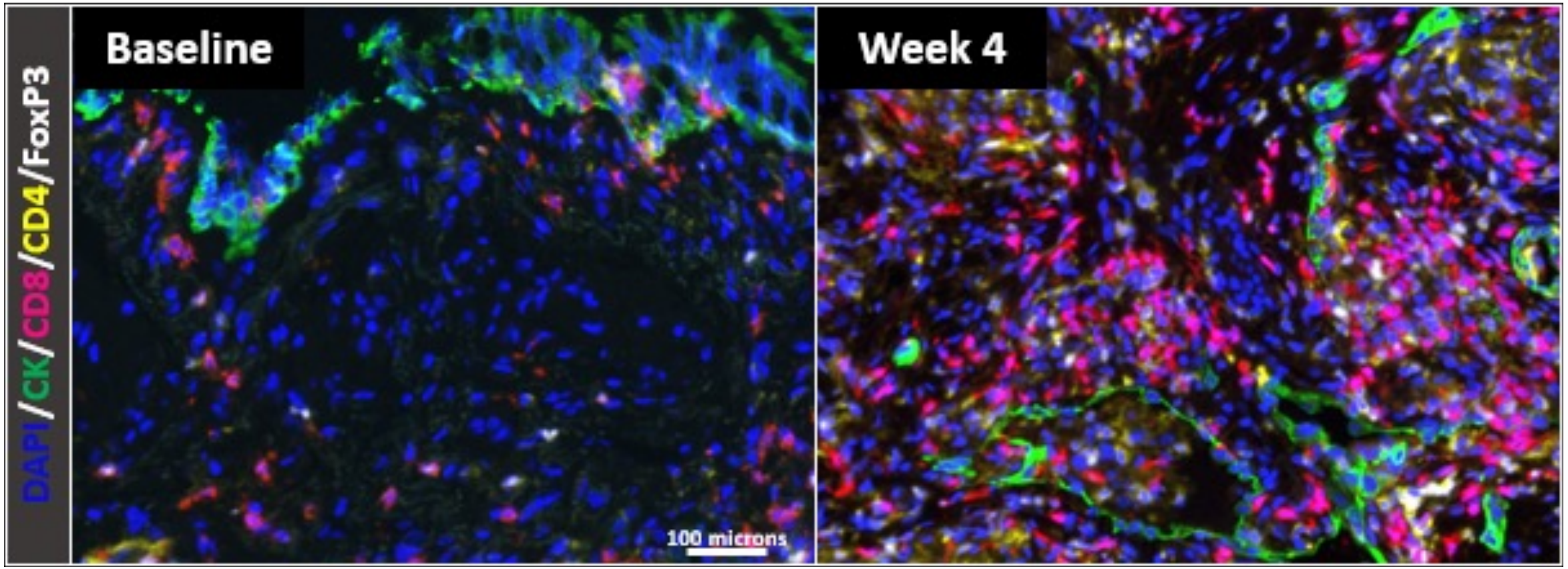
Primary Endpoints: PFS

Secondary Endpoints: OS, Frequency, Severity of Adverse Events

Protocol in Development

• Anne Chiang MD PHD

Targeting the “Immune Desert” in SCLC



A. Chiang, K. Schalper, unpublished data

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.

Tarlatamab Anti-Tumor Activity

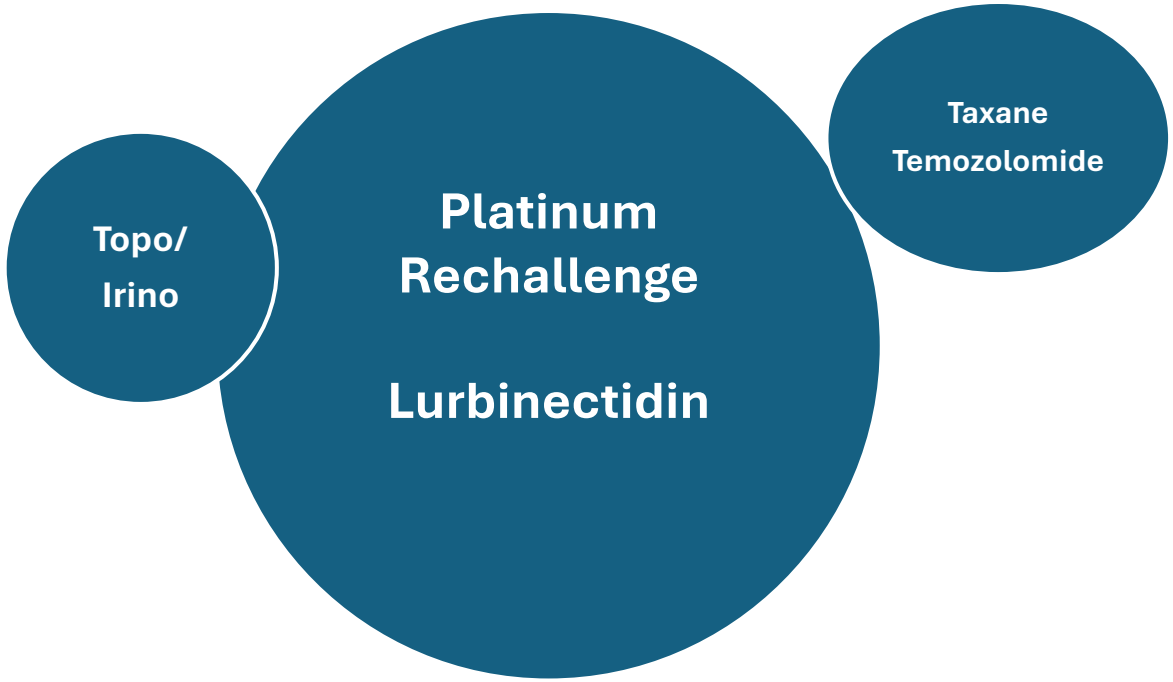
Outcome	Tarlatamab 10 mg (n = 100)	Tarlatamab 100 mg (n = 88)
Objective response rate, n (%) (97.5% CI)	40 (40.0) (29.1, 51.7)	28 (31.8) (21.1, 44.1)
Complete response	1 (1)	7 (8)
Partial respons		21 (24)
Stable disease		27 (31)
Progressive di		13 (15)
Not evaluable	10 (10)	20 (23)
Observed duratio	23/40 (58)	17/28 (61)
Disease control (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

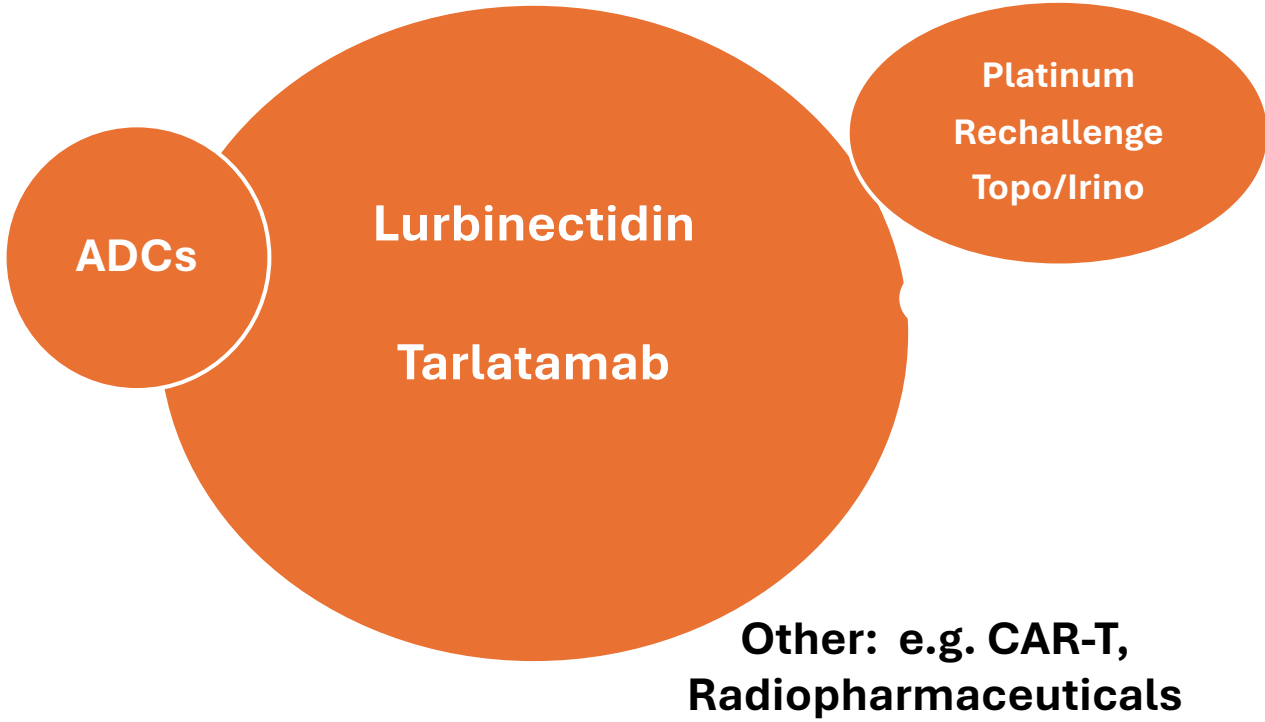
Tarlatamab 10 mg demonstrated anti-tumor activity in heavily pre-treated SCLC with an objective response rate of 40%

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.

A Changing Landscape for Relapsed SCLC



2023: pre Tarlatamab approval



2024: post Tarlatamab approval

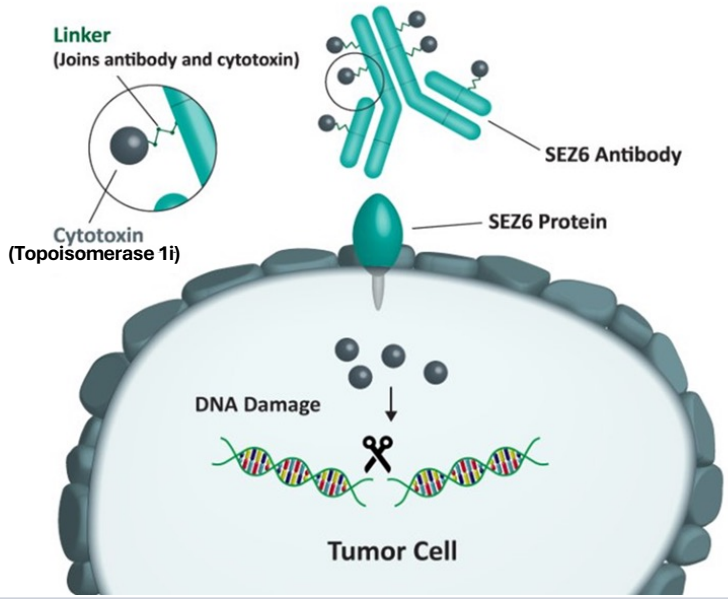
ADCs in SCLC: Summary

Target	Payload/MOA	Agent	Drug Ab ratio (DAR)	SCLC activity RR, DOR	Source
DLL3	Pyrrolobenzodiazepine (PBD)	Rovalpituzumab Tesirine; Rova-T	~2	--	
TROP2	SN-38; topo I inhibitor Deruxtecan; topo I inhibitor	Sacituzumab-govitecan; IMMU-132 Datopotamab deruxtecan; DS-1062a	~7-8 ~4	N=50, ORR 14%; DOR 5.7 mo	NCT01631552 Gray, et al. CCR 2017 NCT03401385
B7-H3 (CD276)	Deruxtecan; topo I inhibitor	Ifinatamab deruxtecan; DS-7300, I-DXd	~4	N=19, 58% ORR; DOR 5.5 mo	NCT04145622
SEZ6	Calicheamycin; induces DS breaks Proprietary	ABBV-011 ABBV-706	~2	N=99, ORR 25%, DOR 4.2 mo	NCT03639194 NCT05599984
CEACAM5	Maytansinoid DM4; MT inhibitor	Tusamitamab ravtansine (SAR408701)	~3.8	--	NCT02187848
B7-H3	Clezutoclax;BCL2/XL inhibitor	Mirzotamab clezutoclax; ABBV-155		--	NCT03595059

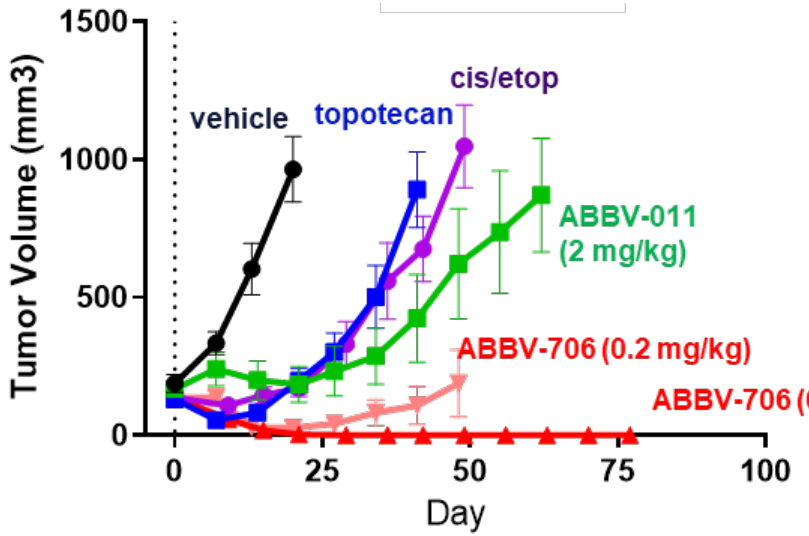
ABBV-706: SEZ6-targeting ADC

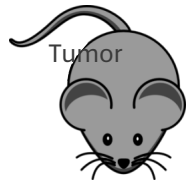
- SEZ6-targeting antibody, conjugated to a topoisomerase 1 inhibitor (Top1i) payload with sub-nM cytotoxic activity
- Drug-to-antibody ratio of 6 with stable attachment via a valine-alanine cathepsin cleavable linker
- Tumor-targeted delivery of Top1i[1] with potential for bystander killing of neighboring cancer cells
- Superior antitumor activity vs chemotherapy and ABBV-011, in a SEZ6-expressing SCLC murine model

ABBV-706 Mechanism of Action



ABBV-706 Preclinical Activity – SCLC (SEZ6+) PDX





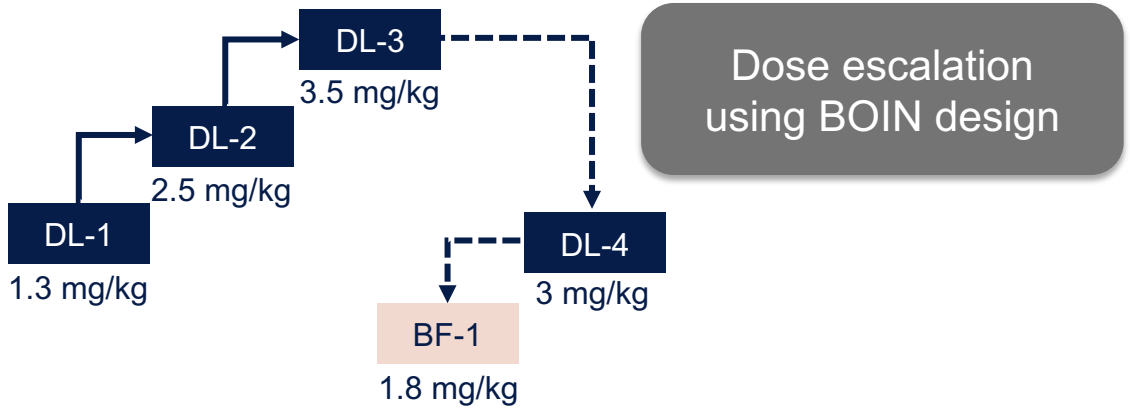
LU124 PDX
(80% tumor cells with 1+ staining intensity by IHC)

ADC, antibody-drug conjugate; cis, cisplatin; etop, etoposide; IHC, immunohistochemistry; nM, nanomolar; PDX, patient-derived xenograft; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6.

1. Han S, et al. *Pharmaceutics*. 2022;14:1707.

Phase 1 dose-escalation and -expansion study: Enrollment in ABBV-706 dose-escalation part is complete (N=53)

Part 1: ABBV-706 Monotherapy Dose Escalation



Backfill doses of 1.8, 2.5, and 3.0 mg/kg were selected to support the selection of doses for dose optimization (N=15 per dose cohort)

ABBV-706 Monotherapy Treatment
IV Q3W in 21-day cycles until disease progression or unacceptable toxicity

Eligible Patients Had R/R Solid Tumors With Potential SEZ6 Expression

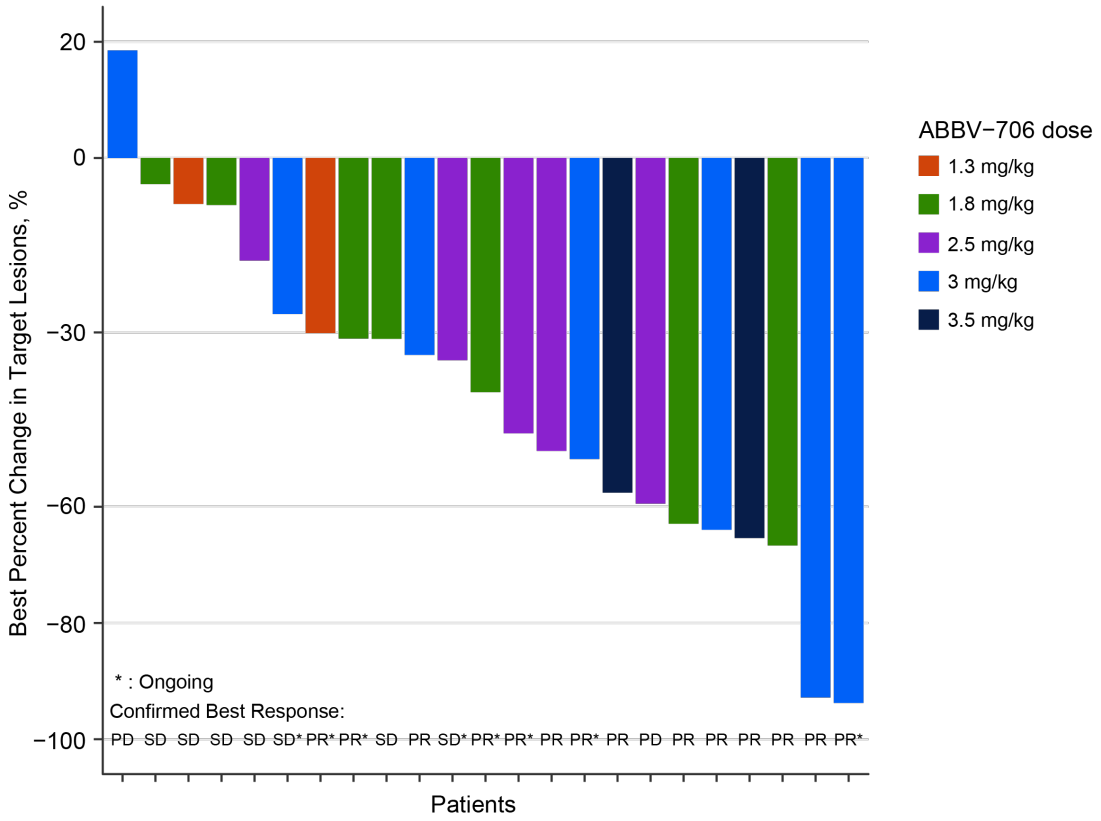
- SCLC
- GBM; anaplastic oligodendroglioma; anaplastic astrocytoma
- NEPC, GEP-NECs, LCNECs, SCLC transformed from m*EGFR* NSCLC, MTC; other NECs or grade 3 NETs

- SEZ6 expression is analyzed retrospectively

BF, backfill; BOIN, Bayesian optimal interval design; DL, dose level; GBM, glioblastoma; GEP, gastroenteropancreatic; IV, intravenous; LCNECs, large cell neuroendocrine carcinomas; m*EGFR*, epidermal growth factor receptor mutant; MTC, medullary thyroid cancer; NECs, neuroendocrine carcinomas; NEPC, neuroendocrine prostate cancer; NETs, neuroendocrine tumors; NSCLC, non-small cell lung cancer; Q3W, once every 3 weeks; R/R, relapsed/refractory; SCLC, small cell lung cancer; SEZ6, seizure-related homolog protein 6.

ABBV-706 is highly efficacious across doses in R/R SCLC (N=23)

Change in Target Lesion Size by Dose



Ongoing	3.0 mg/kg	2.5 mg/kg	1.8 mg/kg	1.3 mg/kg
n=8	3	2	2	1

Outcome	SCLC (N=23)
ORR,[a] n (%) [90% exact CI]	**14 (60.9)** [41.7, 77.8]
Best response,[b] n (%)	
CR	0
PR	14 (60.9)
SD	7 (30.4)
PD	2 (8.7)
CBR,[c] n (%) [90% exact CI]	21 (91.3) [75.1, 98.4]

- 21/23 patients with SCLC were 3L+ at study enrollment
- 11/18 patients with available 1L CTFI data were platinum resistant

[a]Requires a CR or PR confirmed in an assessment ≥4 weeks later; [b]Response according to RECIST v1.1; [c]Requires CR or PR confirmed in an assessment ≥4 weeks later or SD lasting ≥5 weeks.
1L, first-line; 3L+, third-line or later; CBR, clinical benefit rate; CI, confidence interval; CR, complete response; CTFI, chemotherapy-free interval; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; R/R, relapsed/refractory; SCLC, small cell lung cancer; SD, stable disease.

Big Decisions on Small Cell Lung Cancer: A Focus on Clinical Care Updates and Patient Perspectives

Xiao Wang, Anne C. Chiang, ASCO Education Book 2024

"'How long am I going to live?' is an important question. Some people don't want to know, but I would like to have a conversation about that. What should my expectations be? How long before recurrence? What would be my next treatment if this recurred…? *Curative was never a word that was used – they said that they could get rid of the cancer, and I thought that meant it would never come back, but I learned that is definitely not t*

Talk about expectations and prognosis

"I asked to sign a DNR right after my hospitalization for esophagitis. It had not been brought up with me or discussed until I requested it. I think it's very difficult to determine the right time to discuss this – I have ***people in my support group who say, 'Don't even ask about prognosis,' because it's just the average. I don't agree with that. You have SCLC – that's a huge thing introduced in your life, the probability of dying just went way up. You have the opportunity to do what's necessary to prepare yourself and your loved ones.***

SCLC: Key Takeaways

- Immunotherapy is here to stay for ES and LS-SCLC (ADRIATIC)
- SCLC is a heterogeneous disease; understanding the biology may lead to more effective and targeted treatments
  - Obtaining adequate biopsies will be paramount
  - Utilize clinical trials to offer best quality of care
- Stay tuned for the Biomarker-targeted Maintenance Trial S2409 PRISM
- Tarlatamab is an exciting new option to target the SCLC “immune desert”
- ADCs are promising agents to target SCLC as well
- Talk to your patients about prognosis and planning for the future