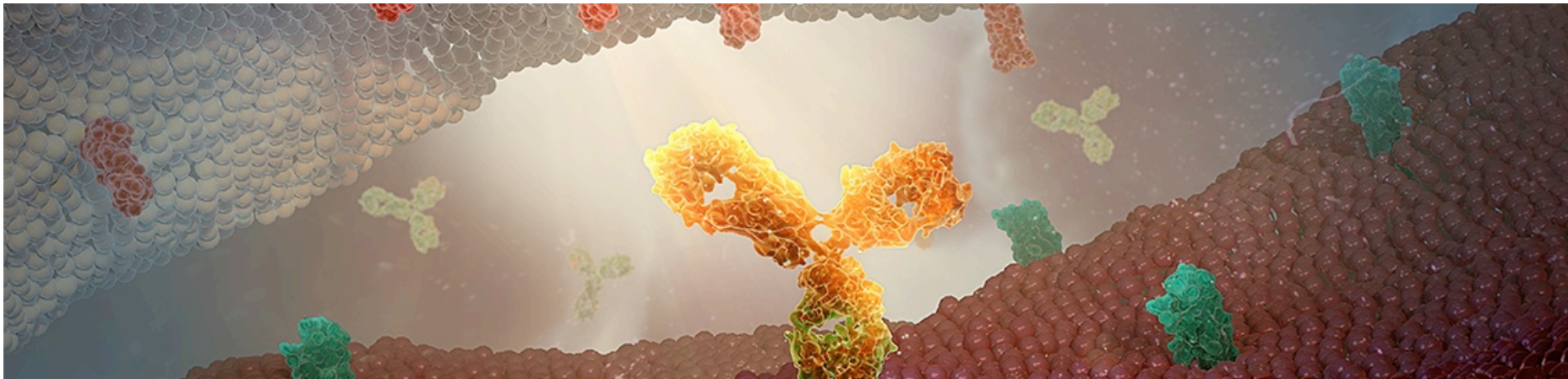


# Durvalumab for the First Line Treatment of Extensive Stage Small Cell Lung Cancer

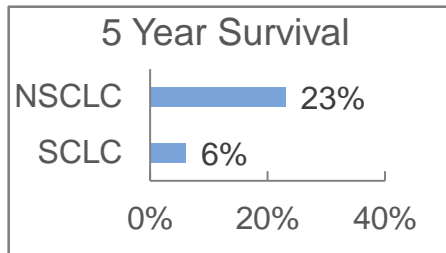
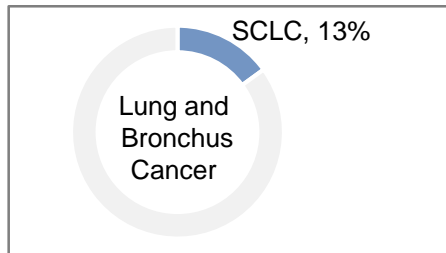
**ICD-10 Coordination & Maintenance Meeting**

Baltimore, MD

17 March 2020



# ES-SCLC: Disease Background



## Epidemiology

- SCLC accounts for about 13% of all patients with lung cancer but is associated with the higher mortality rate
- About 30,000 new cases of SCLC are diagnosed annually in the US
- The majority (80%) of patients are diagnosed in the late/metastatic stage described as Extensive Stage Small Cell Lung Cancer (ES-SCLC)

## Patient Attributes

- The majority of diagnoses occur in patients 65-84 years of age
- Patients present extremely symptomatic with a number of comorbidities
- SCLC is the most rapidly progressive lung cancer. Growth of metastases can be extremely fast, with doubling times of 3-4 days

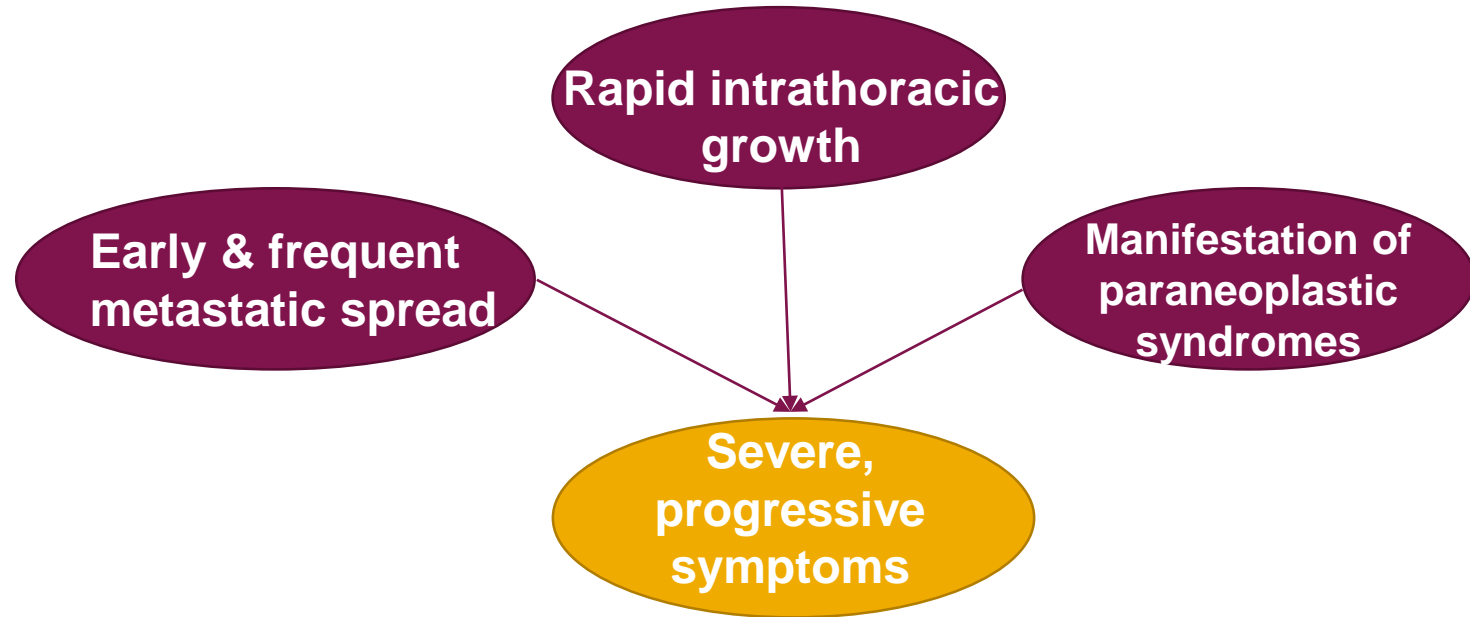
## Outcomes

- Poor prognosis with an estimated 19,000 SCLC patients dying annually
- The median overall survival for ES-SCLC is 9-11 months with chemotherapy standard of care (SOC), representing an ongoing significant unmet need
- The overall 5-year survival rate for SCLC (early and late stage combined) is 6%



# ES-SCLC Patients Present with Significant Symptoms that Often Require Immediate Treatment<sup>1,2,3</sup>

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1. Bennett BM, Wells JR, PanterC, et al. The Humanistic Burden of Small Cell Lung Cancer (SCLC): A Systematic Review of Health-Related Quality of Life (HRQoL) Literature. *Front Pharmacol.* 2017;8:339. 2. Haque N, Raza A, McGoeyR, et al. Small cell lung cancer: time to diagnosis and treatment. *South Med J.* 2012;105(8):418-423. 3. AartsMJ, Aerts JG, van den Borne BE, et al. Comorbidity in Patients With Small-Cell Lung Cancer: Trends and Prognostic Impact. *Clin Lung Cancer.* 2015;16(4):282-291. 4. Cascone T, Gold KA, Glisson BS. Small cell carcinoma of the lung. Chapter 17. In: Kantarjian HM, Wolff RA. eds. *The MD Anderson Manual of Medical Oncology*, 3rd ed. New York, NY: McGraw-Hill..

# Platinum+ Etoposide Had Remained The Standard Of Care For 1L Treatment of ES-SCLC For Over 30 Years<sup>1</sup>

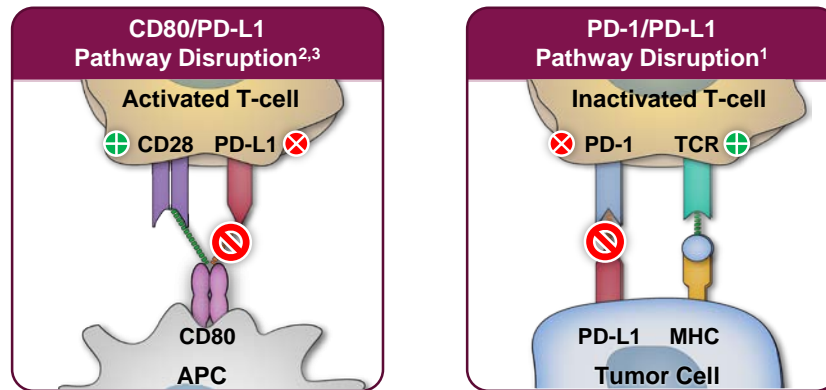
- The most commonly used 1L regimen in the US for ES-SCLC is carboplatin in combination with etoposide administered for 4 to 6 cycles following diagnosis
- SCLC is highly sensitive to carboplatin or cisplatin in combination with etoposide (Platinum + etoposide) in the 1L setting (response rates range from 50%-60% for ES-SCLC)<sup>2</sup>
  - However, the majority of patients will relapse within the first year of treatment, with a median progression-free survival (PFS) of 4-6 months following standard 1L chemotherapy<sup>1,2</sup>
- Platinum + etoposide had remained the SoC for 1L ES-SCLC for nearly 30 years, as numerous trials since the 1990s have failed to demonstrate superiority to this regimen until the entrance of immunotherapy in 2019<sup>1</sup>

1L = first line; ED, extensive-stage disease; SCLC = small-cell lung cancer; SoC = standard of care.

1. Farago AF et al. *Transl Lung Cancer Res*. 2018;7(1):69-79. 2. Hurwitz JL et al. *Oncologist*. 2009;14(10):986-994. 3. Østerlind K. *Eur Respir J*. 2001;18(6):1026-1043. 4.

Sabari JK, Lok BH, Laird JH, Poirier JT, Rudin CM. Unravelling the biology of SCLC: implications for therapy. *Nat Rev Clin Oncol*. 2017;14(9):549-561

# Durvalumab, A PD-L1 Blocking Antibody, Provides A New MOA To The Chemotherapy SOC<sup>4</sup>



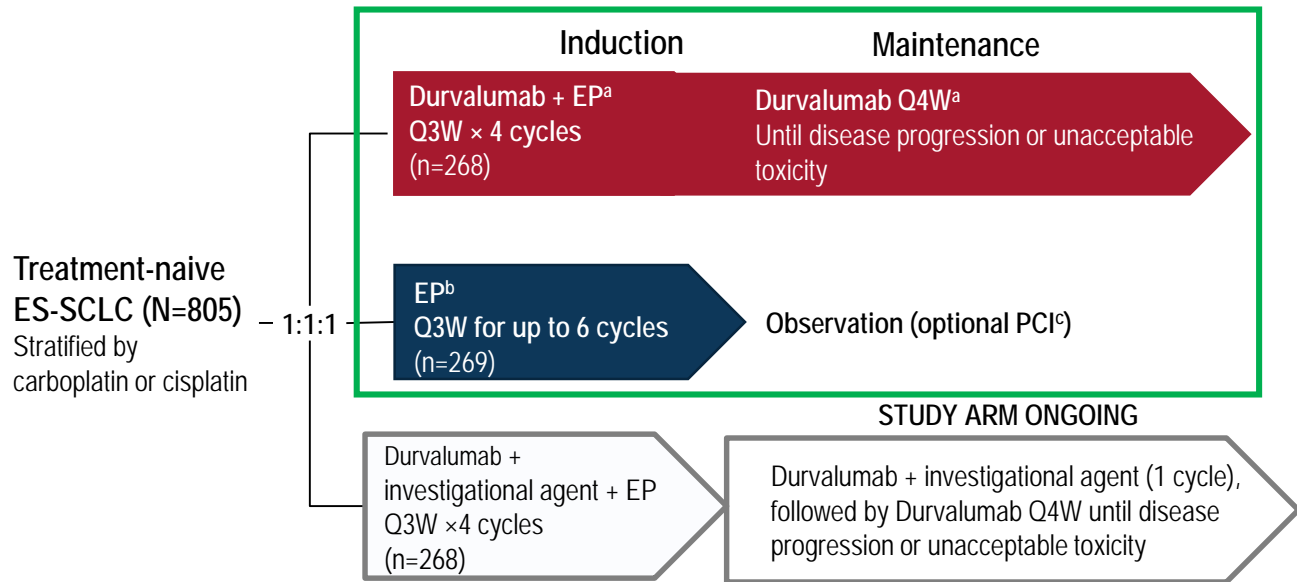
- Durvalumab is a human IgG1κ monoclonal antibody that blocks the interaction of PD-L1 with PD-1 and CD80<sup>4</sup>
- Blockade of PD-L1/PD-1 and PD-L1/CD80 interactions releases the inhibition of immune responses, without inducing ADCC<sup>4</sup>
  - PD-L1 blockade leads to increased T-cell activation in vitro and decreased tumor size in co-engrafted human tumor and immune cell xenograft mouse models

ADCC = antibody dependent cell-mediated cytotoxicity; IgG1κ = immunoglobulin G1 kappa.

1. Intlekofer AM, et al. *J Leukoc Biol.* 2013;94(1):25-39. 2. Topalian SL, et al. *Cancer Cell.* 2015;27:450-461. 3. Park JJ, et al. *Blood.* 2010;116:1291-1298. 4. IMFINZI® (durvalumab) Prescribing Information. AstraZeneca Pharmaceuticals LP, Wilmington, DE; 2019.

# CASPIAN: Study Design

*Large, randomized, open-label, multicenter study of Durvalumab + EP vs EP alone<sup>1,2</sup>*



## Primary Endpoint<sup>1</sup>

- OS

## Key Secondary Endpoints<sup>1</sup>

- PFS<sup>d</sup>
- ORR (unconfirmed)<sup>d</sup>
- OS at 18 months
- PFS at 6 and 12 months
- HRQoL PROs

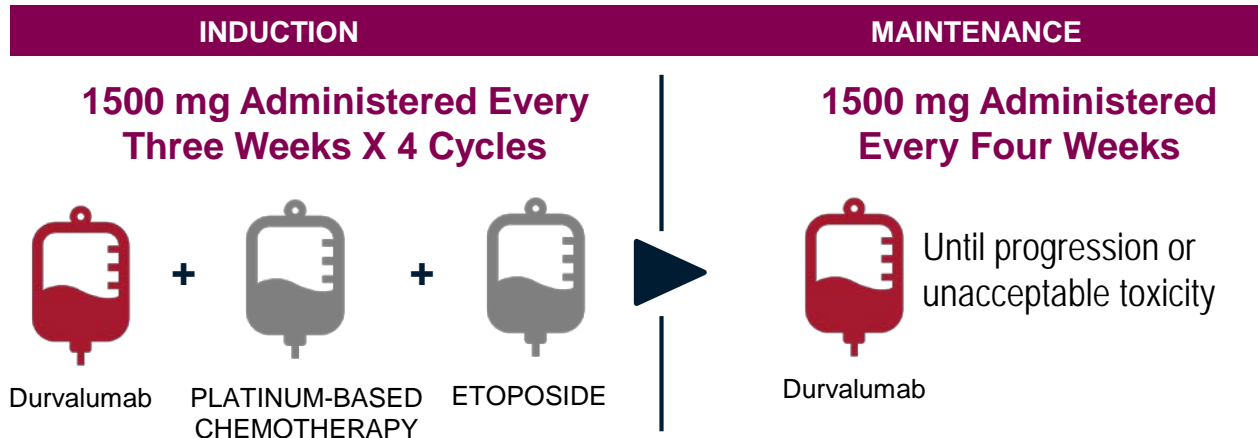
**Following the preplanned interim analysis by the IDMC,  
the durvalumab + tremelimumab + EP vs EP comparison continues to final analysis**

<sup>a</sup>IMFINZI 1500 mg + either carboplatin (AUC 5 or 6 mg/mL/min) or cisplatin (75-80 mg/m<sup>2</sup>) on Day 1 and etoposide (80-100 mg/m<sup>2</sup>) IV on days 1, 2, and 3 of each 21-day cycle for a maximum of 4 cycles, followed by IMFINZI 1500 mg every 4 weeks until disease progression or unacceptable toxicity. <sup>b</sup>Either carboplatin (AUC 5 or 6 mg/mL/min) or cisplatin (75-80 mg/m<sup>2</sup>) on day 1 and etoposide (80-100 mg/m<sup>2</sup>) IV on days 1, 2, and 3 of each 21-day cycle for between 4-6 cycles. <sup>c</sup>Of patients who were treated with EP alone, 8% received PCI after EP. <sup>d</sup>Investigator assessed per RECIST v1.1.

AUC, area under the curve; EP, etoposide/platinum-based chemotherapy; ES-SCLC, extensive-stage small cell lung cancer; HRQoL, health-related quality of life; IV, intravenous; ORR, objective response rate; OS, overall survival; PCI, prophylactic cranial irradiation; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every 3 weeks; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Paz-Ares L, et al. *Lancet*. 2019;394(10212):1929-1939.

# CASPIAN: Dosing and Administration



- Durvalumab will be dosed at 1500 mg every three weeks in combination with etoposide and a platinum-based chemotherapy for four cycles, followed by 1500mg every four weeks until disease progression
- Durvalumab is administered as a 60-minute intravenous (IV) infusion prior to the administration of the chemotherapy regimen
- The chemotherapy regimen is administered on Days 1, 2, and 3 of each of the 4 cycles beginning with a 60-minute IV infusion of carboplatin or cisplatin, followed by etoposide sequentially administered by a 60-minute IV infusion



# CASPIAN: Baseline Characteristics

	<b>Durvalumab + EP (n=268)</b>	<b>EP (n=269)</b>
<b>Median age (range), years</b>	62 (28–82)	62 (35–82)
<b>Male, %</b>	70.9	68.4
<b>White / Asian / Other, %</b>	85.4 / 13.4 / 1.1	82.2 / 15.6 / 2.2
<b>WHO PS 0 / 1, %</b>	36.9 / 63.1	33.5 / 66.5
<b>Disease Stage III / IV,* %</b>	10.4 / 89.6	8.9 / 91.1
<b>Current / Former / Never smoker, %</b>	44.8 / 47.0 / 8.2	46.8 / 47.6 / 5.6
<b>Brain or CNS metastases, %</b>	10.4	10.0

\*All patients were confirmed as having ES-SCLC.

CNS, central nervous system; EP, etoposide and platinum chemotherapy; ES-SCLC, extensive-stage small cell lung cancer; PS, performance status;

WHO, World Health Organization.

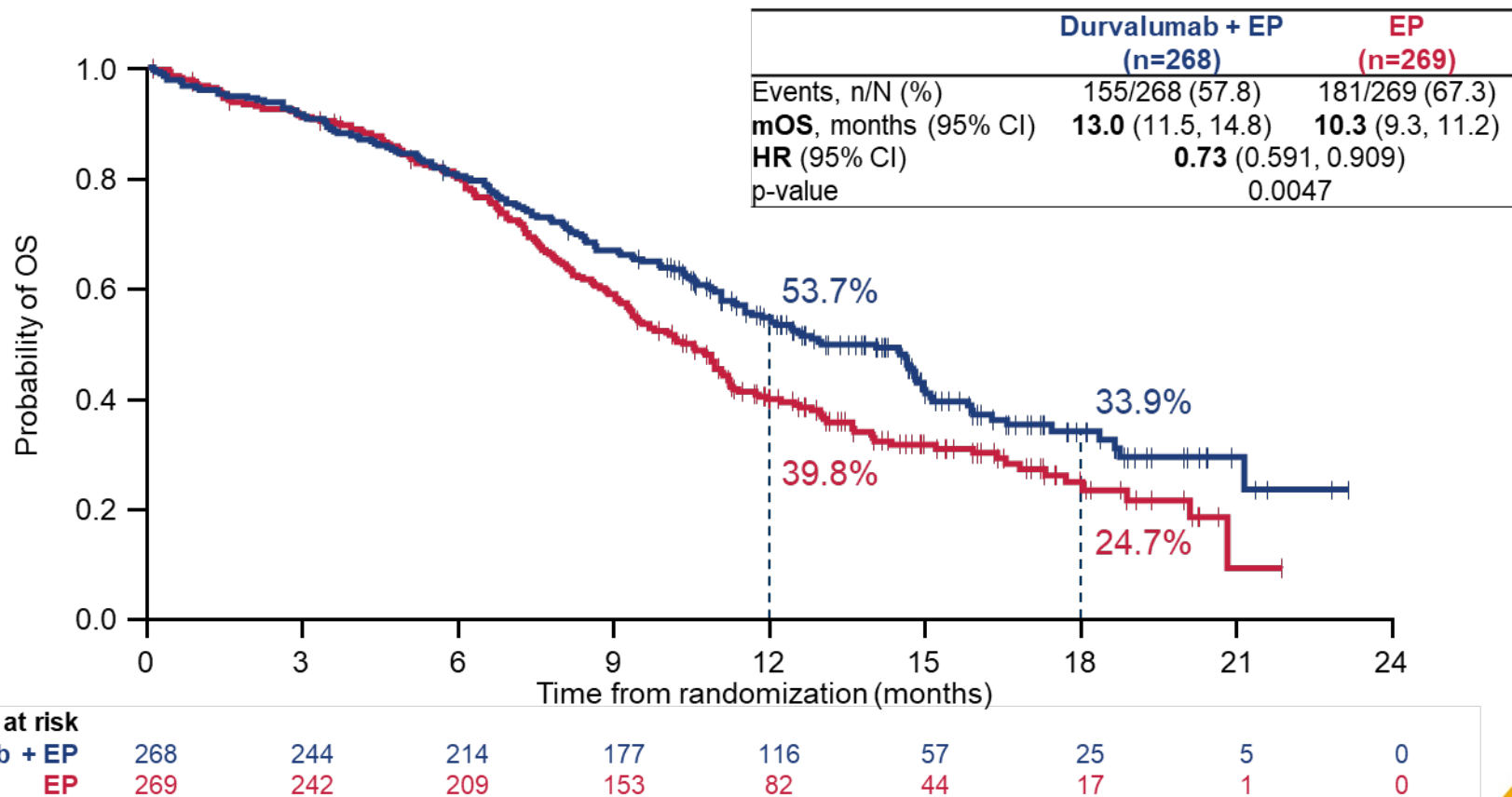
Paz-Ares L, Dvorkin M, Chen Y, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial].

Lancet. 2019. Volume 394 (10212), p1929-1939.





# Overall Survival (Primary Endpoint)



EP, etoposide and platinum chemotherapy; HR, hazard ratio; mOS, median overall survival; OS, overall survival.



# CASPIAN: Safety Profile

	Durvalumab + EP (n=265)	EP (n=266)
Any-grade all-cause AEs, n (%)	260 (98.1)	258 (97.0)
Grade 3/4 AEs	163 (61.5)	166 (62.4)
Serious AEs	82 (30.9)	96 (36.1)
AEs leading to treatment discontinuation*	25 (9.4)	25 (9.4)
Immune-mediated AEs <sup>†</sup>	52 (19.6)	7 (2.6)
AEs leading to death	13 (4.9)	15 (5.6)
Treatment-related AEs leading to death <sup>‡</sup>	5 (1.9)	2 (0.8)

\*Includes patients who permanently discontinued at least one study drug

<sup>†</sup>An event that is associated with drug exposure and consistent with an immune-mediated mechanism of action, where there is no clear alternate aetiology and the event required treatment with systemic corticosteroids or other immunosuppressants and/or, for specific endocrine events, endocrine therapy; majority of imAEs were low grade and thyroid related

<sup>‡</sup>AEs assessed by the investigator as possibly related to any study treatment. Causes of death were cardiac arrest, dehydration, hepatotoxicity, pancytopenia, and sepsis (one patient each) in the durvalumab + EP arm; pancytopenia and thrombocytopenia/haemorrhage (one patient each) in the EP arm

Paz-Ares L, Dvorkin M, Chen Y, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial]. Lancet. 2019. Volume 394 (10212), p1929-1939



# Summary

- SCLC is a rare form of lung cancer that typically presents between 65-84 years of age in advanced stage disease and is associated with a poor prognosis and high mortality rate<sup>1</sup>
- SCLC is a rapidly progressive disease and usually diagnosed in later stages, often requiring urgent treatment due to the acute nature of the symptoms
- Combining Durvalumab with either cisplatin- or carboplatin-etoposide offers a new mechanism of action over chemotherapy SOC with good rationale for positive outcomes in SCLC
- Durvalumab + etoposide plus a platinum-based chemotherapy demonstrated a statistically significant improvement in OS in the treatment of 1L ES-SCLC as compared to etoposide plus a platinum-based chemotherapy alone

Current ICD-10-PCS codes do not uniquely identify administration of durvalumab. AstraZeneca requests that CMS establish a new ICD-10 PCS code in order to accurately report and track administration of Durvalumab in the inpatient setting



# Questions