HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use IMFINZI safely and effectively. See full prescribing information for IMFINZI.

IMFINZI® (durvalumab) injection, for intravenous use
Initial U.S. Approval: 2017

---------- RECENT MAJOR CHANGES ----------

Indications and Usage (1.3)	03/2020
Dosage and Administration (2.1)	11/2020
Dosage and Administration, Dosage Modifications (2.2)	11/2020
Warnings and Precautions (5.1, 5.3)	11/2020

---------- INDICATIONS AND USAGE ----------

IMFINZI is a programmed death-ligand 1 (PD-L1) blocking antibody indicated:

- for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:
  - have disease progression during or following platinum-containing chemotherapy. (1.1)
  - have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. (1.1)

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.1)

- for the treatment of adult patients with unresectable, Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy. (1.2)
- in combination with etoposide and either carboplatin or cisplatin, as first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC). (1.3)

---------- DOSAGE AND ADMINISTRATION ----------

- Administer IMFINZI as an intravenous infusion over 60 minutes. (2.3)
- Urothelial Carcinoma:
  - Weight 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks (2.1)
  - Weight less than 30 kg: 10 mg/kg every 2 weeks (2.1)
- Stage III NSCLC:
  - Weight 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks (2.1)
  - Weight less than 30 kg: 10 mg/kg every 2 weeks (2.1)
- ES-SCLC:
  - Weight 30 kg and more: With etoposide and either carboplatin or cisplatin, administer IMFINZI 1500 mg every 3 weeks in combination with chemotherapy, and then 1500 mg every 4 weeks as a single agent (2.1)
  - Weight less than 30 kg: With etoposide and either carboplatin or cisplatin, administer IMFINZI 20 mg/kg every 3 weeks in combination with chemotherapy, and then 10 mg/kg every 2 weeks as a single agent (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------

- Injection: 500 mg/10 mL (50 mg/mL) solution in a single-dose vial. (3)
- Injection: 120 mg/2.4 mL (50 mg/mL) solution in a single-dose vial. (3)

---------- CONTRAINDICATIONS ----------

None. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Immune-Mediated Adverse Reactions (5.1)
  - Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, immune-mediated nephritis and renal dysfunction, and solid organ transplant rejection.
    - Monitor for early identification and management. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.
    - Withhold or permanently discontinue based on severity and type of reaction.
- Infusion-Related Reactions: Interrupt, slow the rate of infusion, or permanently discontinue IMFINZI based on the severity of the reaction. (5.2)
- Complications of Allogeneic HSCT: Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1 blocking antibody. (5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception. (5.4, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------

- Most common adverse reactions (≥ 15% of patients with urothelial carcinoma) were fatigue, musculoskeletal pain, constipation, decreased appetite, nausea, peripheral edema, and urinary tract infection. (6.1)
- Most common adverse reactions (≥ 20% of patients with unresectable, Stage III NSCLC) were cough, fatigue, pneumonitis/radiation pneumonitis, upper respiratory tract infections, dyspnea, and rash. (6.1)
- Most common adverse reactions (≥ 20% of patients with extensive-stage SCLC) were, nausea, fatigue/asthenia, alopecia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- USE IN SPECIFIC POPULATIONS ----------

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Urothelial Carcinoma

IMFINZI is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma who:

- have disease progression during or following platinum-containing chemotherapy.
- have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials *[see Clinical Studies (14.1)]*.

1.2 Non-Small Cell Lung Cancer

IMFINZI is indicated for the treatment of adult patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

1.3 Small Cell Lung Cancer

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).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosages for IMFINZI as a single agent and IMFINZI in combination with chemotherapy are presented in Table 1 *[see Clinical Studies (14)]*.

IMFINZI is administered as an intravenous infusion over 60 minutes.

Table 1. Recommended Dosages of IMFINZI

Indication	Recommended IMFINZI dosage	Duration of Therapy
Urothelial Carcinoma	Patients with a body weight of 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks	Until disease progression or unacceptable toxicity

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	Patients with a body weight of less than 30 kg: 10 mg/kg every 2 weeks	
Unresectable stage III NSCLC	Patients with a body weight of 30 kg and more: 10 mg/kg every 2 weeks or 1500 mg every 4 weeks Patients with a body weight of less than 30 kg: 10 mg/kg every 2 weeks	Until disease progression, unacceptable toxicity, or a maximum of 12 months
ES-SCLC	Patients with a body weight of 30 kg and more: 1500 mg in combination with chemotherapy[1] every 3 weeks (21 days) for 4 cycles, followed by 1500 mg every 4 weeks as a single agent Patients with a body weight of less than 30 kg: 20 mg/kg in combination with chemotherapy[1] every 3 weeks (21 days) for 4 cycles, followed by 10 mg/kg every 2 weeks as a single agent	Until disease progression or unacceptable toxicity

[1] Administer IMFINZI prior to chemotherapy on the same day. When IMFINZI is administered in combination with chemotherapy, refer to the Prescribing Information for etoposide and carboplatin or cisplatin for dosing information.

2.2 Dosage Modifications for Adverse Reactions

No dose reduction for IMFINZI is recommended. In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids.

Dosage modifications for IMFINZI for adverse reactions that require management different from these general guidelines are summarized in Table 2.

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Table 2. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity[1]	Dosage Modification
Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1)]*		
Pneumonitis	Grade 2	Withhold[2]
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2 or 3	Withhold[2]
	Grade 4	Permanently discontinue

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Adverse Reaction	Severity[1]	Dosage Modification
Hepatitis with no tumor involvement of the liver	ALT or AST increases to more than 3 and up to 8 times the ULN or total bilirubin increases to more than 1.5 and up to 3 times ULN	Withhold[2]
	ALT or AST increases to more than 8 times ULN or total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver[3]	AST or ALT is more than 1 and up to 3 times ULN at baseline and increases to more than 5 and up to 10 times ULN or AST or ALT is more than 3 and up to 5 times ULN at baseline and increases to more than 8 and up to 10 times ULN	Withhold[2]
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[2]
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold[2]

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Adverse Reaction	Severity[1]	Dosage Modification
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological Toxicities	Grade 2	Withhold[2]
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions *[see Warnings and Precautions (5.2)]*	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

ALT = alanine aminotransferase, AST = aspartate aminotransferase, DRESS = Drug Rash with Eosinophilia and Systemic Symptoms, SJS = Stevens Johnson Syndrome, TEN = toxic epidermal necrolysis, ULN = upper limit normal

[1] Based on National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.
[2] Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone 10 mg per day or less (or equivalent) within 12 weeks of initiating steroids.
[3] If AST and ALT are less than or equal to ULN at baseline in patients with liver involvement, withhold or permanently discontinue IMFINZI based on recommendations for hepatitis with no liver involvement.

2.3 Preparation and Administration

Preparation

- Visually inspect drug product for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the vial if the solution is cloudy, discolored, or visible particles are observed.
- Do not shake the vial.
- Withdraw the required volume from the vial(s) of IMFINZI and transfer into an intravenous bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP. Mix diluted solution by gentle inversion. Do not shake the solution. The final concentration of the diluted solution should be between 1 mg/mL and 15 mg/mL.
- Discard partially used or empty vials of IMFINZI.

Storage of Infusion Solution

- IMFINZI does not contain a preservative.
- Administer infusion solution immediately once prepared. If infusion solution is not administered immediately and needs to be stored, the total time from vial puncture to the start of the administration should not exceed:
    - 24 hours in a refrigerator at 2°C to 8°C (36°F to 46°F)

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- 8 hours at room temperature up to 25°C (77°F)

- Do not freeze.
- Do not shake.

Administration

- Administer infusion solution intravenously over 60 minutes through an intravenous line containing a sterile, low-protein binding 0.2 or 0.22 micron in-line filter.
- Do not co-administer other drugs through the same infusion line.

3 DOSAGE FORMS AND STRENGTHS

Injection: 120 mg/2.4 mL (50 mg/mL) and 500 mg/10 mL (50 mg/mL) clear to opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Immune-Mediated Adverse Reactions

IMFINZI is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2)]*. In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month.

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Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

In Patients Who did Not Receive Recent Prior Radiation

In patients who received IMFINZI on clinical trials in which radiation therapy was generally not administered immediately prior to initiation of IMFINZI, the incidence of immune-mediated pneumonitis was 2.0% (28/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. Events resolved in 15 of the 28 patients and resulted in permanent discontinuation in 5 patients. Systemic corticosteroids were required in 17 patients (17/28) with pneumonitis who did not receive chemoradiation prior to initiation of IMFINZI.

In Patients Who Received Recent Prior Radiation

The incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 16.6% (79/475) in patients receiving IMFINZI and 13.2% (31/234) in patients receiving placebo. Of the 79 patients who received IMFINZI, 1.1% were fatal and 2.5% were Grade 3-4 adverse reactions. Events resolved in 43 of the 79 patients and resulted in permanent discontinuation in 24 patients.

Systemic corticosteroids were required in 60 patients (60/79) with pneumonitis who had received chemoradiation prior to initiation of IMFINZI, while 2 patients required use of infliximab with high-dose steroids.

The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar whether IMFINZI was given as a single agent in patients with various cancers in a pooled data set or in patients with ES-SCLC when given in combination with chemotherapy.

Immune-Mediated Colitis

IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.6% (31/1889) of patients receiving IMFINZI, including Grade 4 (0.1%) and Grade 3 (0.3%) adverse reactions. Events resolved in 23 of the 31 patients and resulted in permanent discontinuation in 8 patients. Systemic corticosteroids were required in all patients with

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immune-mediated colitis, while 2 patients (2/31) required other immunosuppressants (e.g., infliximab, mycophenolate).

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis.

Immune-mediated hepatitis occurred in 1.0% (19/1889) of patients receiving IMFINZI, including fatal (<0.1%) and Grade 3 (0.6%) adverse reactions. Events resolved in 12 of the 19 patients and resulted in permanent discontinuation of IMFINZI in 4 patients. Systemic corticosteroids were required in all patients with immune-mediated hepatitis, while 1 patient (1/19) required use of mycophenolate with high-dose steroids.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency:

IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2)]*.

Immune-mediated adrenal insufficiency occurred in 0.4% (7/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Adrenal insufficiency did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, the majority remained on systemic corticosteroids.

Hypophysitis:

IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2)]*.

Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) patients who received IMFINZI. Treatment with systemic corticosteroids was administered in this patient. The event did not lead to permanent discontinuation of IMFINZI.

Thyroid Disorders:

IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated. Withhold or discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2)]*.

Thyroiditis: Immune-mediated thyroiditis occurred in 0.4% (7/1889) of patients receiving IMFINZI. Events resolved in 3 of the 7 patients and none resulted in permanent discontinuation. Systemic

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corticosteroids were required in 3 patients (3/7) with immune-mediated thyroiditis, while 5 patients (5/7) required endocrine therapy.

Hyperthyroidism: Immune-mediated hyperthyroidism occurred in 1.4% (27/1889) of patients receiving IMFINZI. Events resolved in 20 of the 27 patients. Systemic corticosteroids were required in 9 patients (9/27) with immune-mediated hyperthyroidism, while 21 patients (21/27) required endocrine therapy.

Hypothyroidism: Immune-mediated hypothyroidism occurred in 7.3% (137/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Systemic corticosteroids were required in 10 patients (10/137) and the majority of patients (134/137) required long-term thyroid hormone replacement.

Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2)]*.

Grade 3 immune-mediated type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI. This patient required long-term insulin therapy and IMFINZI was permanently discontinued.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis.

Immune-mediated nephritis occurred in 0.3% (5/1889) of patients receiving IMFINZI, including Grade 3 (0.1%) adverse reactions. Events resolved in 3 of the 5 patients and resulted in permanent discontinuation in 4 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis.

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue IMFINZI depending on severity *[see Dosage and Administration (2.2)]*.

Immune-mediated rash or dermatitis occurred in 1.6% (30/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions. Events resolved in 18 of the 30 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI or were reported with the use of other PD-1/PD-L1 blocking antibodies.

Cardiac/vascular: Myocarditis, pericarditis, vasculitis.

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Nervous system: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.

Musculoskeletal and connective tissue disorders: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.

Endocrine: Hypoparathyroidism

Other (hematologic/immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection.

5.2 Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions.

Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity *[see Dosage and Administration (2.2)]*. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

5.3 Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

5.4 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. In animal reproduction studies, administration of durvalumab to cynomolgus monkeys from the onset of organogenesis through delivery resulted in increased premature delivery, fetal loss and premature neonatal death. Advise pregnant women of the potential risk to a fetus.

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Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months after the last dose of IMFINZI *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling.

- Immune-Mediated Adverse Reactions *[see Warnings and Precautions (5.1)]*.
- Infusion-Related Reactions *[see Warnings and Precautions (5.2)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in the Warnings and Precautions section reflect exposure to IMFINZI in 1889 patients from the PACIFIC study (a randomized, placebo-controlled study that enrolled 475 patients with Stage III NSCLC), Study 1108 (an open-label, single-arm, multicohort study that enrolled 191 patients with urothelial carcinoma and 779 patients with other solid tumors), and additional open-label, single-arm trial that enrolled 444 patients with metastatic lung cancer, an indication for which durvalumab is not approved. In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks. Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more. The data also reflects exposure to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC). In the CASPIAN study, IMFINZI was administered at a dose of 1500 mg every 3 or 4 weeks.

The data described in this section reflect exposure to IMFINZI in patients with locally advanced or metastatic urothelial carcinoma enrolled in Study 1108, in patients with Stage III NSCLC enrolled in the PACIFIC study and in patients with ES-SCLC enrolled in the CASPIAN study.

Urothelial Carcinoma

The safety of IMFINZI was evaluated in 182 patients with locally advanced or metastatic urothelial carcinoma in the urothelial carcinoma cohort of Study 1108 whose disease has progressed during or after one standard platinum-based regimen. Patients received IMFINZI 10 mg/kg intravenously every 2 weeks *[see Clinical Studies (14.1)]*. The median duration of exposure was 2.3 months (range: 1 day to 12.1 months).

Thirty-one percent (31%) of patients had a drug delay or interruption for an adverse reaction. The most common (> 2%) were liver injury (4.9%), urinary tract infection (3.3%), acute kidney injury (3.3%), and musculoskeletal pain (2.7%).

The most common adverse reactions (≥ 15%) were fatigue (39%), musculoskeletal pain (24%), constipation (21%), decreased appetite (19%), nausea (16%), peripheral edema (15%), and urinary tract infection (15%). The most common Grade 3 or 4 adverse reactions (≥ 3%) were fatigue, urinary tract infection, musculoskeletal pain, abdominal pain, dehydration, and general physical health deterioration.

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Eight patients (4.4%) who were treated with IMFINZI experienced Grade 5 adverse reactions of cardiorespiratory arrest, general physical health deterioration, sepsis, ileus, pneumonitis, or immune-mediated hepatitis. Three additional patients were experiencing infection and disease progression at the time of death. IMFINZI was discontinued for adverse reactions in 3.3% of patients. Serious adverse reactions occurred in 46% of patients. The most frequent serious adverse reactions (> 2%) were acute kidney injury (4.9%), urinary tract infection (4.4%), musculoskeletal pain (4.4%), liver injury (3.3%), general physical health deterioration (3.3%), sepsis, abdominal pain, and pyrexia/tumor associated fever (2.7% each).

Table 3 summarizes the adverse reactions that occurred in ≥ 10% of patients, while Table 4 summarizes the Grade 3 - 4 laboratory abnormalities that occurred in ≥ 1% of patients treated with IMFINZI in the urothelial carcinoma cohort of Study 1108.

Table 3. Adverse Reactions in ≥ 10% of Patients in Study 1108 Urothelial Carcinoma Cohort

	IMFINZI N = 182	
Adverse Reaction	**All Grades (%)**	**Grades 3 - 4 (%)**
Gastrointestinal Disorders		
Constipation	21	1.1
Nausea	16	1.6
Abdominal pain[1]	14	2.7
Diarrhea/Colitis	13	1.1
General Disorders and Administration		
Fatigue[2]	39	6
Peripheral edema[3]	15	1.6
Pyrexia/Tumor associated fever	14	0.5
Infections		
Urinary tract infection[4]	15	4.4

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	IMFINZI N = 182	
Adverse Reaction	**All Grades (%)**	**Grades 3 - 4 (%)**
Metabolism and Nutrition Disorders		
Decreased appetite/Hypophagia	19	0.5
Musculoskeletal and Connective Tissue Disorders		
Musculoskeletal pain[5]	24	3.8
Respiratory, Thoracic, and Mediastinal Disorders		
Dyspnea/Exertional Dyspnea	13	2.2
Cough/Productive Cough	10	0
Skin and Subcutaneous Tissue Disorders		
Rash[6]	11	0.5

[1] Includes abdominal pain upper, abdominal pain lower, and flank pain
[2] Includes asthenia, lethargy, and malaise
[3] Includes edema, localized edema, edema peripheral, lymphedema, peripheral swelling, scrotal edema, and scrotal swelling
[4] Includes cystitis, candiduria, and urosepsis
[5] Includes back pain, musculoskeletal chest pain, musculoskeletal pain and discomfort, myalgia, and neck pain
[6] Includes dermatitis, dermatitis acneiform, dermatitis psoriasiform, psoriasis, rash maculo-papular, rash pruritic, rash papular, rash pustular, skin toxicity, eczema, erythema, erythema multiforme, rash erythematous, acne, and lichen planus

Table 4. Grade 3-4 Laboratory Abnormalities Worsened from Baseline Occurring in ≥ 1% Patients in Study 1108 Urothelial Carcinoma Cohort

Laboratory Abnormality	Grades 3 - 4 %
Hyponatremia	12
Lymphopenia	11
Anemia	8
Increased alkaline phosphatase	4.1
Hypermagnesemia	4.2
Hypercalcemia	3
Hyperglycemia	3
Increased AST	2.4
Increased ALT	0.6
Hyperbilirubinemia	1.2
Increased creatinine	1.2
Neutropenia	1.2
Hyperkalemia	1.2
Hypokalemia	1.2

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Laboratory Abnormality	Grades 3 - 4 %
Hypoalbuminemia	1.2

Non-Small Cell Lung Cancer

The safety of IMFINZI in patients with Stage III NSCLC who completed concurrent platinum-based chemoradiotherapy within 42 days prior to initiation of study drug was evaluated in the PACIFIC study, a multicenter, randomized, double-blind, placebo-controlled study. A total of 475 patients received IMFINZI 10 mg/kg intravenously every 2 weeks. The study excluded patients who had disease progression following chemoradiation, with active or prior autoimmune disease within 2 years of initiation of the study or with medical conditions that required systemic immunosuppression *[see Clinical Studies (14.2)]*.

The study population characteristics were: median age of 64 years (range: 23 to 90), 45% age 65 years or older, 70% male, 69% White, 27% Asian, 75% former smoker, 16% current smoker, and 51% had WHO performance status of 1. All patients received definitive radiotherapy as per protocol, of which 92% received a total radiation dose of 54 Gy to 66 Gy. The median duration of exposure to IMFINZI was 10 months (range: 0.2 to 12.6).

IMFINZI was discontinued due to adverse reactions in 15% of patients. The most common adverse reactions leading to IMFINZI discontinuation were pneumonitis or radiation pneumonitis in 6% of patients. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions reported in at least 2% of patients were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in < 2% of patients and were similar across arms. The most common adverse reactions (occurring in ≥ 20% of patients) were cough, fatigue, pneumonitis or radiation pneumonitis, upper respiratory tract infections, dyspnea, and rash.

Table 5 summarizes the adverse reactions that occurred in at least 10% of patients treated with IMFINZI.

Table 5. Adverse Reactions Occurring in ≥ 10% Patients in the PACIFIC Study

	IMFINZI **N = 475**		**Placebo**[1] **N = 234**	
Adverse Reaction	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
Respiratory, Thoracic, and Mediastinal Disorders				
Cough/Productive Cough	40	0.6	30	0.4
Pneumonitis[2]/Radiation Pneumonitis	34	3.4	25	3
Dyspnea[3]	25	1.5	25	2.6
Gastrointestinal Disorders				
Diarrhea	18	0.6	19	1.3
Abdominal pain[4]	10	0.4	6	0.4

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	IMFINZI N = 475		Placebo[1] N = 234	
Adverse Reaction	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
Endocrine Disorders				
Hypothyroidism[5]	12	0.2	1.7	0
Skin and Subcutaneous Tissue Disorders				
Rash[6]	23	0.6	12	0
Pruritus[7]	12	0	6	0
General Disorders				
Fatigue[8]	34	0.8	32	1.3
Pyrexia	15	0.2	9	0
Infections				
Upper respiratory tract infections[9]	26	0.4	19	0
Pneumonia[10]	17	7	12	6

[1] The PACIFIC study was not designed to demonstrate statistically significant difference in adverse reaction rates for IMFINZI, as compared to placebo, for any specific adverse reaction listed in Table 4
[2] Includes acute interstitial pneumonitis, interstitial lung disease, pneumonitis, pulmonary fibrosis
[3] Includes dyspnea, and exertional dyspnea
[4] Includes abdominal pain, abdominal pain lower, abdominal pain upper, and flank pain
[5] Includes autoimmune hypothyroidism and hypothyroidism
[6] Includes rash erythematous, rash generalized, rash macular, rash maculopapular, rash papular, rash pruritic, rash pustular, erythema, eczema, rash, and dermatitis
[7] Includes pruritus generalized and pruritus
[8] Includes asthenia and fatigue
[9] Includes laryngitis, nasopharyngitis, peritonsillar abscess, pharyngitis, rhinitis, sinusitis, tonsillitis, tracheobronchitis, and upper respiratory tract infection
[10] Includes lung infection, pneumocystis jirovecii pneumonia, pneumonia, pneumonia adenoviral, pneumonia bacterial, pneumonia cytomegaloviral, pneumonia haemophilus, pneumonia klebsiella, pneumonia necrotising, pneumonia pneumococcal, and pneumonia streptococcal

Other adverse reactions occurring in less than 10% of patients treated with IMFINZI were dysphonia, dysuria, night sweats, peripheral edema, and increased susceptibility to infections.

Table 6 summarizes the laboratory abnormalities that occurred in at least 20% of patients treated with IMFINZI.

Table 6. Laboratory Abnormalities Worsening from Baseline Occurring in ≥ 20% of Patients in the PACIFIC Study

	IMFINZI		Placebo	
Laboratory Abnormality	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**
Chemistry				
Hyperglycemia	52	8	51	8

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	IMFINZI		Placebo	
Laboratory Abnormality	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**	**All Grades[1] (%)[2]**	**Grade 3 or 4 (%)**
Hypocalcemia	46	0.2	41	0
Increased ALT	39	2.3	22	0.4
Increased AST	36	2.8	21	0.4
Hyponatremia	33	3.6	30	3.1
Hyperkalemia	32	1.1	29	1.8
Increased GGT	24	3.4	22	1.7
Hematology				
Lymphopenia	43	17	39	18

[1] Graded according to NCI CTCAE version 4.0
[2] Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: IMFINZI (range: 464 to 470) and placebo (range: 224 to 228)

Small Cell Lung Cancer

The safety of IMFINZI in combination with etoposide and either carboplatin or cisplatin in previously untreated ES-SCLC was evaluated in CASPIAN, a randomized, open-label, multicenter, active-controlled trial. A total of 265 patients received IMFINZI 1500 mg in combination with chemotherapy every 3 weeks for 4 cycles followed by IMFINZI 1500 mg every 4 weeks until disease progression or unacceptable toxicity. The trial excluded patients with active or prior autoimmune disease or with medical conditions that required systemic corticosteroids or immunosuppressants *[see Clinical Studies (14.3)]*. Among 265 patients receiving IMFINZI, 49% were exposed for 6 months or longer and 19% were exposed for 12 months or longer.

Among 266 patients receiving chemotherapy alone, 57% of the patients received 6 cycles of chemotherapy and 8% of the patients received PCI after chemotherapy.

IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. These include pneumonitis, hepatotoxicity, neurotoxicity, sepsis, diabetic ketoacidosis and pancytopenia (1 patient each). 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. These include pancytopenia, sepsis, septic shock, pulmonary artery thrombosis, pulmonary embolism, and hepatitis (1 patient each) and sudden death (2 patients). The most common adverse reactions (occurring in ≥ 20% of patients) were nausea, fatigue/asthenia and alopecia.

Table 7 summarizes the adverse reactions that occurred in patients treated with IMFINZI plus chemotherapy.

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Table 7. Adverse Reactions Occurring in ≥ 10% Patients in the CASPIAN study

	IMFINZI with etoposide and either carboplatin or cisplatin N = 265		Etoposide and either carboplatin or cisplatin N = 266	
Adverse Reaction	**All Grades (%)**	**Grade 3-4 (%)**	**All Grades (%)**	**Grade 3-4 (%)**
Respiratory, thoracic and mediastinal disorders				
Cough/Productive Cough	15	0.8	9	0
Gastrointestinal disorders				
Nausea	34	0.4	34	1.9
Constipation	17	0.8	19	0
Vomiting	15	0	17	1.1
Diarrhea	10	1.1	11	1.1
Endocrine disorders				
Hyperthyroidism[a]	10	0	0.4	0
Skin and subcutaneous tissue disorders				
Alopecia	31	1.1	34	0.8
Rash[b]	11	0	6	0
General disorders and administration site conditions				
Fatigue/Asthenia	32	3.4	32	2.3
Metabolism and nutrition disorders				
Decreased appetite	18	0.8	17	0.8

[a] Includes hyperthyroidism and Basedow's disease
[b] Includes rash erythematous, rash generalized, rash macular, rash maculopapular, rash papular, rash pruritic, rash pustular, erythema, eczema, rash and dermatitis

Table 8 summarizes the laboratory abnormalities that occurred in at least 20% of patients treated with IMFINZI plus chemotherapy.

Table 8. Laboratory Abnormalities Worsening from Baseline Occurring in ≥ 20%[1] of Patients in the CASPIAN study

	IMFINZI with Etoposide and either Carboplatin or Cisplatin	Etoposide and either Carboplatin or Cisplatin
Laboratory Abnormality	**Grade[2] 3 or 4 (%)[3]**	**Grade[2] 3 or 4 (%)[3]**
Chemistry		
Hyponatremia	11	13
Hypomagnesemia	11	6
Hyperglycemia	5	5
Increased Alkaline Phosphatase	4.9	3.5
Increased ALT	4.9	2.7

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Increased AST	4.6	1.2
Hypocalcemia	3.5	2.4
Blood creatinine increased	3.4	1.1
Hyperkalemia	1.5	3.1
TSH decreased < LLN[4] and ≥ LLN at baseline	NA	NA
Hematology		
Neutropenia	41	48
Lymphopenia	14	13
Anemia	13	22
Thrombocytopenia	12	15

[1] The frequency cut off is based on any grade change from baseline
[2] Graded according to NCI CTCAE version 4.03
[3] Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: IMFINZI (range: 258 to 263) and chemotherapy (range: 253 to 262) except magnesium IMFINZI + chemotherapy (18) and chemotherapy (16)
[4] LLN = lower limit of normal

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to durvalumab to the incidence of antibodies to other products may be misleading.

Of 2280 patients who received IMFINZI 10 mg/kg every 2 weeks or 20 mg/kg every 4 weeks as a single-agent, 69 patients (3%) tested positive for treatment-emergent anti-drug antibodies (ADA) and 12 (0.5%) tested positive for neutralizing antibodies. The development of ADA against durvalumab appears to have no clinically relevant effect on its pharmacokinetics or safety.

Of 201 patients in the CASPIAN study who received IMFINZI 1500 mg every 3 weeks in combination with chemotherapy for four doses followed by IMFINZI 1500 mg every 4 weeks no patients tested positive for treatment-emergent ADA.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk summary

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no data on the use of IMFINZI in pregnant women.

In animal reproduction studies, administration of durvalumab to pregnant cynomolgus monkeys from the confirmation of pregnancy through delivery resulted in an increase in premature delivery, fetal loss, and premature neonatal death *(see Data)*. Human immunoglobulin G1 (IgG1) is known to cross the placental

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barrier; therefore, durvalumab has the potential to be transmitted from the mother to the developing fetus. Apprise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

As reported in the literature, the PD-1/PD-L1 pathway plays a central role in preserving pregnancy by maintaining maternal immune tolerance to the fetus. In mouse allogeneic pregnancy models, disruption of PD-L1 signaling was shown to result in an increase in fetal loss. The effects of durvalumab on prenatal and postnatal development were evaluated in reproduction studies in cynomolgus monkeys. Durvalumab was administered from the confirmation of pregnancy through delivery at exposure levels approximately 6 to 20 times higher than those observed at the recommended clinical dose of 10 mg/kg (based on AUC). Administration of durvalumab resulted in premature delivery, fetal loss (abortion and stillbirth), and increase in neonatal deaths. Durvalumab was detected in infant serum on postpartum Day 1, indicating the presence of placental transfer of durvalumab. Based on its mechanism of action, fetal exposure to durvalumab may increase the risk of developing immune-mediated disorders or altering the normal immune response and immune-mediated disorders have been reported in PD-1 knockout mice.

8.2 Lactation

Risk Summary

There is no information regarding the presence of durvalumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG1 is excreted in human milk. Durvalumab was present in the milk of lactating cynomolgus monkeys and was associated with premature neonatal death *(see Data)*.

Because of the potential for adverse reactions in breastfed infants, advise women not to breastfeed during treatment with IMFINZI and for at least 3 months after the last dose.

Data

In lactating cynomolgus monkeys, durvalumab was present in breast milk at about 0.15% of maternal serum concentrations after administration of durvalumab from the confirmation of pregnancy through delivery at exposure levels approximately 6 to 20 times higher than those observed at the recommended clinical dose of 10 mg/kg (based on AUC). Administration of durvalumab resulted in premature neonatal death.

8.3 Females and Males of Reproductive Potential

Contraception

Females

Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with IMFINZI and for at least 3 months following the last dose of IMFINZI.

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8.4 Pediatric Use

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

8.5 Geriatric Use

Of the 182 patients treated with IMFINZI in patients with urothelial carcinoma, 112 patients were 65 years or older and 34 patients were 75 years or older. The overall response rate in patients 65 years or older was 15% (17/112) and was 12% (4/34) in patients 75 years or older. Grade 3 or 4 adverse reactions occurred in 38% (42/112) of patients 65 years or older and 35% (12/34) of patients 75 years or older.

Of the 476 patients treated with IMFINZI in the PACIFIC study, 45% were 65 years or older, while 7.6% were 75 years or older. No overall differences in safety or effectiveness were observed between patients 65 years or older and younger patients. The PACIFIC study did not include sufficient numbers of patients aged 75 years and over to determine whether they respond differently from younger patients.

Of the 265 patients with ES-SCLC treated with IMFINZI in combination with chemotherapy, 101 (38%) patients were 65 years or older and 19 (7.2%) patients were 75 years or older. There were no clinically meaningful differences in safety or efficacy between patients 65 years or older and younger patients.

11 DESCRIPTION

Durvalumab is a programmed cell death ligand 1 (PD-L1) blocking antibody. Durvalumab is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that is produced by recombinant DNA technology in Chinese Hamster Ovary (CHO) cell suspension culture.

IMFINZI (durvalumab) Injection for intravenous use is a sterile, preservative-free, clear to opalescent, colorless to slightly yellow solution, free from visible particles.

Each 500 mg vial of IMFINZI contains 500 mg of durvalumab in 10 mL solution. Each mL contains durvalumab, 50 mg, L-histidine (2 mg), L-histidine hydrochloride monohydrate (2.7 mg), α,α-trehalose dihydrate (104 mg), Polysorbate 80 (0.2 mg), and Water for Injection, USP.

Each 120 mg vial of IMFINZI contains 120 mg of durvalumab in 2.4 mL solution. Each mL contains durvalumab, 50 mg, L-histidine (2 mg), L-histidine hydrochloride monohydrate (2.7 mg), α,α-trehalose dihydrate (104 mg), Polysorbate 80 (0.2 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Expression of programmed cell death ligand-1 (PD-L1) can be induced by inflammatory signals (e.g., IFN-gamma) and can be expressed on both tumor cells and tumor-associated immune cells in the tumor microenvironment. PD-L1 blocks T-cell function and activation through interaction with PD-1 and CD80 (B7.1). By binding to its receptors, PD-L1 reduces cytotoxic T-cell activity, proliferation, and cytokine production.

Durvalumab is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that binds to PD-L1 and blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1). Blockade of PD-L1/PD-1 and PD-

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L1/CD80 interactions releases the inhibition of immune responses, without inducing antibody dependent cell-mediated cytotoxicity (ADCC).

PD-L1 blockade with durvalumab led to increased T-cell activation in vitro and decreased tumor size in co-engrafted human tumor and immune cell xenograft mouse models.

12.2 Pharmacodynamics

The steady state AUC, Ctrough, and Cmax in patients administered with 1500 mg every 4 weeks are 6% higher, 19% lower, and 55% higher than those administered with 10 mg/kg every 2 weeks, respectively. Based on the modeling of pharmacokinetic data and exposure relationships for safety, there are no anticipated clinically meaningful differences in efficacy and safety for the doses of 1500 mg every 4 weeks compared to 10 mg/kg every 2 weeks in patients weighing > 30 kg with UC and NSCLC.

12.3 Pharmacokinetics

The pharmacokinetics of durvalumab as a single agent was studied in patients with doses ranging from 0.1 mg/kg (0.01 times the approved recommended dosage) to 20 mg/kg (2 times the approved recommended dosage) administered once every two, three, or four weeks.

PK exposure increased more than dose-proportionally at doses < 3 mg/kg (0.3 times the approved recommended dosage) and dose proportionally at doses ≥ 3 mg/kg every 2 weeks. Steady state was achieved at approximately 16 weeks.

The pharmacokinetics of durvalumab is similar when assessed as a single agent and when in combination with chemotherapy.

<u>Distribution</u>
The geometric mean (% coefficient of variation [CV%]) steady state volume of distribution (Vss) was 5.6 (18%) L.

<u>Elimination</u>
Durvalumab clearance decreases over time, with a mean maximal reduction (CV%) from baseline values of approximately 23% (57%) resulting in a geometric mean (CV%) steady state clearance (CLss) of 8.2 mL/h (39%) at day 365; the decrease in CLss is not considered clinically relevant. The geometric mean (CV%) terminal half-life, based on baseline CL was approximately 18 (24%) days.

<u>Specific Populations</u>
Age (19–96 years), body weight (31-149 kg), sex, albumin levels, lactate dehydrogenase (LDH) levels, creatinine levels, soluble PD-L1, tumor type, race, mild renal impairment (creatinine clearance (CLcr) 60 to 89 mL/min), moderate renal impairment (CLcr 30 to 59 mL/min), mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin > 1 to 1.5x ULN and any AST), or ECOG/WHO performance status had no clinically significant effect on the pharmacokinetics of durvalumab.

The effect of severe renal impairment (CLcr 15 to 29 mL/min) or moderate hepatic impairment (bilirubin > 1.5 to 3x ULN and any AST) or severe hepatic impairment (bilirubin > 3x ULN and any AST) on the pharmacokinetics of durvalumab is unknown.

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13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic and genotoxic potential of durvalumab have not been evaluated.

Animal fertility studies have not been conducted with durvalumab. In repeat-dose toxicology studies with durvalumab in sexually mature cynomolgus monkeys of up to 3 months duration, there were no notable effects on the male and female reproductive organs.

13.2 Animal Toxicology and/or Pharmacology

In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections and enhanced inflammatory responses. M. tuberculosis-infected PD-1 knockout mice exhibit markedly decreased survival compared with wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout mice have also shown decreased survival following infection with lymphocytic choriomeningitis virus.

14 CLINICAL STUDIES

14.1 Urothelial Carcinoma

The efficacy of IMFINZI was evaluated in the urothelial carcinoma cohort of Study 1108 (NCT01693562), a multicenter, multi-cohort, open-label clinical trial. In Study 1108, 182 patients with locally advanced or metastatic urothelial carcinoma were enrolled. Patients had progressed while on or after a platinum-based therapy, including those who progressed within 12 months of receiving therapy in a neo-adjuvant or adjuvant setting. These patients had initiated IMFINZI at least 13 weeks prior to the data cut-off date. The trial excluded patients with a history of immunodeficiency; medical conditions that required systemic immunosuppression (not to exceed 10 mg per day of prednisone or equivalent); history of severe autoimmune disease; untreated CNS metastases; HIV; active tuberculosis, or hepatitis B or C infection. All patients received IMFINZI 10 mg/kg intravenously every 2 weeks for up to 12 months or until unacceptable toxicity or disease progression. Tumor assessments were performed at Weeks 6, 12, and 16, then every 8 weeks for the first year and every 12 weeks thereafter. The major efficacy outcome measures were confirmed Overall Response Rate (ORR) according to RECIST v1.1 as assessed by Blinded Independent Central Review (BICR), and duration of response (DoR).

The median age was 67 years (range: 34 to 88), 72% were male, 64% were White. Sixty-six percent (66%) of patients had visceral metastasis (bone, liver, or lung), including 34% with liver metastasis. Lymph node only metastasis were present in 13% of patients. Sixty-six percent (66%) of patients had ECOG score of 1 and 41% of patients had a baseline creatinine clearance < 60 mL/min. The Bellmunt risk score (which includes ECOG score, baseline hemoglobin, and liver metastases) was 0 in 23%, 1 in 38%, 2 in 29%, and 3 in 9% of patients. Twenty percent (20%) of patients had disease progression following platinum-containing neoadjuvant or adjuvant chemotherapy as their only prior line of therapy. Seventy percent (70%) of patients received prior cisplatin, 30% prior carboplatin and 35% received ≥ 2 prior lines of systemic therapy.

Tumor specimens were evaluated prospectively for PD-L1 expression on tumor cells (TC) and immune cells (IC) at a central laboratory using the VENTANA PD-L1 (SP263) Assay. Of the 182 patients, 52%

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were classified as PD-L1 high (if ICs involve > 1% of the tumor area, TC ≥ 25% or IC ≥ 25%; if ICs involve ≤ 1% of the tumor area, TC ≥ 25% or IC = 100%), 40% as PD-L1 low/negative (did not meet criterion for PD-L1 high), and samples for 8% were not evaluable.

Table 9 summarizes the results in the urothelial carcinoma cohort of Study 1108. The median follow-up time was 5.6 months. In 37 patients who had received only neoadjuvant or adjuvant therapy prior to study entry, 24% responded.

Among the total 31 responding patients, 45% had ongoing responses of 6 months or longer and 16% had ongoing responses of 12 months or longer.

Table 9. Efficacy Results for Study 1108 Urothelial Carcinoma Cohort

	All Patients N = 182	**PD-L1 High N = 95**	**PD-L1 Low/Negative N = 73**	**PD-L1 NE N = 14**
Overall Response Rate by BICR n (%) (95% CI)	31 (17%) (11.9, 23.3)	25 (26%) (17.8, 36.4)	3 (4%) (0.9, 11.5)	3 (21%) (4.7, 50.8)
Complete Response, n	5	3	1	1
Partial Response, n	26	22	2	2
Median Duration of Response months (range)	NR (0.9+, 19.9+)	NR (0.9+, 19.9+)	12.3 (1.9+, 12.3)	NR (2.3+, 2.6+)

BICR = Blinded Independent Central Review; NR = Not Reached, + denotes a censored value

14.2 Non-Small Cell Lung Cancer (NSCLC)

The efficacy of IMFINZI was evaluated in the PACIFIC study (NCT02125461), a multicenter, randomized, double-blind, placebo-controlled study in patients with unresectable Stage III NSCLC who completed at least 2 cycles of concurrent platinum-based chemotherapy and definitive radiation within 42 days prior to initiation of the study drug and had a WHO performance status of 0 or 1. The study excluded patients who had progressed following concurrent chemoradiation, patients with active or prior documented autoimmune disease within 2 years of initiation of the study or patients with medical conditions that required systemic immunosuppression. Randomization was stratified by sex, age (< 65 years vs. ≥ 65 years), and smoking history (smoker vs. non-smoker). Patients were randomized 2:1 to receive IMFINZI 10 mg/kg or placebo intravenously every 2 weeks for up to 12 months or until unacceptable toxicity or confirmed RECIST v1.1-defined progression. Assessment of tumor status was performed every 8 weeks. The major efficacy outcome measures were progression-free survival (PFS) as assessed by a BICR RECIST v1.1, and overall survival (OS). Additional efficacy outcome measures included ORR and DoR assessed by BICR.

A total of 713 patients were randomized: 476 patients to the IMFINZI arm and 237 to the placebo arm. The study population characteristics were: median age of 64 years (range: 23 to 90); 70% male; 69% White and 27% Asian; 16% current smokers, 75% former smokers, and 9% never smokers; 51% WHO

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performance status of 1; 53% with Stage IIIA and 45% were Stage IIIB; 46% with squamous and 54% with non-squamous histology. All patients received definitive radiotherapy as per protocol, of which 92% received a total radiation dose of 54 Gy to 66 Gy; 99% of patients received concomitant platinum-based chemotherapy (55% cisplatin-based, 42% carboplatin-based chemotherapy, and 2% switched between cisplatin and carboplatin).

At a pre-specified interim analysis for OS based on 299 events (61% of total planned events), the study demonstrated a statistically significant improvement in OS in patients randomized to IMFINZI compared to placebo. The pre-specified interim analysis of PFS based on 371 events (81% of total planned events) demonstrated a statistically significant improvement in PFS in patients randomized to IMFINZI compared to placebo. Table 10 and Figure 1 summarizes the efficacy results for PACIFIC.

Table 10. Efficacy Results for the PACIFIC Study

Endpoint	**IMFINZI (N = 476)[1]**	**Placebo (N = 237)[1]**
Overall Survival (OS)[2]		
Number of deaths	183 (38%)	116 (49%)
Median in months (95% CI)	NR (34.7, NR)	28.7 (22.9, NR)
Hazard Ratio (95% CI)[3]	0.68 (0.53, 0.87)	
p-value[3,4]	0.0025	
Progression-Free Survival (PFS)[5,6]		
Number (%) of patients with event	214 (45%)	157 (66%)
Median in months (95% CI)	16.8 (13.0, 18.1)	5.6 (4.6, 7.8)
Hazard Ratio (95% CI)[3,7]	0.52 (0.42, 0.65)	
p-value[3,8]	< 0.0001	

[1] Among the ITT population, 7% in the IMFINZI arm and 10% in the placebo arm had non-measurable disease as assessed by BICR according to RECIST v1.1
[2] OS results are based on the interim OS analysis conducted at 299 OS events which occurred 46 months after study initiation
[3] Two-sided p-value based on a log-rank test stratified by sex, age, and smoking history
[4] Compared with allocated α of 0.00274 (Lan DeMets spending function approximating O'Brien Fleming boundary) for interim analysis
[5] As assessed by BICR RECIST v1.1
[6] PFS results are based on the interim PFS analysis conducted at 371 PFS events which occurred 33 months after study initiation
[7] Pike estimator
[8] Compared with allocated α of 0.011035 (Lan DeMets spending function approximating O'Brien Fleming boundary) for interim analysis

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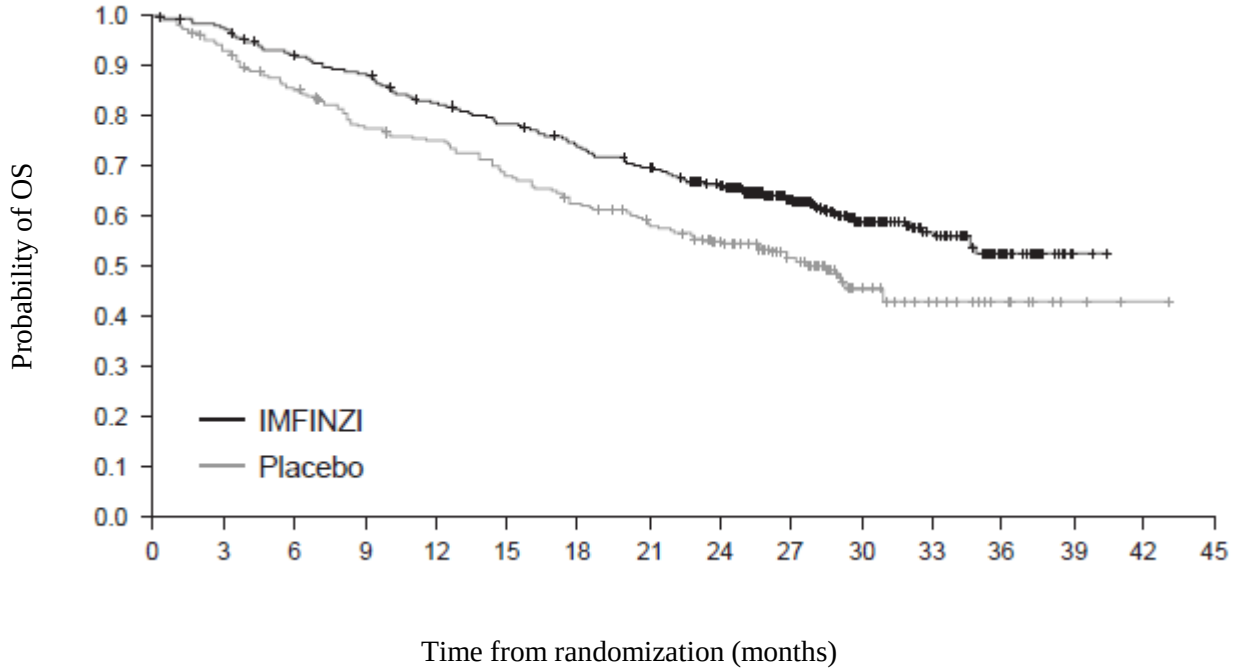
Figure 1. Kaplan-Meier Curves of Overall Survival in the PACIFIC Study



Number of patients at risk

Month	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
IMFINZI	476	464	431	415	385	364	343	319	274	210	115	57	23	2	0	0
Placebo	237	220	198	178	170	155	141	130	117	78	42	21	9	3	1	0

14.3 Small Cell Lung Cancer (SCLC)

The efficacy of IMFINZI in combination with etoposide and either carboplatin or cisplatin in previously untreated ES-SCLC was investigated in CASPIAN, a randomized, multicenter, active-controlled, open-label trial (NCT03043872). Eligible patients had WHO Performance Status of 0 or 1 and were suitable to receive a platinum-based chemotherapy regimen as first-line treatment for SCLC. Patients with asymptomatic or treated brain metastases were eligible. Choice of platinum agent was at the investigator's discretion, taking into consideration the calculated creatinine clearance. Patients with history of chest radiation therapy; a history of active primary immunodeficiency; autoimmune disorders including paraneoplastic syndrome; active or prior documented autoimmune or inflammatory disorders; use of systemic immunosuppressants within 14 days before the first dose of the treatment except physiological dose of systemic corticosteroids were ineligible.

Randomization was stratified by the planned platinum-based therapy in cycle 1 (carboplatin or cisplatin).

The evaluation of efficacy for ES-SCLC relied on comparison between:

- IMFINZI 1500 mg, and investigator's choice of carboplatin (AUC 5 or 6 mg/mL/min) or cisplatin (75-80 mg/m^2) on Day 1 and etoposide (80-100 mg/m^2) intravenously on Days 1, 2, and 3 of each 21-

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day cycle for 4 cycles, followed by IMFINZI 1500 mg every 4 weeks until disease progression or unacceptable toxicity, or

- Investigator's choice of carboplatin (AUC 5 or 6 mg/mL/min) or cisplatin (75-80 mg/m^2) on Day 1 and etoposide (80-100 mg/m^2) intravenously on Days 1, 2, and 3 of each 21-day cycle, up to 6 cycles. After completion of chemotherapy, prophylactic cranial irradiation (PCI) as administered per investigator discretion.

Administration of IMFINZI as a single agent was permitted beyond disease progression if the patient was clinically stable and deriving clinical benefit as determined by the investigator.
The major efficacy outcome measure was overall survival (OS) of IMFINZI plus chemotherapy vs. chemotherapy alone. Additional efficacy outcome measures were investigator-assessed progression-free survival (PFS) and objective response rate (ORR), per RECIST v1.1.

The study population characteristics were: median age of 63 years (range: 28 to 82); 40% age 65 or older; 70% male; 84% White, 15% Asian, and 0.9% Black; 65% WHO/ECOG PS of 1; and 93% were former/current smokers. Ninety percent of patients had Stage IV disease and 10% had brain metastasis at baseline. A total of 25% of the patients received cisplatin and 74% of the patients received carboplatin. In the chemotherapy alone arm, 57% of the patients received 6 cycles of chemotherapy, and 8% of the patients received PCI.

The OS results are summarized in Table 11 and Figure 2.

Table 11. OS Result for the CASPIAN Study

Endpoint	**IMFINZI with Etoposide and either Carboplatin or Cisplatin (n=268)**	**Etoposide and either Carboplatin or Cisplatin (n=269)**
Overall Survival (OS)		
Number of deaths (%)[1]	155 (58)	181 (67)
Median OS (months) (95% CI)	13.0 (11.5, 14.8)	10.3 (9.3, 11.2)
Hazard Ratio (95% CI)[2]	0.73 (0.59, 0.91)	
p-value[1]	0.0047	

[1] At a pre-specified interim analysis, 336 OS events (79% of total planned events) were observed, and the boundary for declaring efficacy (0.0178) was determined by a Lan-Demets alpha spending function with O'Brien Fleming type boundary

[2] The analysis was performed using the stratified log-rank test, adjusting for planned platinum therapy in Cycle 1 (carboplatin or cisplatin) and using the rank tests of association approach

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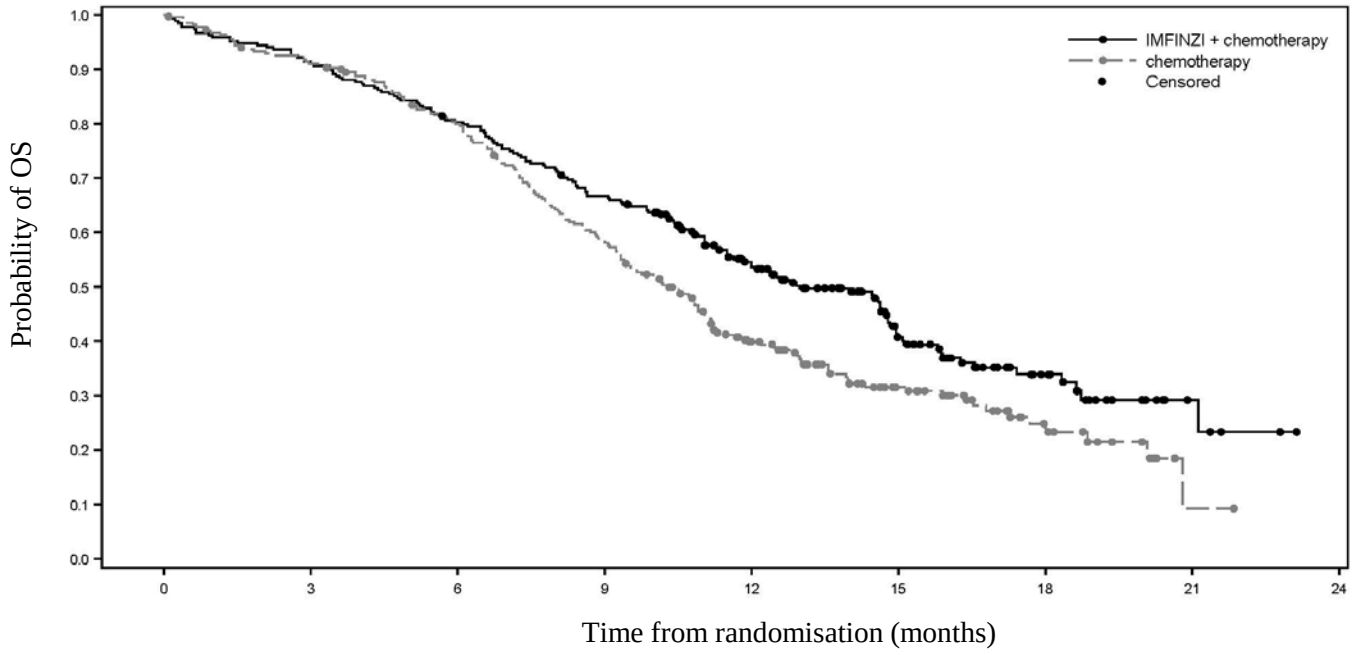
Figure 2. Kaplan-Meier Curves of Overall Survival in the CASPIAN Study



Number of patients at risk	0	3	6	9	12	15	18	21	24
IMFINZI + chemotherapy	268	244	214	177	116	57	25	5	0
chemotherapy	269	242	209	153	82	44	17	1	0

Investigator-assessed PFS (96% of total planned events) showed a HR of 0.78 (95% CI: 0.65, 0.94), with median PFS of 5.1 months (95% CI: 4.7, 6.2) in the IMFINZI plus chemotherapy arm and 5.4 months (95% CI: 4.8, 6.2) in the chemotherapy alone arm. The investigator-assessed confirmed ORR was 68% (95% CI: 62%, 73%) in the IMFINZI plus chemotherapy arm and 58% (95% CI: 52%, 63%) in the chemotherapy alone arm.

In the exploratory subgroup analyses of OS based on the planned platinum chemotherapy received at cycle 1, the HR was 0.70 (95% CI 0.55, 0.89) in patients who received carboplatin, and the HR was 0.88 (95% CI 0.55, 1.41) in patients who received cisplatin.

16 HOW SUPPLIED/STORAGE AND HANDLING

IMFINZI (durvalumab) Injection is a clear to opalescent, colorless to slightly yellow solution supplied in a carton containing one single-dose vial either as:

- 500 mg/10 mL (NDC 0310-4611-50)
- 120 mg/2.4 mL (NDC 0310-4500-12)

Store in a refrigerator at 2°C to 8°C (36°F to 46°F) in original carton to protect from light.
Do not freeze. Do not shake.

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17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Immune-Mediated Adverse Reactions

Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid treatment and interruption or discontinuation of IMFINZI *[see Warnings and Precautions (5.1)]*, including:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for any new or worsening cough, chest pain, or shortness of breath.
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, pain on the right side of abdomen, lethargy, or easy bruising or bleeding.
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood or mucus in stools, or severe abdominal pain.
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, adrenal insufficiency, type 1 diabetes mellitus, or hypophysitis.
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis.
- Dermatological Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of severe dermatological reactions.
- Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of aseptic meningitis, immune thrombocytopenia, myocarditis, hemolytic anemia, myositis, uveitis, keratitis, and myasthenia gravis.

Infusion-Related Reactions:

- Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions *[see Warnings and Precautions (5.2)]*.

Complications of Allogeneic HSCT:

- Advise patients of potential risk of post-transplant complications *[see Warnings and Precautions (5.3)]*.

Embryo-Fetal Toxicity:

- Advise females of reproductive potential that IMFINZI can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.1, 8.3)]*.
- Advise females of reproductive potential to use effective contraception during treatment and for at least 3 months after the last dose of IMFINZI *[see Use in Specific Populations (8.3)]*.

Lactation:

- Advise female patients not to breastfeed while taking IMFINZI and for at least 3 months after the last dose *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.2)]*.

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Manufactured for:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

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MEDICATION GUIDE

IMFINZI® (im-FIN-zee)

(durvalumab)

injection

What is the most important information I should know about IMFINZI?

IMFINZI is a medicine that may treat certain cancers by working with your immune system.

IMFINZI can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worsening signs or symptoms, including:

Lung problems.

- cough
- shortness of breath
- chest pain

Intestinal problems.

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems.

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach-area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems.

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increase sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual
- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems.

- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

Skin problems.

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

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Problems can also happen in other organs and tissues. These are not all of the signs and symptoms of immune system problems that can happen with IMFINZI. Call or see your healthcare provider right away for any new or worsening signs or symptoms, which may include:

- Chest pain, irregular heartbeats, shortness of breath or swelling of ankles
- Confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- Double vision, blurry vision, sensitivity to light, eye pain, changes in eye slight
- Persistent or severe muscle pain or weakness, muscle cramps
- Low red blood cells, bruising.

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feel like passing out
- fever
- back or neck pain

Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic).
These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with IMFINZI. Your healthcare provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious.
Your healthcare provider will check you for these problems during your treatment with IMFINZI. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with IMFINZI, if you have severe side effects.

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What is IMFINZI?

IMFINZI is a prescription medicine used to treat adults with:

- **a type of cancer in the bladder and urinary tract called urothelial carcinoma**. IMFINZI may be used when your urothelial carcinoma:
  - has spread or cannot be removed by surgery, **and**
  - you have tried chemotherapy that contains platinum, and it did not work or is no longer working.
- **a type of lung cancer called non-small cell lung cancer (NSCLC)**. IMFINZI may be used when your NSCLC:
  - has not spread outside your chest
  - cannot be removed by surgery, **and**
  - has responded or stabilized with initial treatment with chemotherapy that contains platinum, given at the same time as radiation therapy.
- **a type of lung cancer called small cell lung cancer (SCLC)**. IMFINZI may be used **with the chemotherapy medicines etoposide and carboplatin or cisplatin as your first treatment when your SCLC**:
  - has spread within your lungs or to other parts of the body, (extensive-stage small cell lung cancer, or ES-SCLC).

It is not known if IMFINZI is safe and effective in children.

Before you receive IMFINZI, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. IMFINZI can harm your unborn baby.
  Females who are able to become pregnant
  - You should use an effective method of birth control during your treatment and for at least 3 months after the last dose of IMFINZI. Talk to your healthcare provider about birth control methods that you can use during this time.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with IMFINZI.
- are breastfeeding or plan to breastfeed. It is not known if IMFINZI passes into your breast milk. Do not breastfeed during treatment and for at least 3 months after the last dose of IMFINZI.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive IMFINZI?

- Your healthcare provider will give you IMFINZI into your vein through an intravenous (IV) line over 60 minutes.
- IMFINZI is usually given every 2, 3 or 4 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will test your blood to check you for certain side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

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What are the possible side effects of IMFINZI?
IMFINZI can cause serious side effects, including:
See "What is the most important information I should know about IMFINZI?"
The most common side effects of IMFINZI in people with urothelial carcinoma include:

- feeling tired
- muscle or bone pain
- constipation
- decreased appetite
- nausea
- swelling of your arms and legs
- urinary tract infection

The most common side effects of IMFINZI in people with NSCLC include:

- cough
- feeling tired
- inflammation in the lungs
- upper respiratory tract infections
- shortness of breath
- rash

The most common side effects of IMFINZI when used with other anticancer medicines in people with ES-SCLC include:

- nausea
- hair loss
- feeling tired or weak

Tell your doctor if you have any side effect that bothers you or that does not go away.
These are not all the possible side effects of IMFINZI. Ask your healthcare provider or pharmacist for more information.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of IMFINZI.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about IMFINZI, talk with your healthcare provider. You can ask your healthcare provider for information about IMFINZI that is written for health professionals.

What are the ingredients in IMFINZI?
Active ingredient: durvalumab
Inactive ingredients: L-histidine, L-histidine hydrochloride monohydrate, α,α-trehalose dihydrate, polysorbate 80, water for injection, USP.

Manufactured for: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850
By: AstraZeneca UK Limited, 1 Francis Crick Ave. Cambridge, England CB2 0AA
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For more information, call 1-800-236-9933 or go to www.IMFINZI.com
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