# Updates in Small Cell lung cancer

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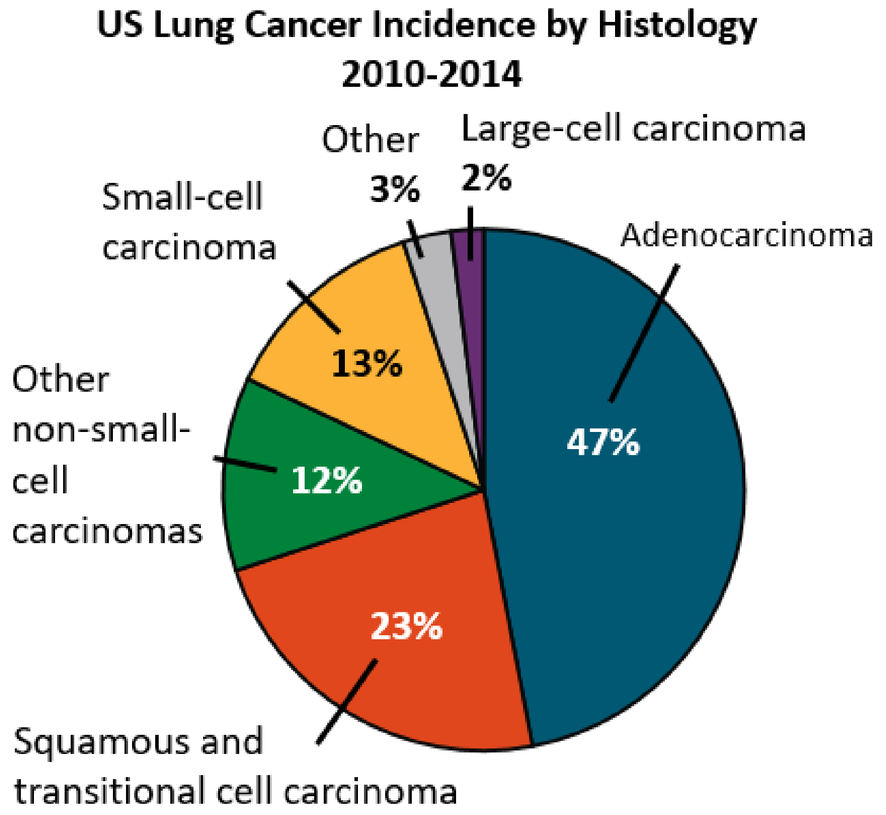
# Disclosure of Conflicts of Interest

Abhirami Vivekanandarajah, MD, has the following financial relationships to disclose:

- Speaker – Astra Zaneca
- Consultant – Aptitude

# Small Cell Lung Cancer

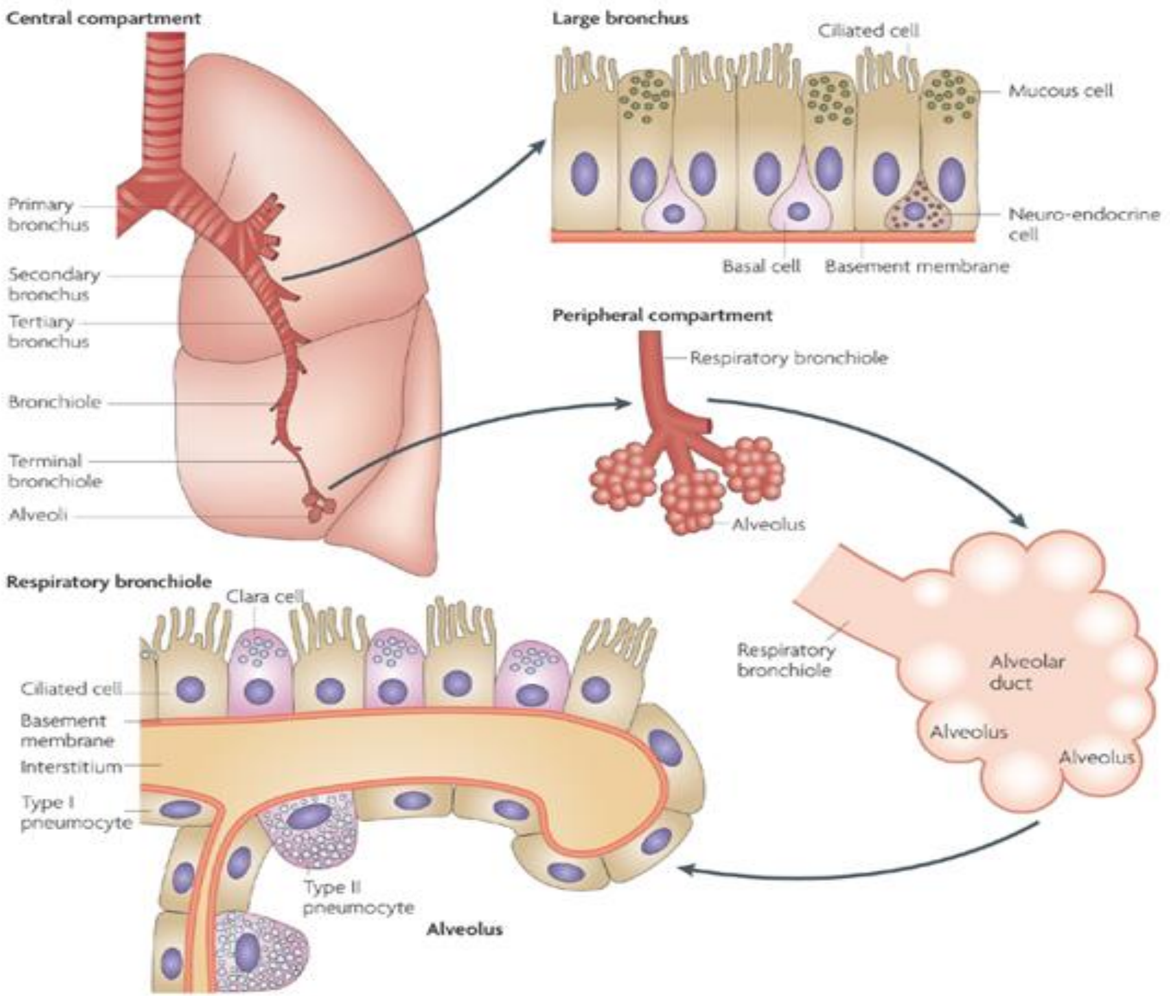
- SCLC accounts for ~ 13% of all lung cancers in the US
- Previously called oat-cell carcinoma
- Associated with a history of significant tobacco use
- Unique biology: rapid proliferation, abrupt presentation, bulky central tumor, hematogenous metastases at onset
- Poor outcomes




Oronsky. Neoplasia. 2017;19:842. Alvarado-Luna. Transl Lung Cancer Res. 2016;5:26. Howlander. SEER Cancer Statistics Review, 1975-2014.

# Pathogenesis of Lung Cancer

| Other Putative Causes | Relative Risk |
|---|---|
| 2nd-hand smoke | 1.2 |
| Radon | 10 |
| Cooking oil vapors | 2.1 |
| Indoor coal and wood burning | 2 |
| Genetic | 2 |
| Viral-HPV | 10 |

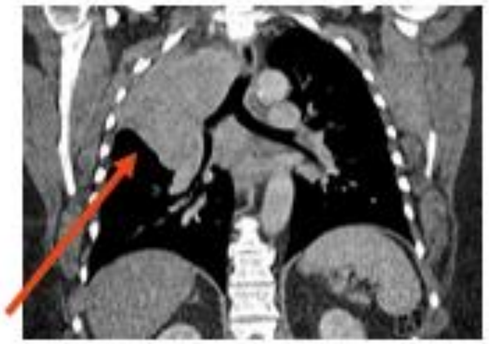


# Clinical Presentation

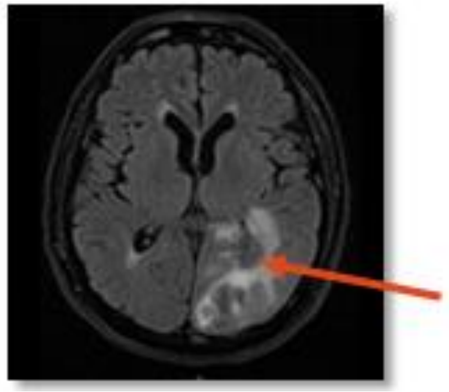
- Local symptoms: cough, 50%; dyspnea, 40%; chest pain, 35%; hemoptysis, 20%; hoarseness, 10%
- Distant symptoms: weight loss, 50%; weakness, 40%; anorexia, 30%; paraneoplastic syndrome, 15%; fever, 10%
- Paraneoplastic syndromes: ectopic hormone-associated syndromes, immune-mediated neurologic syndromes

| Metastatic Site, % | At Presentation | At Autopsy |
|---|---|---|
| Mediastinal LNs | 66-80 | 73-87 |
| Liver | 21-27 | 69 |
| Bone | 27-41 | 54 |
| Adrenal glands | 5-31 | 35-65 |
| Bone marrow | 15-30 | NA |
| Brain | 10-14 | 28-50 |
| Retroperitoneal LNs | 3-12 | 29-52 |
| Supraclavicular LNs | 17 | 42 |
| Pleural effusion | 16-20 | 30 |
| Contralateral lung | 1-12 | 8-27 |
| Soft tissues | 5 | 19 |

Chest CT

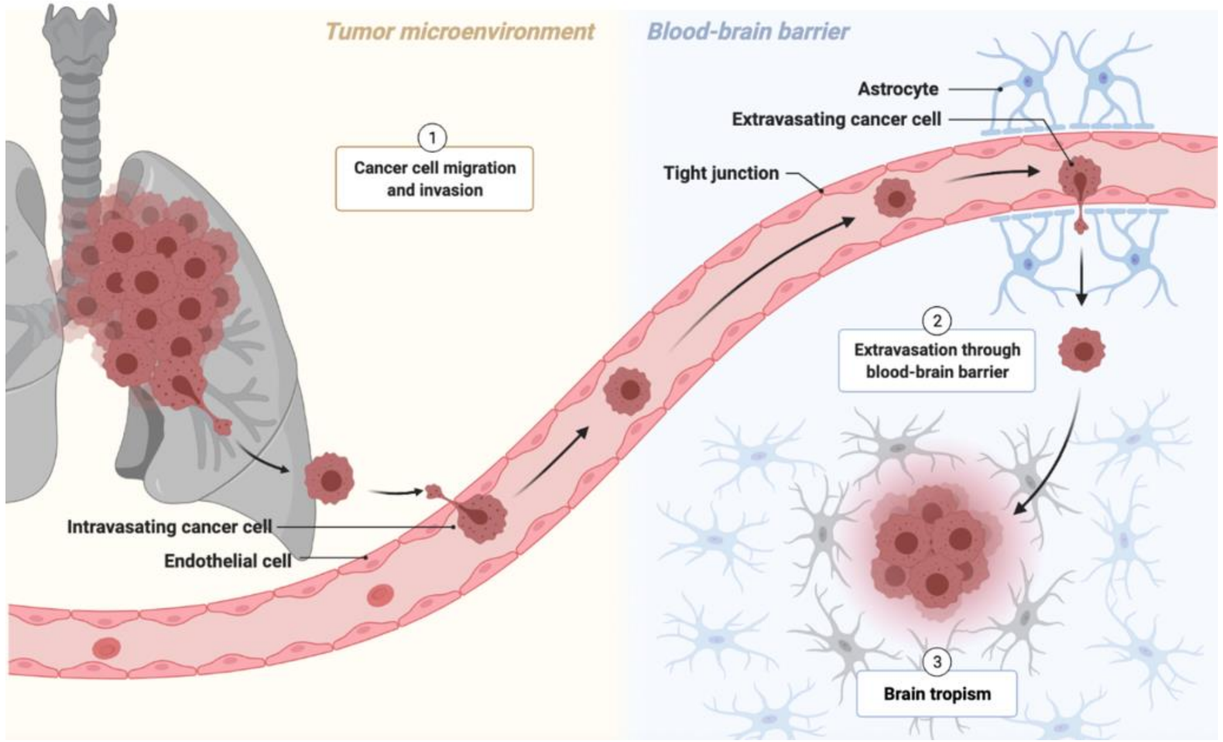


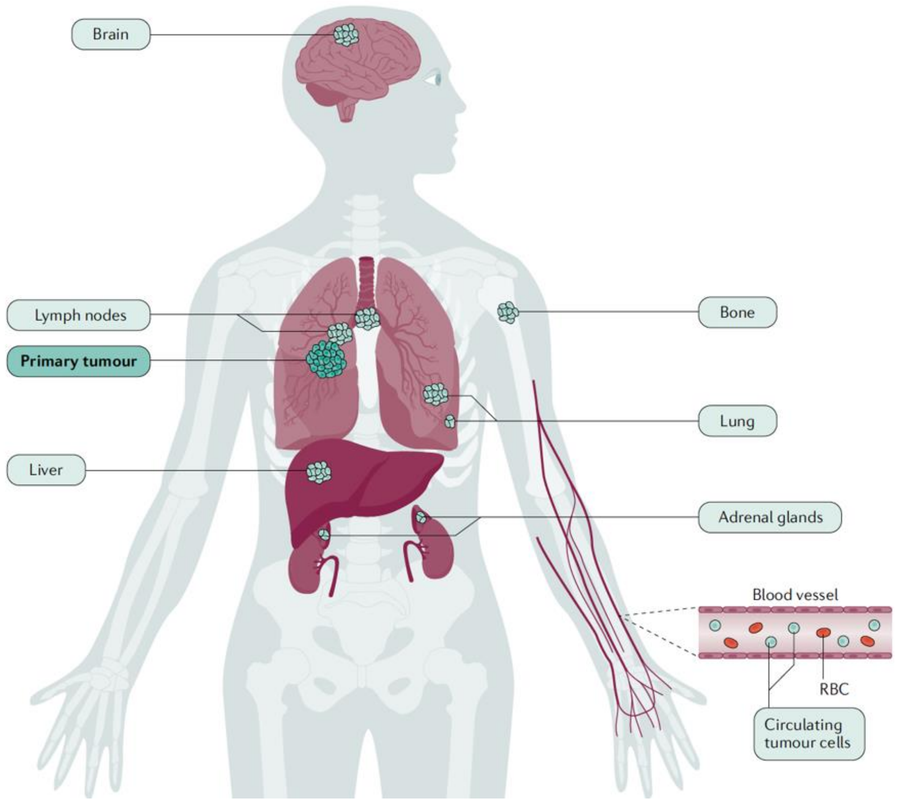
Brain MRI



Jackman. Lancet. 2005;366:1385. Images courtesy of Anna F. Farago, MD, PhD.

# Sites of metastases



# Staging – TNM staging

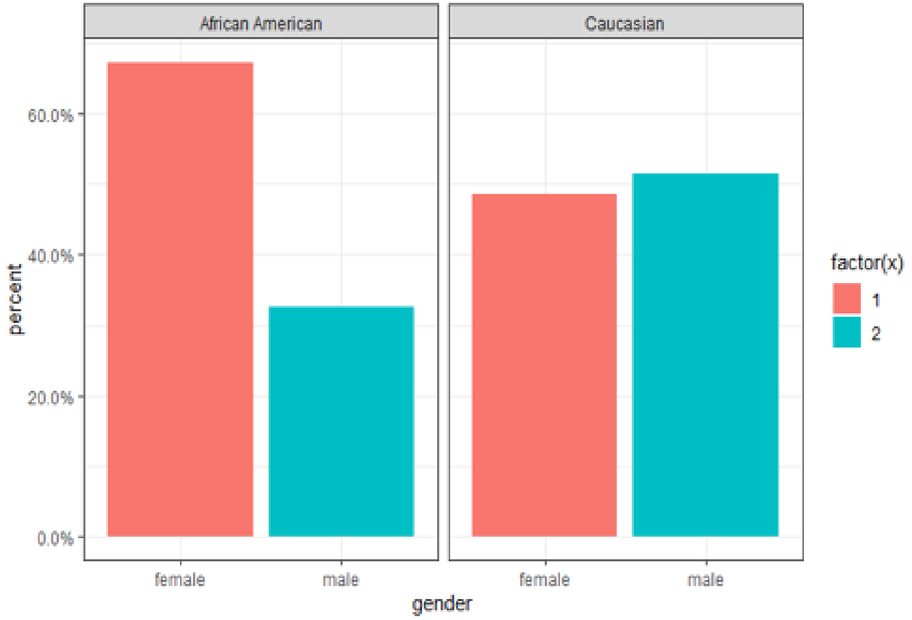
- Diagnosis by FNA or biopsy
- Staging workup
  - CT chest/abdomen/pelvis
  - Brain MRI
  - PET scan to rule out distant metastases

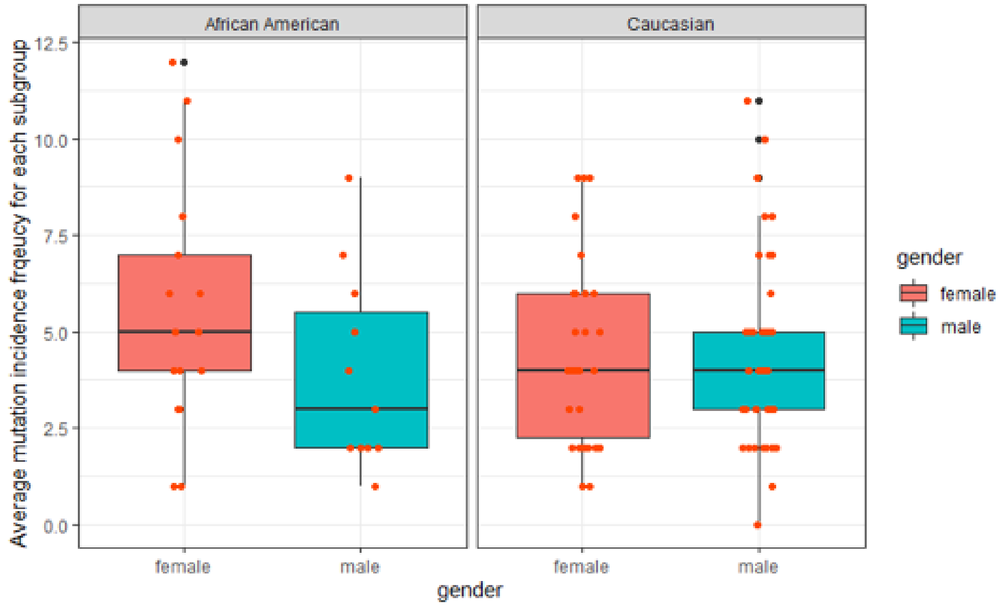
| TNM Staging | VA Staging | Incidence, % |
|---|---|---|
| T1-T2, N0, M0 (stage I) | Limited stage | ~ 5 |
| T any, N any, M0 (stage I-III) | Limited stage; disease burden contained within radiation field | ~ 30 |
| T any, N any, M1 (stage IV) | Extensive stage; disease burden beyond radiation field | ~ 65 |

Kalemkerian. Cancer Imaging. 2011;11:253. Alvarado-Luna. Transl Lung Cancer Res. 2016;5:26. Sabari. Nat Rev Clin Oncol. 2017;14:549

# Epidemiology of SCLC

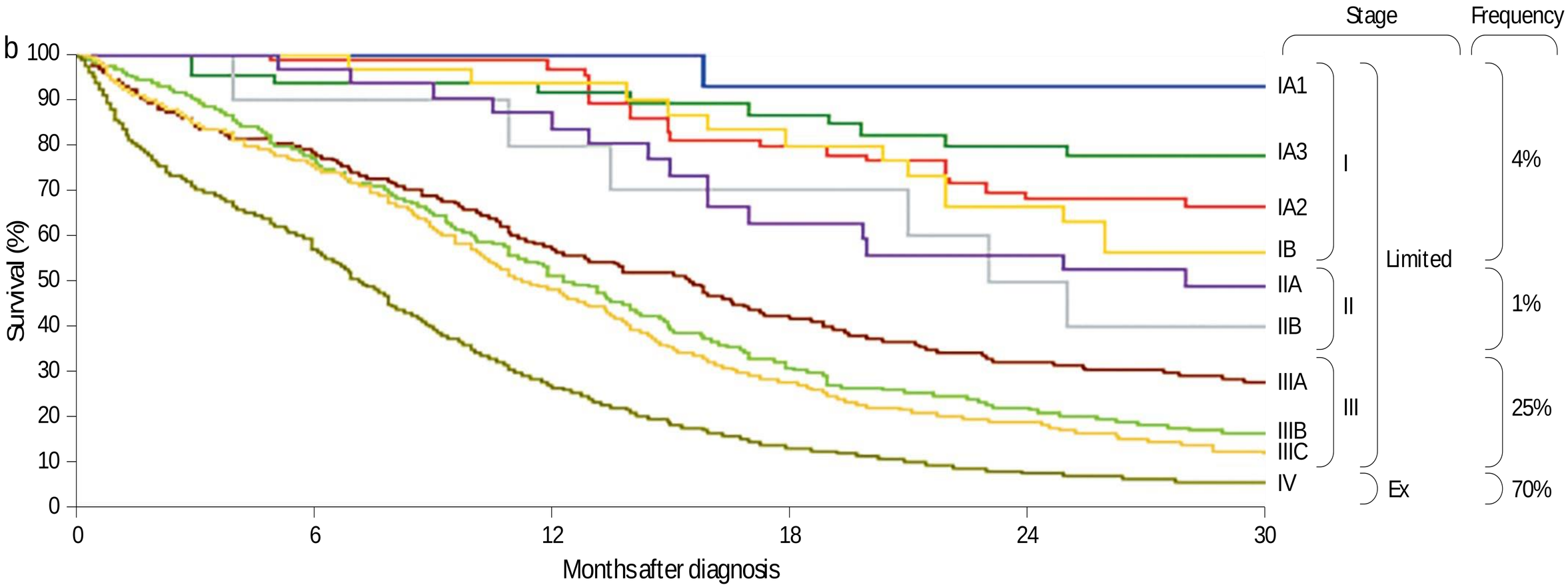
- 13% of all lung cancers = 20,000 – 30,000/yr in US



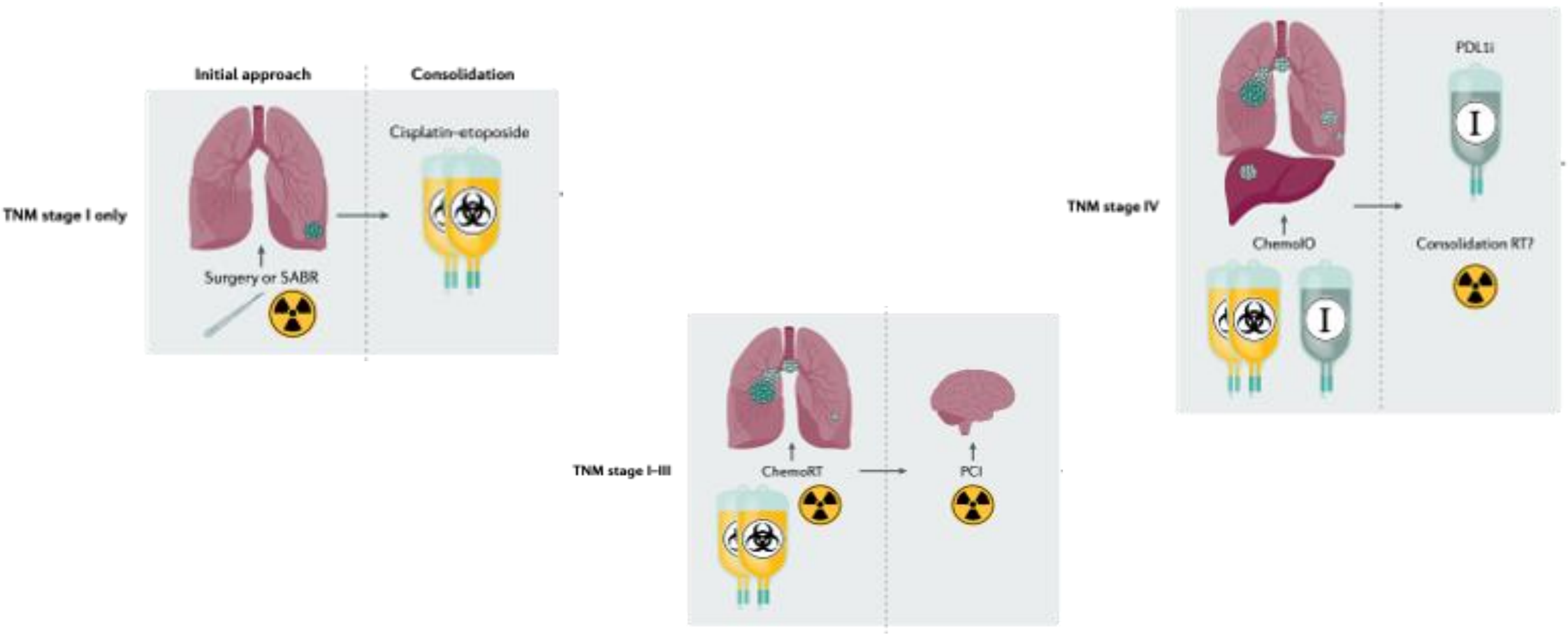




Bayal et. Al.

# Survival according to the stage



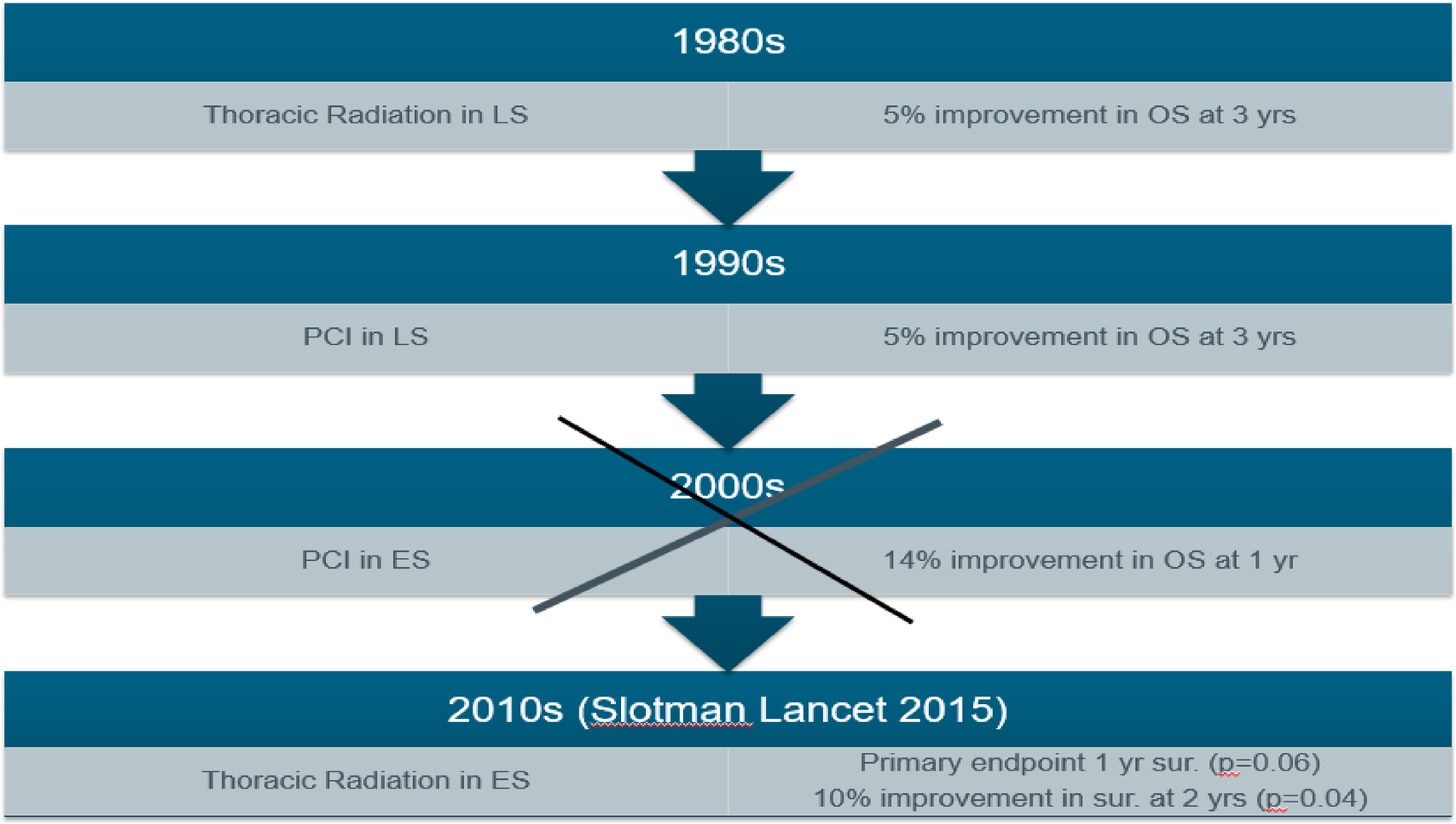
# Treatment


Initial approach
Consolidation
TNM stage I only
Cisplatin-etoposide
Surgery or SABR
TNM stage IV
PDL1i
I
ChemoIO
Consolidation RT?
I
TNM stage I–III
ChemoRT
PCI

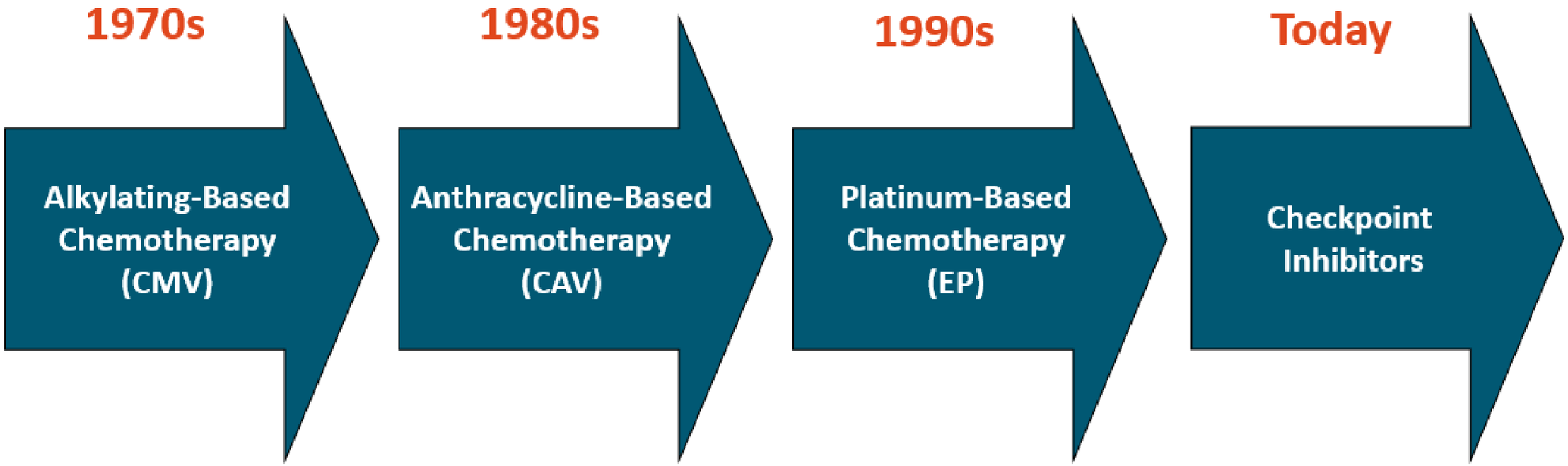
# Cisplatin Etoposide compared to other doublets

| Regimen | No of Trials | No. Patients | Results | Population studied |
|---|---|---|---|---|
| Cisplatin and Irinotecan | 3 | Trial 1 – Japan - 154<br>Trial 2 – Pfizer - 331<br>Trial 3 – SWOG -671 | Superior<br>Equivalent<br>Equivalent | Ext-SCLC |
| Carboplatin and Gemcitabine | 1 | 241 | Equivalent | Ext-SCLC and Lim-SCLC |
| Carboplatin and Etoposide | 1 | 220 | Equivalent | Ext-SCLC<br>Poor risk |
| Cisplatin and Topotecan | 1 | 780 | Equivalent | Ext-SCLC |
| Carboplatin and Pemetrexed | 1 | 909 | Inferior | Ext-SCLC |
| Carboplatin and Irinotecan | 1 | 209 | Equivalent | Ext-SCLC compared to carbo/etop |

# Overall Survival with Radiation

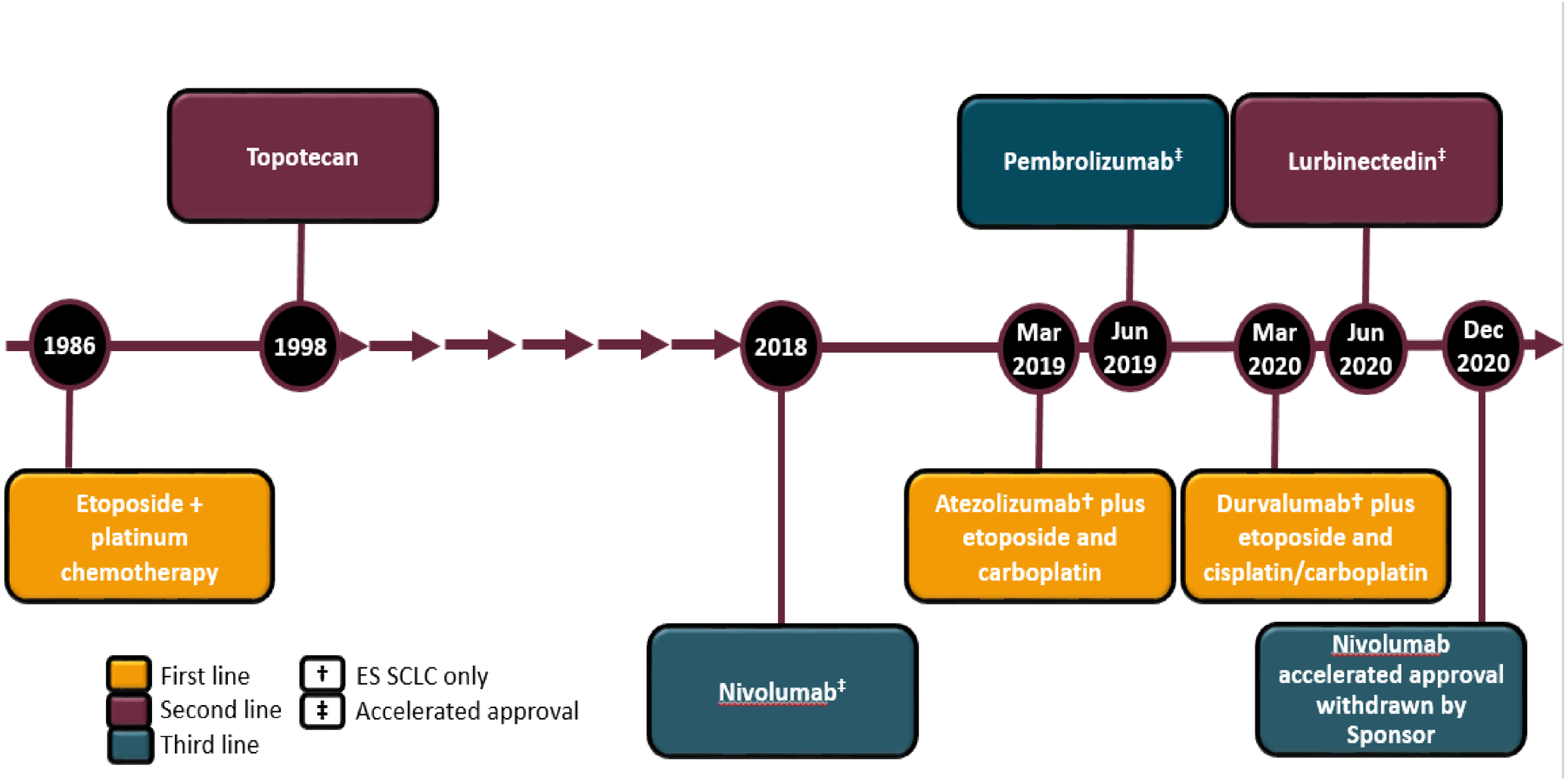


# Evolution of Systemic therapy in SCLC

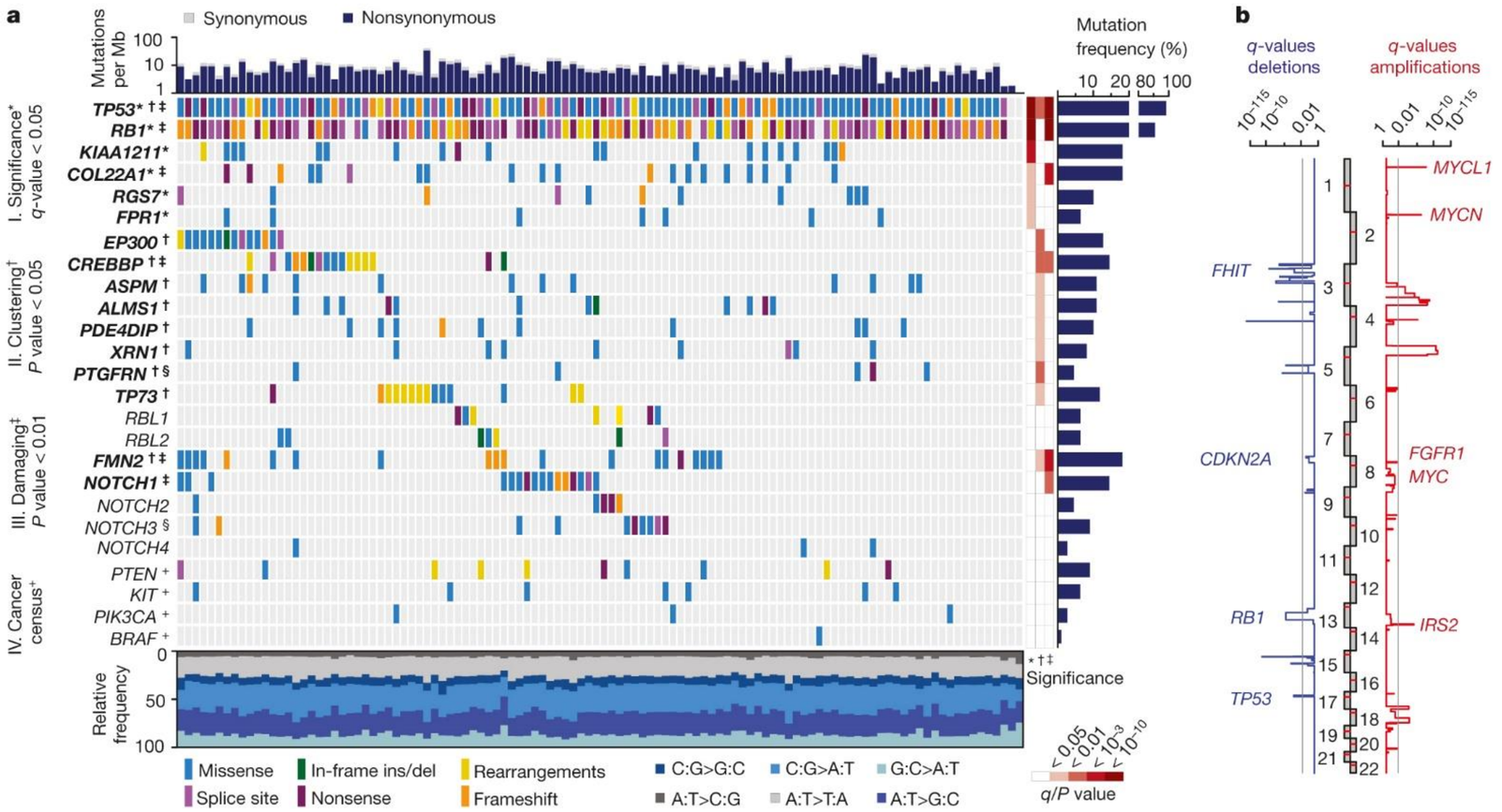



Sabari. Nat Rev Clin Oncol. 2017;14:549. Saleh. Immunotherapy. 2019;11:457

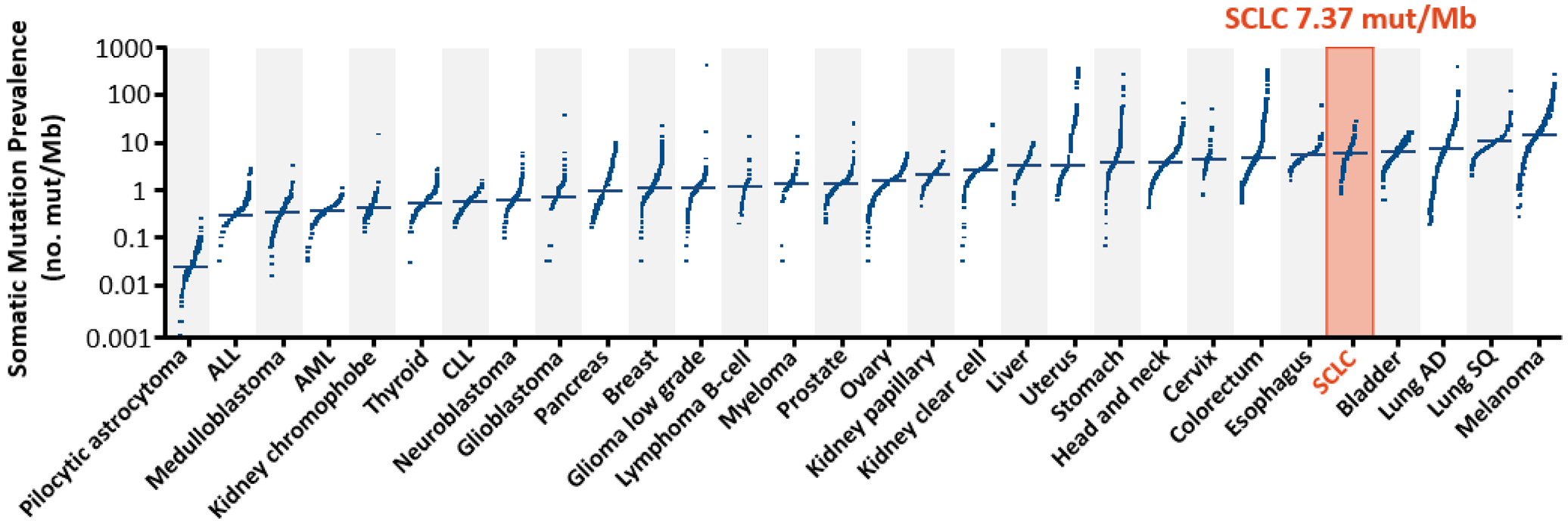
# Evolution of Systemic therapy in SCLC



# SCLC – lack of expression of driver mutations



# SCLC has high tumor mutational burden




Peifer. Nat Genet. 2012;44:1104. Alexandrov. Nature. 2013;500:415

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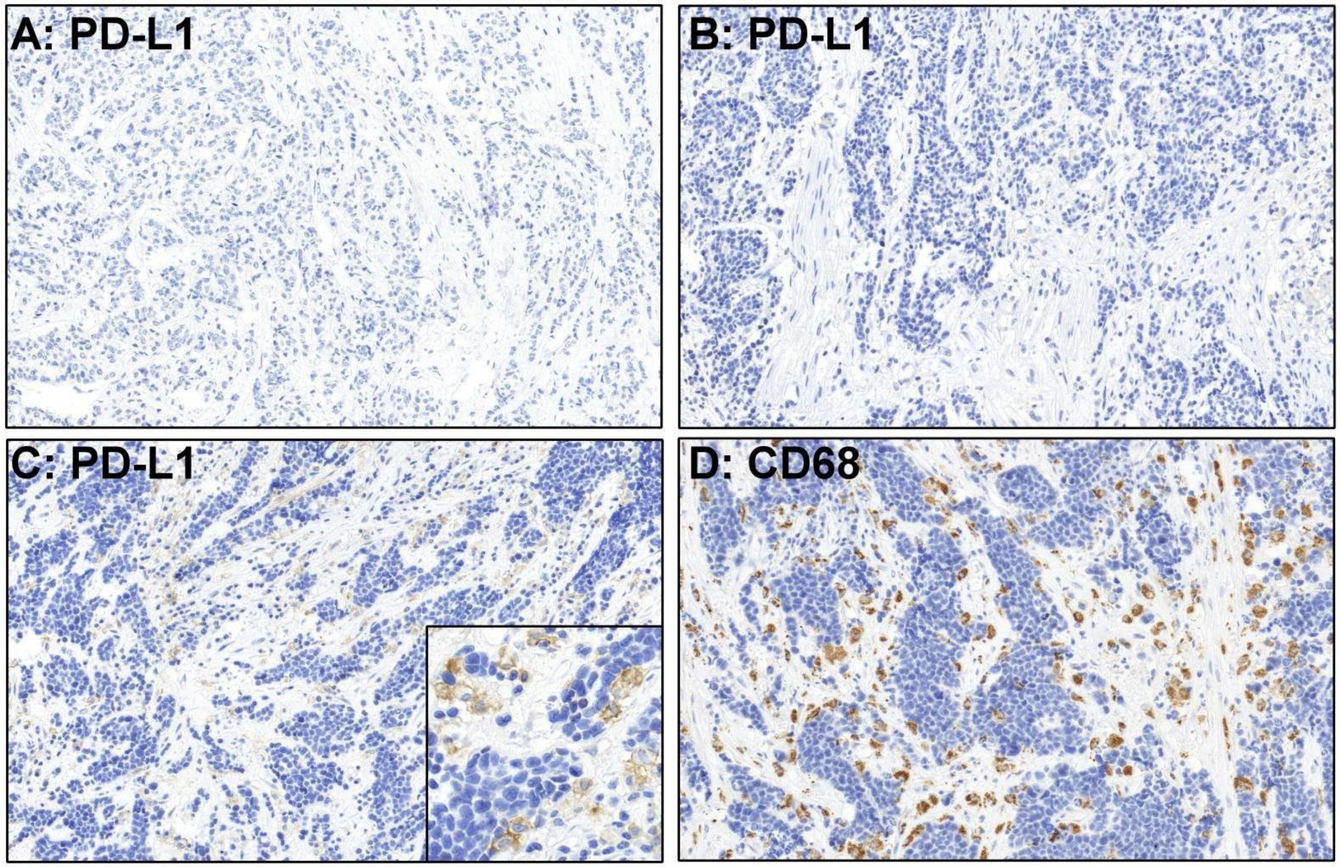
# PDL1 Expression

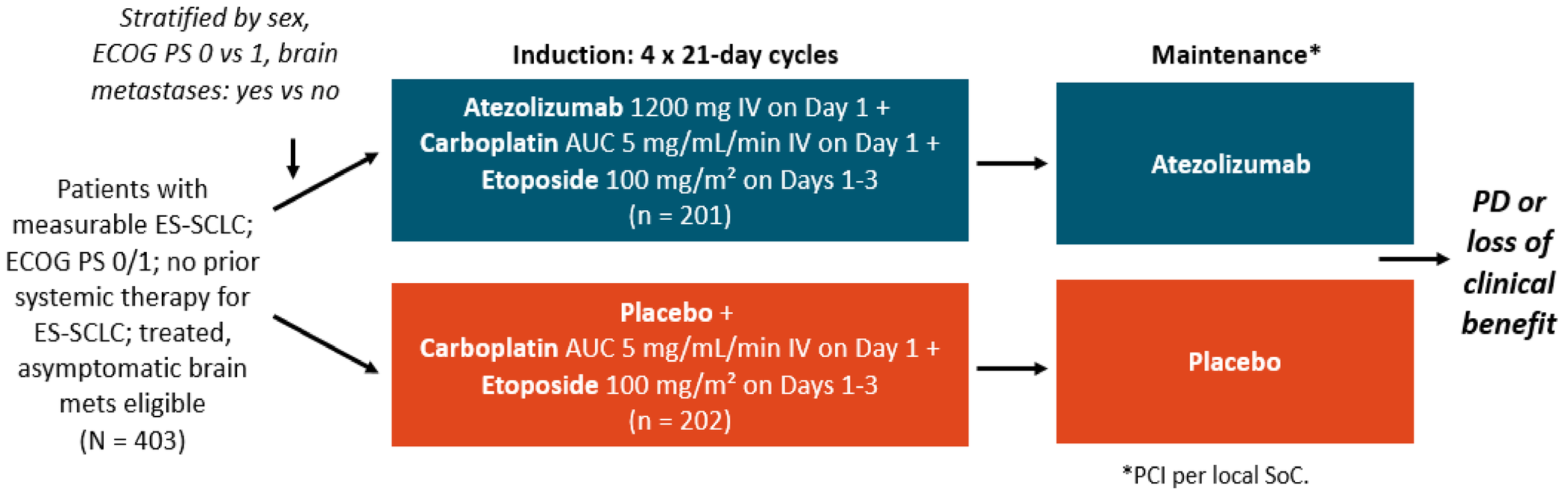



- No PD-L1 expression detected by IHC on tumor cells in 94 SCLC cases
- 18.5% of cases (17/92) showed PD-L1 expression in tumor-infiltrating macrophages
- 48% (45/94) of cases showed PD-1–positive T-lymphocytes

Schultheis. Eur J Cancer. 2015;51:421

# IMpower133: Atezolizumab + Chemotherapy for Advanced SCLC

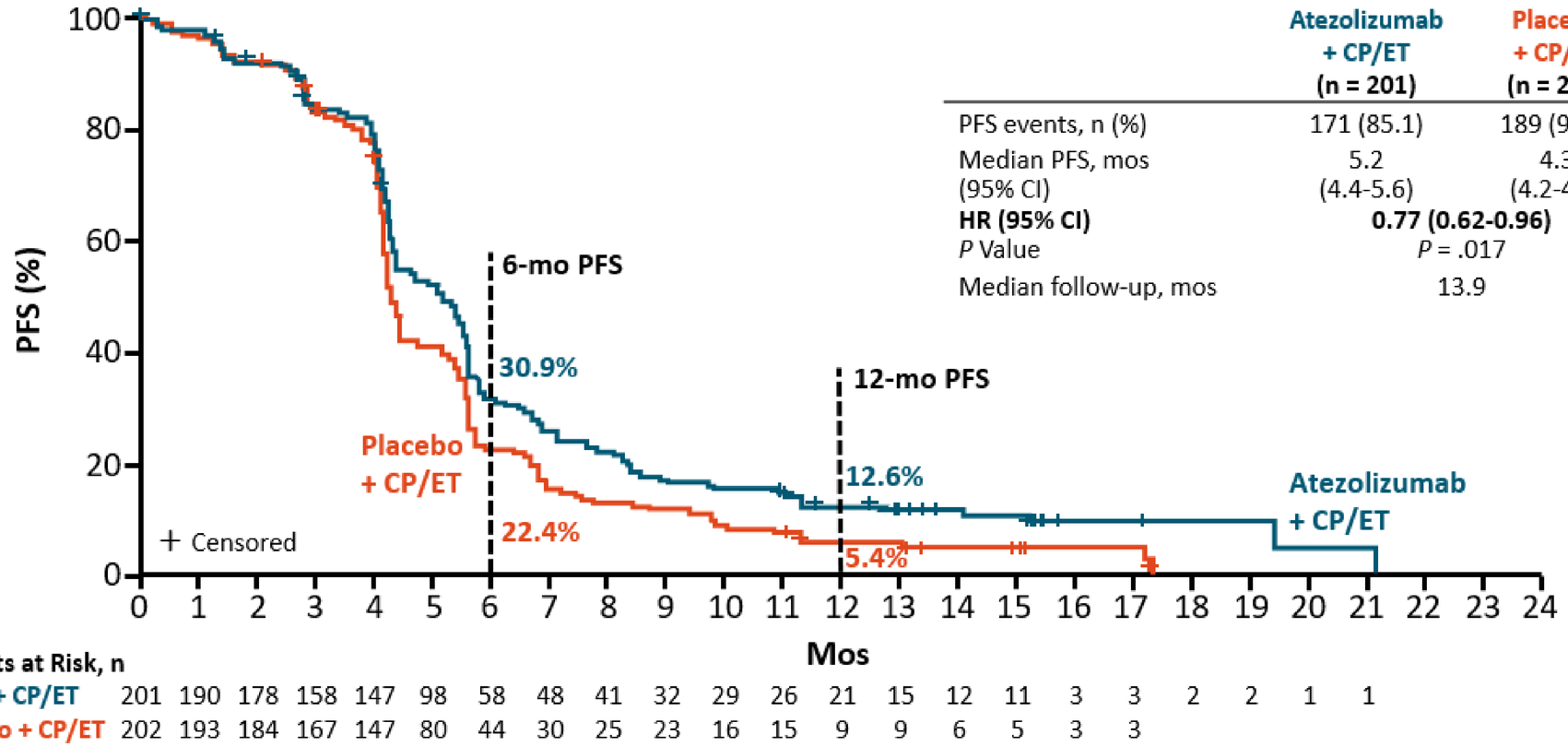
- Double-blind, randomized, placebo-controlled phase I/III trial




- Coprimary endpoints: OS, PFS by investigator assessment
- Secondary endpoints: ORR, DoR, safety

Liu. IASLC WCLC. 2018. Abstr PL0-207. Horn. NEJM. 2018;379:2220. Horn. AACR 2020. Abstract 9759.

# IMpower133: PFS



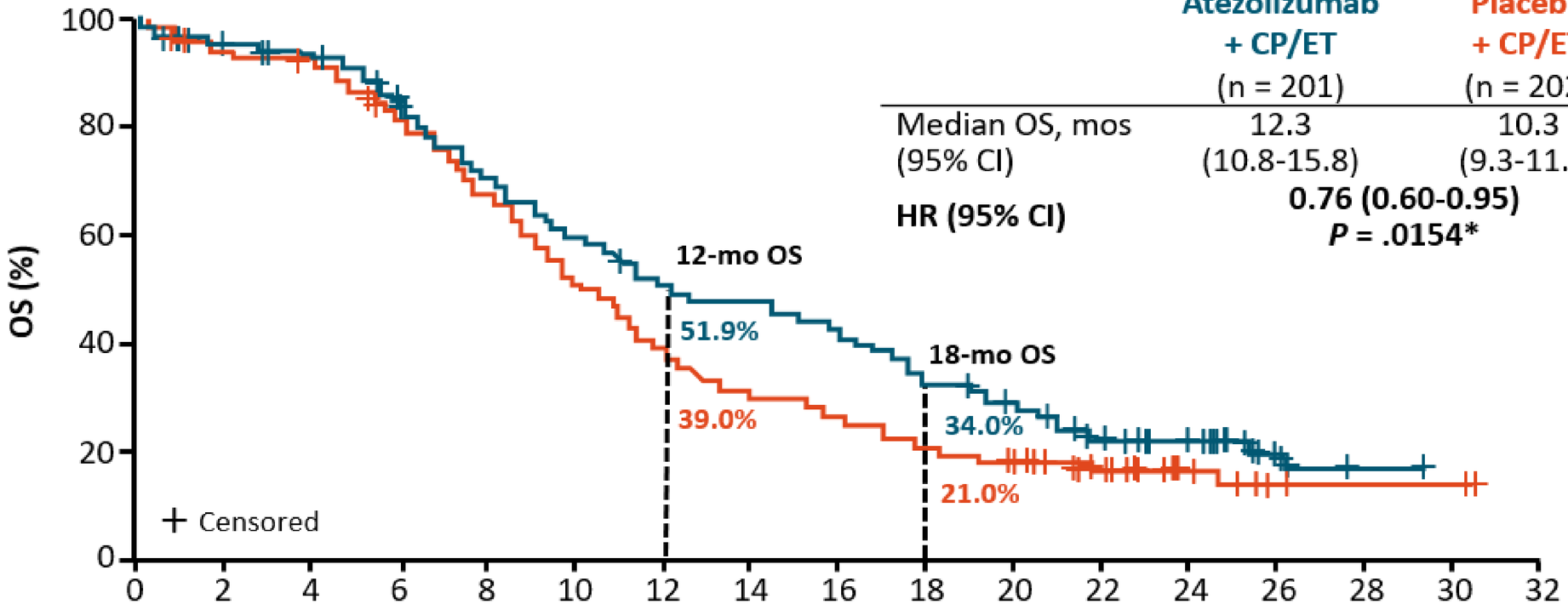

| | Atezolizumab + CP/ET (n = 201) | Placebo + CP/ET (n = 202) |
|---|---|---|
| PFS events, n (%) | 171 (85.1) | 189 (93.6) |
| Median PFS, mos (95% CI) | 5.2 (4.4-5.6) | 4.3 (4.2-4.5) |
| **HR (95% CI)** | **0.77 (0.62-0.96)** | |
| *P* Value | *P* = .017 | |
| Median follow-up, mos | 13.9 | |

**Patients at Risk, n**

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Atezo + CP/ET | 201 | 190 | 178 | 158 | 147 | 98 | 58 | 48 | 41 | 32 | 29 | 26 | 21 | 15 | 12 | 11 | 3 | 3 | 2 | 2 | 1 | 1 |
| Placebo + CP/ET | 202 | 193 | 184 | 167 | 147 | 80 | 44 | 30 | 25 | 23 | 16 | 15 | 9 | 9 | 6 | 5 | 3 | 3 | | | | |

Horn. NEJM. 2018;379:2220

# IMpower133: Updated OS




| | Atezolizumab + CP/ET (n = 201) | Placebo + CP/ET (n = 202) |
|---|---|---|
| Median OS, mos (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*** | |

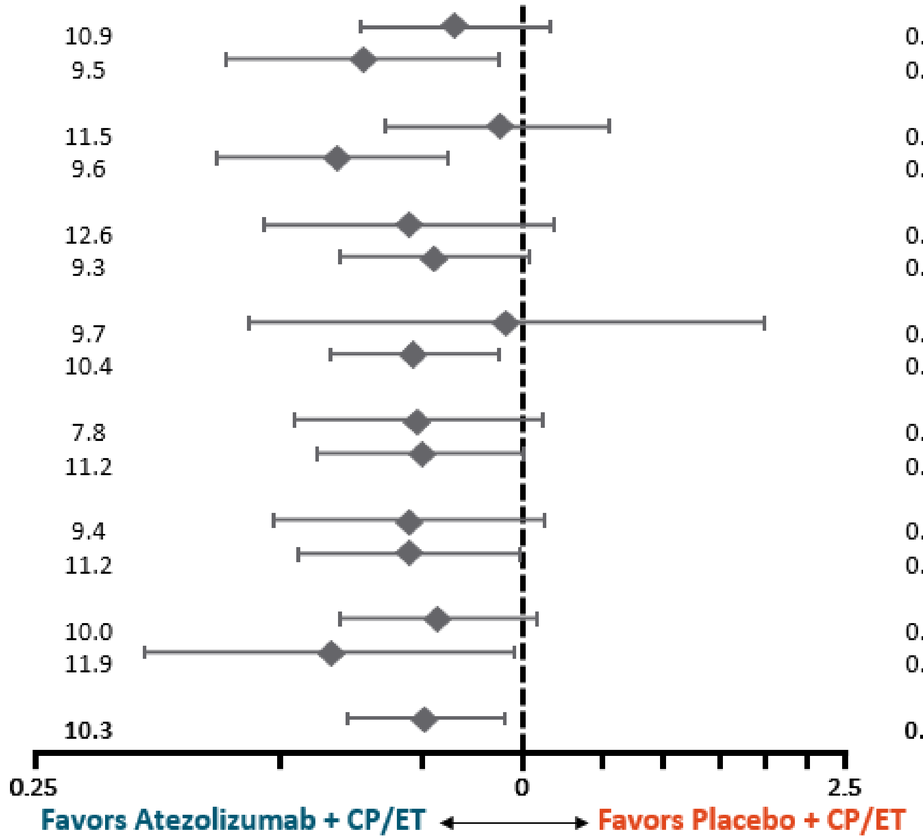
**Patients at Risk, n**

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Atezo + CP/ET | 201 | 187 | 180 | 159 | 130 | 109 | 98 | 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 |

Horn. NEJM. 2018;379:2220

# IMpower133: Updated OS by Subgroup

| Subgroup | Median OS, Mos: Atezolizumab + CP/ET | Median OS, Mos: Placebo + CP/ET | OS HR (95% CI) |
|---|---|---|---|
| Male (n = 261) | 12.2 | 10.9 | 0.83 (0.63-1.10) |
| Female (n = 142) | 13.6 | 9.5 | 0.64 (0.43-0.94) |
| < 65 yrs (n = 217) | 12.1 | 11.5 | 0.94 (0.68-1.28) |
| ≥ 65 yrs (n = 186) | 14.4 | 9.6 | 0.59 (0.42-0.82) |
| ECOG PS 0 (n = 140) | 16.8 | 12.6 | 0.73 (0.48-1.10) |
| ECOG PS 1 (n = 263) | 11.3 | 9.3 | 0.78 (0.60-1.03) |
| Brain metastases (n = 35) | 8.5 | 9.7 | 0.96 (0.46-2.01) |
| No brain metastases (n = 368) | 12.6 | 10.4 | 0.74 (0.58-0.94) |
| Liver metastases (n = 149) | 9.3 | 7.8 | 0.75 (0.52-1.07) |
| No liver metastases (n = 254) | 16.3 | 11.2 | 0.76 (0.56-1.01) |
| bTMB < 10 mut/Mb (n = 134) | 11.8 | 9.4 | 0.73 (0.49-1.08) |
| bTMB ≥ 10 mut/Mb (n = 212) | 14.9 | 11.2 | 0.73 (0.53-1.00) |
| bTMB < 16 mut/Mb (n = 266) | 12.5 | 10.0 | 0.79 (0.60-1.04) |
| bTMB ≥ 16 mut/Mb (n = 80) | 17.1 | 11.9 | 0.58 (0.34-0.99) |
| **ITT (N = 403)** | **12.3** | **10.3** | **0.76 (0.60-0.95)** |




Horn. NEJM. 2018;379:2220

# IMpower133: Updated Safety

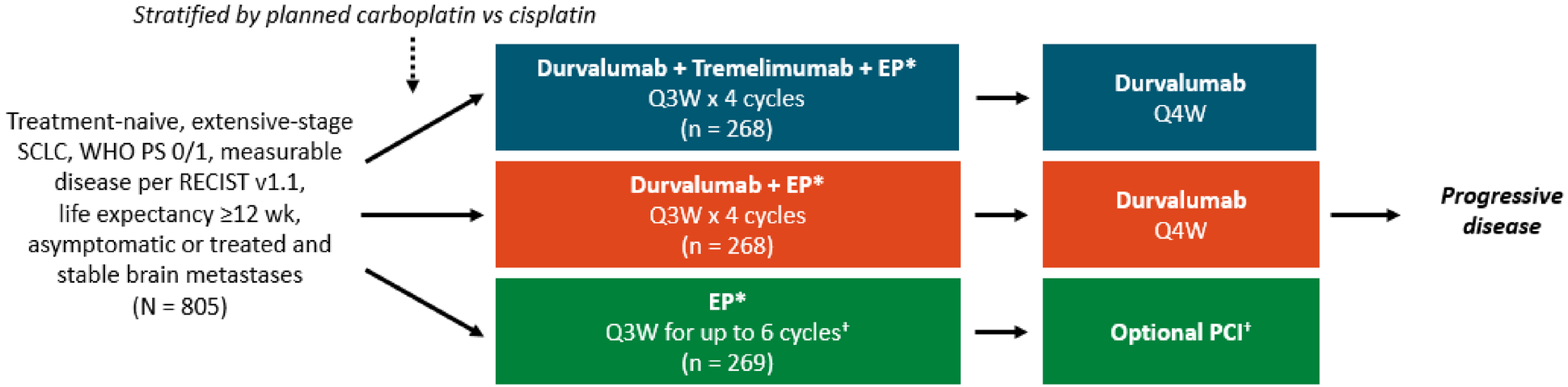
| Events, n (%) | Atezolizumab + CP/ET (n = 198) | Placebo + CP/ET (n = 196) |
|---|---|---|
| ≥ 1 AE | 198 (100) | 189 (96.4) |
| Grade 3/4 AEs | 134 (67.7) | 124 (63.3) |
| Treatment-related AEs | 188 (94.9) | 181 (92.3) |
| Serious AEs | 77 (38.9) | 69 (35.2) |
| Immune-related AEs | 82 (41.4) | 48 (24.5) |
| AEs leading to withdrawal from any study medication | 24 (12.1) | 6 (3.1) |
| ▪ Atezolizumab or placebo | 23 (11.6) | 5 (2.6) |
| ▪ Carboplatin | 5 (2.5) | 1 (0.5) |
| ▪ Etoposide | 8 (4.0) | 2 (1.0) |
| Treatment-related deaths | 3 (1.5) | 3 (1.5) |

- Median duration of treatment: atezolizumab, 4.7 mos (range: 0-29); placebo, 4.1 mos (range: 0-26)
- Median no. of doses received: atezolizumab, 7.0 (range: 1-39); placebo, 6.0 (range: 1-38)

Horn. NEJM. 2018;379:2220

# CASPIAN 3-Yr Update: Study Design

- Randomized, open-label, multicenter phase III study




*Etoposide 80-100 mg/m$^2$ with either carboplatin AUC 5-6 or cisplatin 75-80 mg/m$^2$, durvalumab 1500 mg, tremelimumab 75 mg.
†Per investigator discretion, additional 2 cycles of EP (6 cycles total) and PCI.

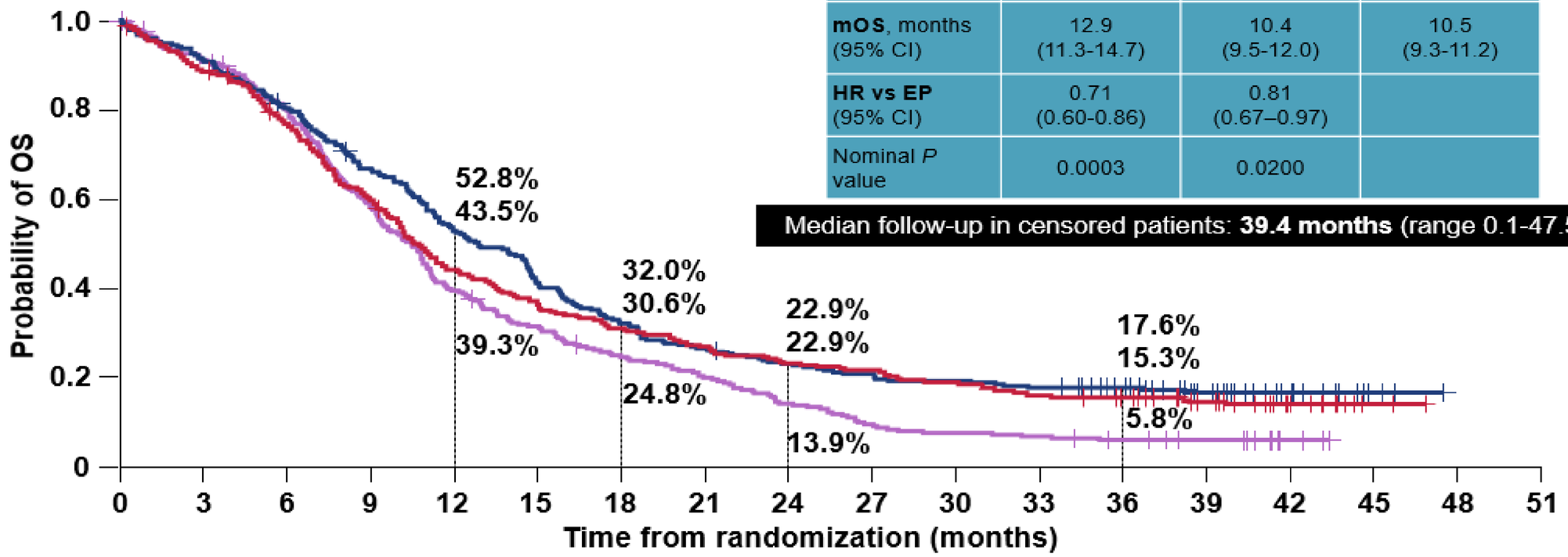
- **Primary endpoint:** OS
- **Secondary endpoints:** PFS and ORR (not collected since last data cutoff), safety (limited to serious AEs, including death)

Paz-Ares. ESMO 2021. Abstr LBA61

# CASPIAN 3 year OS update

| | D + EP | D + T + EP | EP |
|---|---|---|---|
| Events, n/N (%) | 221/268 (82.5) | 226/268 (84.3) | 248/269 (92.2) |
| **mOS**, months (95% CI) | 12.9 (11.3-14.7) | 10.4 (9.5-12.0) | 10.5 (9.3-11.2) |
| **HR vs EP** (95% CI) | 0.71 (0.60-0.86) | 0.81 (0.67–0.97) | |
| Nominal *P* value | 0.0003 | 0.0200 | |

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




| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| D + EP | 268 | 244 | 214 | 177 | 140 | 109 | 85 | 70 | 60 | 54 | 50 | 46 | 39 | 25 | 13 | 3 | 0 | 0 |
| D + T + EP | 268 | 243 | 200 | 156 | 114 | 92 | 80 | 70 | 60 | 56 | 48 | 41 | 37 | 26 | 11 | 2 | 0 | 0 |
| EP | 269 | 243 | 212 | 156 | 104 | 82 | 64 | 51 | 36 | 24 | 19 | 17 | 13 | 10 | 3 | 0 | 0 | 0 |

Paz-Ares L, et al. Presented at: ESMO Congress; September 16-21, 2021; virtual. Abs LBA61.

# CASPIAN 3-Yr Update: OS With Durvalumab + EP vs EP Alone

| Outcome | D + EP (n = 268) | EP (n = 269) | HR (95% CI) |
|---|---|---|---|
| Median OS, mo (95% CI) | 12.9 (11.3-14.7) | 10.5 (9.3-11.2) | 0.71 (0.60-0.86)<br>Nominal *P* = .0003 |
| 12-mo OS, % | 52.8 | 39.3 | |
| 18-mo OS, % | 32.0 | 24.8 | |
| 24-mo OS, % | 22.9 | 13.9 | |
| 36-mo OS, % | 17.6 | 5.8 | |

- Median follow-up (range) – 39.4 months (0.1-47.5)

Paz-Ares. ESMO 2021. Abstr LBA61

# CASPIAN 3-Yr Update: Subgroup Analysis of OS With Durvalumab + EP vs EP Alone

| Subgroup | | HR (95% CI) |
|---|---|---|
| All patients (n = 537) | | 0.71 (0.60-0.86) |
| Planned platinum agent | Carboplatin (n = 402) | 0.74 (0.60-0.91) |
| | Cisplatin (n = 135) | 0.65 (0.45-0.94) |
| Age | <65 yr (n = 324) | 0.68 (0.54-0.87) |
| | ≥65 yr (n = 213) | 0.78 (0.59-1.04) |
| Sex | Male (n = 374) | 0.76 (0.62-0.95) |
| | Female (n = 163) | 0.60 (0.42-0.84) |
| Performance status | 0 (n = 189) | 0.70 (0.51-0.95) |
| | 1 (n = 348) | 0.73 (0.58-0.92) |
| Smoking status | Smoker (n = 500) | 0.71 (0.59-0.86) |
| | Nonsmoker (n = 37) | 0.82 (0.41-1.69) |

| Subgroup | | HR (95% CI) |
|---|---|---|
| Brain/CNS metastases | Yes (n = 55) | 0.76 (0.43-1.33) |
| | No (n = 482) | 0.71 (0.59-0.86) |
| AJCC disease stage at diagnosis | Stage III (n = 52) | 0.82 (0.45-1.49) |
| | Stage IV (n = 485) | 0.71 (0.59-0.86) |
| Race | Asian (n = 78) | 0.81 (0.50-1.28) |
| | Non-Asian (n = 458) | 0.71 (0.58-0.87) |
| Region | Asia (n = 76) | 0.82 (0.51-1.31) |
| | Europe (n = 405) | 0.69 (0.56-0.85) |
| | North/South America (n = 56) | 0.84 (0.46-1.54) |

Paz-Ares. ESMO 2021. Abstr LBA61

# CASPIAN 3-Yr Update: Treatment Exposure

| Parameter | D + T + EP (n = 266) | D + EP (n = 265) |
|---|---|---|
| Receiving durvalumab at cutoff, n (%) | 19 (7.1) | 27 (10.2) |
| Median number of durvalumab doses (range) | 6.0 (1-46) | 7.0 (1-52) |
| Total duration of durvalumab exposure, n (%) | | |
| ▪ ≥1 yr | 49 (18.4) | 54 (20.4) |
| ▪ ≥2 yr | 30 (11.3) | 32 (12.1) |
| ▪ ≥3 yr | 21 (7.9) | 24 (9.1) |
| Median total duration of durvalumab, wk (range) | 23.1 (0.1-190.0) | 28.0 (0.3-198.7) |

- Most patients at risk at Yr 3 in the durvalumab-containing arms remained on durvalumab treatment at the data cutoff (March 22, 2021)
- Exposure to chemotherapy and tremelimumab remained unchanged at these data cutoff compared with previous analysis

Paz-Ares. ESMO 2021. Abstr LBA61

# CASPIAN 3-Yr Update: Serious Adverse Events

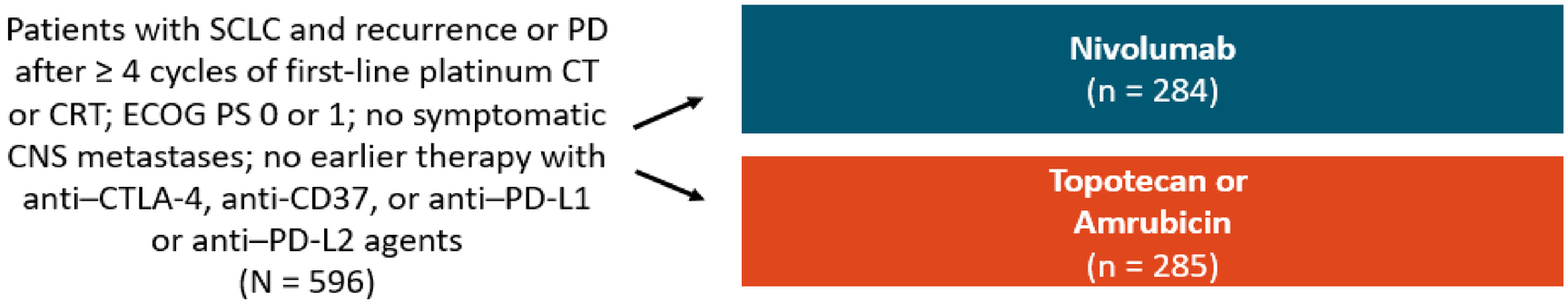
| Serious AEs ≥2% | D + T + EP (n = 266) | D + EP (n = 265) | EP (n = 266) |
|---|---|---|---|
| Any, n (%) | 126 (47.4) | 86 (32.5) | 97 (36.5) |
| Febrile neutropenia | 11 (4.1) | 12 (4.5) | 12 (4.5) |
| Pneumonia | 16 (6.0) | 6 (2.3) | 11 (4.1) |
| Anemia | 9 (3.4) | 5 (1.9) | 12 (4.5) |
| Thrombocytopenia | 6 (2.3) | 1 (0.4) | 9 (3.4) |
| Hyponatremia | 9 (3.4) | 2 (0.8) | 4 (1.5) |
| Neutropenia | 5 (1.9) | 2 (0.8) | 7 (2.6) |
| Diarrhea | 7 (2.6) | 2 (0.8) | 4 (1.5) |
| Pulmonary embolism | 7 (2.6) | 1 (0.4) | 0 |
| Fatal AE (any cause), n (%)* | 29 (10.9) | 14 (5.3) | 16 (6.0) |
| Fatal TRAE, n (%) | 12 (4.5) | 6 (2.3) | 2 (0.8) |

*4 more deaths that were not treatment-related were reported since the previous analysis: 1 each in the D + EP and EP arms (aspiration and small intestine leiomyosarcoma, respectively), and 2 in the D + T + EP arm (drowning and *Pneumocystis jirovecii* pneumonia).

Paz-Ares. ESMO 2021. Abstr LBA61

# CheckMate 331: Second-line Nivolumab in Patients With Relapsed SCLC

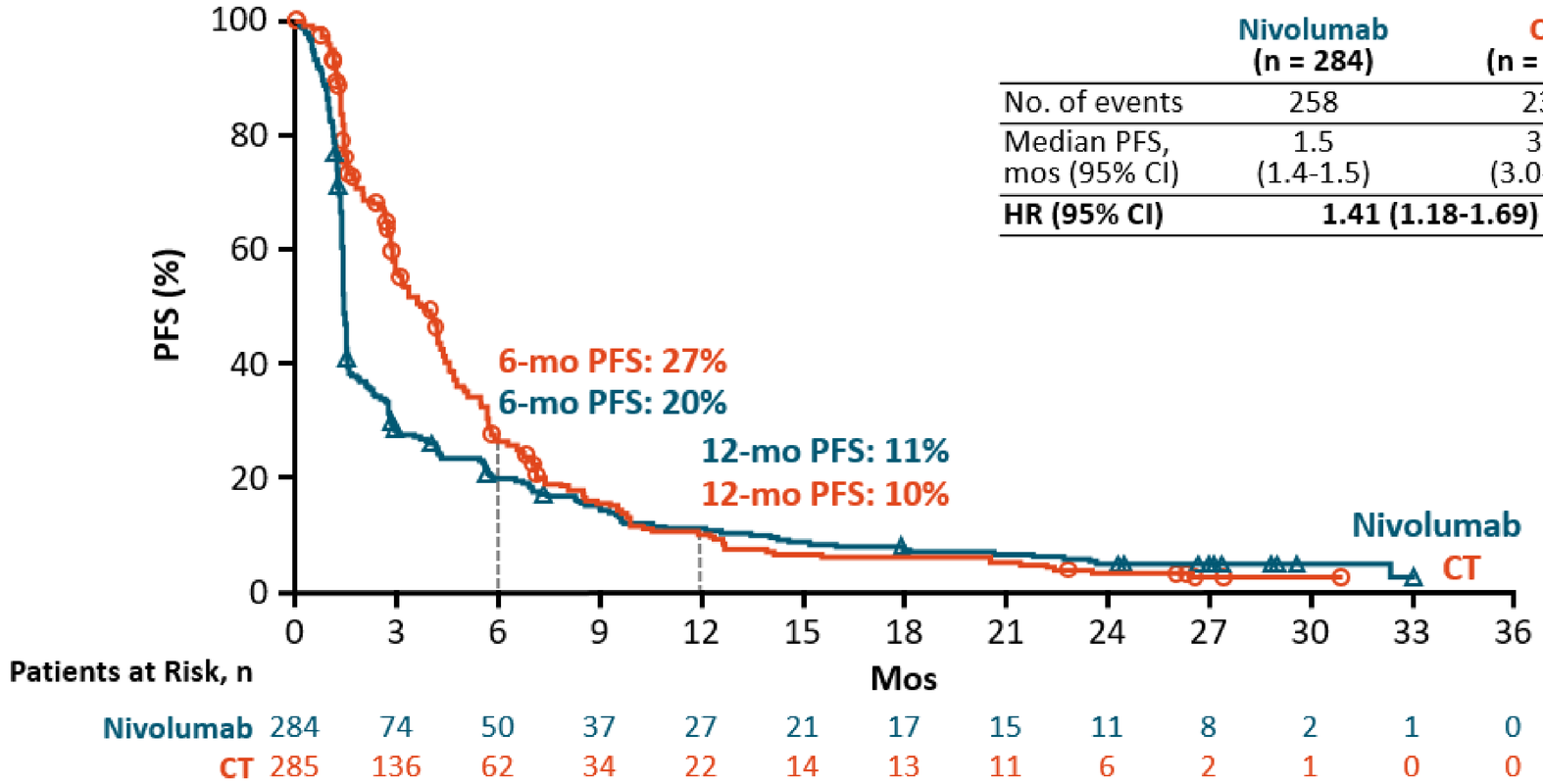
- Randomized, open-label phase III trial (database lock: September 28, 2018)
  - Median follow-up: nivolumab, 7.0 mos; CT, 7.6 mos
  - Minimum follow-up for OS: 15.8 mos




- Primary endpoint: OS
- Secondary endpoints: PFS, ORR

Reck. ESMO IO Congress 2018. Abstr LBA5

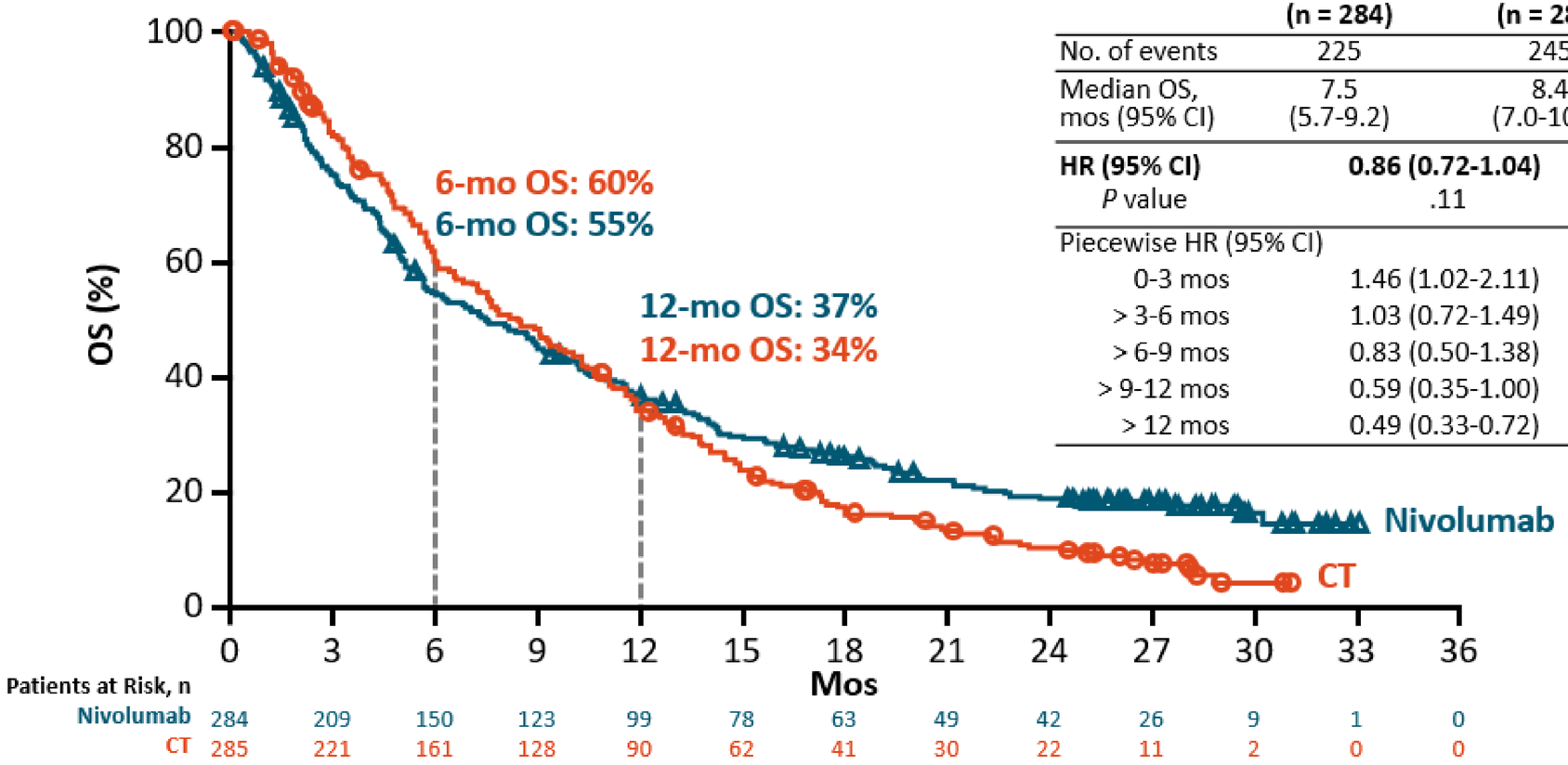
# CheckMate 331: PFS With Nivolumab vs Chemotherapy




| | Nivolumab (n = 284) | CT (n = 285) |
|---|---|---|
| No. of events | 258 | 235 |
| Median PFS, mos (95% CI) | 1.5 (1.4-1.5) | 3.8 (3.0-4.2) |
| **HR (95% CI)** | **1.41 (1.18-1.69)** | |

Reck. ESMO IO Congress 2018. Abstr LBA5

# CheckMate 331: OS With Nivolumab vs Chemotherapy

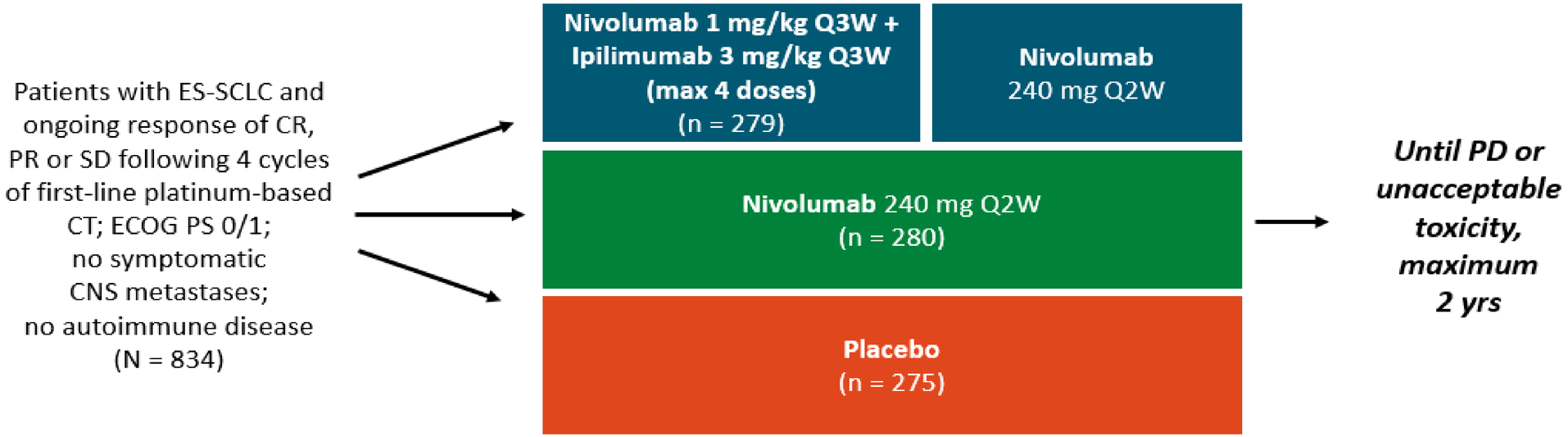



| | Nivolumab (n = 284) | CT (n = 285) |
|---|---|---|
| No. of events | 225 | 245 |
| Median OS, mos (95% CI) | 7.5 (5.7-9.2) | 8.4 (7.0-10.0) |
| **HR (95% CI)** | **0.86 (0.72-1.04)** | |
| *P* value | .11 | |
| Piecewise HR (95% CI) | | |
| 0-3 mos | 1.46 (1.02-2.11) | |
| > 3-6 mos | 1.03 (0.72-1.49) | |
| > 6-9 mos | 0.83 (0.50-1.38) | |
| > 9-12 mos | 0.59 (0.35-1.00) | |
| > 12 mos | 0.49 (0.33-0.72) | |

Reck. ESMO IO Congress 2018. Abstr LBA5

# CheckMate 451: Nivolumab + Ipilimumab vs Nivolumab vs Placebo as Maintenance Therapy for ES-SCLC

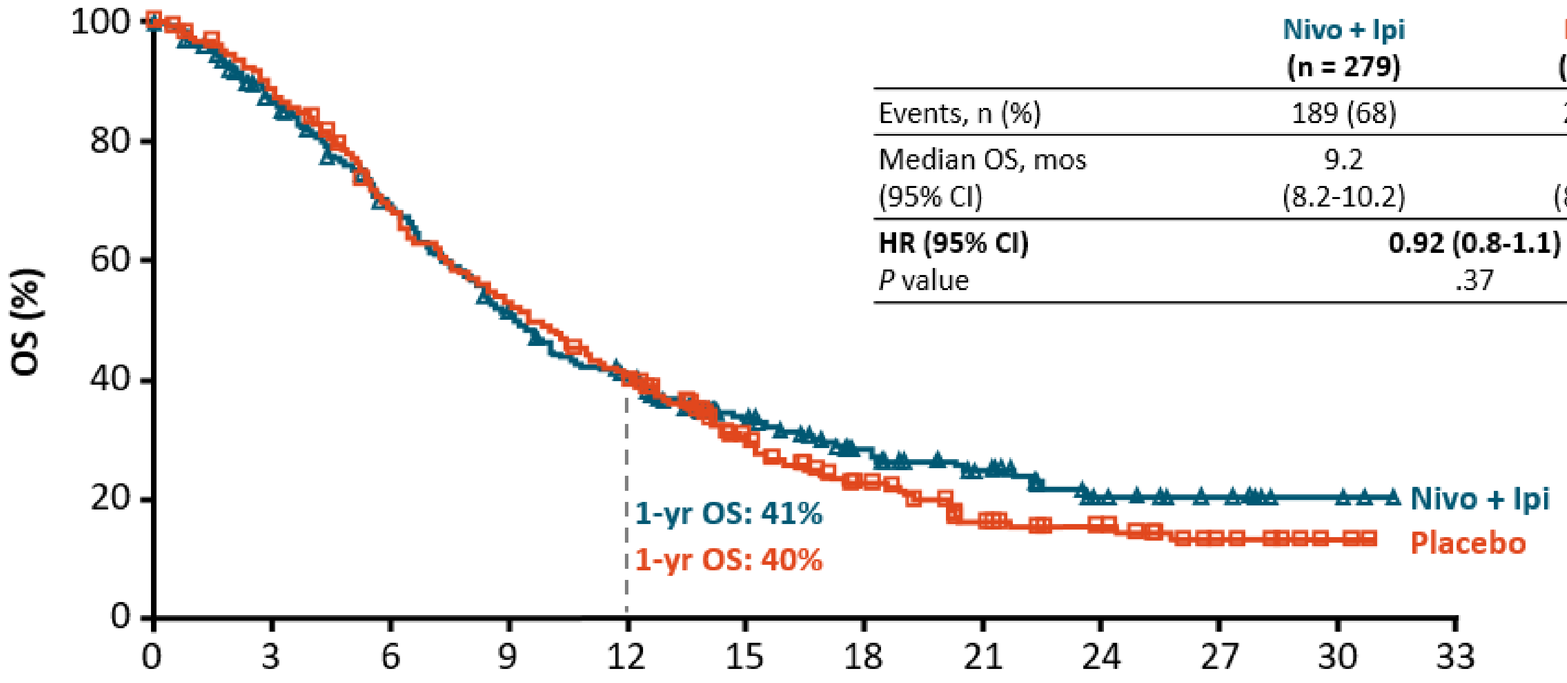
- Randomized, double-blind phase III study (minimum follow-up: 9 mos)




- Primary endpoint: OS, nivolumab + ipilimumab vs placebo
- Secondary endpoints: PFS, nivolumab + ipilimumab vs placebo; PFS and OS, nivolumab vs placebo
- Exploratory endpoints: ORR; DoR; safety and tolerability

Owonikoko. ELCC 2019. Abstr LBA1_PR.

# CheckMate 451: OS With Nivolumab + Ipilimumab vs Placebo (Primary Endpoint)



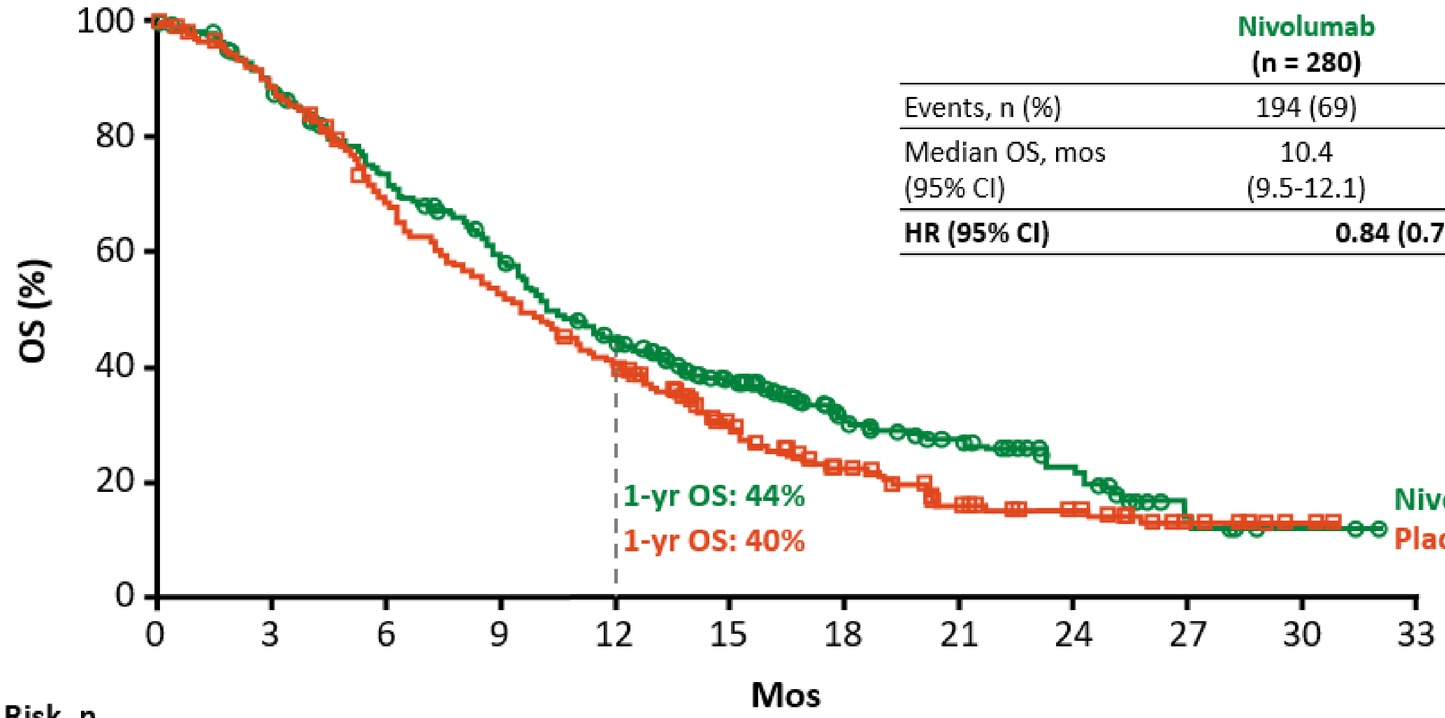

| | Nivo + Ipi (n = 279) | Placebo (n = 275) |
|---|---|---|
| Events, n (%) | 189 (68) | 211 (77) |
| Median OS, mos (95% CI) | 9.2 (8.2-10.2) | 9.6 (8.2-11.0) |
| **HR (95% CI)** | **0.92 (0.8-1.1)** | |
| *P* value | .37 | |

**Patients at Risk, n**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Nivo + Ipi** | 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 |

Owonikoko. ELCC 2019. Abstr LBA1_PR.

# CheckMate 451: OS Nivolumab + Ipilimumab vs Nivolumab vs Placebo



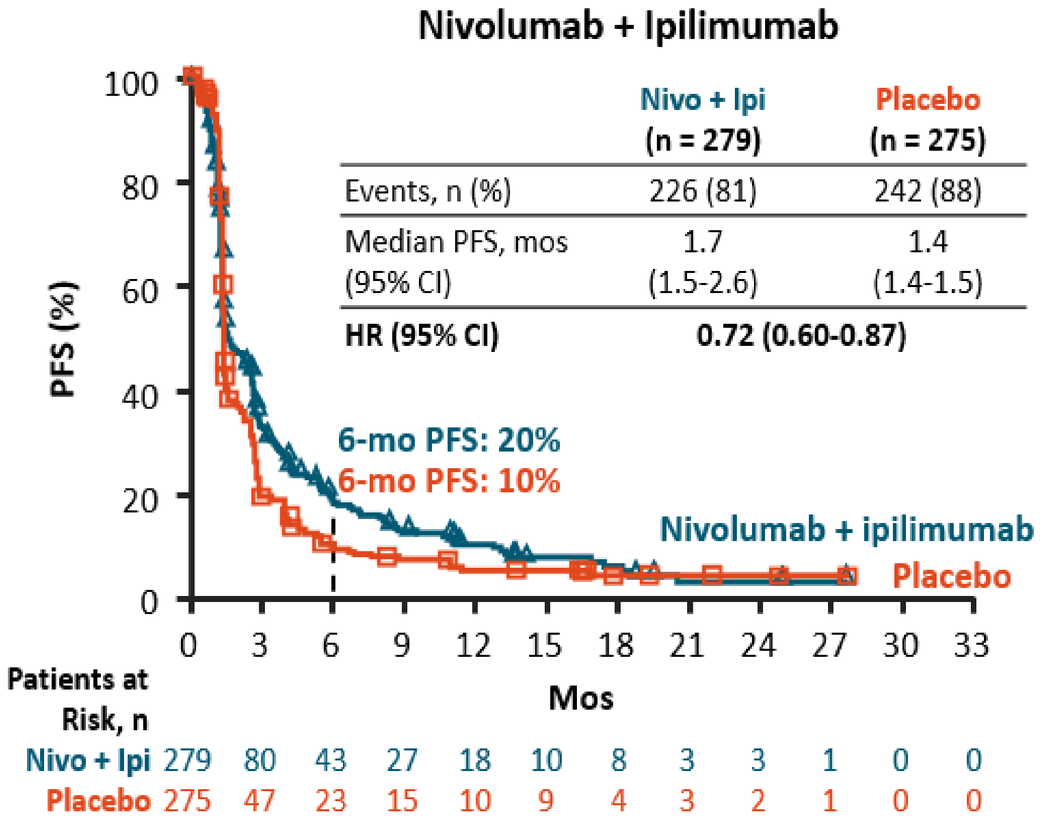

| | Nivolumab (n = 280) | Placebo (n = 275) |
|---|---|---|
| Events, n (%) | 194 (69) | 211 (77) |
| Median OS, mos (95% CI) | 10.4 (9.5-12.1) | 9.6 (8.2-11.0) |
| **HR (95% CI)** | **0.84 (0.7-1.0)** | |

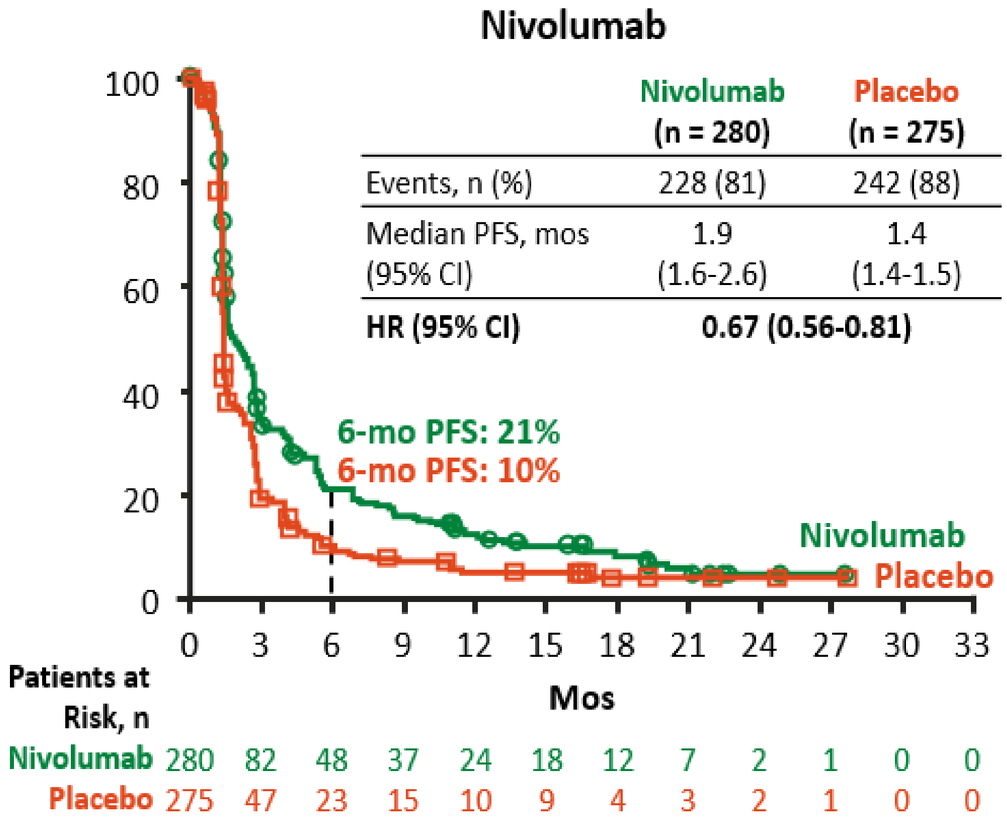
**Patients at Risk, n**

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Nivolumab | 280 | 242 | 195 | 155 | 114 | 81 | 49 | 37 | 21 | 6 | 2 | 0 |
| Placebo | 275 | 237 | 181 | 139 | 105 | 65 | 41 | 23 | 16 | 7 | 2 | 0 |

Owonikoko. ELCC 2019. Abstr LBA1_PR.

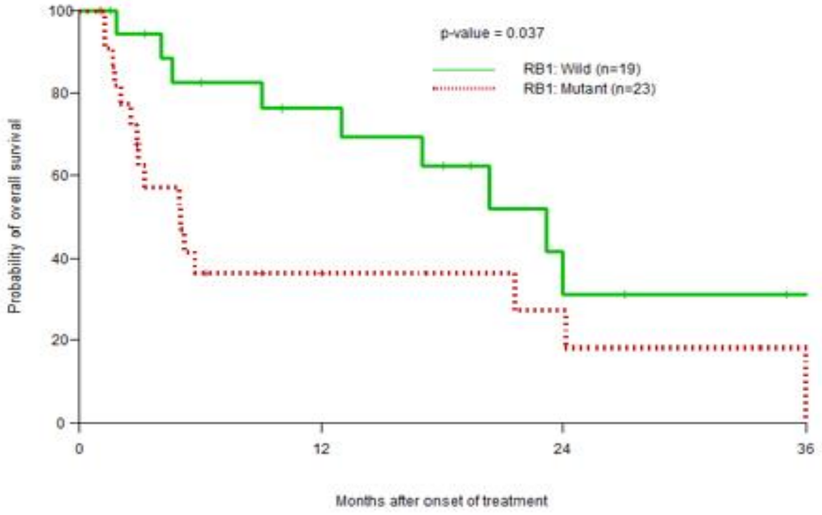
# CheckMate 451: PFS for Nivolumab + Ipilimumab or Nivolumab vs Placebo

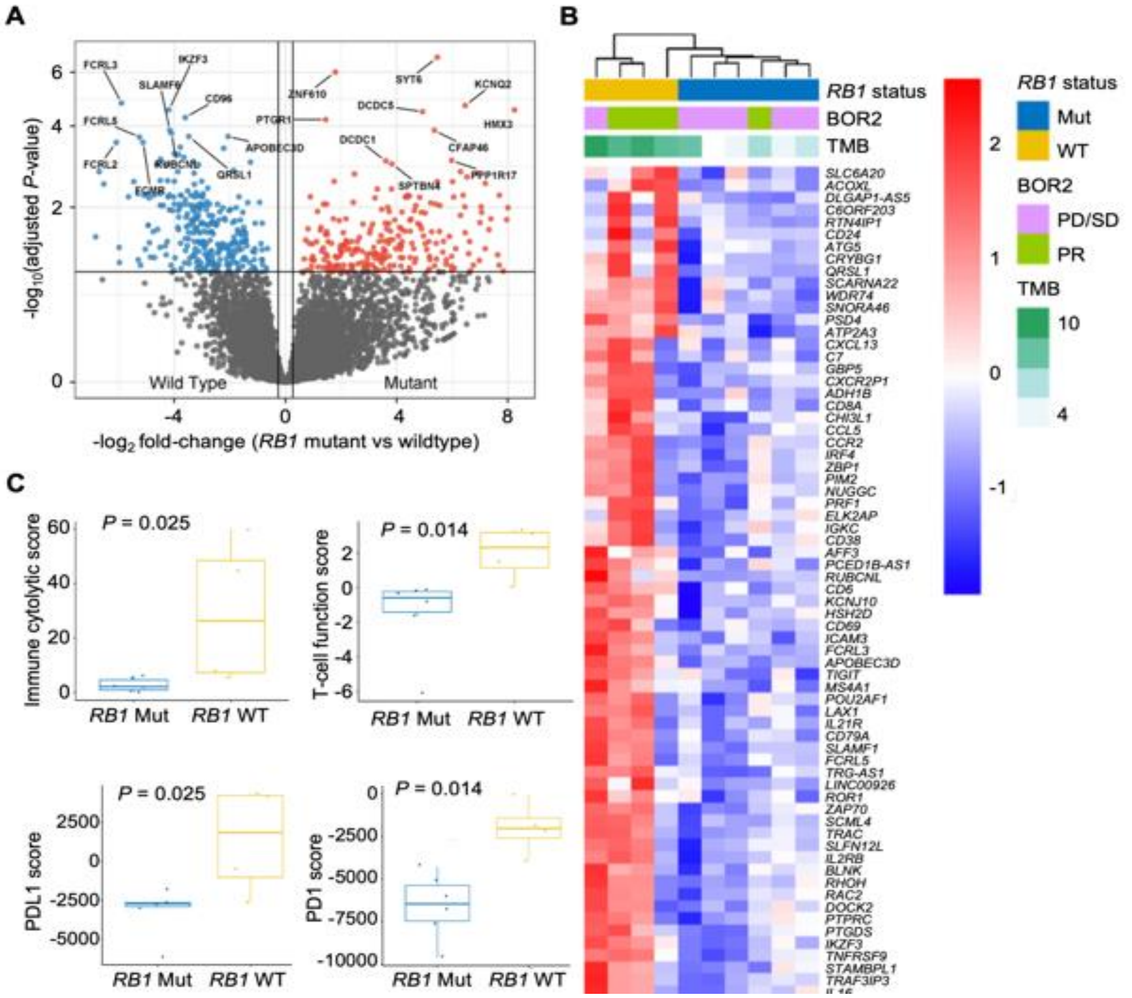



Owonikoko. ELCC 2019. Abstr LBA1_PR.

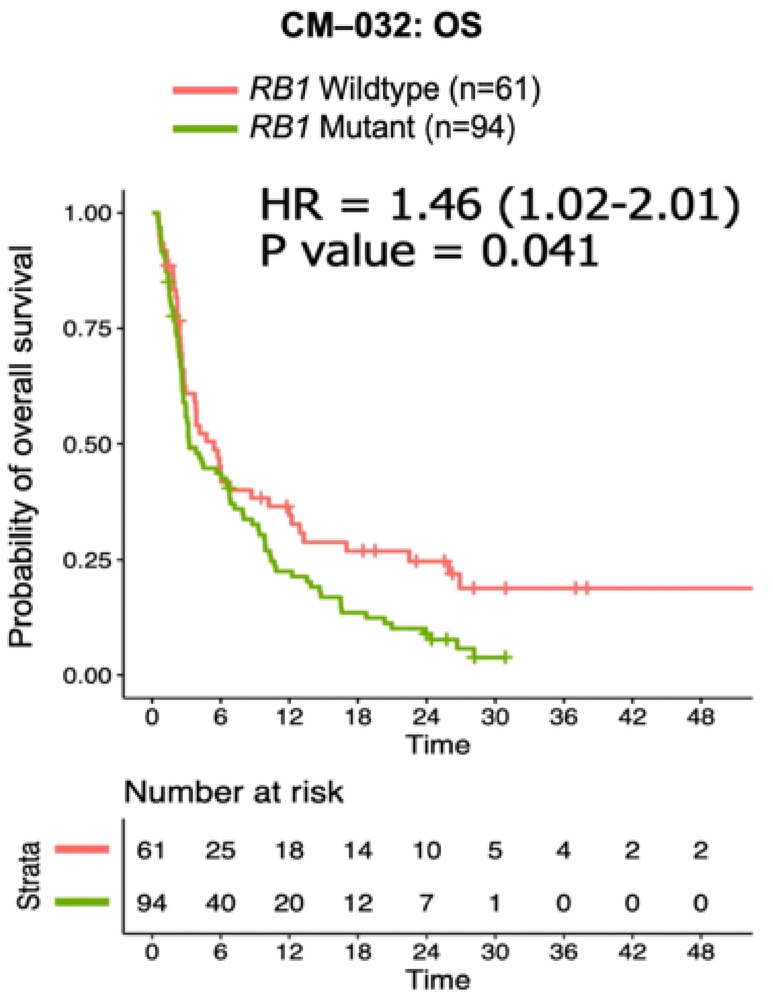
# RB1 Wildtype SCLC – Benefit from ICI

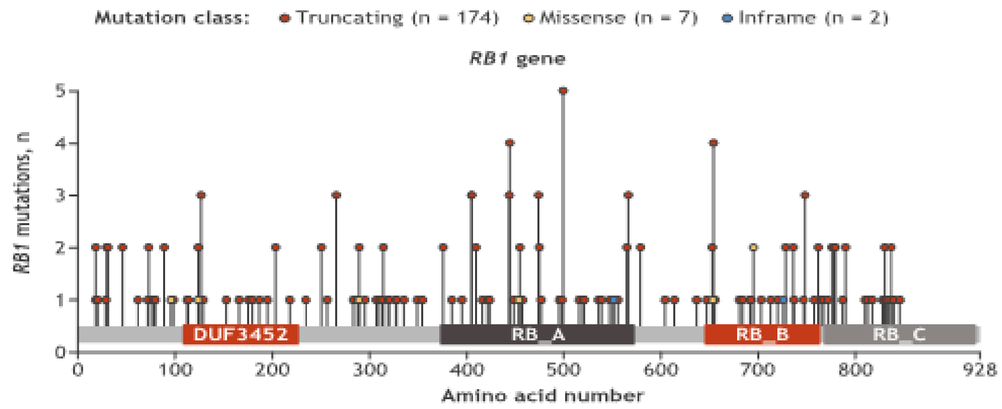


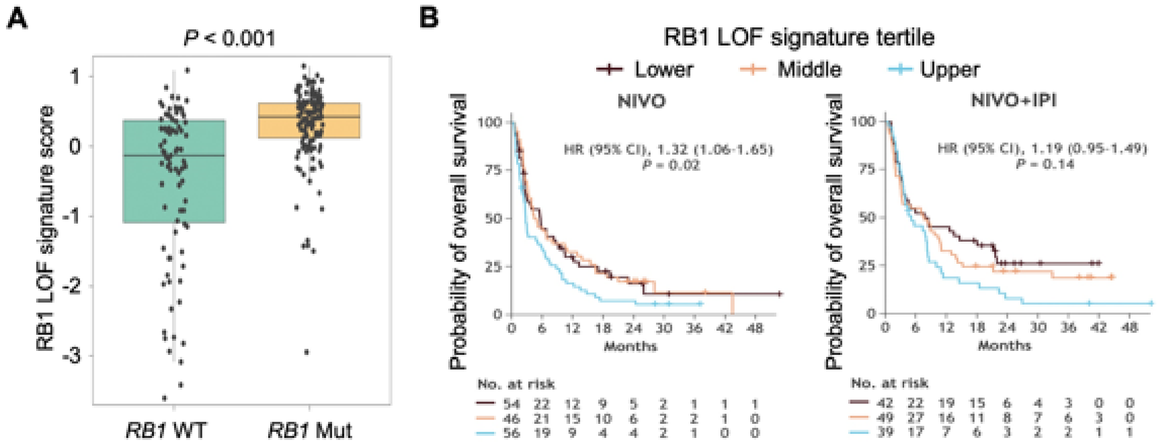

Dowlati lab

# Checkmate 032 – Validation of RB WT and ICI




DUF3452, domain of unknown function (DUF3452); RB_A, Rb-associated protein A domain; RB_B, Rb-associated protein B domain; RB_C, Rb C-terminal domain.



# Phase II Update: Second-line Lurbinectedin Monotherapy in Patients with Relapsed Advanced SCLC

- Confirmed ORR of 35.2% with second-line lurbinectedin surpassed ≥ 30% statistical cut off for a positive trial[1]
  - Follow-up: 6.1 mos (range: 1-33)
- Outcomes with second-line lurbinectedin numerically higher than historical outcomes with second-line topotecan[1,2]
  - Topotecan ORR: 5-24%, mOS: 6-8 mos

| Outcome[1] | All patients (N = 105) | Platinum sensitive† (n = 60) | Platinum resistant‡ (n = 45) |
|---|---|---|---|
| ORR, % | 35.2* | 45.0* | 22.2* |
| DCR, % | 68.6 | 81.7 | 51.1 |
| Median DoR, mos | 5.3 | 6.2 | 4.7 |
| Median PFS, mos | 3.9 | 4.6 | 2.6 |
| ▪ 6-mo PFS, % | 33.6 | 44.6 | 18.8 |
| Median OS, mos | 9.3 | 11.9 | 5.0 |
| ▪ 12-mo OS, % | 34.2 | 48.3 | 15.9 |

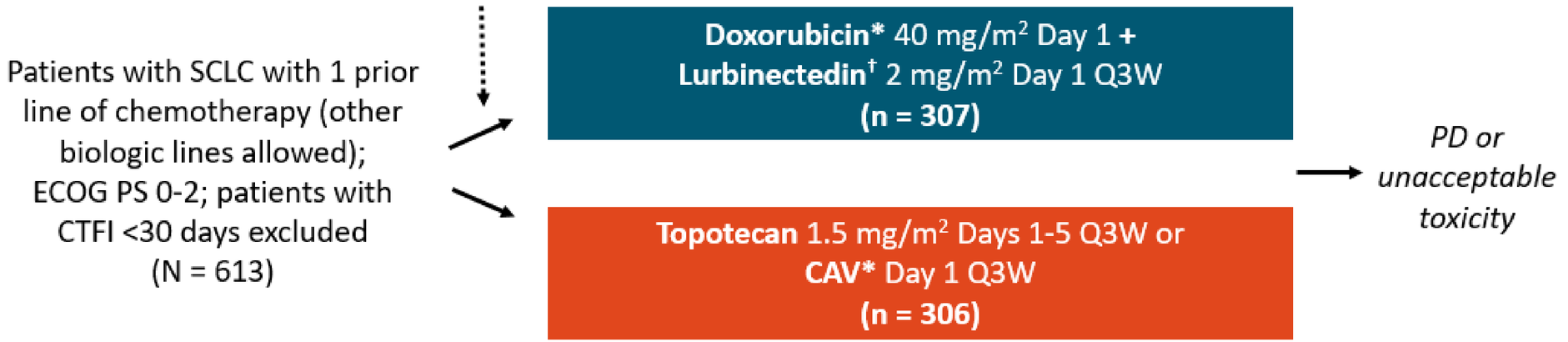
*All confirmed PRs. †CTFI ≥ 90 days. ‡CTFI < 90 days.

Paz-Ares. ASCO 2019. Abstract 8506. 2. Yang. J Hematol Oncol. 2019;12:47. 3. NCT02566993.

# ATLANTIS: Study Design

- Multicenter, randomized phase III trial

*Stratified by ECOG PS (0 vs 1-2), CTFI (≥180 vs 90-179 vs <90 days), CNS involvement (yes vs no), prior PD-1/PD-L1 inhibitor (yes vs no), investigator preference for control arm*

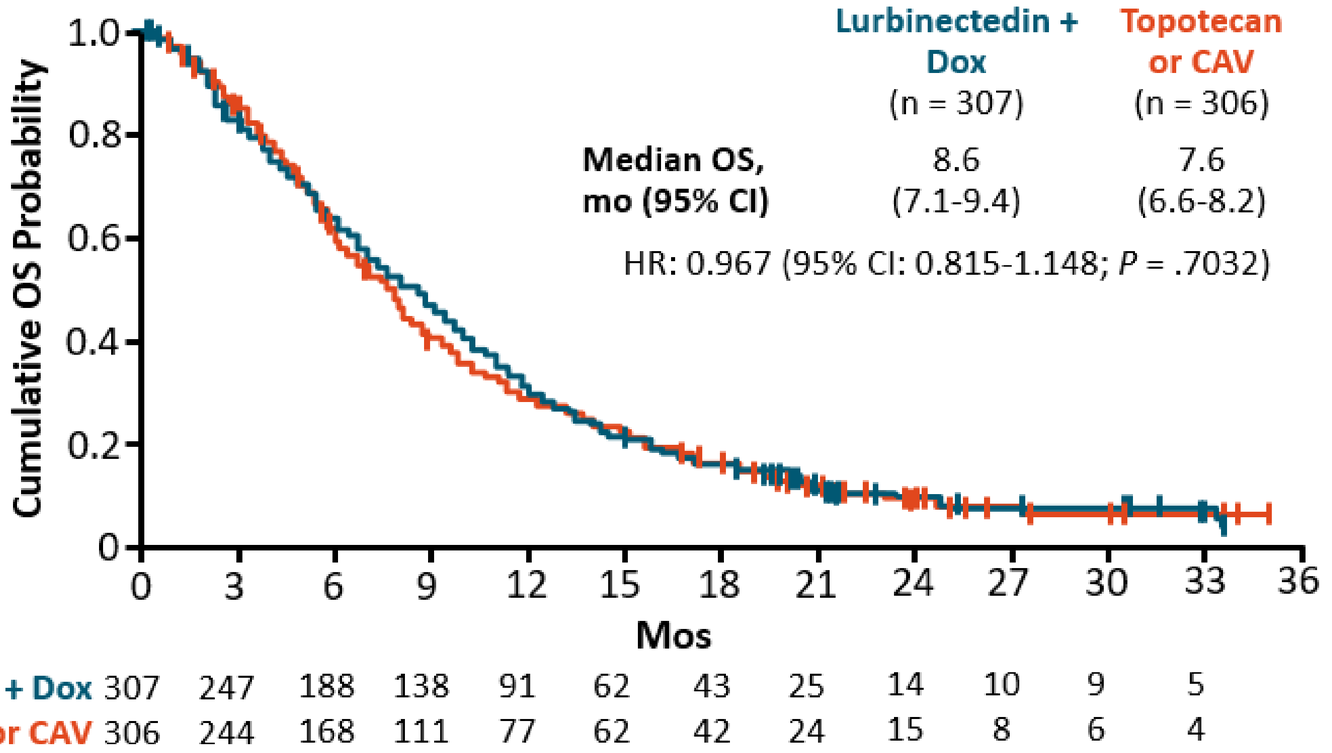



*Maximum 10 cycles of doxorubicin.
†Lurbinectedin continued as maintenance at 3.2 mg/m² Day 1 Q3W.
G-CSF prophylaxis mandatory in both arms.

- **Primary endpoint:** OS
- **Secondary endpoints:** PFS, tumor response, DoR, safety

Paz-Ares. WCLC 2021. Abstr PL02.03.

# ATLANTIS: OS in ITT Population




- No significant difference in OS between arms in ITT population
- Subset analyses also showed no significant differences between arms based on stratification factors

Paz-Ares. WCLC 2021. Abstr PL02.03. Reproduced with permission.

# Summary

- The majority of progress in SCLC over the past 30 years has been in radiation oncology
- However, the addition of checkpoint inhibitors durvalumab and atezolizumab has made a modest impact in overall survival.
- Long-term follow-up from the Caspian trial shows a 17.6% 3 year survival rate for extensive stage SCLC, a major advancement in SCLC treatment.
- Novel drugs are likely to make further impact in the near future.

# Acknowledgment


- Dr. Afshin Dowlati
- Dr. Joshua Sabari