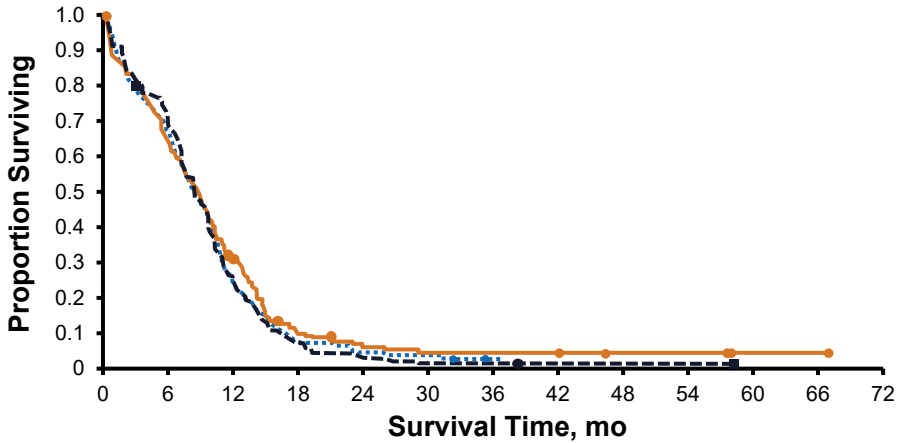
Agenda

1. **Welcome and Introduction**
2. **MasterClass and Practicum Sessions**
    - Implications of the Immuno-Oncology Revolution and the Potential to Improve Outcomes in Patients With SCLC With Cancer Immunotherapies: What Managed Care Professionals Need to Know
    - Integrating Immuno-Oncology Into the Plan for Patients With SCLC in Managed Care Settings: Challenges, Practicalities, and Implications
3. **Audience Q&A**
4. **Summary, Reflections, and Take-Home Points**

SCLC, small cell lung cancer.

Managing SCLC[1]

- Historic standard for ES-SCLC was chemotherapy
  - Cisplatin + etoposide introduced in the 1970s
  - Relatively well-tolerated chemotherapy
- SCLC initially highly responsive to therapy
  - Cisplatin + etoposide RR 61%
    - 10% complete response
- Responses transient
  - PFS 4.0 months
- OS 8.6 months



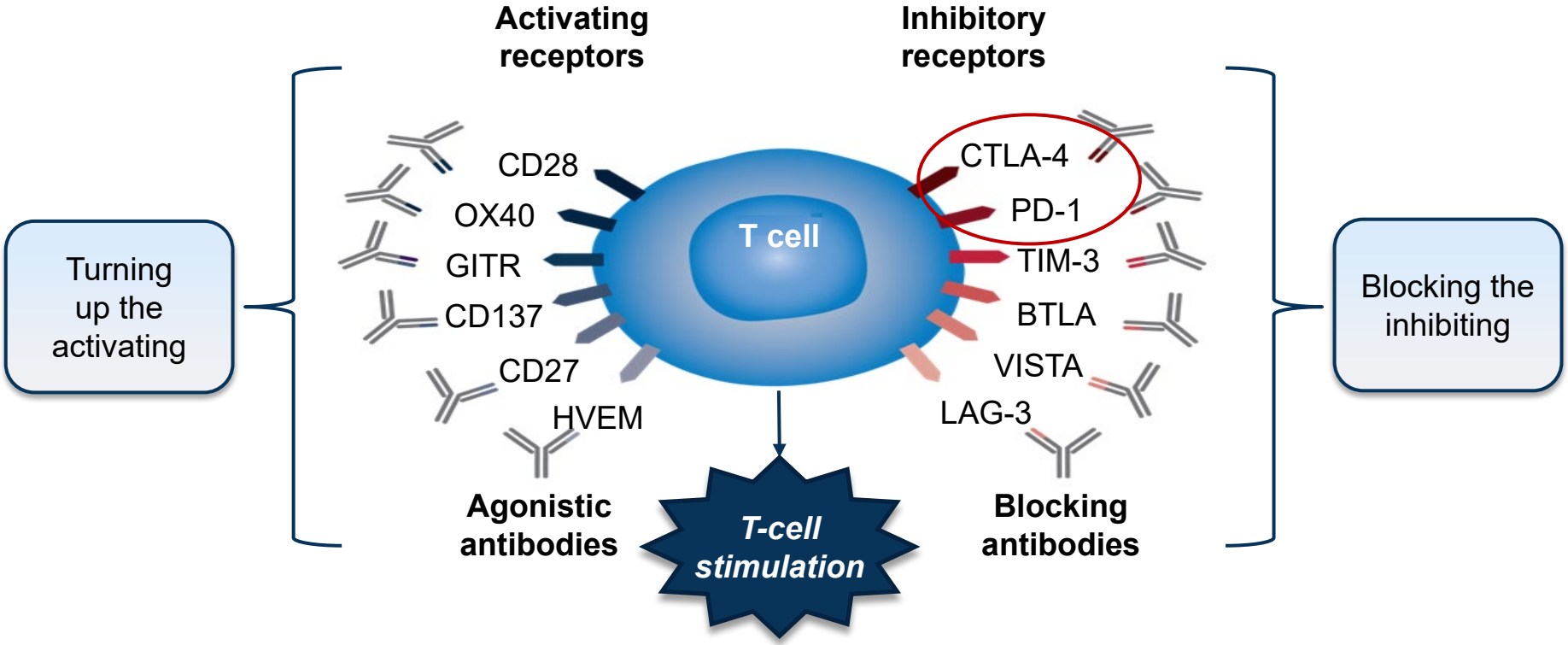
ES-SCLC, extensive-stage small cell lung cancer; OS, overall survival; PFS, progression-free survival; RR, response rate.

1. Roth JB et al. *J Clin Oncol*. 1992;10:282-291.

Managing SCLC (Cont'd)

- Dozens of failed randomized trials
  - Despite impressive initial responses, countless novel strategies failed to extend patient survival
  - Numerous challenges to drug development in SCLC
    - Smoking-related cancer = patient comorbidities
    - Rapid clinical course not tolerant of treatment delays (trial screening)
    - Standard chemotherapy easy to administer (fewer referrals)
    - Limited understanding of the biology, scant tumor specimens
    - Inadequate preclinical models

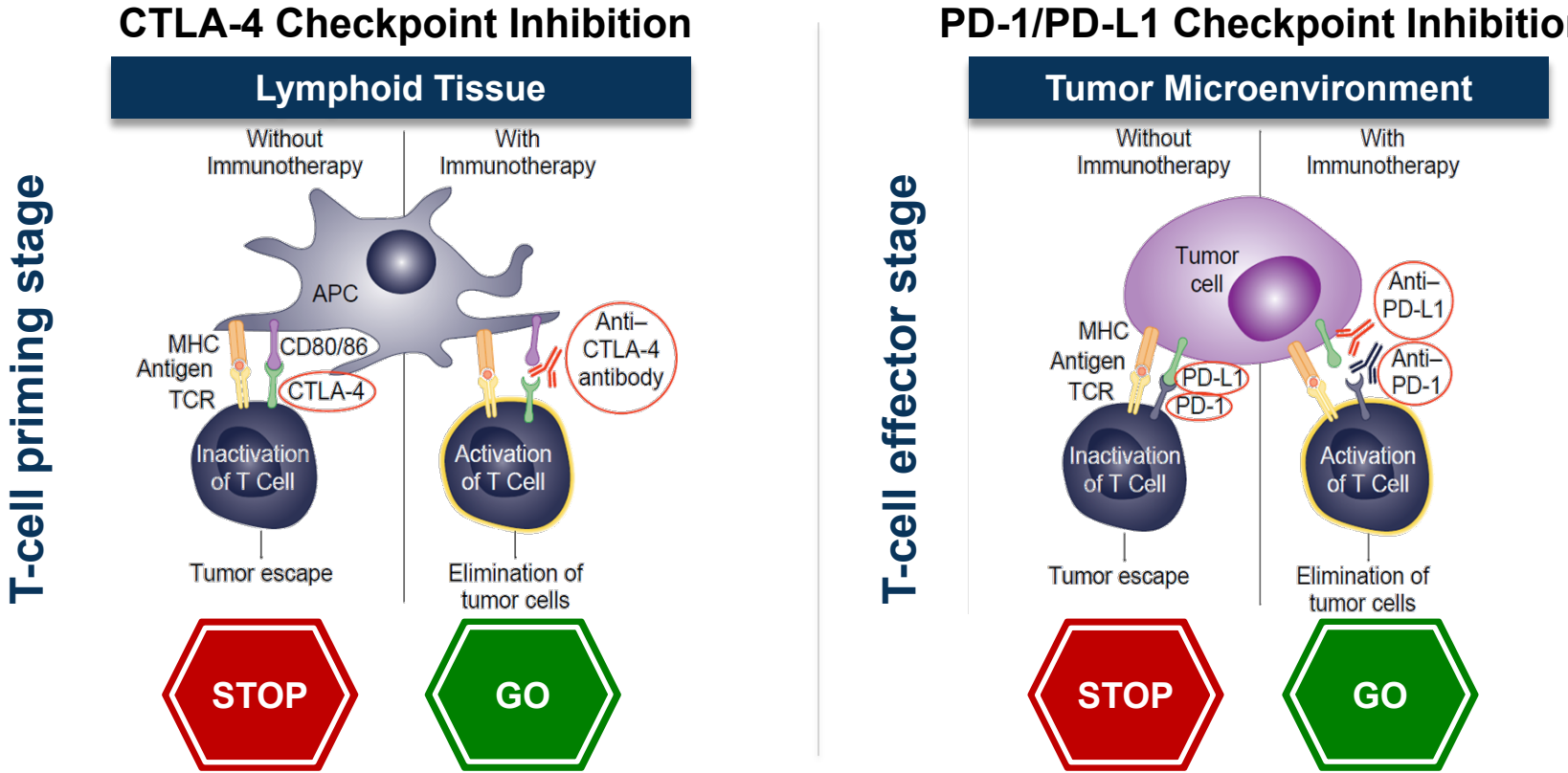
Ways to Enhance T-Cell Attack[1]



BTLA, B-lymphocyte and T-lymphocyte attenuator; CTLA-4, cytotoxic T-lymphocyte–associated protein 4; GITR, glucocorticoid-induced TNFR-related protein; HVEM, herpes virus entry mediator; LAG-3, lymphocyte activation gene-3; PD-1, programmed cell death protein 1; TIM-3, T-cell immunoglobulin and mucin-containing protein 3; VISTA, V-domain immunoglobulin-containing suppressor of T-cell activation.

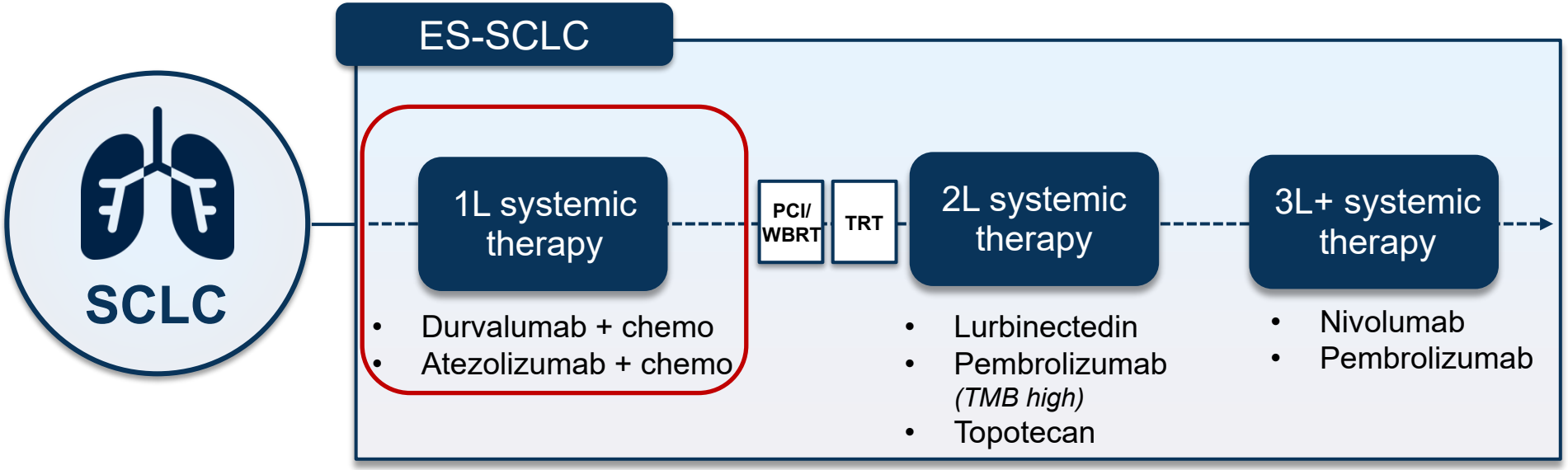
1. Mellman I et al. *Nature*. 2011;480:480-489.

Immune Checkpoint Inhibitors Block T-Cell Inhibitory Signals



MHC, major histocompatibility complex; PD-L1, programmed cell death ligand 1; TCR, T-cell receptor.

Current Treatment Landscape in ES-SCLC



1L, first line; 2L, second line; 3L, third line; chemo, chemotherapy; PCI, prophylactic cranial irradiation; TMB, tumor mutational burden; TRT, thoracic radiotherapy; WBRT, whole brain radiotherapy.

CheckMate -032: Nivolumab ± Ipilimumab Efficacy and Safety Summary[1]

- N = 216 patients (nonrandomized)
  - Previously treated SCLC, primary endpoint: ORR

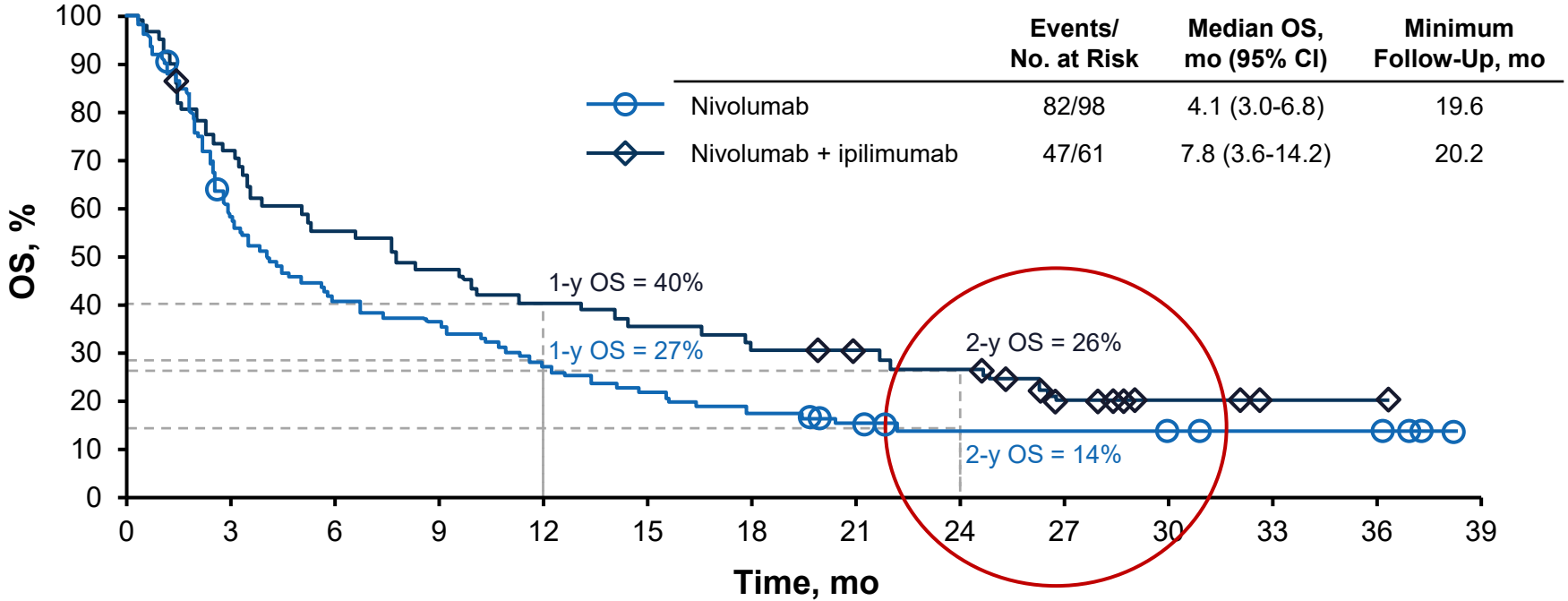
Endpoint	Nivolumab 3 mg/kg (n = 98)	Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg (n = 61)	Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n = 54)
Response rate, %	10	23	19
Median PFS, mo	1.4	2.6	1.4
1-year OS rate, %	33	43	35
Median OS, mo	4.4	7.7	6.0
Grade ≥3 AEs, %	13	30	19

AE, adverse event; ORR, objective reponse rate.

1. Antonia SJ et al. *Lancet Oncol*. 2016;17:883-895.

CheckMate -032: Nivolumab ± Ipilimumab OS[1]

- CheckMate -032, nonrandomized cohort



OS, overall survival.

1. Hellmann MD et al. 2017 American Society of Clinical Oncology Annual Meeting (ASCO 2017). Abstract 8503.

Salvage Immunotherapy Approvals

3L Nivolumab[1]

- RR 11.9%, DOR 17.9 mo
- 18-mo survival rate 20%
- Accelerated approval as 3L therapy: August 16, 2018

3L Pembrolizumab[2]

- RR 19%, median DOR not reached
- Accelerated approval as 3L therapy: June 18, 2019

DOR, duration of response; RR, response rate.

1. Ready N et al. *J Thorac Oncol*. 2019;14:237-244. 2. Chung HC et al. *J Thorac Oncol*. 2020;15:618-627.

Late-Line Immunotherapy Options for ES-SCLC[1-3]

Nivolumab approved for 3L therapy based on data from CheckMate -032 subgroup

- ORR 12% (95% CI, 6.5-19.5)
- Responses durable for ≥6 months in 77%, ≥12 months in 62%, and ≥18 months in 39% of responding patients

Pembrolizumab approved for 3L therapy based on KEYNOTE-158 cohort G and KEYNOTE-028 cohort C1

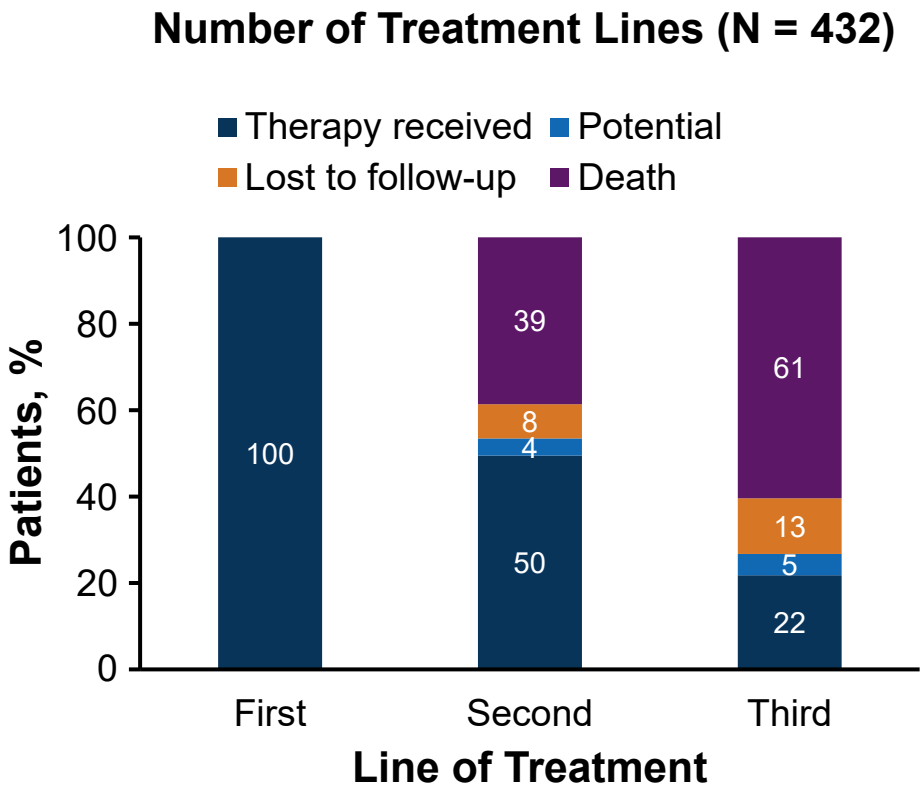
- ORR was 19% (95% CI, 11-29); CR rate was 2%
- Responses were durable for ≥6 months in 94%, ≥12 months in 63%, and ≥18 months in 56% of responding patients

3L, third line; CI, confidence interval; CR, complete response; ORR, overall response rate.

1. Antonia SJ et al. *Lancet Oncol*. 2016;17:883-895. 2. Chung HC et al. *J Clin Oncol*. 2018;36(suppl 15):8506. 3. Ott PA et al. *J Clin Oncol*. 2017;35:3823-3829.

Nivolumab and Pembrolizumab in ES-SCLC[1]

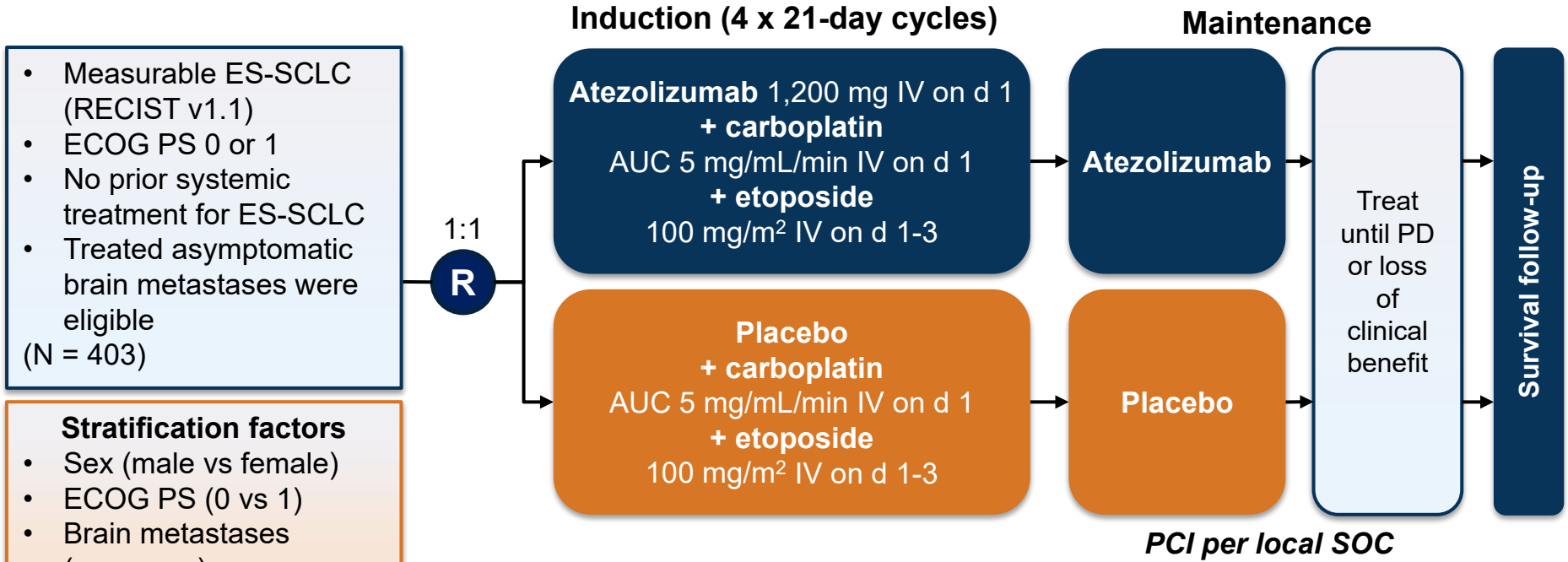
- Important FDA approvals in 3L setting
  - High attrition rate in SCLC, few patients receive 3L therapy
- Prospective data collection
- 432 patients with ES-SCLC
  - 93% received 1L therapy
  - 50% received 2L therapy
  - 22% received 3L therapy
- Potentially transformative drugs
  - How do we increase potential impact?



1L, first line; 2L, second line; 3L, third line; ES-SCLC, extensive-stage small cell lung cancer, FDA: Food and Drug Administration; SCLC, small cell lung cancer.

1. Steffens C-C et al. *Lung Cancer.* 2019;130:216-225.

IMpower133 Study Design: Atezolizumab + Chemo in ES-SCLC[1]



- **Coprimary endpoints:** OS, investigator-assessed PFS
- **Key secondary endpoints:** ORR, DOR, safety

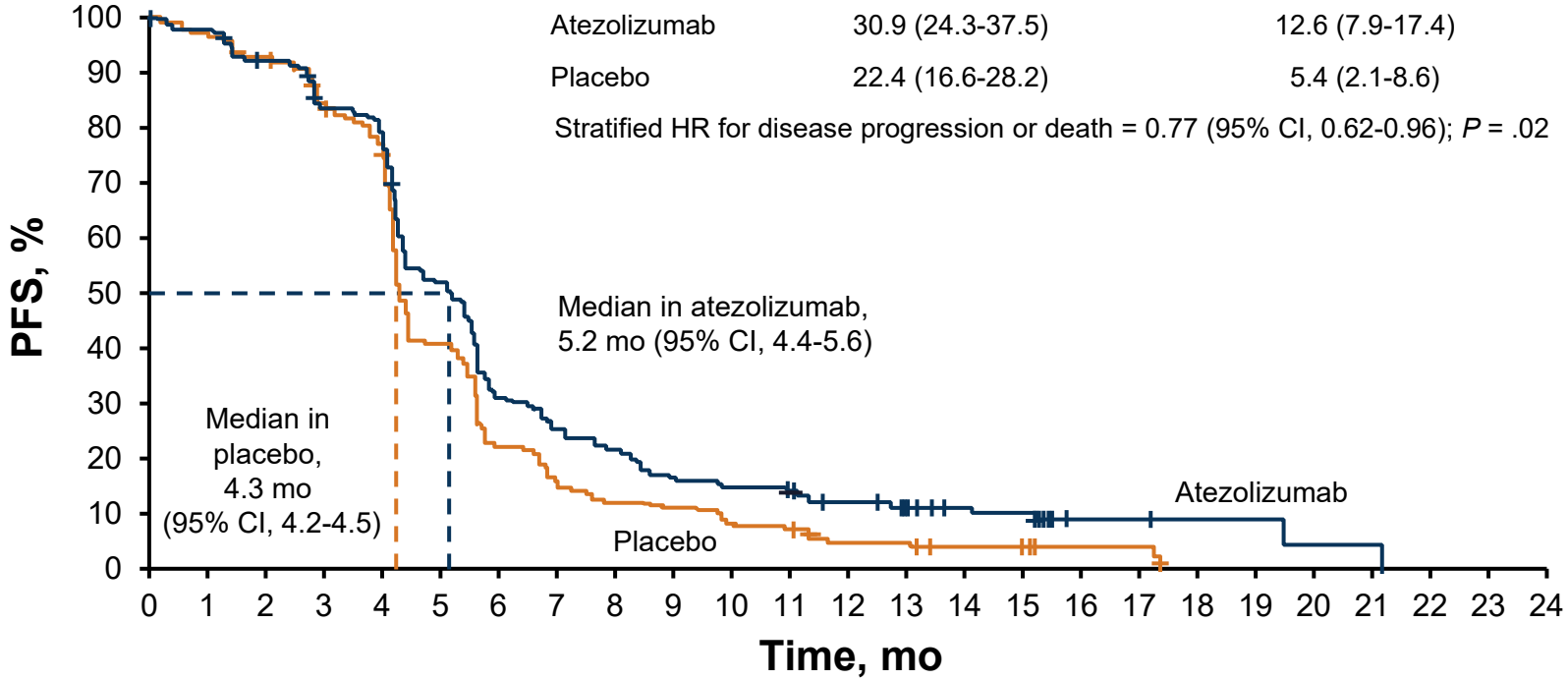
AUC, area under the curve; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; ORR, overall response rate; OS, overall survival; PCI, prophylactic cranial irradiation; PD, progressive disease; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SOC, standard of care.

1. Horn L et al. *N Engl J Med*. 2018;379:2220-2229.

IMpower133: Atezolizumab + Chemo PFS[1]

	6-mo PFS (95% CI), %	12-mo PFS (95% CI), %
Atezolizumab	30.9 (24.3-37.5)	12.6 (7.9-17.4)
Placebo	22.4 (16.6-28.2)	5.4 (2.1-8.6)

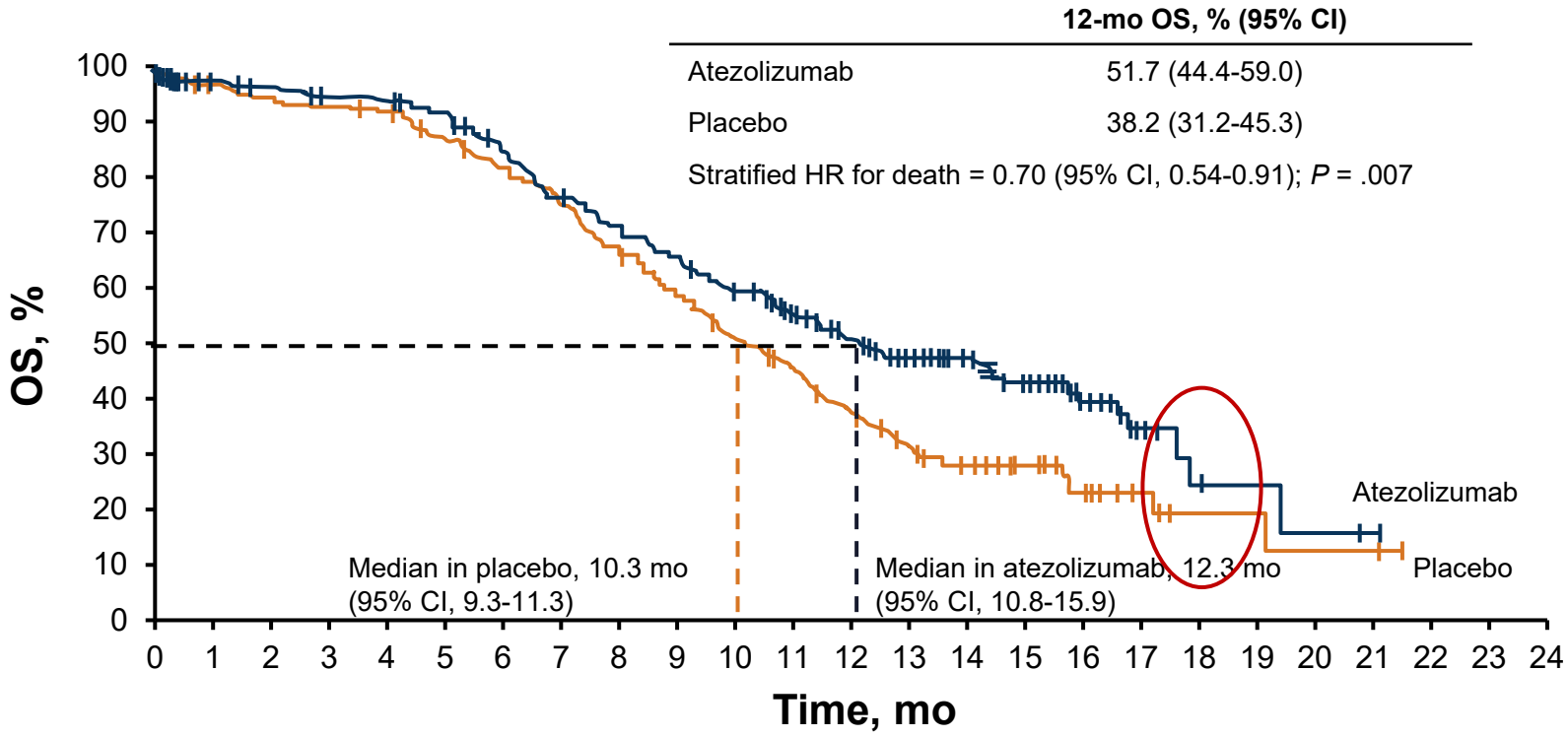
Stratified HR for disease progression or death = 0.77 (95% CI, 0.62-0.96); *P* = .02



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

1. Horn L et al. *N Engl J Med*. 2018;379:2220-2229.

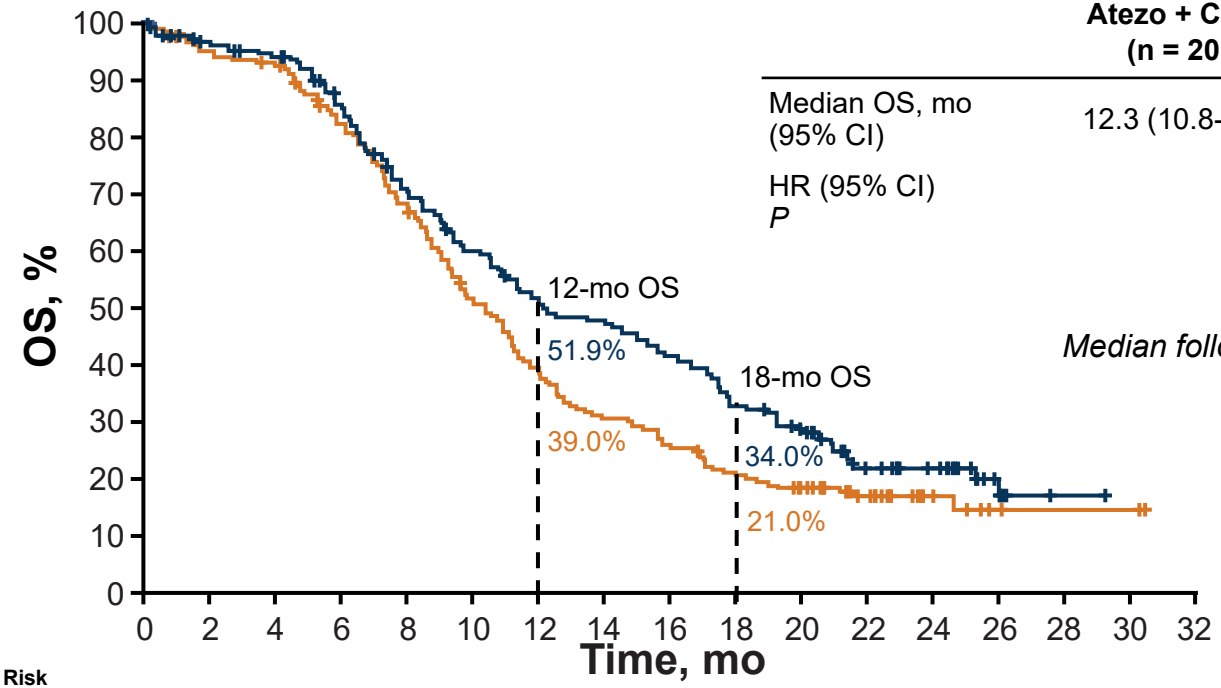
IMpower133: Atezolizumab + Chemo OS[1]



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

1. Horn L et al. *N Engl J Med*. 2018;379:2220-2229.

IMpower133: Atezolizumab + Chemo Updated OS[1]



	Atezo + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8-15.8)	10.3 (9.3-11.3)
HR (95% CI)	0.76 (0.60-0.95)	
P	.0154[a]	

Median follow-up, 22.9 months

No. at Risk

Atezo + 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

Atezo, atezolizumab; CI, confidence interval; CP, carboplatin; ET, etoposide; HR, hazard ratio; OS, overall survival.

[a] *P* value is provided for descriptive purpose. CCOD 24 January 2019.

1. Reck M et al. European Society for Medical Oncology Congress 2019 (ESMO 2019). Abstract 2374.

IMpower133: Safety Results[1]

Patients, n (%)	Atezolizumab (n = 198)	Placebo (n = 196)
Patients with ≥1 AE	198 (100)	189 (96.4)
Grade 3-4 AEs	133 (67.2)	125 (63.8)
Treatment-related AEs	188 (94.9)	181 (92.3)
Serious AEs	74 (37.4)	68 (34.7)
Immune-related AEs	79 (39.9)	48 (24.5)
AEs leading to withdrawal from any treatment	22 (11.1)	6 (3.1)
From atezolizumab/placebo	21 (10.6)	5 (2.6)
From carboplatin	5 (2.5)	1 (0.5)
From etoposide	8 (4.0)	2 (1.0)
Treatment-related deaths	3 (1.5)	3 (1.5)

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

AE, adverse event.

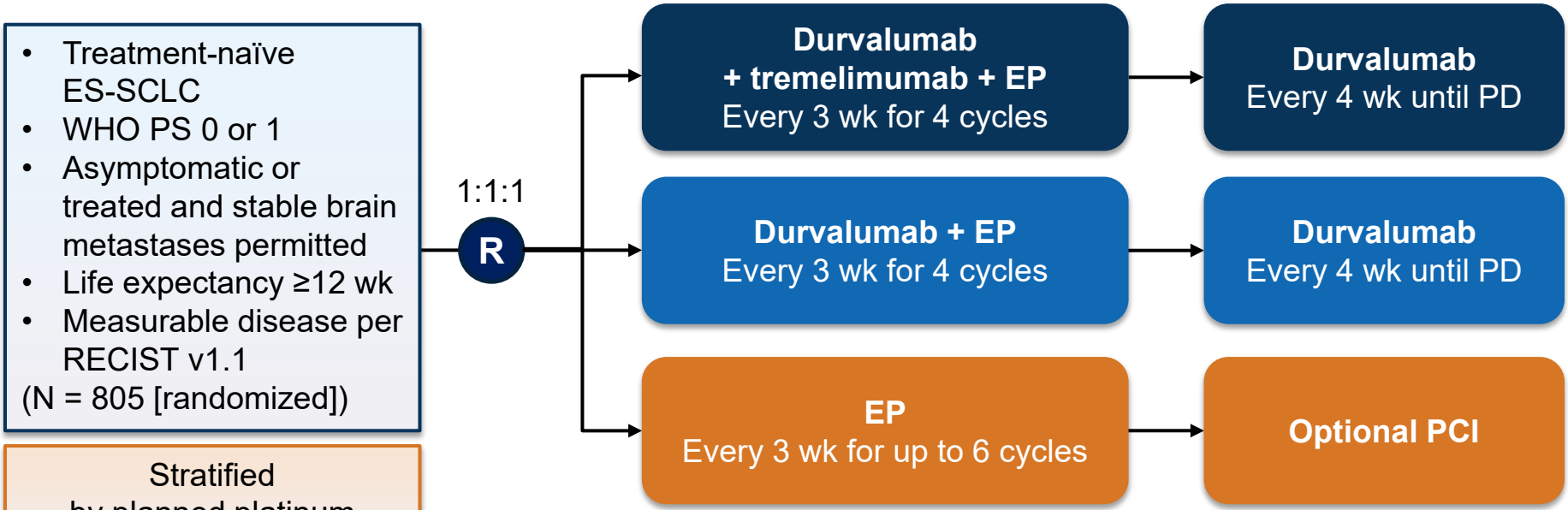
1. Liu S et al. International Association for the Study of Lung Cancer 18th World Conference on Lung Cancer (WCLC 2018). Abstract PL02.07.

Atezolizumab + Carboplatin/Etoposide

- FDA approved March 18, 2019
- EMA approved September 6, 2019
- NCCN category 1, preferred option

EMA, European Medicines Agency; FDA, Food and Drug Administration; NCCN, National Comprehensive Cancer Network.

CASPIAN Study Design: Durvalumab ± Tremelimumab ± EP in ES-SCLC[1]

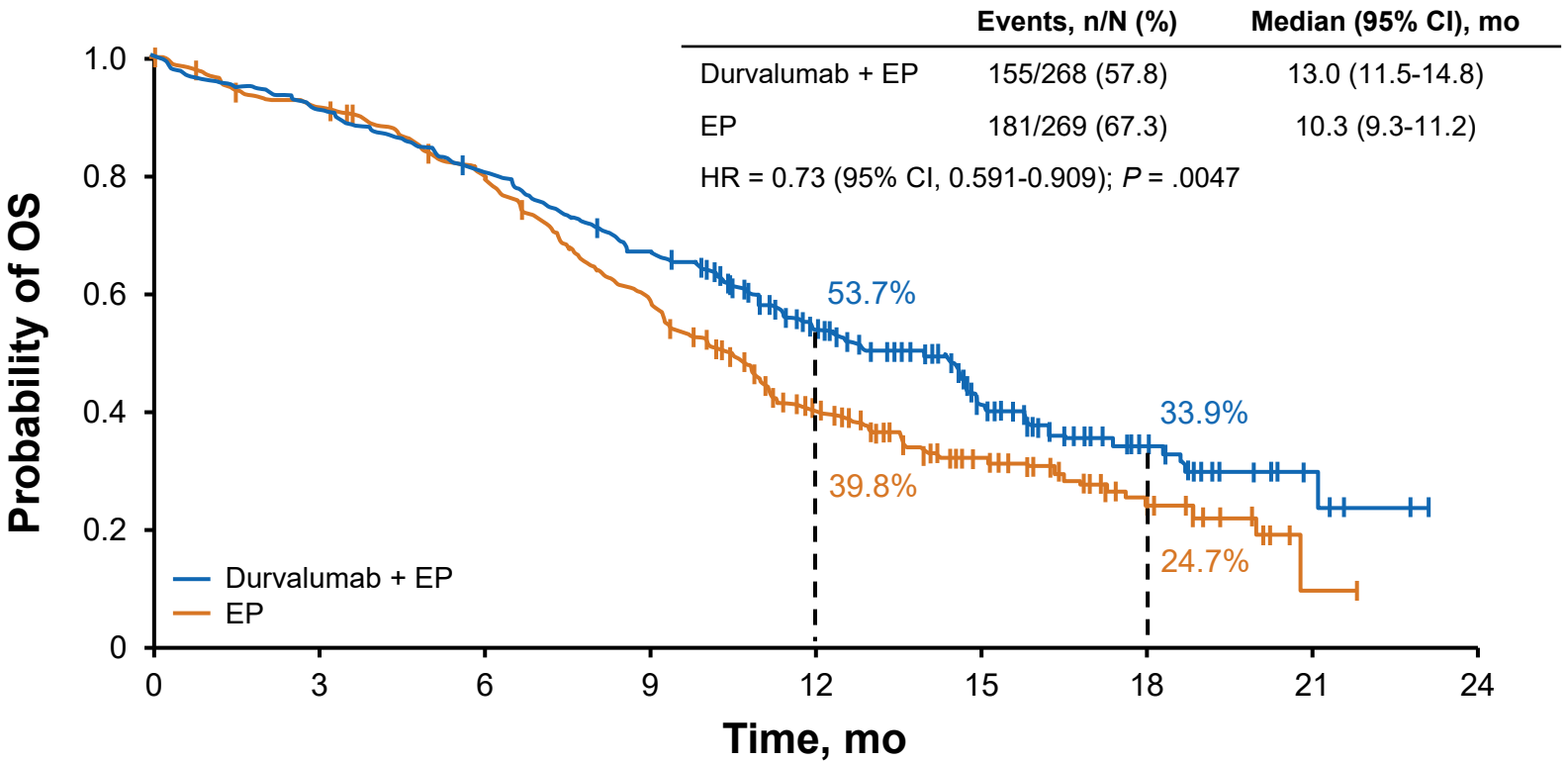


- **Primary endpoint: OS**
- **Secondary endpoints:** PFS, ORR, safety and tolerability, patient-reported outcomes

EP, etoposide and cisplatin; ES-SCLC, extensive-stage small cell lung cancer; ORR, overall response rate; OS, overall survival; PCI, prophylactic cranial irradiation; PD, progressive disease; PFS, progression-free survival; PS, performance status; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

CASPIAN: Durvalumab + EP vs EP OS[1]



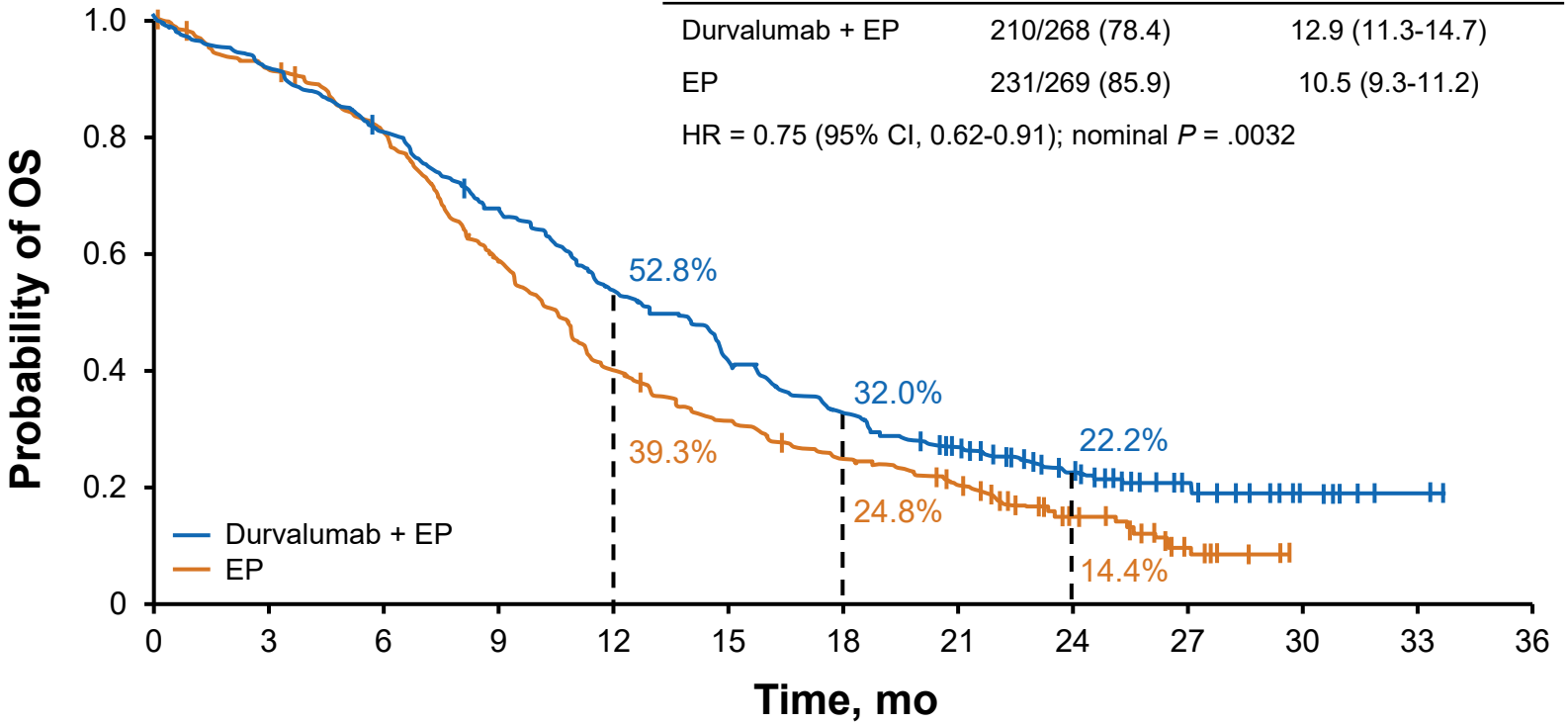
CI, confidence interval; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival.

1. Paz-Ares L et al. WCLC 2019. Abstract PL02.11.

CASPIAN: Durvalumab + EP vs EP Updated OS[1]

	Events, n/N (%)	Median (95% CI), mo
Durvalumab + EP	210/268 (78.4)	12.9 (11.3-14.7)
EP	231/269 (85.9)	10.5 (9.3-11.2)

HR = 0.75 (95% CI, 0.62-0.91); nominal *P* = .0032



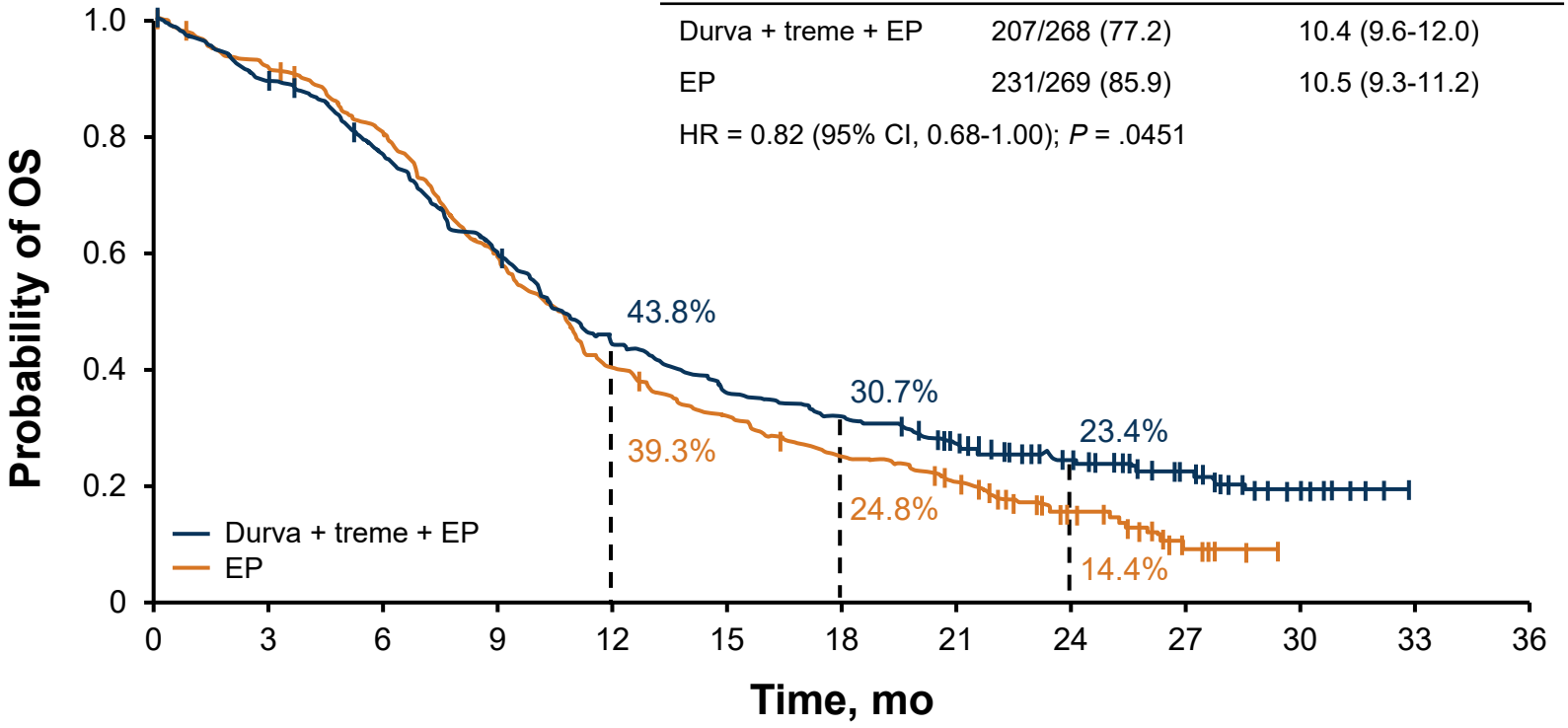
CI, confidence interval; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

CASPIAN: Durvalumab + Tremelimumab + EP vs EP OS[1]

	Events, n/N (%)	Median (95% CI), mo
Durva + treme + EP	207/268 (77.2)	10.4 (9.6-12.0)
EP	231/269 (85.9)	10.5 (9.3-11.2)

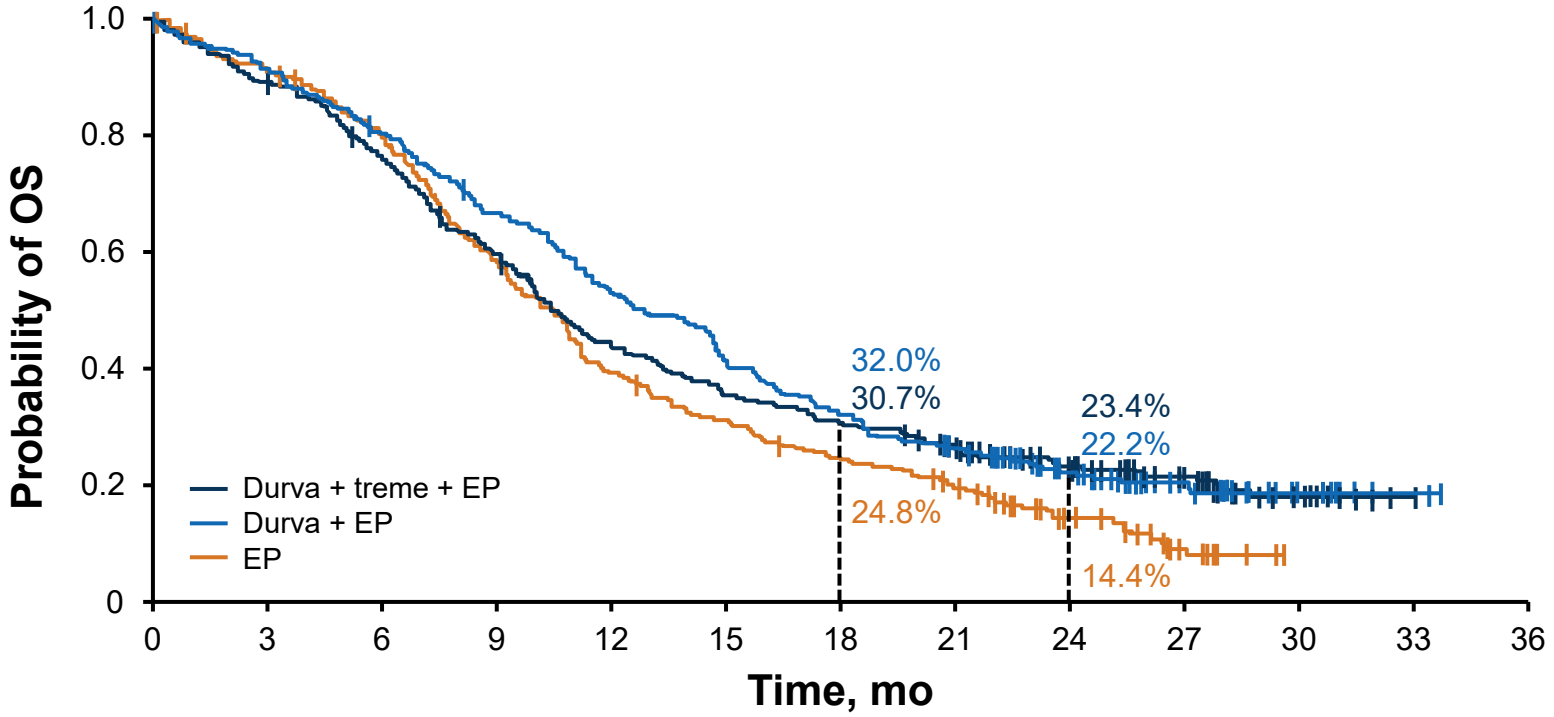
HR = 0.82 (95% CI, 0.68-1.00); *P* = .0451



CI, confidence interval; durva, durvalumab; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival; treme, tremelimumab.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

CASPIAN: Durvalumab + Tremelimumab + EP vs Durvalumab + EP vs EP OS[1]



- Median duration of follow-up in censored patients: 25.1 mo (range, 0.1-33.7)

Durva, durvalumab; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival; treme, tremelimumab.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

CASPIAN: Safety Results[1]

	Durvalumab + Tremelimumab + EP (n = 266)	Durvalumab + EP (n = 265)	EP (n = 266)
Any-grade all-cause AEs, n (%)	264 (99.2)	260 (98.1)	258 (97.0)
Grade 3/4 AEs	187 (70.3)	165 (62.3)	167 (62.8)
Serious AEs	121 (45.5)	85 (32.1)	97 (36.5)
AEs leading to treatment discontinuation	57 (21.4)	27 (10.2)	25 (9.4)
Immune-related AEs	96 (36.1)	53 (20.0)	7 (2.6)
AEs leading to death	27 (10.2)	13 (4.9)	15 (5.6)
Treatment-related AEs leading to death	12 (4.5)	6 (2.3)	2 (0.8)

AE, adverse event; EP, etoposide and cisplatin.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

Durvalumab + Platinum/Etoposide

- FDA approved March 30, 2020
- NCCN category 1, preferred option

FDA, Food and Drug Administration; NCCN, National Comprehensive Cancer Network.

First-Line Chemo-Immunotherapy

IMpower133[1,2] — FDA approved March 2019

- Addition of anti–PD-L1 (atezolizumab) to 1L chemotherapy improves OS without significant toxicity

CASPIAN[3] — FDA approved March 2020

- Addition of anti–PD-L1 (durvalumab) to 1L chemotherapy improves OS without significant toxicity
- Addition of tremelimumab to durvalumab + 1L chemotherapy increased toxicity, did not prolong survival

Two additional randomized trials at #ASCO20

1L, first line; ASCO, American Society of Clinical Oncology; FDA, Food and Drug Administration; OS, overall survival; PD-L1, programmed cell death ligand 1.

1. Horn L et al. *N Engl J Med*. 2018;379:2220-2229. 2. Reck M et al. ESMO 2019. Abstract 2374. 3. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

KEYNOTE-604: Pembrolizumab in Advanced SCLC[1]

- Stage IV SCLC (*AJCC 7th edition*)
- No prior systemic therapy
- ECOG PS 0 or 1
- Provision of a sample for biomarker assessment
- No unstable brain metastases
- Adequate organ function
- Life expectancy ≥3 mo

Stratification factors
- Platinum (cisplatin vs carboplatin)
- ECOG PS (0 vs 1)
- LDH (≤ULN vs >ULN)

1:1

R

(n = 228)

Pembrolizumab 200 mg on d 1
+ etoposide 100 mg/m^2 on d 1-3
+ carboplatin AUC 5 on d 1 ***OR***
cisplatin 75 mg/m^2 on d 1
for 4 every-3-wk cycles

Pembrolizumab
200 mg on d 1 for up
to 31 every-3-wk cycles
+ optional PCI

(n = 225)

Placebo (normal saline) on d 1
+ **etoposide** 100 mg/m^2 on d 1-3
+ **carboplatin** AUC 5 on d 1 ***OR***
cisplatin 75 mg/m^2 on d 1
for 4 every-3-wk cycles

Placebo
(normal saline)
on d 1 for up
to 31 every-3-wk cycles
+ optional PCI

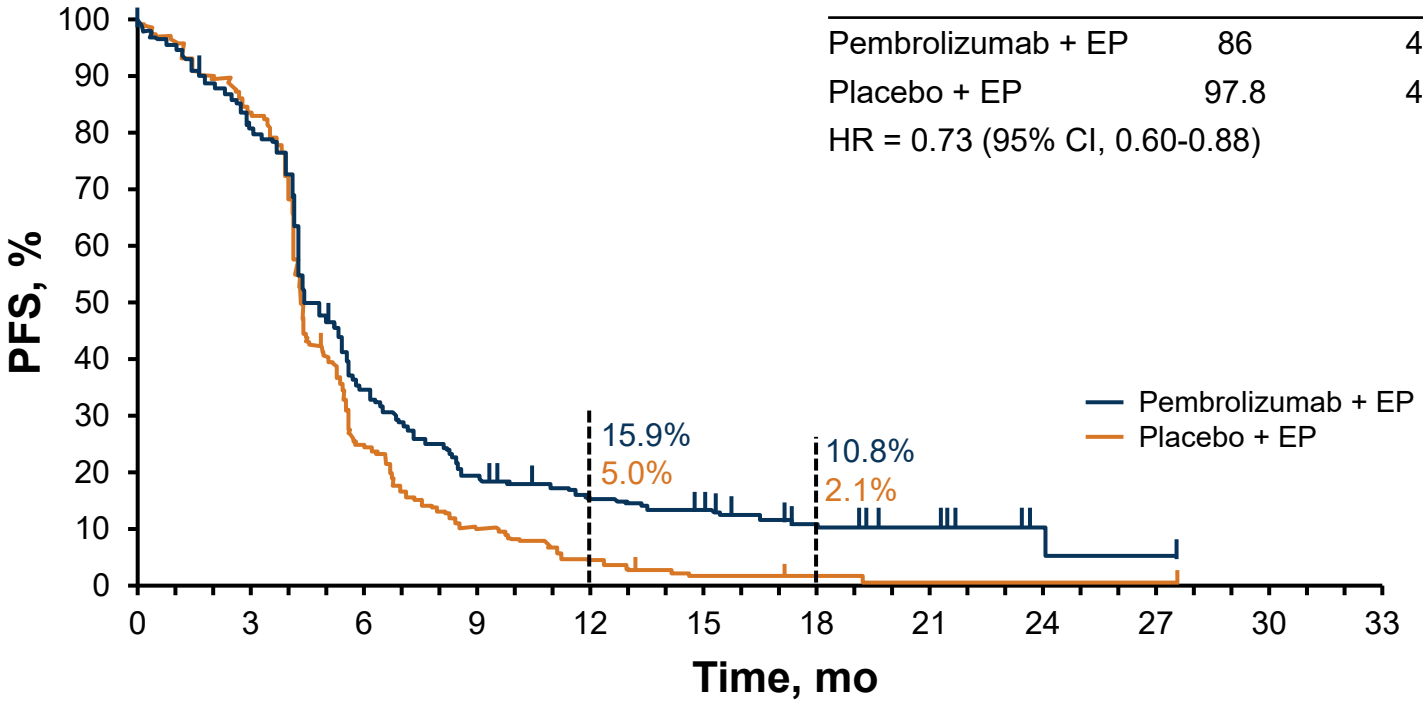
- **Primary endpoints:** PFS per RECIST v1.1 by BICR and OS
- **Secondary endpoints:** ORR and DOR per RECIST v1.1 by BICR and safety

AJCC, American Joint Committee on Cancer; AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; ECOG PS: Eastern Cooperative Oncology Group performance status; LDH, lactose dehydrogenase; ORR, overall response rate; OS, overall survival; PCI, prophylactic cranial irradiation; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SCLC, small cell lung cancer; ULN, upper limit of normal.

1. Rudin CM et al. ASCO 2020. Abstract 9001.

KEYNOTE-604: PFS Results[1]

	Events, %	Median, mo (95% CI)
Pembrolizumab + EP	86	4.8 (4.3-5.4)
Placebo + EP	97.8	4.3 (4.2-4.5)
HR = 0.73 (95% CI, 0.60-0.88)		



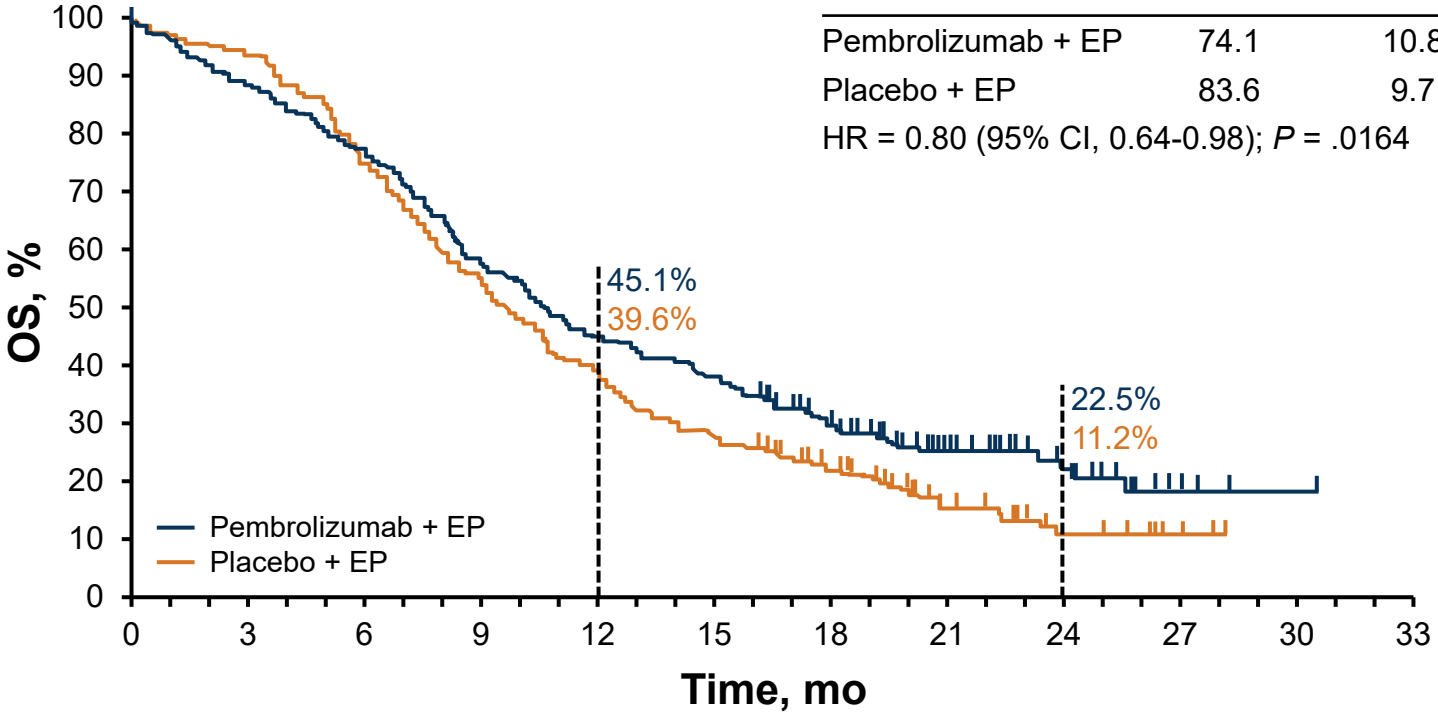
CI, confidence interval; EP, etoposide and cisplatin; HR, hazard ratio; PFS, progression-free survival.

1. Rudin CM et al. ASCO 2020. Abstract 9001.

KEYNOTE-604: OS Results[1]

	Events, %	Median, mo (95% CI)
Pembrolizumab + EP	74.1	10.8 (9.2-12.9)
Placebo + EP	83.6	9.7 (8.6-10.7)

HR = 0.80 (95% CI, 0.64-0.98); *P* = .0164



CI, confidence interval; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival.

1. Rudin CM et al. ASCO 2020. Abstract 9001.

Cross-Trial Comparison

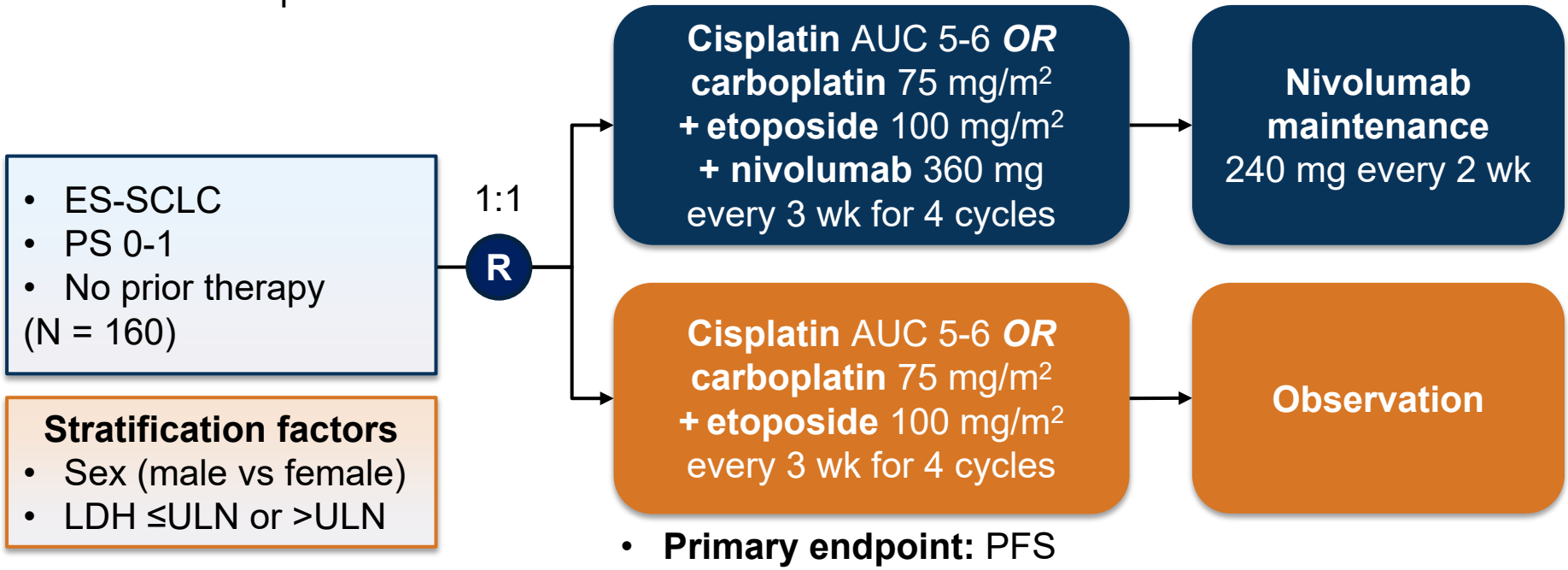
Study	Arm	n	Median OS, mo	12-mo OS, %	18-mo OS, %
IMpower133[1]	Atezolizumab + CP/ET	201	12.3	51.9	34.0
	CP/ET	202	10.3	39.0	21.0
			HR = 0.76 (95% CI, 0.60-0.95)		
CASPIAN[2]	Durvalumab + EP	268	12.9	52.8	32.0
	EP	269	10.5	43.8	30.7
	Durvalumab + tremelimumab + EP	268	10.4	39.3	24.8
			HR = 0.75 (durvalumab); HR = 0.82 (durvalumab + tremelimumab)		
KEYNOTE-604[3]	Pembrolizumab + EP	228	10.8	45.1	
	EP	225	9.7	39.6	
			HR = 0.80		

CI, confidence interval; CP, carboplatin; EP, etoposide and cisplatin; HR, hazard ratio; OS, overall survival.

1. Reck M et al. ESMO 2019. Abstract 2374. 2. Paz-Ares LG et al. ASCO 2020. Abstract 9002. 3. Rudin CM et al. ASCO 2020. Abstract 9001.

EA5161: Nivolumab + Chemo in ES-SCLC[1]

- Randomized phase 2 trial



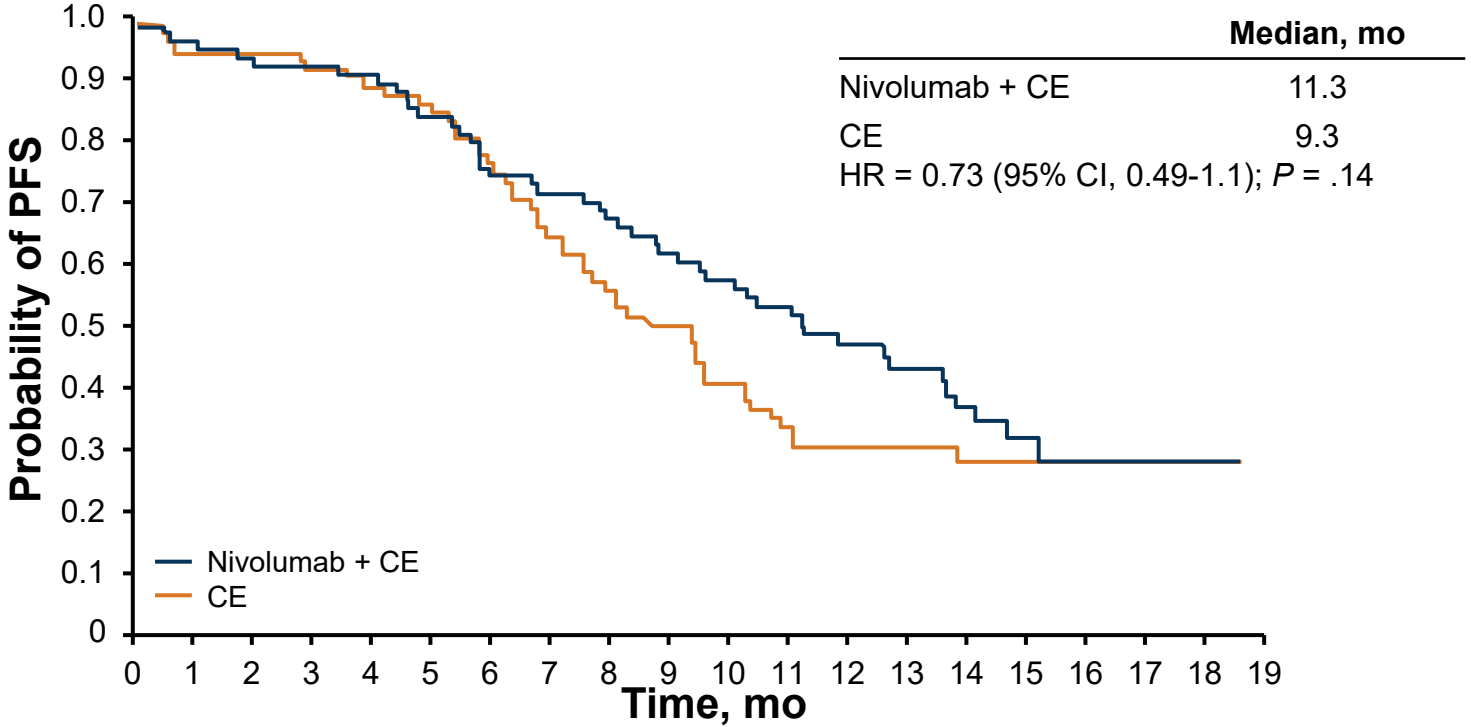
- **Primary endpoint:** PFS

AUC, area under the curve; ES-SCLC, extensive-stage small cell lung cancer; LDH, lactate dehydrogenase; PFS, performance-free survival; PS, performance status; ULN, upper limit of normal.

1. Leal T et al. ASCO 2020. Abstract 9000.

EA5161: Nivolumab ± CE Efficacy[1]

- Addition of nivolumab improved OS



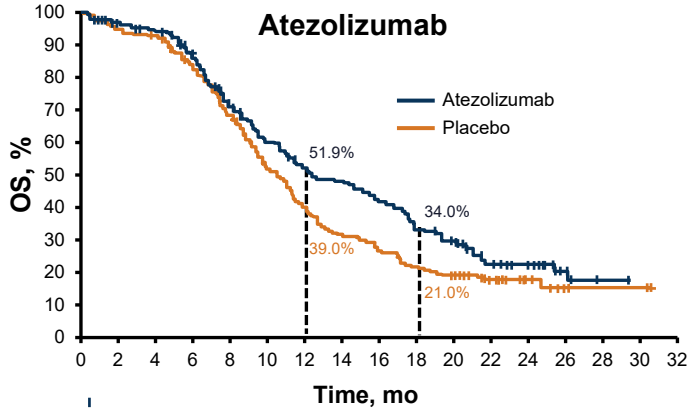
	Median, mo
Nivolumab + CE	11.3
CE	9.3

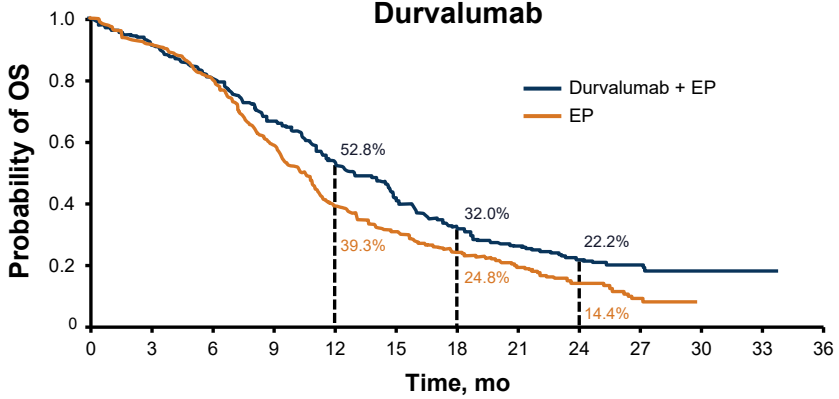
HR = 0.73 (95% CI, 0.49-1.1); *P* = .14

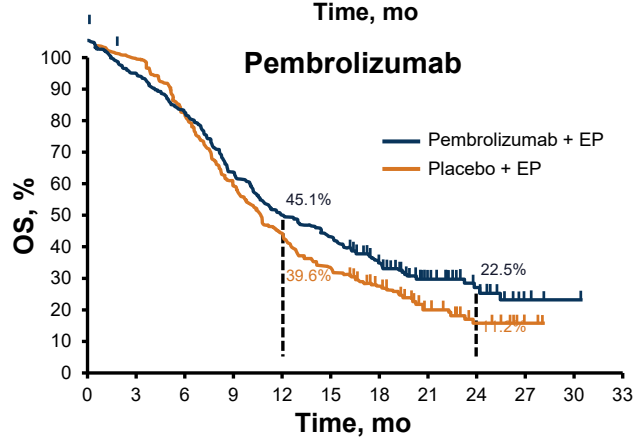
CE, cisplatin/carboplatin and etoposide; CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

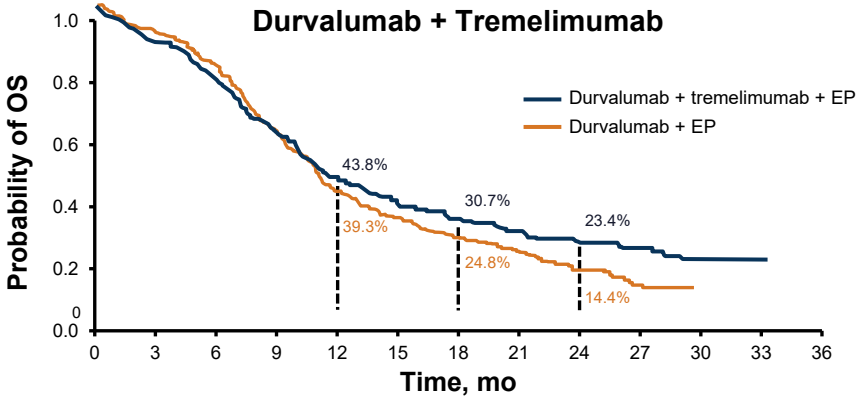
1. Leal T et al. ASCO 2020. Abstract 9000.

Immune Checkpoint Inhibitors in ES-SCLC[1-3]









EP, etoposide and cisplatin; ES-SCLC, extensive-stage small cell lung cancer; OS, overall survival.

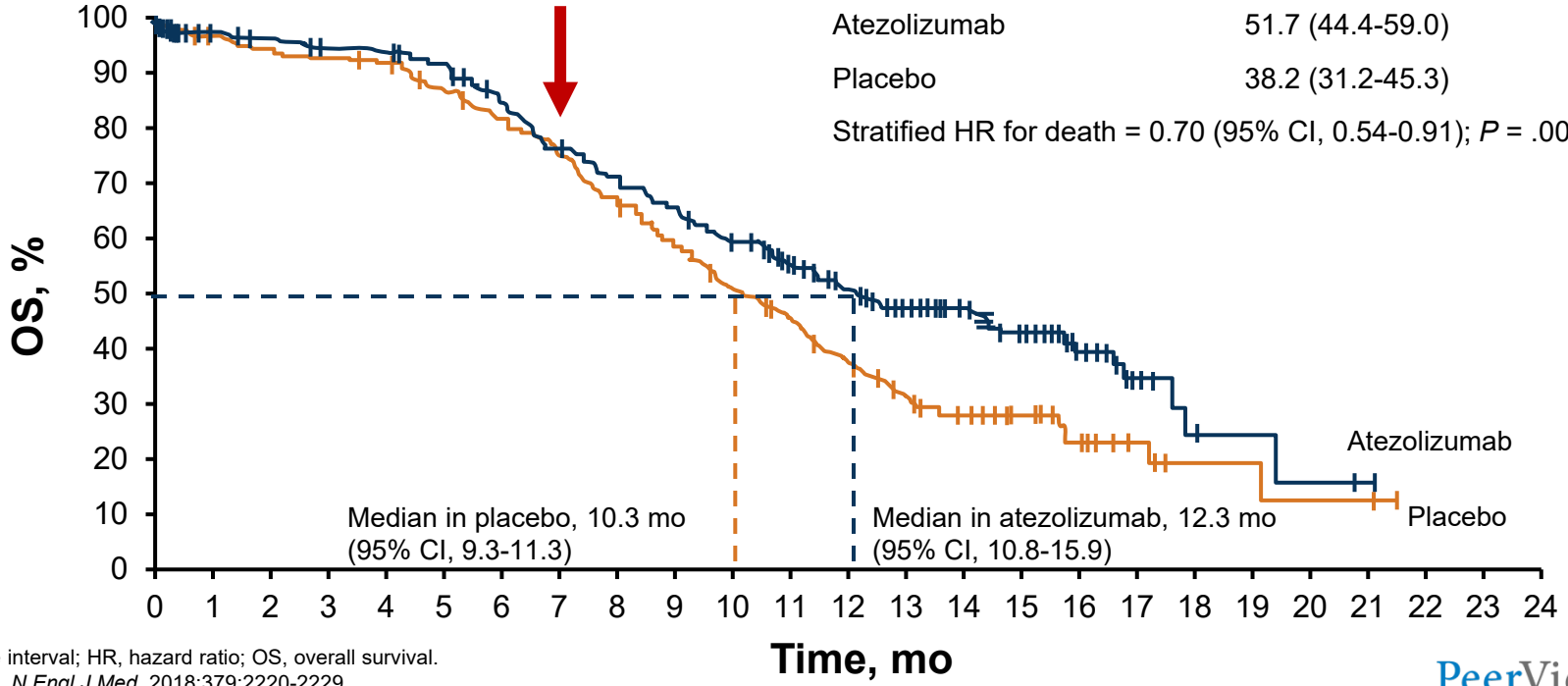
1. Reck M et al. ESMO 2019. Abstract 2374. 2. Paz-Ares LG et al. ASCO 2020. Abstract 9002. 3. Rudin CM et al. ASCO 2020. Abstract 9001.

Timing of Immunotherapy[1]

- Can initiation of immunotherapy be delayed?

	12-mo OS, % (95% CI)
Atezolizumab	51.7 (44.4-59.0)
Placebo	38.2 (31.2-45.3)

Stratified HR for death = 0.70 (95% CI, 0.54-0.91); *P* = .007



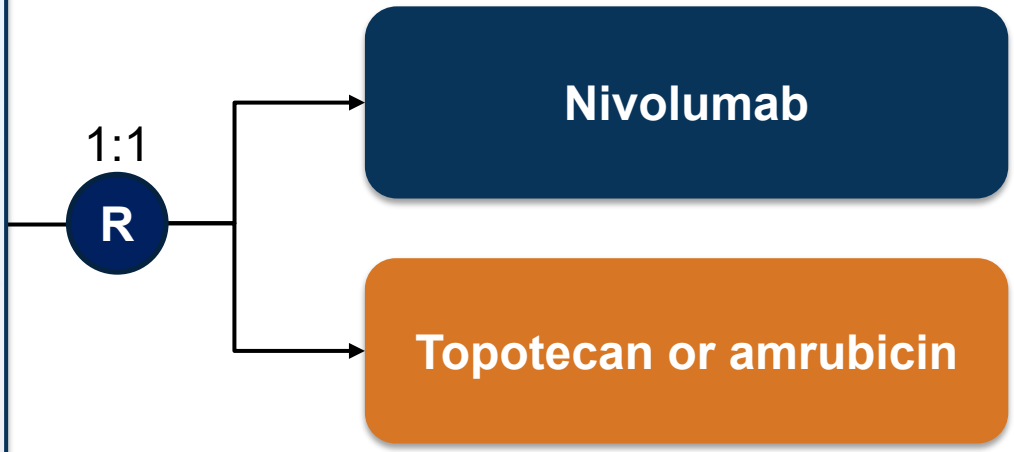
CI, confidence interval; HR, hazard ratio; OS, overall survival.

1. Horn L et al. *N Engl J Med*. 2018;379:2220-2229.

CheckMate -331: Second-Line Nivolumab[1]

- SCLC
- Recurrence/PD after 1L platinum CT or CRT (≥4 cycles)
- ECOG PS ≤1
- No symptomatic CNS metastases
- No prior therapy with anti–CTLA-4, anti–CD137, anti–PD-1/PD-L1/PD-L2

(N = 480)



- **Primary outcome measure:** OS

CD, cluster of differentiation; CNS, central nervous system; CT, chemotherapy; CTLA, cytotoxic T-lymphocyte–associated protein 4; CRT, chemoradiotherapy; ECOG PS: Eastern Cooperative Oncology Group performance status; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PD-L2, programmed cell death ligand 2; SCLC, small cell lung cancer.

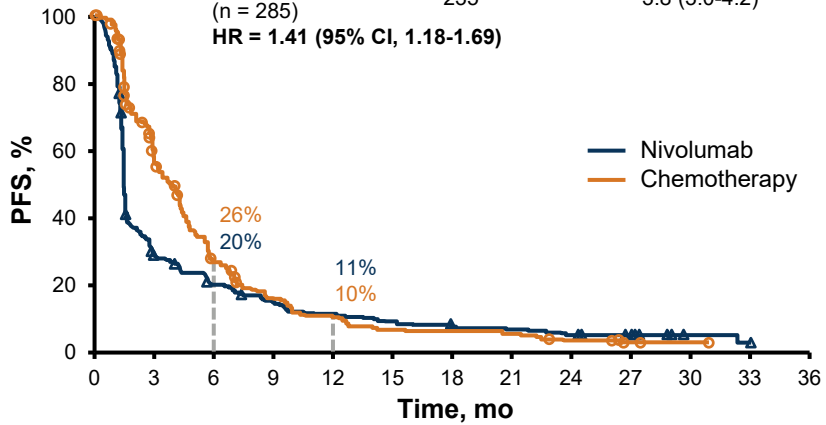
1. Reck M et al. ESMO 2018. Abstract 489.

CheckMate -331: Second-Line Nivolumab Efficacy[1]

- Recurrent/progressive SCLC
  - Randomization to nivolumab or topotecan/ambubicin, n = 480

	Events, n	Median PFS, mo (95% CI)
Nivolumab (n = 284)	258	1.4 (1.4-1.5)
Chemotherapy (n = 285)	235	3.8 (3.0-4.2)

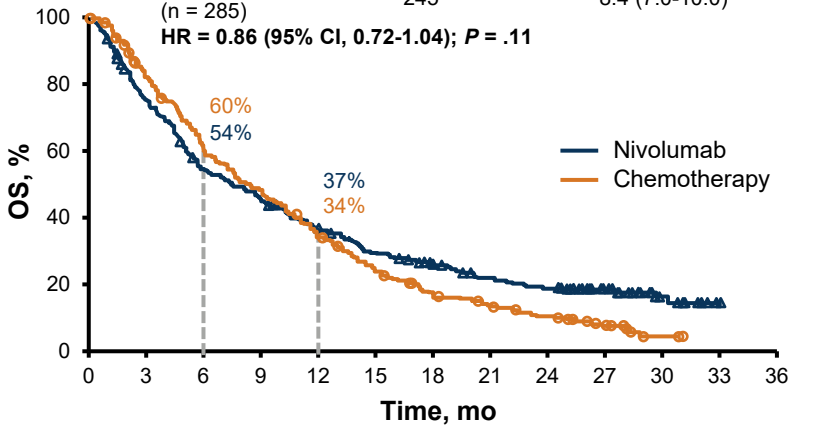
HR = 1.41 (95% CI, 1.18-1.69)



No. at Risk													
Nivolumab	284	74	50	37	27	21	17	15	11	8	2	1	0
Chemotherapy	285	136	62	34	22	14	13	11	6	2	1	0	0

	Events, n	Median PFS, mo (95% CI)
Nivolumab (n = 284)	225	7.5 (5.6-9.2)
Chemotherapy (n = 285)	245	8.4 (7.0-10.0)

HR = 0.86 (95% CI, 0.72-1.04); *P* = .11



No. at Risk													
Nivolumab	284	209	150	123	99	78	63	49	42	26	9	1	0
Chemotherapy	285	221	161	128	90	62	41	30	22	11	2	0	0

HR, hazard ratio; PFS, progression-free survival; SCLC, small cell lung cancer.

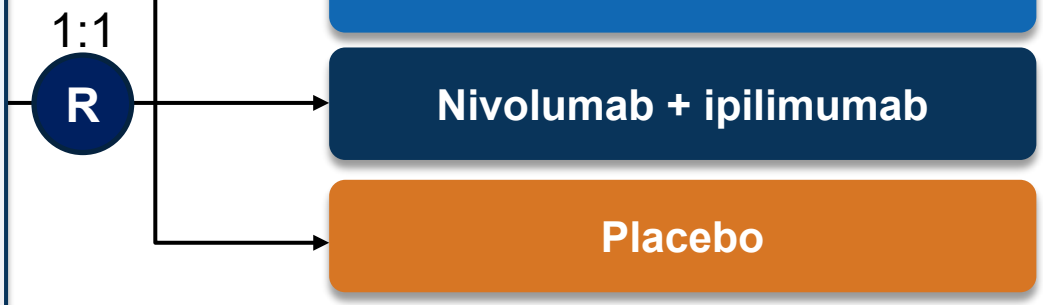
1. Reck M et al. ESMO 2018. Abstract 489.

CheckMate -451

- Randomized phase 3 maintenance trial[1]

- ≥ stable disease following 1L, platinum-based CT
- ECOG PS 0 to 1
- No symptomatic CNS metastases
- No autoimmune disease

(N = 834)

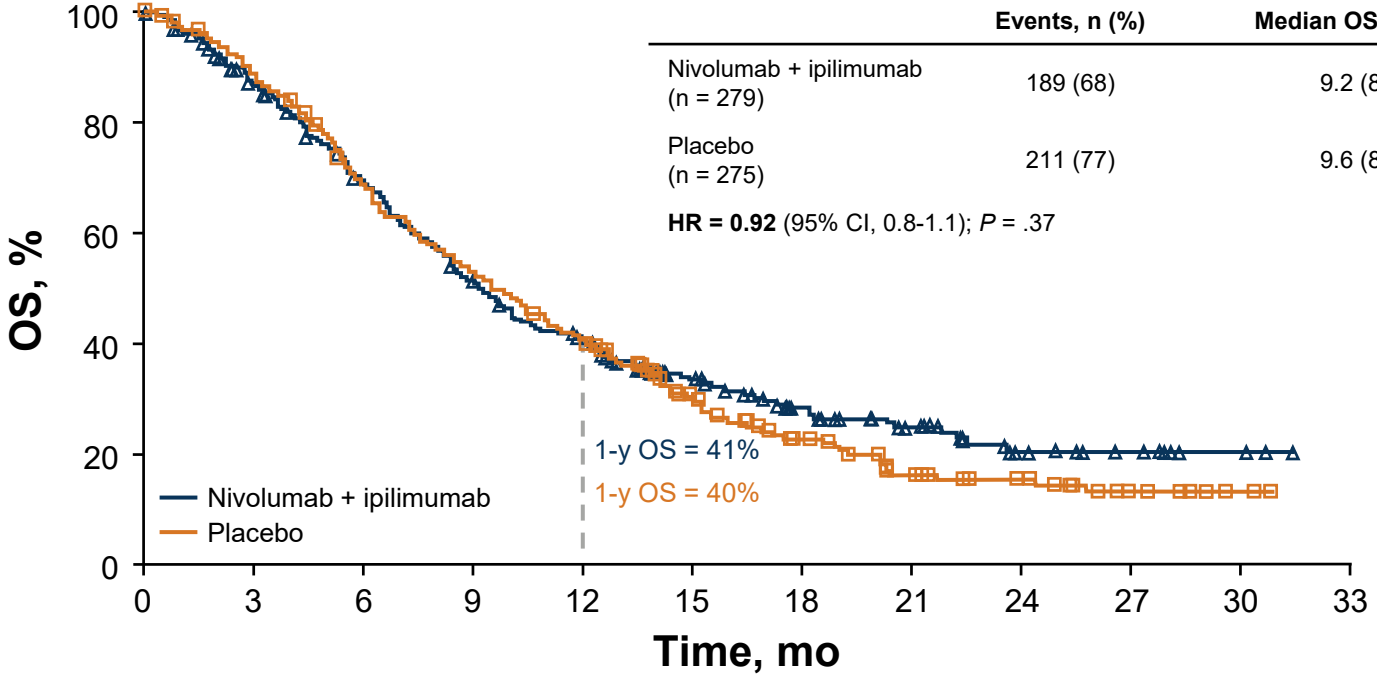


- **Primary endpoint:** OS
- **Secondary endpoints:** ORR and PFS

1L, first line; CNS, central nervous system; CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; PFS, progression-free survival; ORR, overall response rate; OS, overall survival.

1. https://clinicaltrials.gov/ct2/show/NCT02538666.

Maintenance Nivolumab/Ipilimumab[1]



	Events, n (%)	Median OS, mo (95% CI)
Nivolumab + ipilimumab (n = 279)	189 (68)	9.2 (8.2-10.2)
Placebo (n = 275)	211 (77)	9.6 (8.2-11.0)

HR = 0.92 (95% CI, 0.8-1.1); *P* = .37

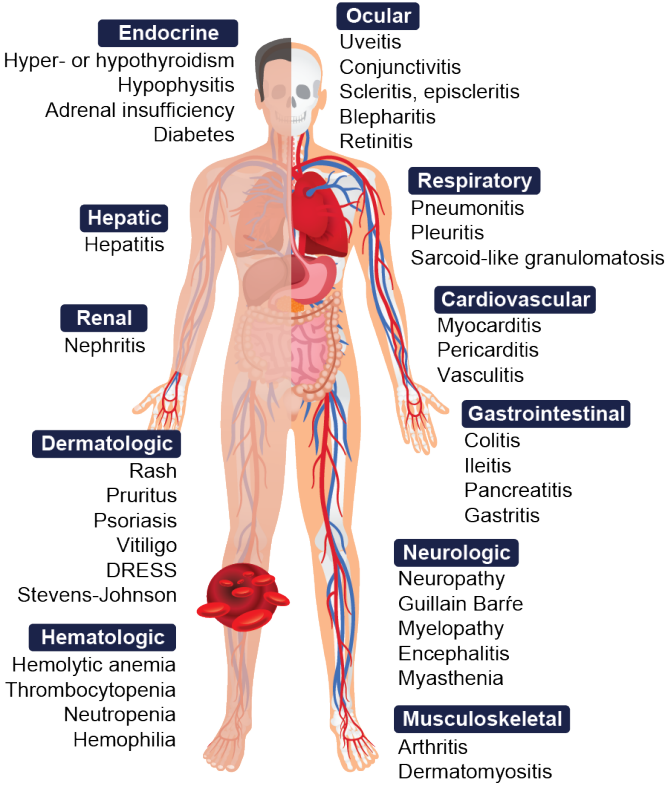
No. at Risk

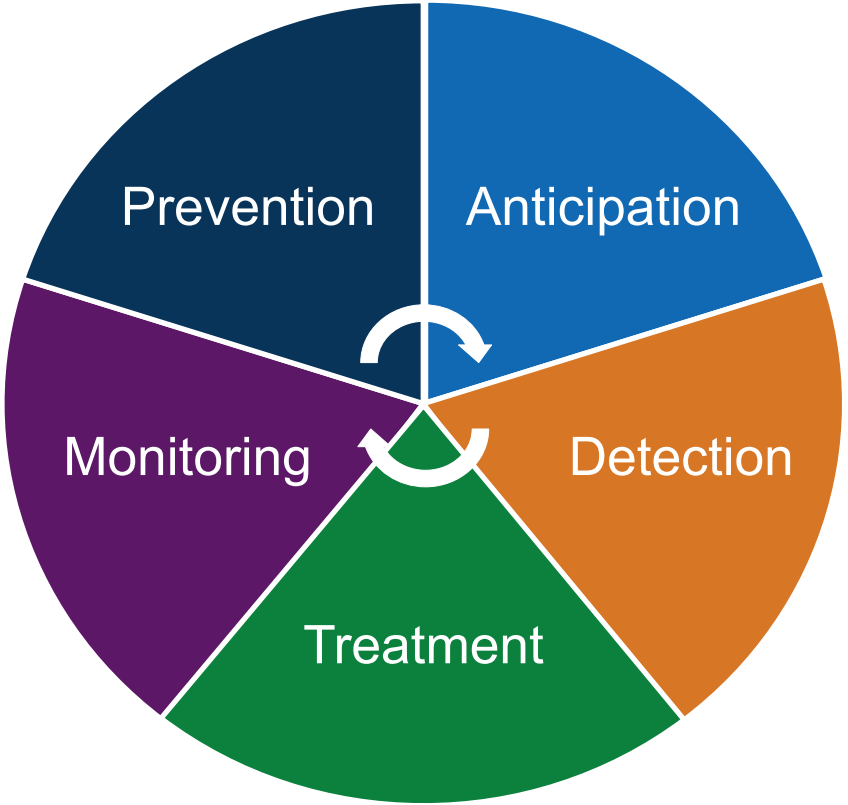
Nivolumab + ipilimumab	279	230	177	130	100	65	43	30	14	8	3	0
Placebo	275	237	181	139	105	65	41	23	16	7	2	0

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

1. Owonikoko T et al. European Lung Cancer Congress 2019 (ELCC 2019). Abstract LBA1_PR.

irAEs Can Affect Any Organ System and Require Close Monitoring by Patients and Clinicians[1,2]





DRESS, drug rash with eosinophilia and systemic symptoms; irAE, immune-related adverse event.

1. Gordon R et al. *Clin J Oncol Nurs*. 2017;21(suppl 2):45-52. 2. Champiat S et al. *Ann Oncol.* 2016;27:559-574.

Grading and General Recommendations for Managing irAEs[1-3]

Questions: Continue, suspend, or discontinue immune checkpoint inhibitor? Use of steroids? Referral to specialists?

Grade	Assessment and Management
Grade 1	Asymptomatic; diagnostic changes only; continue immunotherapy
Grade 2	Mild to moderate symptoms; grade 2 diagnostic abnormalities • Hold treatment; provide supportive care • Methylprednisolone 0.5-1.0 mg/kg/day until stable (or oral equivalent) **If improving:** transition to oral steroid at start of taper • Dosage suggested: 60 mg prednisone daily for 2 weeks • Taper over ≥4 weeks to reduce recurrence of symptoms • May consider reinitiation of immunotherapy **If progressing:** treat as grade 3/4 • Consider hospitalization of patient; multidisciplinary evaluation of toxicity
Grade 3/4	Discontinue immunotherapy (consider organ-specific algorithms; endocrine) • Hospitalization indicated • Methylprednisolone 1.0-2.0 mg/kg/day until stable
Refractory	If no improvement or progression, additional immunosuppressant treatment may be needed • Infliximab 5 mg/kg (except if contraindicated) • Mycophenolate mofetil 1 g twice daily • Cyclosporine or IVIG

CTCAE Guide

CTCAE, Common Terminology Criteria for Adverse Events; irAE, immune-related adverse event; IVIG, intravenous immunoglobulin.

1. https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. 2. Brahmer JR et al. *J Clin Oncol*. 2018;36:1714-1768.
3. Puzanov I et al. *J Immunother Cancer*. 2017;5:95.

Can We Select Patients?

- Can we identify the right patients for immunotherapy?
- Are there appropriate biomarkers?

Implications of PD-L1 Expression[1,2]

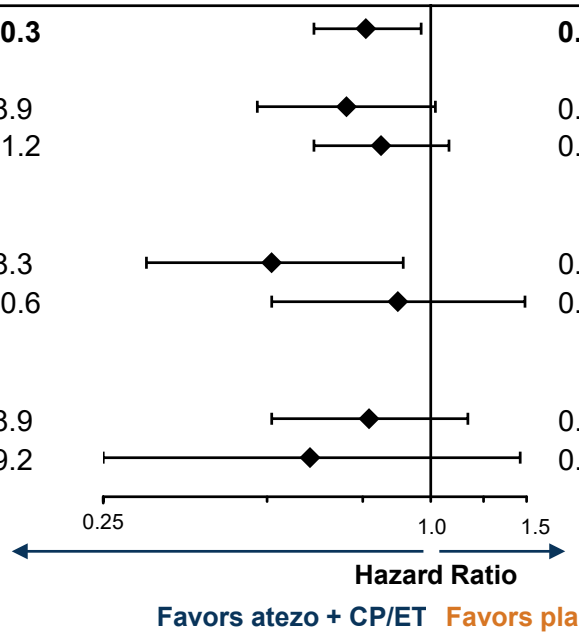
- IMpower133 using SP263 PD-L1 assay
  - Only 34% of samples evaluable
  - 94% PD-L1 <1% based on tumor cell expression
  - 50% PD-L1 <1% based on immune cell expression
- CASPIAN using SP263 PD-L1 assay
  - Only 52% of samples evaluable
  - 95% PD-L1 <1% based on tumor cell expression
  - 78% PD-L1 <1% based on immune cell expression

PD-L1, programmed cell death ligand 1.

1. Reck M et al. ESMO 2019. Abstract 2374. 2. Paz-Ares L et al. ESMO 2019. Abstract 3837.

PD-L1 Expression: IMpower133[1]

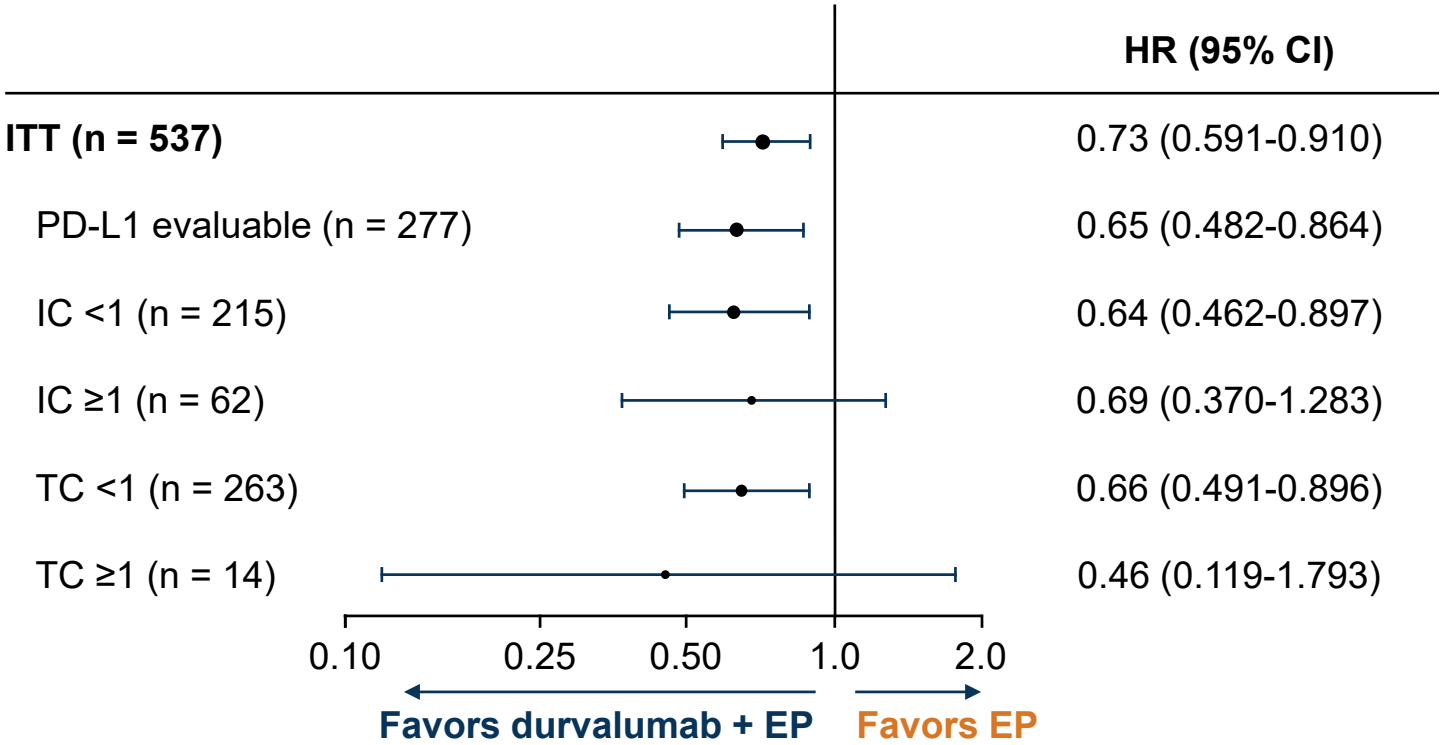
Subgroup	Median OS, mo: Atezo + CP/ET	Median OS, mo: Placebo + CP/ET	OS HR (95% CI)
ITT (N = 403)	**12.3**	**10.3**	**0.76 (0.61-0.96)**
ITT-BEP (n = 137)	9.9	8.9	0.70 (0.48-1.02)
Non-BEP (n = 266)	14.6	11.2	0.81 (0.61-1.08)
PD-L1 expression 1% TC or IC			
<1% PD-L1 (n = 65)	10.2	8.3	0.51 (0.30-0.89)
≥1% PD-L1 (n = 72)	9.7	10.6	0.87 (0.51-1.49)
PD-L1 expression 5% TC or IC			
<5% PD-L1 (n = 108)	9.2	8.9	0.77 (0.51-1.17)
≥5% PD-L1 (n = 29)	21.6	9.2	0.60 (0.25-1.46)



Atezo, atezolizumab; BEP, biomarker-evaluable population; CI, confidence interval; CP, carboplatin; ET, etoposide; HR, hazard ratio; IC, immune cell; ITT, intent to treat; OS, overall survival; PD-L1, programmed cell death ligand 1; TC, tumor cell.

1. Reck M et al. ESMO 2019. Abstract 2374.

PD-L1 Expression: CASPIAN[1]



CI, confidence interval; EP, etoposide and carboplatin; HR, hazard ratio; IC, immune cells; ITT, intent to treat; PD-L1, programmed cell death ligand 1; TC, tumor cells.

1. Paz-Ares L et al. ESMO 2019. Abstract 3837.

PD-L1 Expression: KEYNOTE-604[1]

- Randomized phase 3 trial for 1L ES-SCLC
  - Platinum + etoposide + pembrolizumab/placebo
    - PFS benefit achieved, did not achieve OS endpoint
    - PD-L1 evaluable in majority of patients (~80%)
    - Higher rates of PD-L1 positivity than other trials

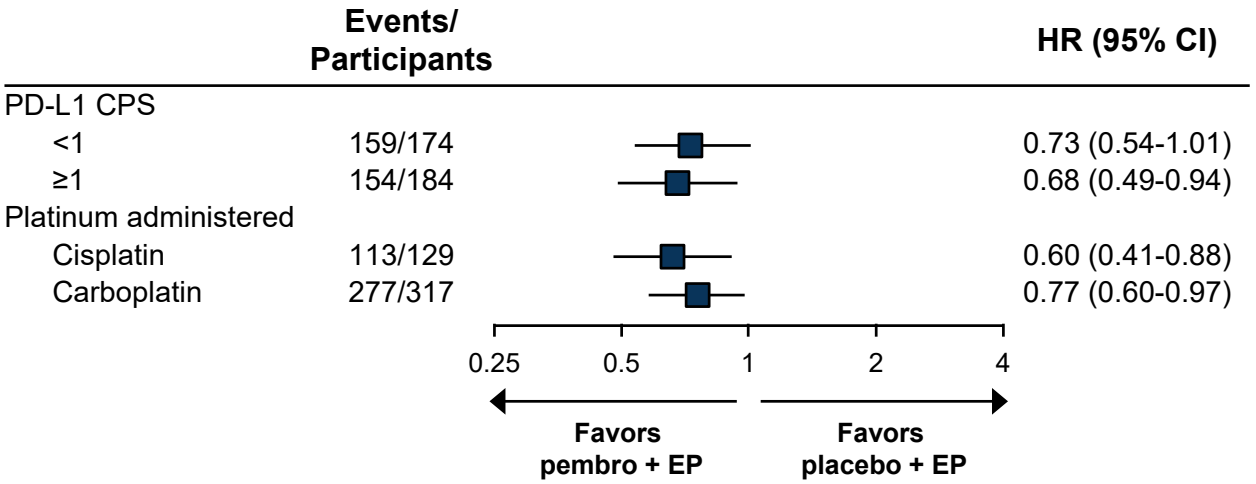
PD-L1 CPS	Pembrolizumab + EP (n = 228)	Placebo + EP (n = 225)
<1	97 (42.5)	78 (34.7)
≥1	88 (38.6)	97 (43.1)
Unknown	43 (18.9)	50 (22.2)

CPS, combined positive score; EP, etoposide and cisplatin; ES-SCLC, extensive-stage small cell lung cancer; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; OS, overall survival.

1. Rudin CM et al. *J Clin Oncol*. 2020;38:2369-2379.

PD-L1 Expression: KEYNOTE-604[1] (Cont'd)

- PD-L1 expression (CPS, 22C3) did not correlate with survival benefit from pembrolizumab in ES-SCLC



CI, confidence interval; CPS, combined positive score; EP, etoposide and carboplatin; ES-SCLC, extensive stage small cell lung cancer; HR, hazard ratio; PD-L1, programmed cell death ligand 1; pembro, pembrolizumab.

1. Rudin CM et al. *J Clin Oncol*. 2020;38:2369-2379.

Blood TMB[1,2]

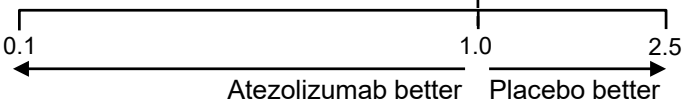
- Blood TMB in IMpower133
  - Blood collected for TMB at study entry
  - Predictive role for PFS with second-line atezolizumab in NSCLC
    - OAK, POPLAR
  - Prespecified cutoffs of 10 and 16 mutations/Mb

NSCLC, non–small cell lung cancer; PFS, progression-free survival; TMB, tumor mutational burden.

1. Liu S et al. WCLC 2018. Abstract PL02.07. 2. Gandara DR et al. *Nat Med*. 2018;24:1441-1448.

Blood TMB: IMpower133[1]

Population	Median OS, mo: Atezolizumab + CP/ET	Median OS, mo: Placebo + CP/ET	OS HR[a] (95% CI)
Male (n = 261)	12.3	10.9	0.74 (0.54-1.02)
Female (n = 142)	12.5	9.5	0.65 (0.42-1.00)
<65 y (n = 217)	12.1	11.5	0.92 (0.64-1.32)
≥65 y (n = 186)	12.5	9.6	0.53 (0.36-0.77)
ECOG PS 0 (n = 140)	16.6	12.4	0.79 (0.49-1.27)
ECOG PS 1 (n = 263)	11.4	9.3	0.68 (0.50-0.93)
Brain metastases (n = 35)	8.5	9.7	1.07 (0.47-2.43)
No brain metastases (n = 368)	12.6	10.4	0.68 (0.52-0.89)
Liver metastases (n = 149)	9.3	7.8	0.81 (0.55-1.20)
No liver metastases (n = 254)	16.8	11.2	0.64 (0.45-0.90)
bTMB <10 mut/mb (n = 139)	11.8	9.2	0.70 (0.45-1.07)
bTMB ≥10 mut/mb (n = 212)	14.6	11.2	0.68 (0.47-0.97)
bTMB <16 mut/mb (n = 271)	12.5	9.9	0.71 (0.52-0.98)
bTMB ≥16 mut/mb (n = 80)	17.8	11.9	0.63 (0.35-1.15)
ITT (N = 403)	12.3	10.3	0.70 (0.54-0.91)



bTMB, blood tumor mutational burden; CI, confidence interval; CP, carboplatin; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, etoposide; HR, hazard ratio; ITT, intent to treat; mut/mb, mutations per megabase; OS, overall survival; TMB, tumor mutational burden.

Clinical data cutoff date: April 24, 2018.

[a] HRs are unistratified for patient subgroups and stratified for the ITT. [b] TMB assessed as reported in Gandara DR et al.[2]

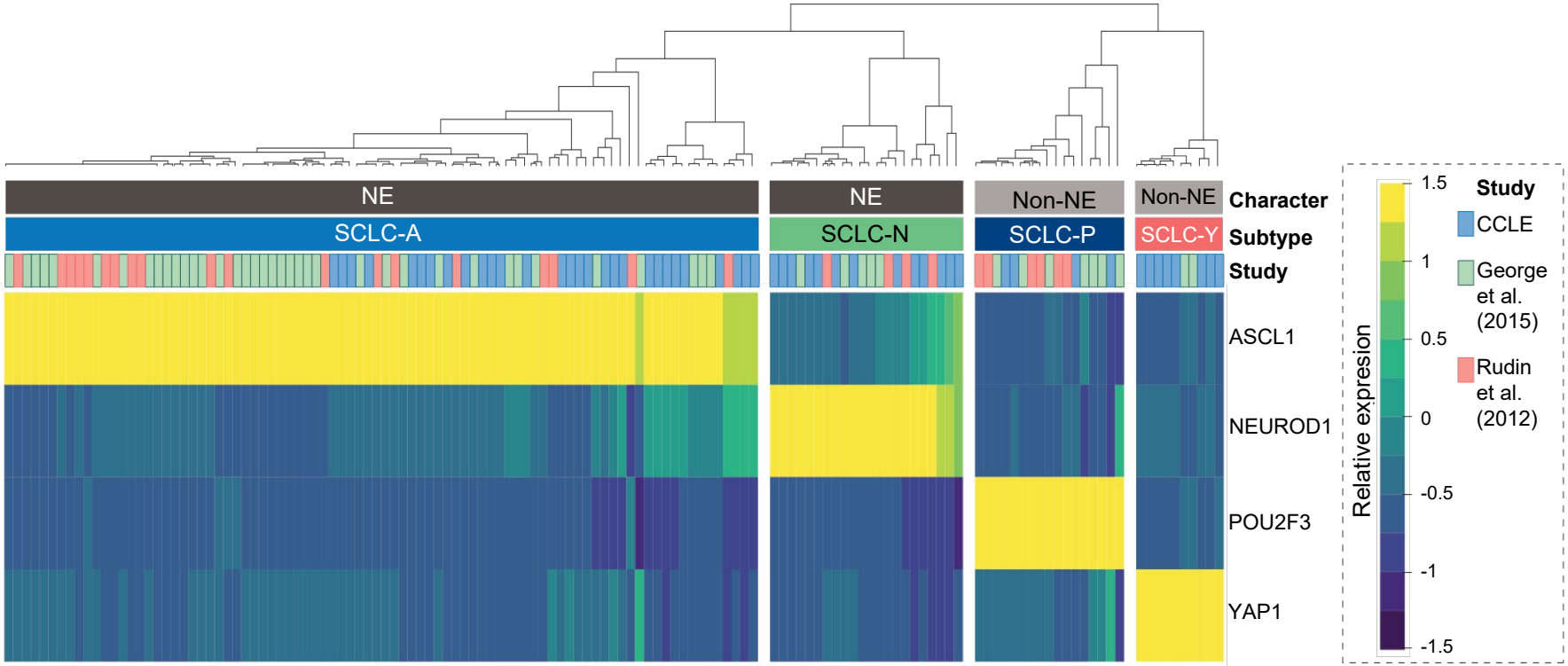
1. Liu S et al. WCLC 2018. Abstract PL02.07. 2. Gandara DR et al. *Nat Med.* 2018;24:1441-1448.

SCLC Subtypes

- Biologic subtypes can be established by differential expression of four key transcription regulators
  - ASCL1 (achaete-scute homologue 1)
  - NeuroD1 (neurogenic differentiation factor 1)
  - YAP1 (yes-associated protein)
  - POU2F3 (POU class 2 homeobox 3)

SCLC, small cell lung cancer.

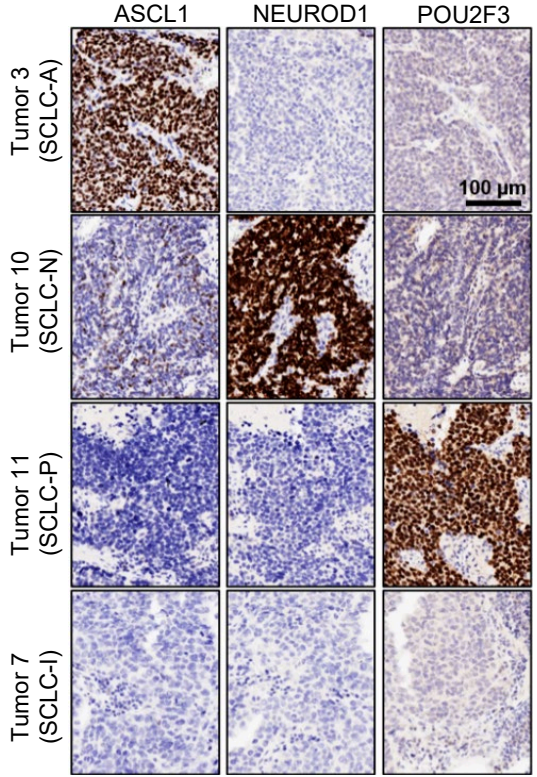
Distinct SCLC Subsets[1]

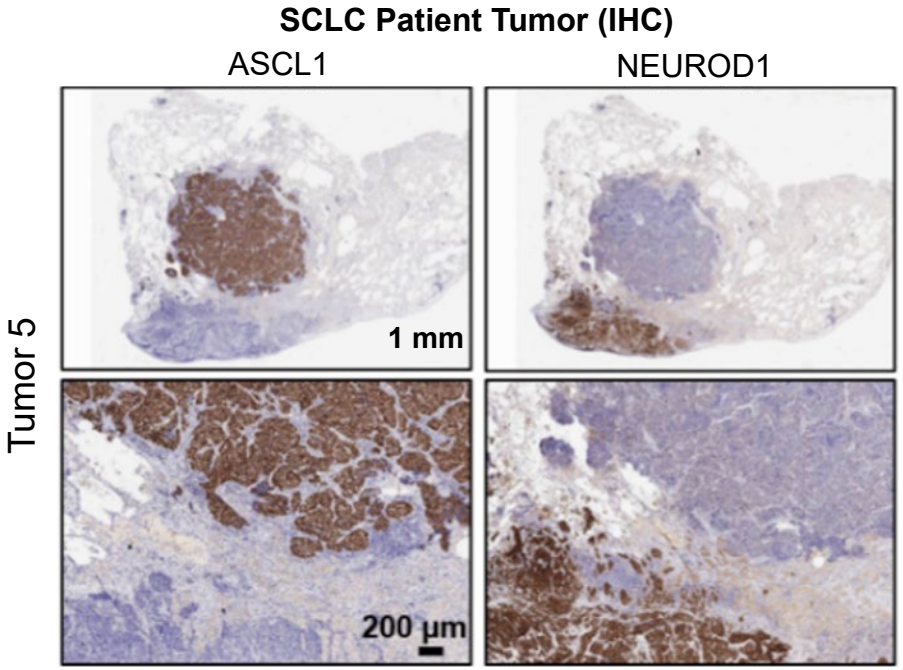


ASCL1, achaete-scute homologue 1; NE, neuroendocrine; NEUROD1, neurogenic differentiation factor 1; POU2F3, POU class 2 homeobox 3; SCLC, small cell lung cancer; YAP1, yes-associated protein 1.

1. Rudin CM et al. *Nat Rev Cancer*. 2019;19:289-297.

SCLC Transcription Factor Subtypes[1]





ASCL1, achaete-scute homologue 1; IHC, immunohistochemistry; NEUROD1, neurogenic differentiation factor 1; POU2F3, POU class 2 homeobox 3; SCLC, small cell lung cancer.

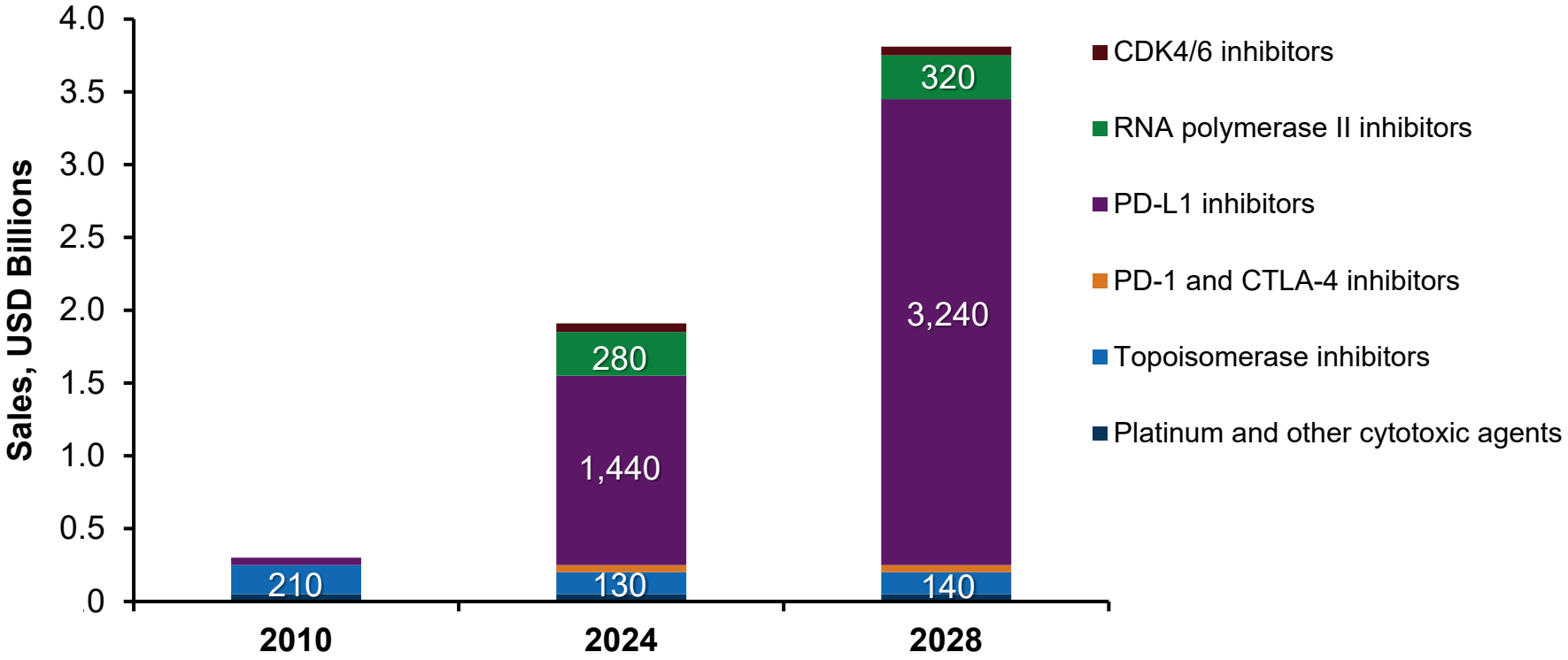
1. Gay CM et al. WCLC 2019. Abstract OA03.06.

Conclusions

- SCLC is a highly lethal subtype of lung cancer
- Concurrent chemo-immunotherapy is the new first-line standard of care for ES-SCLC
  - Platinum + etoposide + durvalumab
  - Carboplatin + etoposide + atezolizumab
- Second-line and maintenance approaches have not had the same effect as concurrent first-line use

ES-SCLC, extensive-stage small cell lung cancer; SCLC, small cell lung cancer.

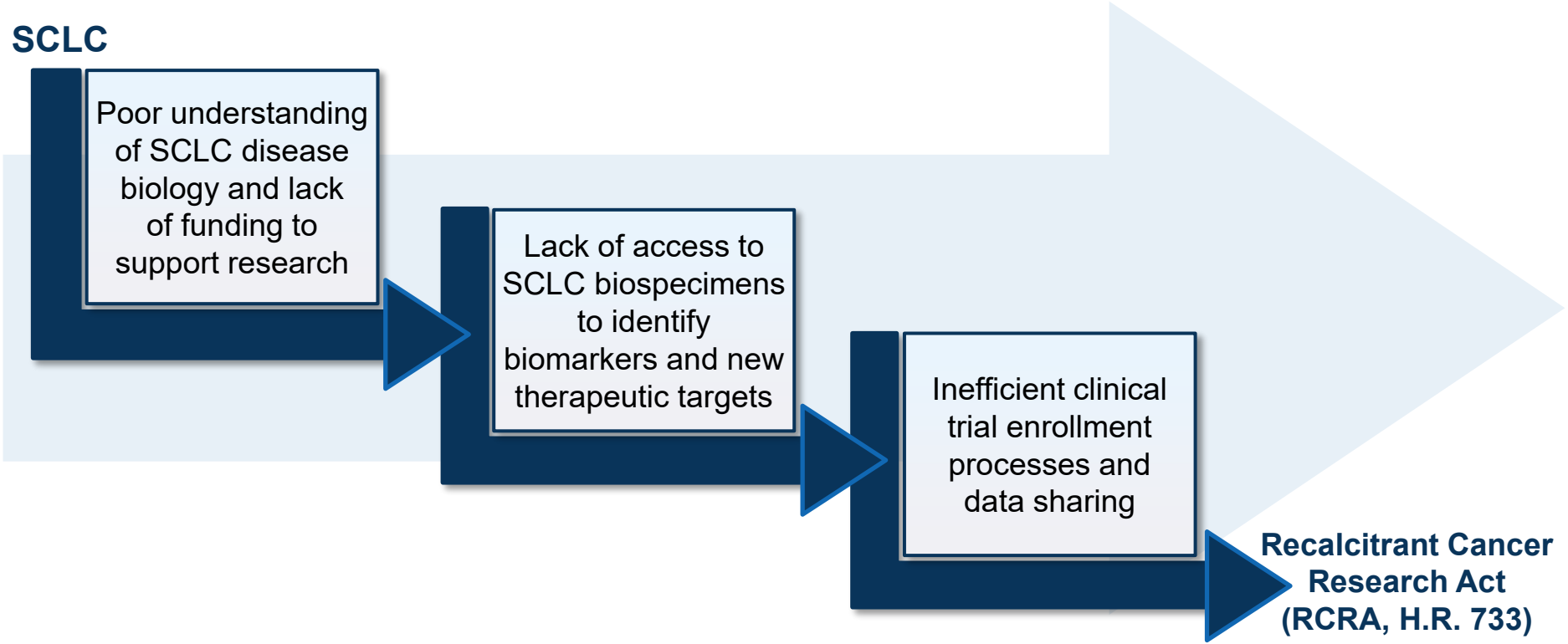
Estimated Major Market Sales of Key Therapies for SCLC: 2018 to 2028[1]



CDK4, cyclin-dependent kinase 4; CDK6, cyclin-dependent kinase 6; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; RNA, ribonucleic acid; SCLC, small cell lung cancer; USD, US dollar.

1. Dawkins JBN, Webster RM. *Nat Rev Drug Discov*. 2020;19:507-508.

Path to Innovation for SCLC



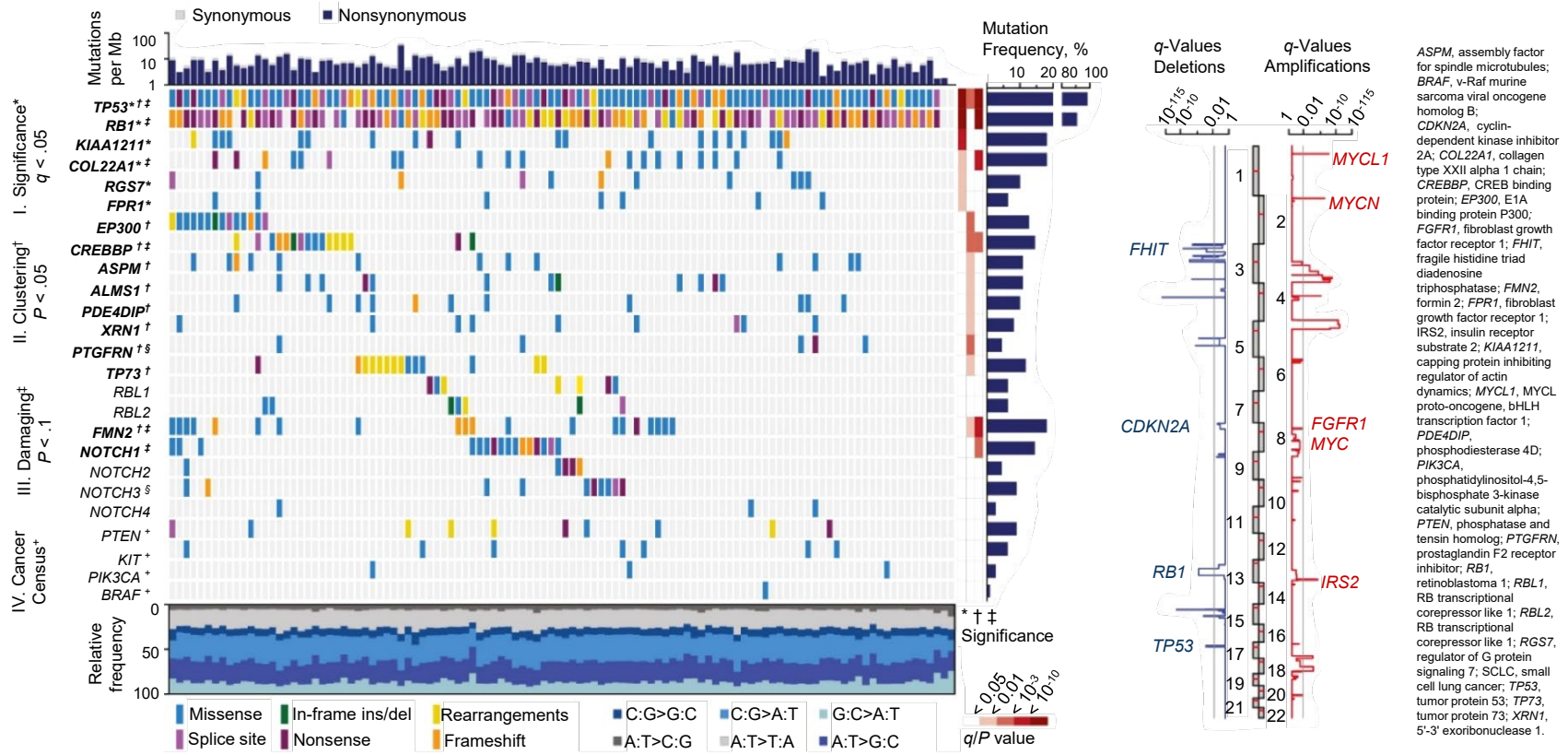
SCLC, small cell lung cancer.

SCLC Working Group

1. Develop better research tools for the study of SCLC
2. Perform comprehensive genomic profiling of tumors from patients with SCLC
3. Develop new diagnostic approaches
4. Enhance therapeutic development efforts
5. Elucidate mechanisms underlying both initial rate of response and the rapid emergence of drug and radiation resistance

SCLC, small cell lung cancer.

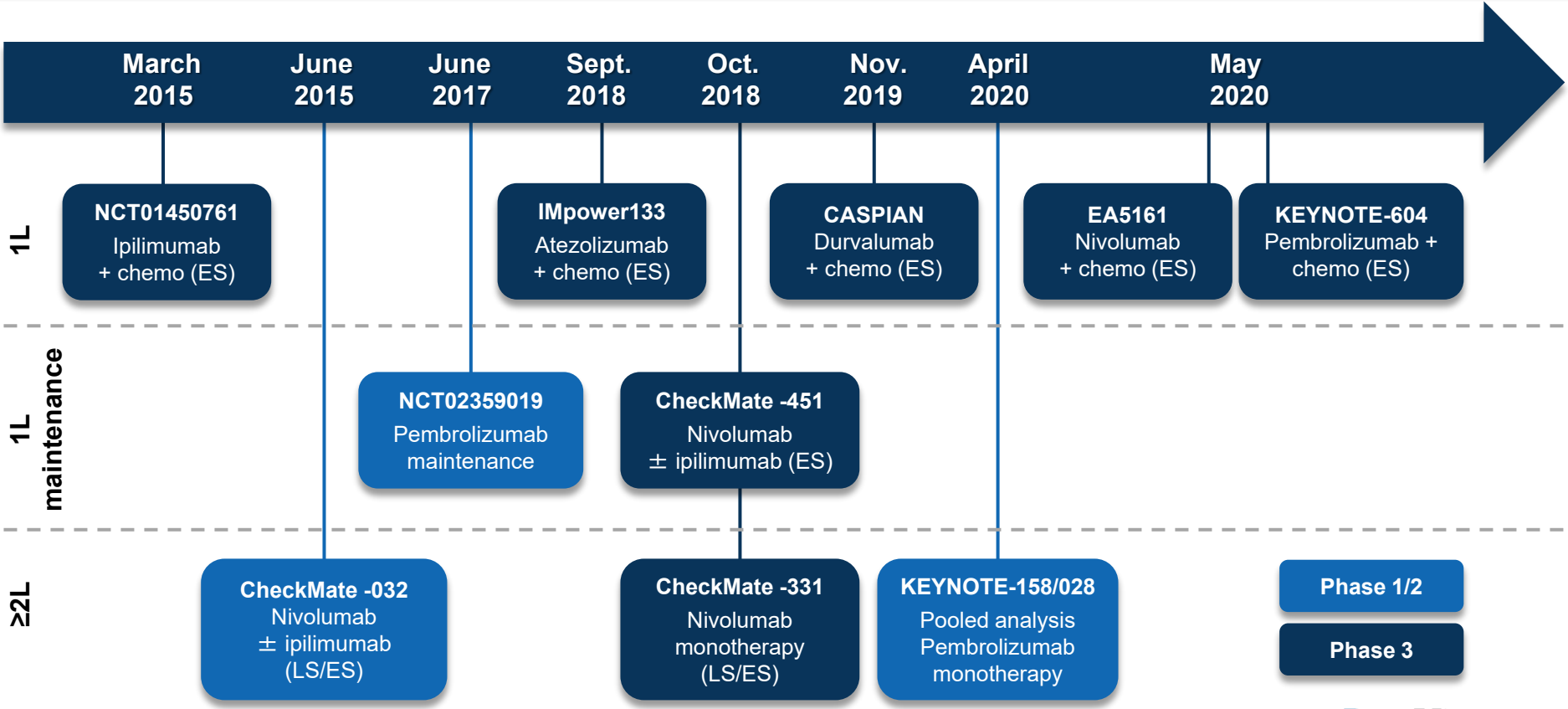
Why Progress Has Been Slow: Absence of Driver Mutations in SCLC[1]



ASPM, assembly factor for spindle microtubules; *BRAF*, v-Raf murine sarcoma viral oncogene homolog B; *CDKN2A*, cyclin-dependent kinase inhibitor 2A; *COL22A1*, collagen type XXII alpha 1 chain; *CREBBP*, CREB binding protein; *EP300*, E1A binding protein P300; *FGFR1*, fibroblast growth factor receptor 1; *FHIT*, fragile histidine triad diadenosine triphosphatase; *FMN2*, formin 2; *FPR1*, fibroblast growth factor receptor 1; IRS2, insulin receptor substrate 2; *KIAA1211*, capping protein inhibiting regulator of actin dynamics; *MYCL1*, MYCL proto-oncogene, bHLH transcription factor 1; *PDE4DIP*, phosphodiesterase 4D; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*, phosphatase and tensin homolog; *PTGFRN*, prostaglandin F2 receptor inhibitor; *RB1*, retinoblastoma 1; *RBL1*, RB transcriptional corepressor like 1; *RBL2*, RB transcriptional corepressor like 1; *RGS7*, regulator of G protein signaling 7; SCLC, small cell lung cancer; *TP53*, tumor protein 53; *TP73*, tumor protein 73; *XRN1*, 5'-3' exoribonuclease 1.

1. George J et al. *Nature*. 2015;524:47-53.

Explosion of Immunotherapy Treatments in SCLC



1L, first line; 2L, second line; chemo, chemotherapy; ES, extensive stage; LS, limited stage; SCLC, small cell lung cancer.

Cancer Health Disparities[1]

- According to the NCI, cancer health disparities in the United States are adverse differences in cancer measures such as number of new cases, number of deaths, cancer-related health complications, survivorship and QOL after cancer treatment, screening rates, and stage at diagnosis that exist among certain population groups including

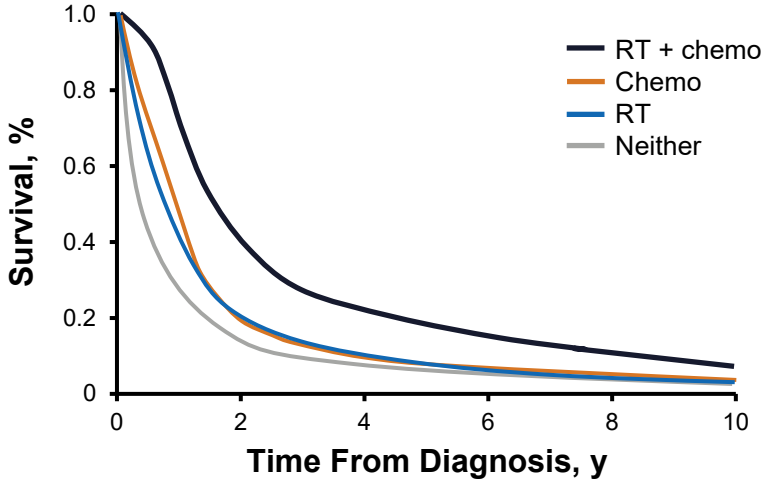
- Racial and ethnic minority groups
- Individuals of different ancestry
- Individuals of low socio-economic status
- Individuals with disabilities
- Individuals who lack or have limited health insurance coverage
- Residents in certain geographic locations, including rural areas
- Members of the lesbian, gay, bisexual, and transgender community
- Immigrants
- Refugees or asylum seekers
- Adolescents and young adults
- The elderly

NCI, National Cancer Institute; QOL, quality of life.

1. http://www.CancerDisparitiesProgressReport.org.

Survival of Patients With Limited-Stage SCLC Captured in the National Cancer Database, 2004-2013[1]

- Uninsured LS-SCLC were 35% less likely to receive chemotherapy and 25% less likely to receive RT



No. at Risk						
RT + CT	38,979	13,611	5,636	2,589	875	111
CT	14,383	2,481	940	423	148	15
RT	2,465	439	161	68	12	1
Neither	14,087	1,659	671	304	112	11

Chemo, chemotherapy; CT, chemotherapy; LC-SCLC, limited-stage small cell lung cancer; SCLC, small cell lung cancer; RT, radiotherapy.

1. Pezzi TA et al. *JAMA Oncol*. 2018;4:e174504.

Economic Burden of SCLC

Direct Costs

- Chemotherapy
- Surgery
- Radiation
- Diagnostics
- Hospitalizations
- ED utilization
- Direct cost of prophylactic therapies
- Bone metastatic disease
- Average monthly total cost
  - $11,158 (without treatment)
  - $16,309 (with chemotherapy)
  - $17,321 (chemotherapy + RT)

Predominant cost drivers were hospitalizations and office visits

Indirect Costs

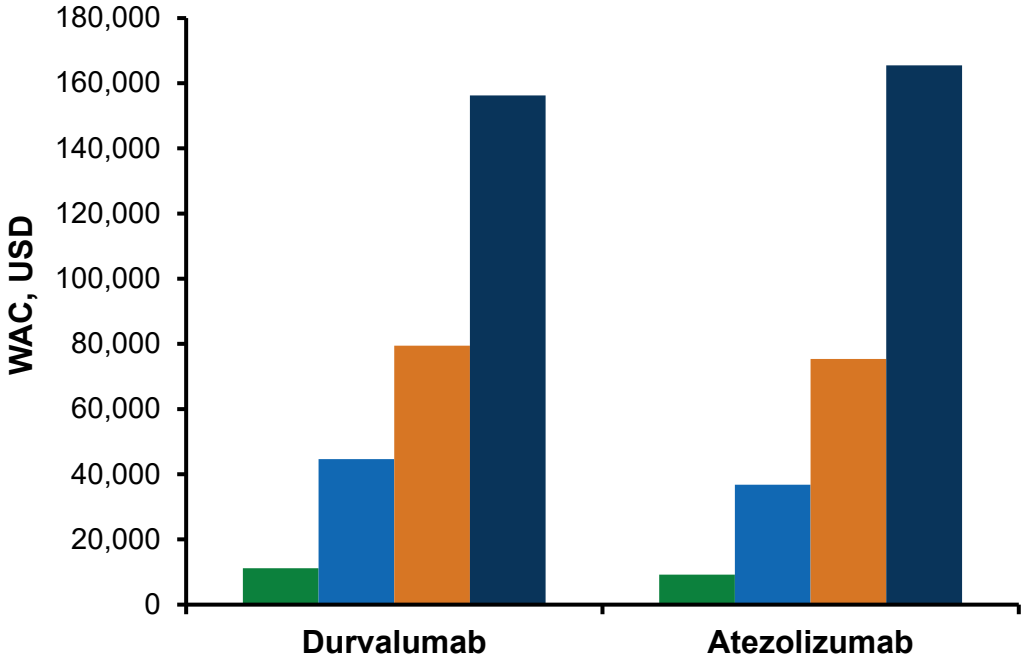
- Loss in productivity
- Caregiver burden

ED, emergency department; RT, radiotherapy; SCLC, small cell lung cancer.

Formulary Considerations From Managed Care and Health System Perspective

Annual Cost of Frontline Therapy for Extensive-Stage SCLC

- Durvalumab $11,160 (1st cycle), $44,640 (4 cycles), $79,470 (6 mo), $156,240 (12 mo)
- Atezolizumab $9,194 (1st cycle), $36,776 (4 cycles), $75,386 (6 mo), $165,476 (12 mo)



- Carboplatin/etoposide $640 (12 mo)
- Cisplatin/etoposide $472 (12 mo)
- Irinotecan/etoposide $604 (12 mo)
- Irinotecan/carboplatin $1,020 (12 mo)
- Irinotecan/cisplatin $852 (12 mo)

SCLC, small cell lung cancer; USD, US dollar; WAC, wholesale acquisition cost.

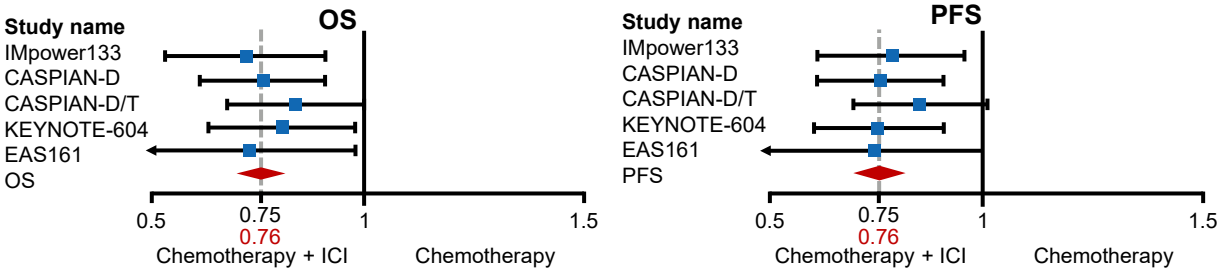
Reimbursement Considerations From Payor and Health System

- Durvalumab annual Medicare spend: $159,648
- Atezolizumab annual Medicare spend: $169,080
- NTAP
  - Durvalumab approved for NTAP
  - Atezolizumab approved for NTAP
- ICD-10-PCS procedure code XW03336 or XW04336
  - Place of service code
  - Revenue code
  - ICD-10-CM code
- Additional payment (65% of the costs of the new medical service or technology) ***or*** 65% of the amount by which the costs of the case exceed the standard MS-DRG payment
- CMS has set the maximum add-on payment at $6,875.90 for qualifying cases

ICD-10, International Classification of Diseases, Tenth Revision; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS, International Classification of Diseases, Tenth Revision, Procedure Coding System. MS-DRG, Medicare Severity–Diagnosis-Related Group; NTAP, new technology add-on payment.

Formulary Justification of Cost vs Benefit

Frontline Chemoimmunotherapy in SCLC: Summary of Efficacy



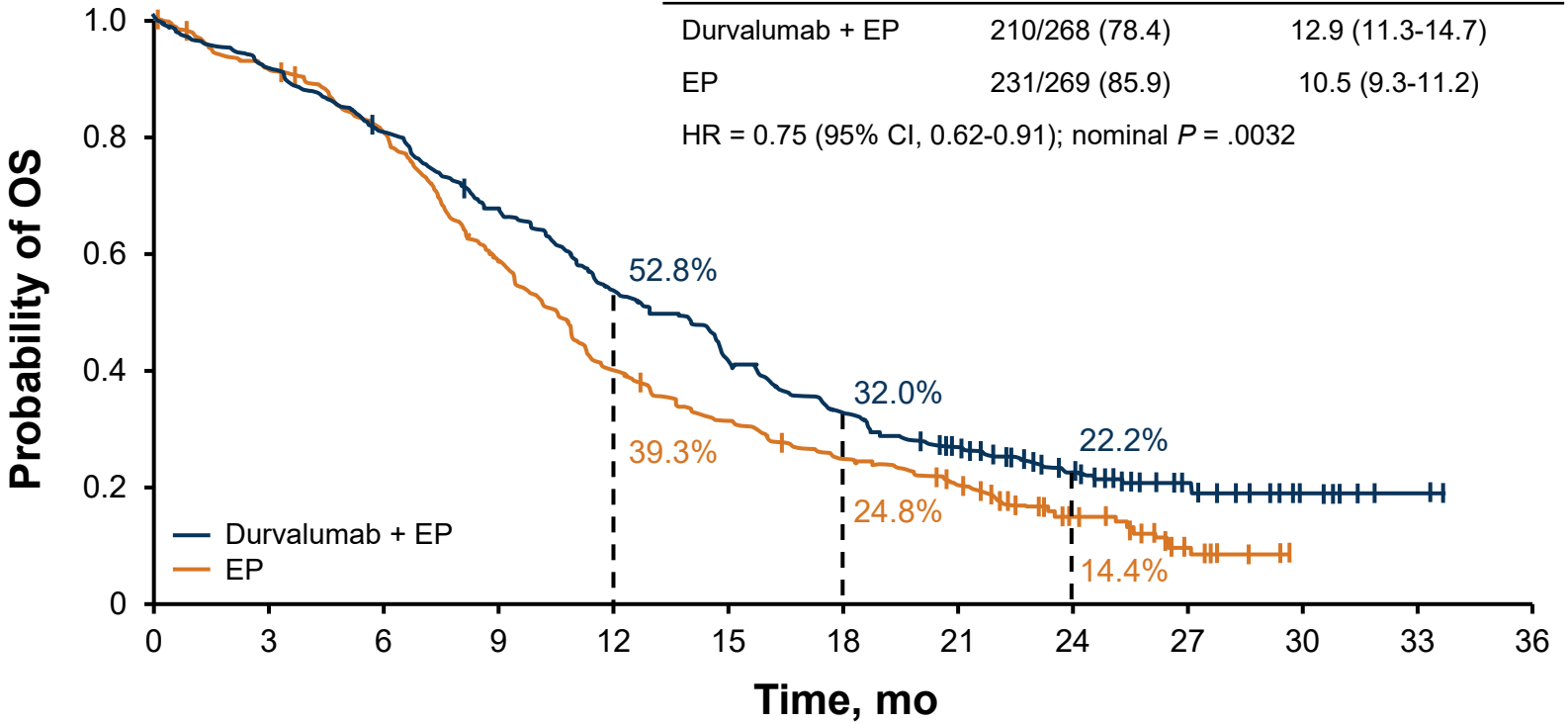
	IMpower133	CASPIAN		KEYNOTE-604	EA5161
		Durvalumab	Durvalumab/ Tremelimumab		
Median PFS, mo HR (95% CI)	5.2 0.77 (0.62-0.96)	5.1 0.78 (0.65-0.94)	4.9 0.84 (0.70-1.01)	4.5 0.75 (0.61-0.91)	5.5 0.68 (0.48-1.0)
Median OS, mo HR (95% CI)	12.3 0.70 (0.54-0.91)	13 0.73 (0.59-0.91)	10.4 0.82 (0.68-1.00)	10.8 0.80 (0.64-1.00)	11.3 0.67 (0.46-0.98)
12-mo OS, %	51.7	52.8	43.8	45.1	~48
24-mo OS, %	~22	22.2	23.4	22.5	NR

ICI, immune checkpoint inhibitor; NR, not reached; OS, overall survival; PFS, progression-free survival; SCLC, small cell lung cancer.

CASPIAN: OS for Durvalumab + EP vs EP[1]

	Events, n/N (%)	Median (95% CI), mo
Durvalumab + EP	210/268 (78.4)	12.9 (11.3-14.7)
EP	231/269 (85.9)	10.5 (9.3-11.2)

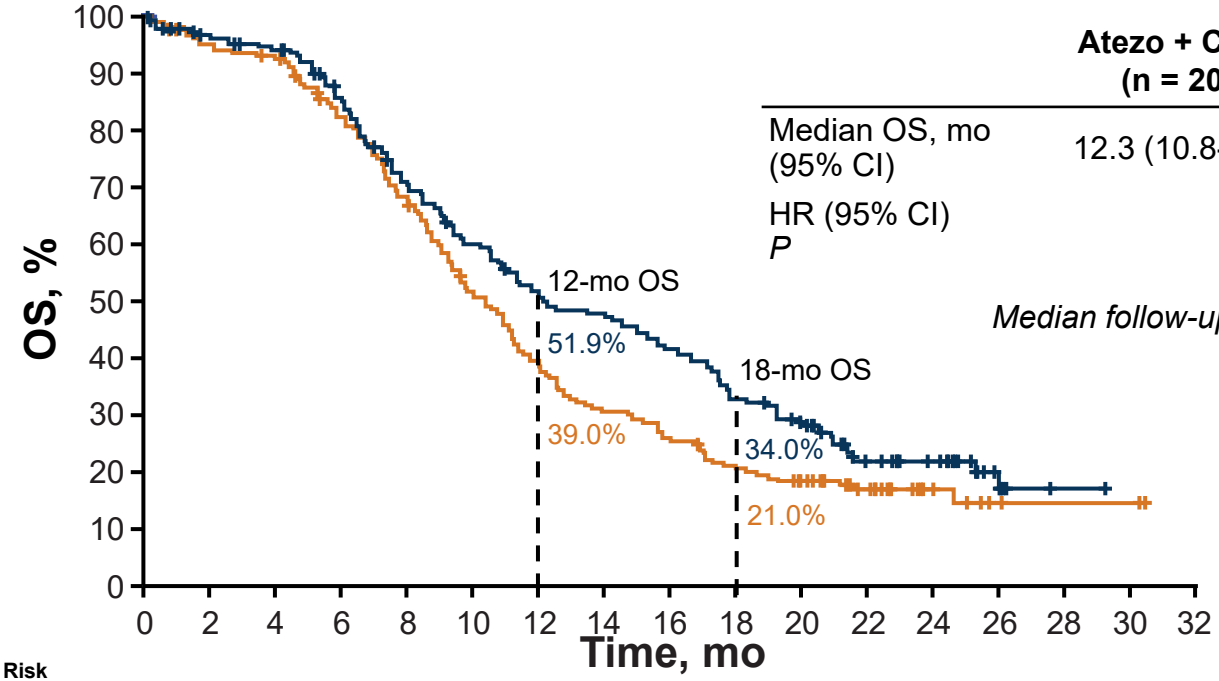
HR = 0.75 (95% CI, 0.62-0.91); nominal *P* = .0032



CI, confidence interval; EP, etoposide and carboplatin; HR, hazard ratio; OS, overall survival.

1. Paz-Ares LG et al. ASCO 2020. Abstract 9002.

IMpower133: Updated OS (Coprimary Endpoint)[1]



	Atezo + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8-15.8)	10.3 (9.3-11.3)
HR (95% CI)	0.76 (0.60-0.95)	
P	.0154[a]	

Median follow-up, 22.9 months

No. at Risk

Atezo + 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

Atezo, atezolizumab; CCOD, clinical cutoff date; CI, confidence interval; CP, carboplatin; ET, etoposide; HR, hazard ratio; OS, overall survival.
CCOD 24 January 2019.
[a] *P* value is provided for descriptive purposes.
1. Reck M et al. ESMO 2019. Abstract 2374.

Value Framework Tools

- Are value framework tools ready in the United States to help payors and providers drive more cost-effective treatments?
  - Cancer treatments seem to be significant drivers of innovation and cost
- Institute for Clinical and Economic Review (ICER)
- ASCO value framework
- National Comprehensive Cancer Network (NCCN) evidence blocks
- Memorial Sloan Kettering (Abacus)

ASCO Value Framework: Adjuvant and Advanced Disease[1]

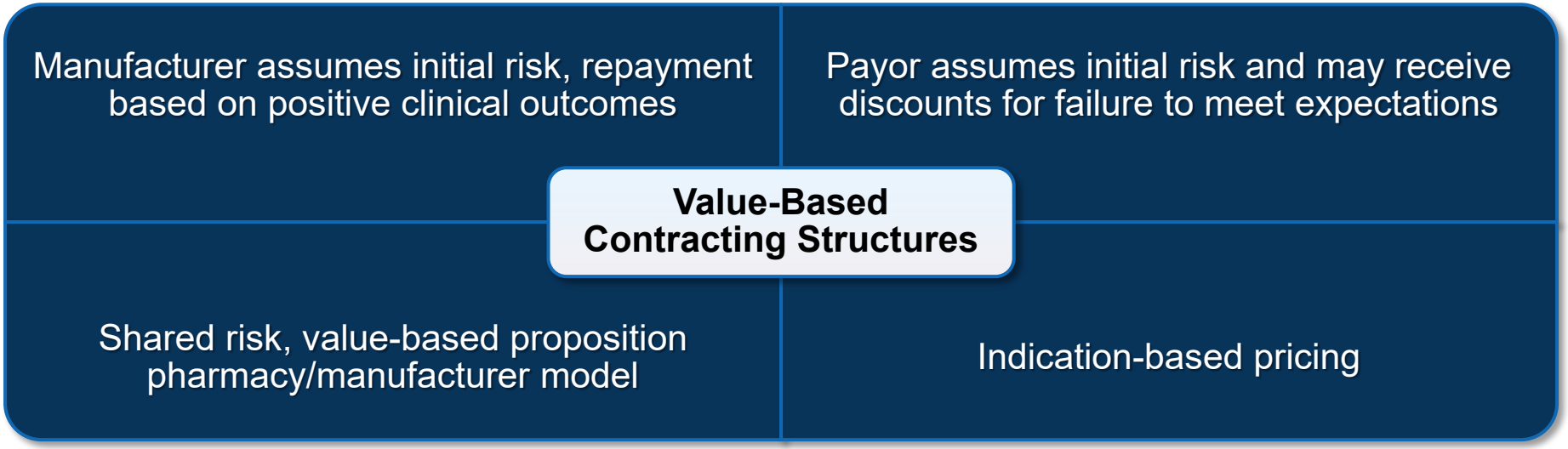
Item	Points	Notes
Clinical benefit (OS, PFS, RR)	Up to 80 points	Reflects endpoint and magnitude of benefit; preference given to OS if available
Toxicity	±20 points	Rate of grade 3-5 toxic effects with treatment relative to SOC
Bonus points		
Palliation	10 points	– If treatment improves symptoms
Time off all treatment	<20 points	– For increased time off all treatment

- **Cost per month:** no points
- **Total:** up to 100 points (adjuvant disease) or 130 points (advanced disease)

ASCO, American Society of Clinical Oncology; OS, overall survival; PFS, progression-free survival; RR, response rate; SOC, standard of care.

1. https://www.asco.org/practice-policy/cancer-care-initiatives/value-cancer-care.

Options for Structuring Value-Based Contracting



- Medication cost for each individual indication should be aligned with degree of clinical benefit
- When drug is used for low-efficacy indications, initial payment for the drug is low and manufacturer has opportunity to earn back payment based on positive treatment outcomes
- Repayment structure is based on risk calculation

Bevacizumab as an Example[1]

- Manufacturer collaborated with payor on an outcome-based contract for bevacizumab (category 1 recommendation by NCCN guidelines for NSCLC treatment)
- Payor received rebates if patients did not achieve progression-free status at defined timepoints
- Rebate was calculated with equation, taking into consideration actual survival, expected survival, duration of treatment, and risk-sharing percentage

Median PFS for 1L disease in pivotal RCT	6 mo
Expected PFS	6 mo
Patient actual assessments	
Actual PFS	3 mo
Goal/missed by/unrealized benefit	3 mo
Risk-sharing agreement if median PFS is not met	50%
Realized benefit	3/6 = 50%
Unrealized benefit	3/6 = 50%
Duration of treatment	3 mo
Cost/month	$10,000

Risk-Share Calculation

$$\frac{\text{(Expected - Actual)}}{\text{Expected}} \times \text{Risk Share \%} \times \text{Treatment Duration} \times \text{Cost/Month} = \text{Refund amount}$$

$$\frac{(6 - 3)}{6} \times 50\% \times 3 \times \$10{,}000 = \$7{,}500 \text{ rebate}$$

1L, first line; NCCN, National Comprehensive Cancer Network; NSCLC, non–small cell lung cancer; PFS, progression-free survival; RCT, randomized controlled trial.

1. https://www.healthaffairs.org/do/10.1377/hblog20170403.059442/full.

NICE Position on Atezolizumab for ES-SCLC

January 2020[1]

Atezolizumab + carboplatin and etoposide is not recommended, within its marketing authorization, for untreated ES-SCLC in adults

July 2020[2]

Atezolizumab + carboplatin and etoposide is recommended as an option for untreated ES-SCLC in adults, only if

- They have an ECOG PS of 0 or 1, ***AND***
- The company provides atezolizumab according to the commercial arrangement

ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; NICE, National Institute for Health and Care Excellence.

1. https://www.nice.org.uk/guidance/ta638/documents/129. 2. https://www.nice.org.uk/guidance/ta638.

Unmet Need for Research Gaps and Opportunities in SCLC Based on SCLC Working Group[1]

Research Gaps	Biology and Genetics/Genomics
• Tumor heterogeneity • Mechanisms of metastasis • Molecular drivers of resistance	• Molecular characterization of late-stage disease, metastases, pre- and post-therapy, and exceptional responders
Models	**Prevention/Screening/Diagnosis**
• Preclinical models specific to therapeutic targets and development of resistance, including models for testing of immunotherapy approaches	• Molecularly targeted imaging agents for detection and/or response assessment
Therapy and Resistance	
• New approaches to clinical trials in SCLC • Studies focused on understanding the unique features of SCLC that could be used to develop new therapeutics • Methods to improve palliative and supportive care, including optimization of pain management and end-of-life care	

SCLC, small cell lung cancer.

1. https://deainfo.nci.nih.gov/advisory/ctac/0719/Att%2013_SCLC%20PWG%20Final%20Report_CTAC%20071719_v2.pdf.

Future Pipeline Agents

Agent/Route	Clinical Trial ID	Phase	Therapeutic Approach/Target	Clinical Setting
Atezolizumab IV	NCT03811002	3	PD-L1 inhibitor	LS-SCLC
Durvalumab IV ± tremelimumab	NCT03043872	3	PD-L1 inhibitor ± CTLA-4 inhibitor	LS-SCLC
Trilaciclib IV	NCT03041311 NCT02514447 NCT02499770	PDFUA date: 2/15/21	CDK 4/6 inhibitor	Myelopreservation ES-SCLC
Tiragolumab IV + atezolizumab + EP	NCT04256421	3	Anti-TIGIT antibody	ES-SCLC
Niraparib PO	NCT03516084	3	PARP inhibitor	Maintenance ES-SCLC first line
Nanoliposomal pegylated irinotecan IV	NCT03088813	3	Topoisomerase I inhibitor	LS-SCLC or ES-SCLC second line
RRx001 IV	NCT03699956	3	Immunotherapy targeting CD47–SIRPα	SCLC third line
Abemaciclib PO	NCT04010357	2	CDK 4/6 inhibitor	Retinoblastoma wild-type ES-SCLC

CDK4, cyclin-dependent kinase 4; CDK6, cyclin-dependent kinase 6; CTLA-4, cytotoxic T-lymphocyte–associated protein 4; EP, etoposide; ES-SCLC, extensive-stage small cell lung cancer; IV, intravenous; LS-SCLC, limited-stage small cell lung cancer; PARP, poly ADP-ribose polymerase; PDFUA, Prescription Drug User Fee Act; PD-L1, programmed cell death ligand 1; PO, orally; SCLC, small cell lung cancer; SIRPα, signal regulatory protein α; TIGIT, T-cell immunoreceptor with Ig and ITIM domains.

Durva ± Treme After Concurrent Chemoradiotherapy for Patients With Limited-Stage SCLC: The ADRIATIC Study[1]

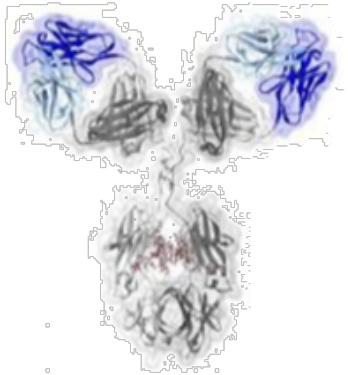
Arm	Intervention
Experimental: durvalumab + placebo Durvalumab monotherapy (1,500 mg IV Q4W in combination with placebo saline solution IV Q4W for up to 4 doses/cycles each, followed by durvalumab 1,500 mg Q4W); first durvalumab dose will be 4 wk after final dose of durvalumab in combination with placebo saline solution	Durvalumab IV Placebo IV
Experimental: durvalumab + tremelimumab Durvalumab in combination with tremelimumab: durvalumab (1,500 mg IV) Q4W in combination with tremelimumab (75 mg IV) Q4W for up to 4 doses/cycles each, followed by durvalumab 1,500 mg Q4W; first durvalumab dose will be 4 wk after final dose of durvalumab in combination with tremelimumab	Durvalumab IV Tremelimumab IV
Comparator: placebo + placebo Placebo: placebo saline solution (IV) Q4W in combination with a second placebo saline solution (IV) Q4W for up to 4 doses/cycles each, followed by a single placebo saline solution Q4W; first placebo saline solution monotherapy dose Q4W will be 4 wk after the final dose of the 2 placebo saline solutions in combination	Placebo IV

Durva, durvalumab; IV, intravenously; Q4W, every 4 weeks; SCLC, small cell lung cancer; treme, tremelimumab.

1. https://clinicaltrials.gov/ct2/show/NCT03703297.

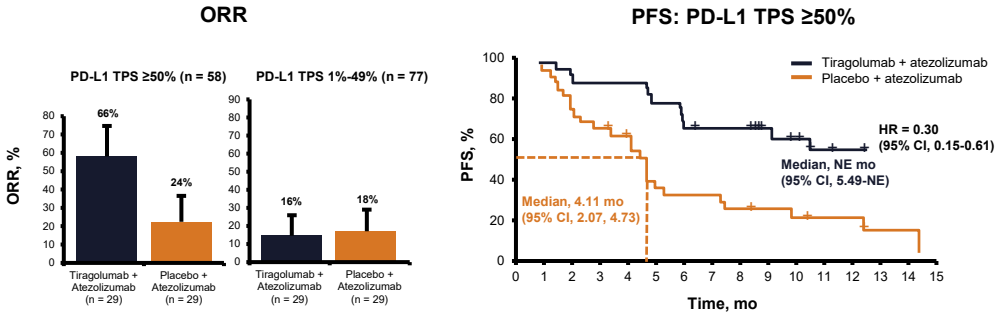
Tiragolumab + Atezolizumab in NSCLC and SCLC[1]

Anti-TIGIT mAb



- Fully human IgG1/kappa Ab with intact Fc region that blocks the binding of TIGIT to PVR
- Could restore antitumor response and could complement the activity of anti–PD-L1/PD-1 antibodies

Randomized Phase 3 (CITYSCAPE) in 1L NSCLC



- Tiragolumab + atezolizumab showed clinically meaningful improvement in ORR and PFS in the ITT population with a greater magnitude of improvement in the PD-L1 TPS ≥50% subgroup
- Tiragolumab + atezolizumab was well tolerated with a safety profile similar to the control arm
- Phase 3 in 1L PD-L1 + NSCLC (SKYSCRAPER-01), 1L ES-SCLC (SKYSCRAPER-02), and stage III NSCLC (SKYSCRAPER-03) ongoing

1L, first line; Ab, antibody; CI, confidence interval; ES-SCLC, extensive-stage small cell lung cancer; Fc, fragment crystallizable; HR, hazard ratio; IgG1, immunoglobulin G1; ITT, intent to treat; mAb, monoclonal antibody; NE, not evaluable; NSCLC, non–small cell lung cancer; ORR, objective response rate; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PVR, poliovirus receptor; SCLC, small cell lung cancer; TIGIT, T-cell immunoreceptor with Ig and ITIM domains; TPS, tumor proportion score.

1. Rodriguez-Abreu D et al. ASCO 2020. Abstract 9503.

Trilaciclib[1]

- Data pooled from patients enrolled in the studies are outlined in the table below
  - In each study, patients received IV trilaciclib 240 mg/m^2 or placebo on each day prior to chemo administration

Study	Patient Population	Treatment Schedule
G1T28-02 (NCT0249970)	1L ES-SCLC	Trilaciclib or placebo on d 1-3 of each 21-d EP cycle
G1T28-05 (NCT03041311)	1L ES-SCLC	Trilaciclib or placebo on d 1-3 of each 21-d EPA cycle for up to 4 cycles (induction), followed by A every 21 d (maintenance)
G1T28-03 (NCT02514447)	2/3L ES-SCLC	Trilaciclib or placebo on d 1-5 of each 21-d topotecan cycle

- Effect of trilaciclib evaluated in terms of myelopreservation and antitumor efficacy
  - Primary myelopreservation endpoints were duration of grade 4 neutropenia in cycle 1 and occurrence of severe neutropenia across the treatment period
    - Secondary myelopreservation endpoints were assessed by hematopoietic lineage
- Antitumor efficacy measures included ORR, PFS, and OS

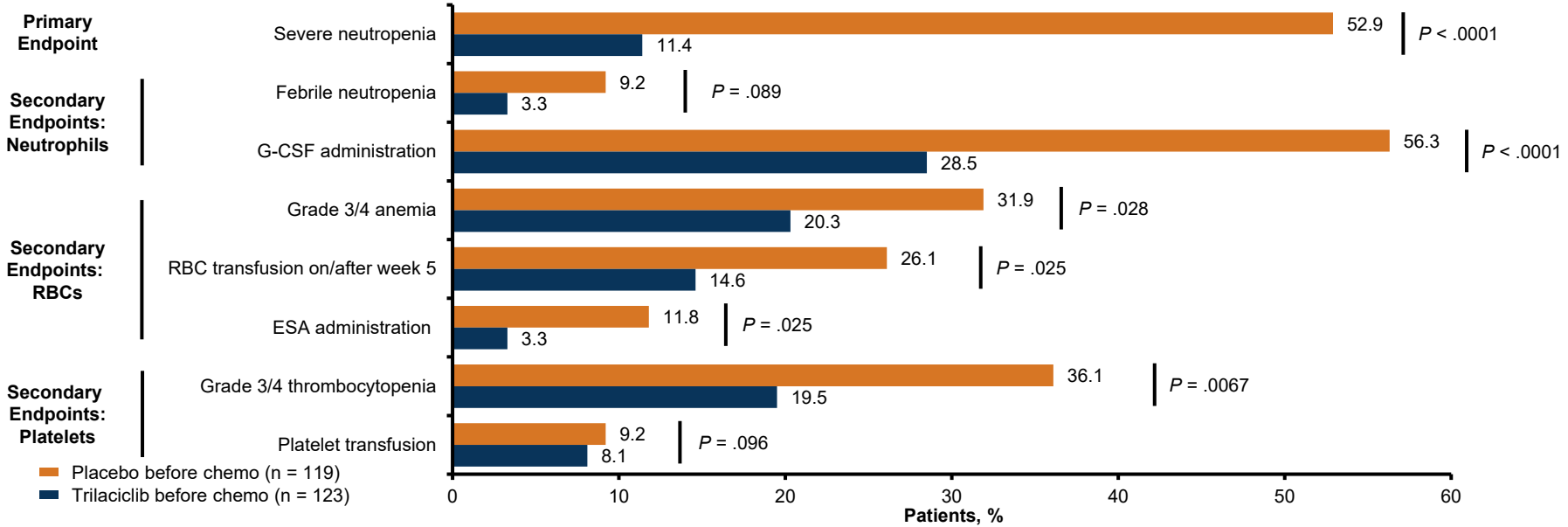
A, atezolizumab; Chemo, chemotherapy; EP, etoposide and carboplatin; EPA, etoposide, carboplatin, and aztezolizumab; ES-SCLC, extensive-stage small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

1. Weiss J et al. American Association for Cancer Research Annual Meeting 2020 (AACR 2020). Poster 384.

Myelopreservation Endpoints in the Pooled Efficacy Analysis[1]

Myelopreservation efficacy of trilaciclib administered before chemo

- Addition of trilaciclib before chemo significantly decreased most measures of multilineage CIM and the need for supportive care interventions
- The primary endpoints of DSN in cycle 1 (a surrogate for febrile neutropenia and infections) and occurrence of SN were both significantly reduced with trilaciclib vs placebo
- Mean (SD) DSN was 0 (1.8) days with trilaciclib vs 4 (5.1) days with placebo ($P < .0001$)



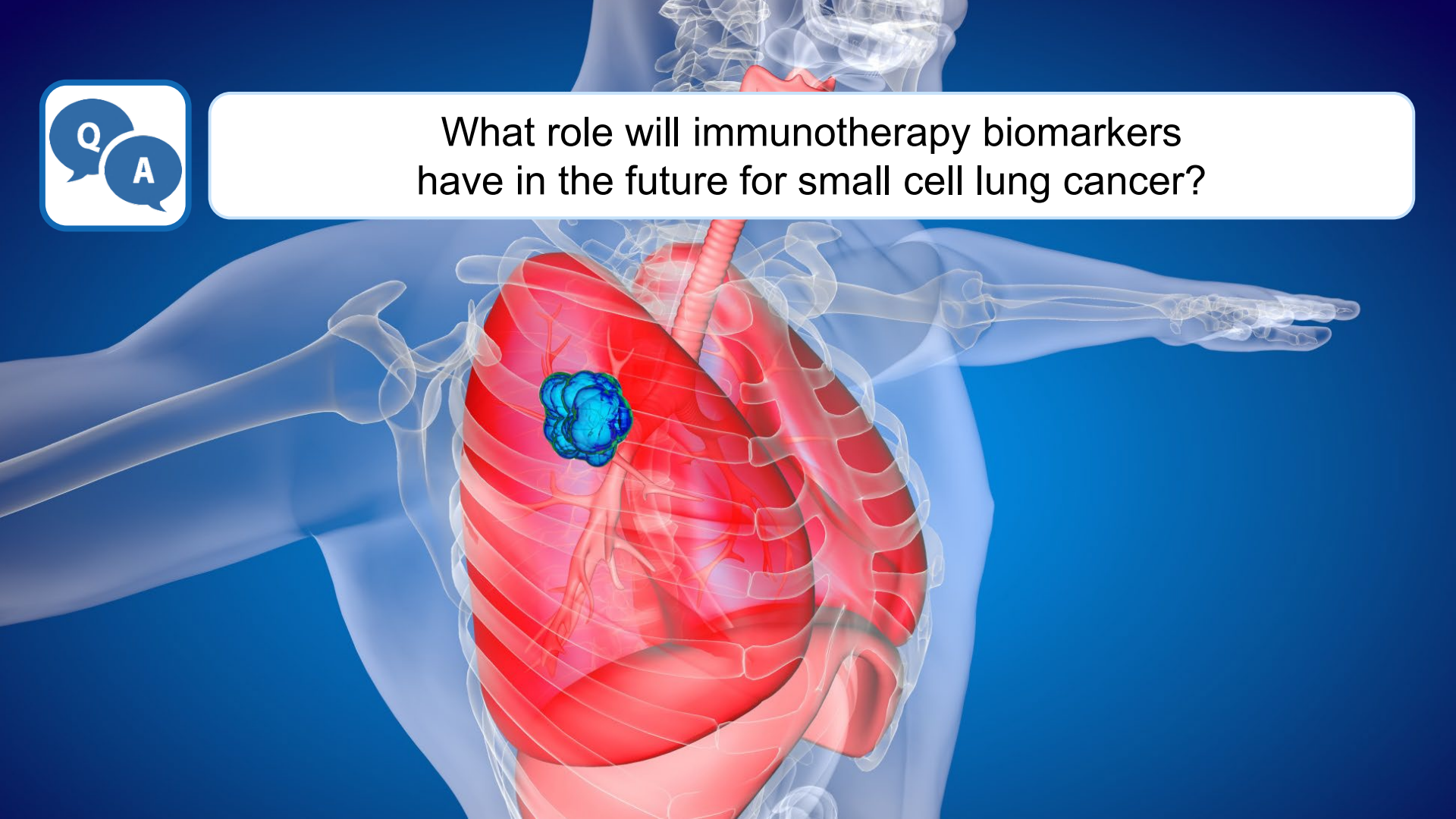
Chemo, chemotherapy; CIM, chemotherapy-induced myelosuppression; DSN, duration of severe neutropenia; ESA, erythropoietin-stimulating agent; G-CSF, granulocyte colony-stimulating factor; RBC, red blood cell; SD, standard deviation; SN, severe neutropenia.

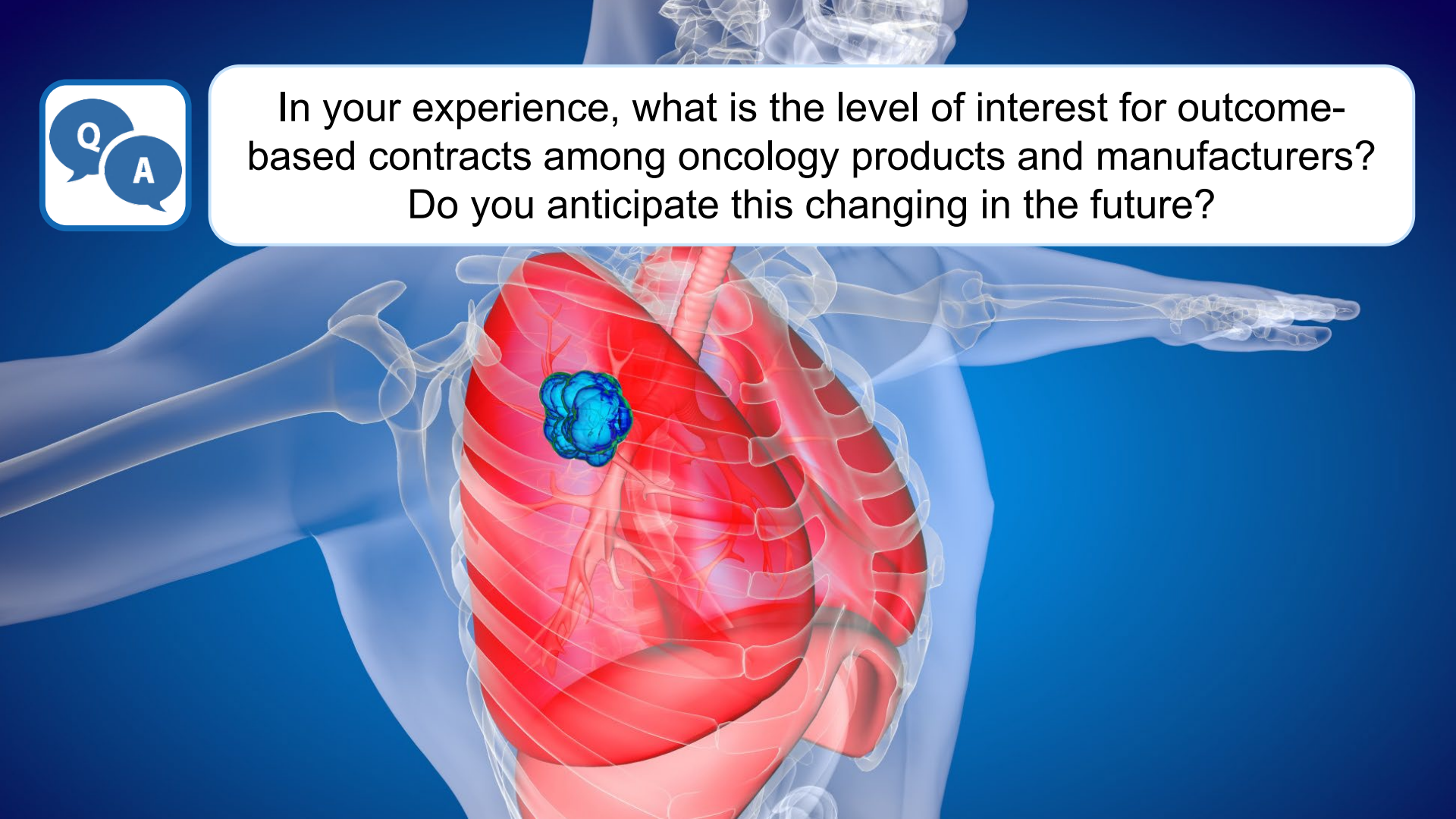
1. Weiss J et al. AACR 2020. Poster 384.

Conclusions

- Significant innovations in treatments—immunotherapies in particular—have helped make progress against SCLC as a recalcitrant cancer in the past 5 years
- There continues to be progress with focus on incorporating immunotherapy in early-stage disease
- There are unique immunotherapy combinations and other novel agents under investigation
- Total cost-of-care models and value-based frameworks are lacking for this dramatically underserved malignancy to help patients, providers, pharmacists, and payors in choosing appropriate cost-effective treatments, as the market is forecasted to grow to $3.8 billion by 2028

SCLC, small cell lung cancer.


Q
A
What role will immunotherapy biomarkers
have in the future for small cell lung cancer?



In your experience, what is the level of interest for outcome-based contracts among oncology products and manufacturers? Do you anticipate this changing in the future?