

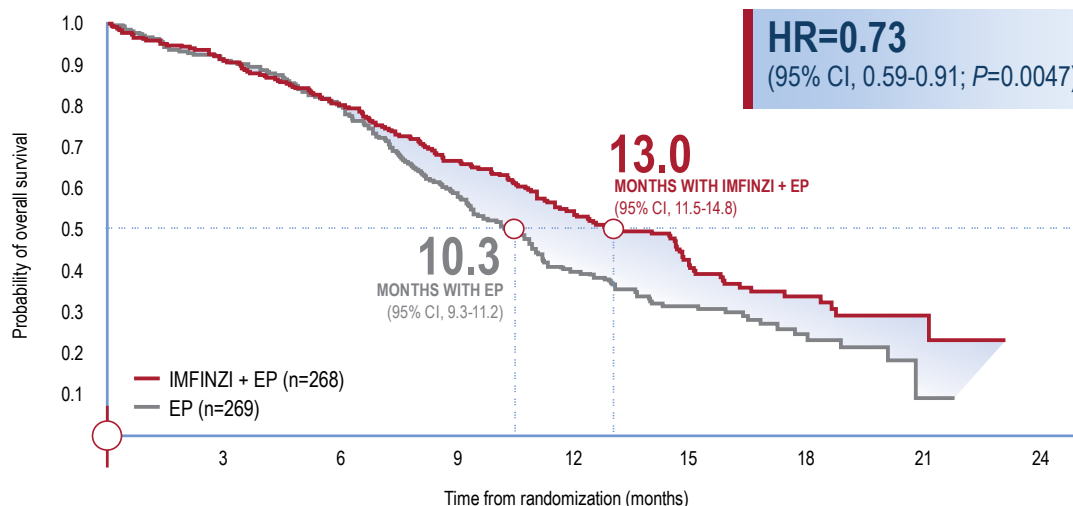
IMFINZI + EP: APPROVED IN FIRST-LINE ES-SCLC

Study design: Approval for IMFINZI was based on the CASPIAN study, a Phase 3, randomized, open-label study in 805 patients with treatment-naïve ES-SCLC. Patients were randomized 1:1:1 to receive IMFINZI with or without an investigational agent + EP^a followed by maintenance IMFINZI or EP alone.^b FDA approval was based on the results from the planned interim analysis of the IMFINZI + EP and EP alone arms. Patients with asymptomatic or treated brain metastases were allowed. The primary endpoint was OS. Key secondary endpoints included PFS, ORR (unconfirmed), OS at 18 months, PFS at 6 and 12 months, and HRQoL patient-reported outcomes.^{1,2}



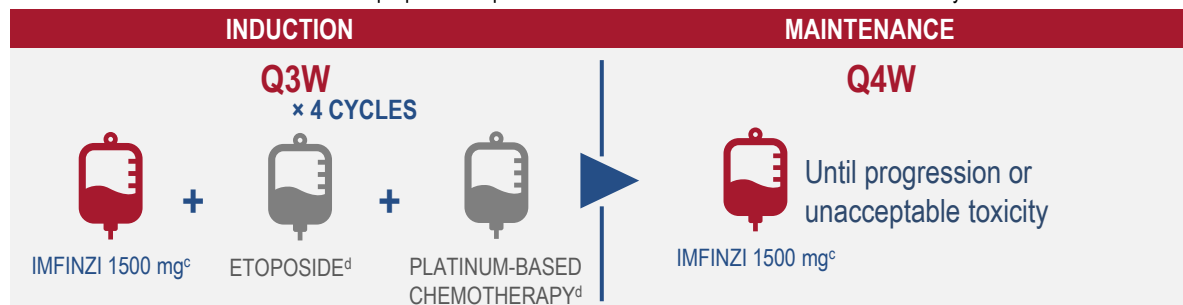
ES-SCLC

OVERALL SURVIVAL^{1,2}



	IMFINZI + EP (n=268)	EP alone (n=269)
OS rate at 18 months (secondary endpoint)	34% (95% CI, 26.9-41.0)	25% (95% CI, 18.4-31.6)

• OS rate at 18 months is the estimated proportion of patients alive at 18 months based on the interim analysis.^{1,2}



**NCCN
Guidelines®**

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend durvalumab (IMFINZI) in combination with either carboplatin/etoposide or cisplatin/etoposide followed by maintenance durvalumab (IMFINZI) as preferred first-line treatment options (category 1 for all) for ES-SCLC.^{3,e,f}

^aIMFINZI 1500 mg + either carboplatin (AUC 5 mg/mL/min or 6 mg/mL/min) or cisplatin (75-80 mg/m²) on day 1 and etoposide (80-100 mg/m²) intravenously 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.^{1,2} ^bEither carboplatin (AUC 5 mg/mL/min or 6 mg/mL/min) or cisplatin (75-80 mg/m²) on day 1 and etoposide (80-100 mg/m²) intravenously on days 1, 2, and 3 of each 21-day cycle for 4 to 6 cycles. The EP alone control arm allowed for prophylactic cranial irradiation following treatment at the investigator's discretion.^{1,2} ^cPatients with a body weight of 30 kg or less must receive weight-based dosing, equivalent to IMFINZI 20 mg/kg, according to the same dosing schedule as above. IMFINZI may be given as 1500 mg fixed dose once body weight increases to >30 kg. IMFINZI is administered as a 60-minute IV infusion. No premedication is required for IMFINZI treatment. ^dEP consists of etoposide 80-100 mg/m² with either carboplatin AUC 5 or 6 mg/mL/min or cisplatin 75-80 mg/m². For more information, please refer to the Prescribing Information for each treatment. ^ePreferred indicates interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability; category 1 recommendations are based upon high-level evidence, and there is uniform NCCN consensus that the intervention is appropriate. ^fSee the NCCN Guidelines for detailed recommendations, including other preferred options.³

Indication

IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Important Safety Information

There are no contraindications for IMFINZI® (durvalumab).

IMFINZI can cause serious, potentially fatal adverse reactions including immune-mediated pneumonitis, hepatitis, colitis, endocrinopathies, nephritis, dermatologic reactions, other immune-mediated adverse reactions, infection, and infusion-related reactions. Please refer to the full Prescribing Information for important dosage modification and management information specific to adverse reactions.

IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3 or 4 pneumonitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, pneumonitis occurred in 5% of patients, including Grade 3 (0.8%), Grade 4 (<0.1%), and Grade 5 (0.3%) pneumonitis. Pneumonitis led to discontinuation of IMFINZI in 1.5% of the 1889 patients. The incidence of pneumonitis (including radiation pneumonitis) was higher in patients in the PACIFIC study who completed treatment with definitive chemoradiation within 42 days prior to initiation of IMFINZI (34%) compared to patients in other clinical studies (2.3%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI. In the PACIFIC study, the incidence of Grade 3 pneumonitis was 3.4% and of Grade 5 pneumonitis was 1.1% in the IMFINZI arm. In the PACIFIC study, pneumonitis led to discontinuation of IMFINZI in 6% of patients.

The frequency and severity of immune-mediated pneumonitis were similar whether IMFINZI was given as a single agent in patients with various cancers or in combination with chemotherapy in patients with ES-SCLC.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of hepatitis during and after discontinuation of IMFINZI, including clinical chemistry monitoring. Administer corticosteroids for Grade 2 or higher elevations of ALT, AST, and/or total bilirubin. Withhold IMFINZI for ALT or AST greater than 3 but less than or equal to 8 times the ULN or total bilirubin greater than 1.5 but less than or equal to 5 times the ULN; permanently discontinue IMFINZI for ALT or AST greater than 8 times the ULN or total bilirubin greater than 5 times the ULN or concurrent ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times the ULN with no other cause.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hepatitis occurred in 12% of patients, including Grade 3 (4.4%), Grade 4 (0.4%), and Grade 5 (0.2%) hepatitis. Hepatitis led to discontinuation of IMFINZI in 0.7% of the 1889 patients.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis, defined as requiring use of corticosteroids.

Administer corticosteroids for Grade 2 or greater colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3 or 4 colitis or diarrhea.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, colitis or diarrhea occurred in 18% of patients, including Grade 3 (1.0%) and Grade 4 (0.1%) immune-mediated colitis. Diarrhea or colitis led to discontinuation of IMFINZI in 0.4% of the 1889 patients.

Immune-Mediated Endocrinopathies

IMFINZI can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus, and hypophysitis/hypopituitarism. Monitor patients for clinical signs and symptoms of endocrinopathies.

- **Thyroid disorders**—Monitor thyroid function prior to and periodically during treatment. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Withhold IMFINZI for Grades 2–4 hyperthyroidism, until clinically stable. Continue IMFINZI for hypothyroidism. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hypothyroidism occurred in 11% of patients, while hyperthyroidism occurred in 7% of patients. Thyroiditis occurred in 0.9% of patients, including Grade 3 (<0.1%) thyroiditis. Hypothyroidism was preceded by thyroiditis or hyperthyroidism in 25% of patients.
- **Adrenal insufficiency**—Administer corticosteroids as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher adrenal insufficiency. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, adrenal insufficiency occurred in 0.7% of patients, including Grade 3 (<0.1%) adrenal insufficiency.
- **Type 1 diabetes mellitus**—Initiate treatment with insulin as clinically indicated. Withhold IMFINZI for Grades 2–4 type 1 diabetes mellitus, until clinically stable. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, type 1 diabetes mellitus occurred in <0.1% of patients.
- **Hypophysitis**—Administer corticosteroids and hormone replacement as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher hypophysitis. Hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in <0.1% of 1889 patients with various cancers who received IMFINZI.

Immune-Mediated Nephritis

IMFINZI can cause immune-mediated nephritis, defined as evidence of renal dysfunction requiring use of corticosteroids. Fatal cases have occurred. Monitor patients for abnormal renal function tests prior to and periodically during treatment with IMFINZI. Administer corticosteroids as clinically indicated. Withhold IMFINZI for creatinine greater than 1.5 to 3 times the ULN; permanently discontinue IMFINZI and administer corticosteroids in patients with creatinine greater than 3 times the ULN.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, nephritis (reported as any of the following: increased creatinine or urea, acute kidney injury, renal failure, decreased glomerular filtration rate, tubulointerstitial nephritis, decreased creatinine clearance, glomerulonephritis, and nephritis) occurred in 6.3% of the patients including Grade 3 (1.1%), Grade 4 (0.2%), and Grade 5 (0.1%) nephritis. IMFINZI was discontinued in 0.3% of the 1889 patients.

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AUC, area under the curve; EP, etoposide + platinum-based chemotherapy; ES-SCLC, extensive-stage small cell lung cancer; HR, hazard ratio; HRQoL, health-related quality of life; IV, intravenous; NCCN, National Comprehensive Cancer Network; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; Q4W, every 4 weeks.

Please see accompanying complete Prescribing Information, including Medication Guide.

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Immune-Mediated Dermatologic Reactions

IMFINZI can cause immune-mediated rash. Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN) has occurred with other products in this class. Administer corticosteroids for Grade 2 rash or dermatitis lasting for more than 1 week or for Grade 3 or 4 rash or dermatitis. Withhold IMFINZI for Grade 2 rash or dermatitis lasting longer than 1 week or Grade 3 rash or dermatitis; permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, 26% of patients developed rash or dermatitis and 0.4% of the patients developed vitiligo. Rash or dermatitis led to discontinuation of IMFINZI in 0.1% of the 1889 patients.

Other Immune-Mediated Adverse Reactions

IMFINZI can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with IMFINZI, immune-mediated adverse reactions can also manifest after discontinuation of IMFINZI. For suspected immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. Withhold IMFINZI for Grade 3 immune-mediated adverse reactions, unless clinical judgment indicates discontinuation; permanently discontinue IMFINZI for Grade 4 adverse reactions.

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in 1889 patients who received IMFINZI: aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, and ocular inflammatory toxicity, including uveitis and keratitis. Additional clinically significant immune-mediated adverse reactions have been seen with other products in this class (see Warnings and Precautions Section 5.7 of IMFINZI full Prescribing Information).

Infection

IMFINZI can cause serious infections, including fatal cases. Monitor patients for signs and symptoms of infection and treat as clinically indicated. Withhold IMFINZI for Grade 3 or 4 infection, until clinically stable.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infections occurred in 43% of patients, including Grade 3 (8%), Grade 4 (1.9%), and Grade 5 (1.0%). The overall incidence of infections in IMFINZI-treated patients in the PACIFIC study (56%) was higher compared to patients in other clinical studies (38%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI. In patients with UC in Study 1108 (n=182), the most common Grade 3 or higher infection was urinary tract infections, which occurred in 4% of patients. In patients with Stage III NSCLC in the PACIFIC study, the most common Grade 3 or higher infection was pneumonia, which occurred in 5% of patients.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor patients for signs and symptoms of an infusion-related reaction. Interrupt or slow the rate of infusion for Grades 1–2 infusion-related reactions; permanently discontinue for Grades 3–4 infusion-related reactions.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infusion-related reactions occurred in 2.2% of patients, including Grade 3 (0.3%).

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. There are no data on the use of IMFINZI in pregnant women. Advise pregnant women of the potential risk to a fetus and advise women of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI.

Lactation

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- In patients with extensive-stage SCLC in the CASPIAN study (n=265), the most common adverse reactions (≥20%) were nausea, fatigue/asthenia, and alopecia. The most common Grade 3 or 4 adverse reaction (≥3%) was fatigue/asthenia (3.4%).
- In patients with extensive-stage SCLC in the CASPIAN study (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy.

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

References: 1. IMFINZI® [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. 2. Paz-Ares L, Chen Y, Reinmuth N, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomized, controlled, open-label, phase 3 trial. *Lancet*. 2019;394(10212):1929-1939. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer V3.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed February 11, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org.

Small Cell Lung Cancer-Extensive Disease

Durvalumab/Etoposide/CARBOplatin or CISplatin followed by Durvalumab Maintenance

Laboratory Studies^{1,a}		
CBC with differential	Baseline, D1 and D8 q3weeks for Cycles 1-4, then q4weeks thereafter. Upon discontinuation, once monthly for 3 months.	
Clinical chemistry	Baseline, D1 and D8 q3weeks for Cycles 1-4, then q4weeks thereafter. Upon discontinuation, once monthly for 3 months.	Recommended to have CrCl ≥ 60 mL/min for patients on cisplatin and >45 mL/min for patients on carboplatin (using Cockcroft-Gault equation) ³
Liver Panel (bilirubin, LFTs)	Baseline, D1 and D8 q3weeks for Cycles 1-4, then q4weeks thereafter. Upon discontinuation, once monthly for 3 months.	Recommended to have total bilirubin less than or equal to 1.5x ULN, AST/ALT less than or equal to 2.5x ULN (or less than or equal to 5x ULN for liver metastases) ³
Thyroid Panel (TSH, fT4, fT3)	Baseline, D1 q3weeks for Cycles 1-4, then q4weeks thereafter. Upon discontinuation, once monthly for 3 months.	Free T3 and free T4 will only be measured if TSH is abnormal or if there is clinical suspicion of an AE related to the endocrine system. ¹
Urine pregnancy test	Baseline, D1 q3weeks for Cycles 1-4, then q4weeks thereafter. Upon discontinuation, at 28 days, and as clinically indicated thereafter.	Recommended for premenopausal women of childbearing potential. ³ Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for ≥ 3 months after last dose. ²
Other monitoring	Per institution-preferred protocol	Signs and symptoms of pneumonitis, hepatitis, colitis or diarrhea, adrenal insufficiency, hypophysitis or hypopituitarism, nephritis, rash or dermatitis, aseptic meningitis, hemolytic anemia, immune thrombocytopenia purpura, myocarditis, myositis, ocular inflammatory toxicity, including uveitis and keratitis, infection, and infusion-related reactions; clinical signs and symptoms of endocrinopathies; symptoms of diabetes. ²
^a Per CASPIAN study protocol or institution-preferred protocol		

Please see full indication for IMFINZI (durvalumab), Important Safety Information on pages 4-7, and complete [Prescribing Information](#), including Medication Guide.

Treatment Conditions and Parameters

<p>Recommended Hold/Discontinuation Parameters</p> <p>Please see complete Prescribing Information for additional information regarding therapeutic interventions</p>	<p>Pneumonitis or colitis/diarrhea: For Grade 2, withhold until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent); permanently discontinue for Grade 3 or 4.²</p> <p>Rash or dermatitis: For Grade 2 for longer than 1 week or Grade 3, withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent); permanently discontinue for Grade 4.²</p> <p>Hepatitis: For ALT or AST greater than 3 but less than or equal to 8 times the ULN or total bilirubin greater than 1.5 but less than or equal to 5 times the ULN, withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent); permanently discontinue for ALT or AST >8x the ULN or total bilirubin >5x the ULN or concurrent ALT or AST >3x the ULN and total bilirubin >2x the ULN with no other cause.²</p> <p>Endocrinopathy (hyperthyroidism, adrenal insufficiency, hypophysitis/hypopituitarism, type 1 diabetes mellitus): For Grade 2-4, withhold dose until clinically stable.²</p> <p>Nephritis: For creatinine greater than 1.5 to 3 times the ULN, withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent); permanently discontinue for creatinine greater than 3 times the ULN.²</p> <p>Infection: For Grade 3 or 4, withhold dose until clinically stable.²</p> <p>Other immune-mediated adverse reactions: For Grade 3, withhold dose until Grade 1 or resolved and corticosteroid dose is less than or equal to prednisone 10 mg per day (or equivalent); permanently discontinue for Grade 4.²</p> <p>Persistent Grade 2 or 3 adverse reactions (excluding endocrinopathies): Permanently discontinue for Grade 2 or 3 adverse reaction that does not recover to Grade 0 or 1 within 12 weeks after last IMFINZI dose.²</p> <p>Inability to taper corticosteroid: Permanently discontinue if inability to reduce to less than or equal to prednisone 10 mg per day (or equivalent) within 12 weeks after the last IMFINZI dose.</p> <p>Recurrent Grade 3 or 4 adverse reaction: Permanently discontinue for recurrent Grade 3 or 4 (severe or life-threatening) adverse reaction.²</p> <p>^bNational Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.</p>
<h2>PreHydration and PreMedications</h2>	
<p>PreHydration</p>	<p>For Durvalumab: Per institution-preferred protocol For Chemotherapy: Per institution-preferred protocol</p>
<p>PreMedications</p>	<p>For Durvalumab: Per institution-preferred protocol For Chemotherapy: Per institution-preferred protocol</p>

Chemotherapy Orders

Cycle 1-4 Cycle Length=3 weeks(21 days)	
Durvalumab 1500 mg IV over 60 minutes in combination with chemotherapy* *Chemotherapy CARBOplatin (AUC 5 or 6 mg/mL/min) or CISplatin (75-80 mg/m ²) IV on Day 1 and etoposide IV (80-100 mg/m ²) intravenously on Days 1, 2, and 3	Durvalumab: Dilute to final concentration 1 mg/mL to 15 mg/mL with 0.9% sodium chloride injection, USP or 5% dextrose injection, USP and administer over 60 minutes. Use sterile, low-protein binding 0.2 or 0.22 micron in-line filter. Administer infusion solution immediately once prepared. The total time from vial puncture to the start of the administration should not exceed 24 hr refrigerated (2°C to 8°C) or 8 hr at room temperature (up to 25°C). Discard partially used or empty vials of IMFINZI. Do not co-administer other drugs through the same infusion line. Chemotherapy: Dilute and administer per institution-preferred protocol, following administration of durvalumab

Cycle 5 and beyond (until disease progression or unacceptable toxicity) Cycle length= 4 weeks	
Durvalumab 1500 mg IV over 60 minutes	Durvalumab: Dilute to final concentration 1 mg/mL to 15 mg/mL with 0.9% sodium chloride injection, USP or 5% dextrose injection, USP and administer over 60 minutes. Use sterile, low-protein binding 0.2 or 0.22 micron in-line filter. Administer infusion solution immediately once prepared. The total time from vial puncture to the start of the administration should not exceed 24 hr refrigerated (2°C to 8°C) or 8 hr at room temperature (up to 25°C). Discard partially used or empty vials of IMFINZI. Do not co-administer other drugs through the same infusion line.

Rescue Medications and Flush

IV Flush	Per institution-preferred protocol
Infusion Related Reactions	Per institution-preferred protocol
For imAE management	Durvalumab: Prednisone or equivalent Refer to IMFINZI Prescribing Information for specific corticosteroid treatment Chemotherapy: Per institution-preferred protocol, for cycles 1-4

Take Home Medications

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Abbreviations:

BMP=basic metabolic panel; CBC=complete blood count; CrCl=creatinine clearance; D1=day 1; ft3=free triiodothyronine; ft4=free thyroxine; imAEs=immune-mediated adverse events; IV=intravenous; LFT=liver function test; MDV=multiple-dose vial; Q2W=every 2 weeks; SDV=single-dose vial; TSH=thyroid stimulating hormone; ULN=upper limit of normal; USP=US Pharmacopeia.

References:

1. Data on File, REF-73243, AstraZeneca Pharmaceuticals LP.
2. IMFINZI [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020
3. 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 randomized, controlled, open-label, phase 3 trial [article and supplementary appendix]. *Lancet*. 2019;394(10212):1929-1939.

Important Safety Information

There are no contraindications for IMFINZI® (durvalumab).

IMFINZI can cause serious, potentially fatal adverse reactions including immune-mediated pneumonitis, hepatitis, colitis, endocrinopathies, nephritis, dermatologic reactions, other immune-mediated adverse reactions, infection, and infusion-related reactions. Please refer to the full Prescribing Information for important dosage modification and management information specific to adverse reactions.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of pneumonitis and evaluate with radiographic imaging when suspected. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold IMFINZI for Grade 2 pneumonitis; permanently discontinue for Grade 3 or 4 pneumonitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, pneumonitis occurred in 5% of patients, including Grade 3 (0.8%), Grade 4 (<0.1%), and Grade 5 (0.3%) pneumonitis. Pneumonitis led to discontinuation of IMFINZI in 1.5% of the 1889 patients. The incidence of pneumonitis (including radiation pneumonitis) was higher in patients in the PACIFIC study who completed treatment with definitive chemoradiation within 42 days prior to initiation of IMFINZI (34%) compared to patients in other clinical studies (2.3%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI. In the PACIFIC study, the incidence of Grade 3 pneumonitis was 3.4% and of Grade 5 pneumonitis was 1.1% in the IMFINZI arm. In the PACIFIC study, pneumonitis led to discontinuation of IMFINZI in 6% of patients.

The frequency and severity of immune-mediated pneumonitis were similar whether IMFINZI was given as a single agent in patients with various cancers or in combination with chemotherapy in patients with ES-SCLC.

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis, defined as requiring use of corticosteroids. Fatal cases have been reported. Monitor patients for signs and symptoms of hepatitis during and after discontinuation of IMFINZI, including clinical chemistry monitoring. Administer corticosteroids for Grade 2 or higher elevations of ALT, AST, and/or total bilirubin. Withhold IMFINZI for ALT or AST greater than 3 but less than or equal to 8 times the ULN or total bilirubin greater than 1.5 but less than or equal to 5 times the ULN; permanently discontinue IMFINZI for ALT or AST greater than 8 times the ULN or total bilirubin greater than 5 times the ULN or concurrent ALT or AST greater than 3 times the ULN and total bilirubin greater than 2 times the ULN with no other cause.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hepatitis occurred in 12% of patients, including Grade 3 (4.4%), Grade 4 (0.4%), and Grade 5 (0.2%) hepatitis. Hepatitis led to discontinuation of IMFINZI in 0.7% of the 1889 patients.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis, defined as requiring use of corticosteroids. Administer corticosteroids for Grade 2 or greater colitis or diarrhea. Withhold IMFINZI for Grade 2 colitis or diarrhea; permanently discontinue for Grade 3 or 4 colitis or diarrhea.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, colitis or diarrhea occurred in 18% of patients, including Grade 3 (1.0%) and Grade 4 (0.1%) immune-mediated colitis. Diarrhea or colitis led to discontinuation of IMFINZI in 0.4% of the 1889 patients.

Immune-Mediated Endocrinopathies

IMFINZI can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, type 1 diabetes mellitus, and hypophysitis/hypopituitarism. Monitor patients for clinical signs and symptoms of endocrinopathies.

- **Thyroid disorders**—Monitor thyroid function prior to and periodically during treatment. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated. Withhold IMFINZI for Grades 2–4 hyperthyroidism, until clinically stable. Continue IMFINZI for hypothyroidism.
In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, hypothyroidism occurred in 11% of patients, while hyperthyroidism occurred in 7% of patients. Thyroiditis occurred in 0.9% of patients, including Grade 3 (<0.1%) thyroiditis. Hypothyroidism was preceded by thyroiditis or hyperthyroidism in 25% of patients.
- **Adrenal insufficiency**—Administer corticosteroids as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher adrenal insufficiency. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, adrenal insufficiency occurred in 0.7% of patients, including Grade 3 (<0.1%) adrenal insufficiency.
- **Type 1 diabetes mellitus**—Initiate treatment with insulin as clinically indicated. Withhold IMFINZI for Grades 2–4 type 1 diabetes mellitus, until clinically stable. In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, type 1 diabetes mellitus occurred in <0.1% of patients.
- **Hypophysitis**—Administer corticosteroids and hormone replacement as clinically indicated and withhold IMFINZI until clinically stable for Grade 2 or higher hypophysitis. Hypopituitarism leading to adrenal insufficiency and diabetes insipidus occurred in <0.1% of 1889 patients with various cancers who received IMFINZI.

Immune-Mediated Nephritis

IMFINZI can cause immune-mediated nephritis, defined as evidence of renal dysfunction requiring use of corticosteroids. Fatal cases have occurred. Monitor patients for abnormal renal function tests prior to and periodically during treatment with IMFINZI. Administer corticosteroids as clinically indicated. Withhold IMFINZI for creatinine greater than 1.5 to 3 times the ULN; permanently discontinue IMFINZI and administer corticosteroids in patients with creatinine greater than 3 times the ULN.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, nephritis (reported as any of the following: increased creatinine or urea, acute kidney injury, renal failure, decreased glomerular filtration rate, tubulointerstitial nephritis, decreased creatinine clearance, glomerulonephritis, and nephritis) occurred in 6.3% of the patients including Grade 3 (1.1%), Grade 4 (0.2%), and Grade 5 (0.1%) nephritis. IMFINZI was discontinued in 0.3% of the 1889 patients.

Immune-Mediated Dermatologic Reactions

IMFINZI can cause immune-mediated rash. Stevens Johnson Syndrome (SJS)/toxic epidermal necrolysis (TEN) has occurred with other products in this class. Administer corticosteroids for Grade 2 rash or dermatitis lasting for more than 1 week or for Grade 3 or 4 rash or dermatitis. Withhold IMFINZI for Grade 2 rash or dermatitis lasting longer than 1 week or Grade 3 rash or dermatitis; permanently discontinue IMFINZI in patients with Grade 4 rash or dermatitis.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, 26% of patients developed rash or dermatitis and 0.4% of the patients developed vitiligo. Rash or dermatitis led to discontinuation of IMFINZI in 0.1% of the 1889 patients.

Other Immune-Mediated Adverse Reactions

IMFINZI can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with IMFINZI, immune-mediated adverse reactions can also manifest after discontinuation of IMFINZI. For suspected immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. Withhold IMFINZI for Grade 3 immune-mediated adverse reactions, unless clinical judgment indicates discontinuation; permanently discontinue IMFINZI for Grade 4 adverse reactions.

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in 1889 patients who received IMFINZI: aseptic meningitis, hemolytic anemia, immune thrombocytopenic purpura, myocarditis, myositis, and ocular inflammatory toxicity, including uveitis and keratitis. Additional clinically significant immune-mediated adverse reactions have been seen with other products in this class (see Warnings and Precautions Section 5.7 of IMFINZI full Prescribing Information).

Infection

IMFINZI can cause serious infections, including fatal cases. Monitor patients for signs and symptoms of infection and treat as clinically indicated. Withhold IMFINZI for Grade 3 or 4 infection, until clinically stable.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infections occurred in 43% of patients, including Grade 3 (8%), Grade 4 (1.9%), and Grade 5 (1.0%). The overall incidence of infections in IMFINZI-treated patients in the PACIFIC study (56%) was higher compared to patients in other clinical studies (38%) in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI. In patients with UC in Study 1108 (n=182), the most common Grade 3 or higher infection was urinary tract infections, which occurred in 4% of patients. In patients with Stage III NSCLC in the PACIFIC study, the most common Grade 3 or higher infection was pneumonia, which occurred in 5% of patients.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor patients for signs and symptoms of an infusion-related reaction. Interrupt or slow the rate of infusion for Grades 1–2 infusion-related reactions; permanently discontinue for Grades 3–4 infusion-related reactions.

In clinical studies enrolling 1889 patients with various cancers who received IMFINZI, infusion-related reactions occurred in 2.2% of patients, including Grade 3 (0.3%).

Embryo-Fetal Toxicity

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. There are no data on the use of IMFINZI in pregnant women. Advise

pregnant women of the potential risk to a fetus and advise women of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI.

Lactation

There is no information regarding the presence of IMFINZI in human milk; however, because of the potential for adverse reactions in breastfed infants from IMFINZI, advise women not to breastfeed during treatment and for at least 3 months after the last dose.

Most Common Adverse Reactions

- In patients with extensive-stage SCLC in the CASPIAN study (n=265), the most common adverse reactions ($\geq 20\%$) were nausea, fatigue/asthenia, and alopecia. The most common Grade 3 or 4 adverse reaction ($\geq 3\%$) was fatigue/asthenia (3.4%)
- In patients with extensive-stage SCLC in the CASPIAN study (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy

The safety and effectiveness of IMFINZI have not been established in pediatric patients.

Indication

IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Please see complete [Prescribing Information](#), including Medication Guide.