IMMUNE-MEDIATED ADVERSE REACTIONS GUIDE AND DOSING MODIFICATIONS

For adults receiving IMFINZI + gem-cis in the first-line treatment of locally advanced or metastatic biliary tract cancers, including cholangiocarcinoma and gallbladder cancer

Study design: TOPAZ-1 was a randomized, double-blind, placebo-controlled, multicenter, Phase III study in patients with previously untreated locally advanced or metastatic intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer. Patients who developed recurrent disease >6 months after surgery and/or completion of adjuvant therapy were eligible. Patients were randomized 1:1 to receive IMFINZI 1500 mg (n=341) or placebo (n=344) on Day 1 + gem-cis on Days 1 and 8 Q3W for up to 8 cycles followed by IMFINZI 1500 mg or placebo Q4W until disease progression or unacceptable toxicity. The primary endpoint was overall survival.[1,2]

BTCs=biliary tract cancers; gem-cis=gemcitabine-cisplatin; Q3W=every 3 weeks; Q4W=every 4 weeks.

Indication:

IMFINZI, in combination with gemcitabine and cisplatin, is indicated for the treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC).

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

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 or after discontinuation. 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 USPI Dosing and Administration for specific details.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

In the treatment of locally advanced or metastatic biliary tract cancers

Start with IMFINZI and chemotherapy, then continue with IMFINZI monotherapy[1]

For patients with a body weight of ≥30 kg

START

IMFINZI + gem-cis Q3W

Up to 8 cycles

IMFINZI + GEMCITABINE + CISPLATIN

1500-mg fixed dose*†

Administer IMFINZI prior to chemotherapy on the same day. Refer to Prescribing Information for appropriate chemotherapeutic agent for dosage information.

CONTINUE

IMFINZI Q4W

Until disease progression or unacceptable toxicity

IMFINZI

1500-mg fixed dose*†

NO CHEMOTHERAPY NEEDED WITH IMFINZI Q4W

In the TOPAZ-1 study, IMFINZI 1500 mg was administered on Day 1 of each cycle in combination with gemcitabine 1000 mg/m^2 and cisplatin 25 mg/m^2 on Days 1 and 8 of each 21-day cycle for up to 8 cycles, followed by IMFINZI 1500 mg every 4 weeks until disease progression or unacceptable toxicity.

*IMFINZI is administered as a 60-minute IV infusion after dilution.

†Patients with a body weight of <30 kg: 20 mg/kg in combination with chemotherapy every 3 weeks (21 days) for up to 8 cycles, followed by 20 mg/kg every 4 weeks as a single agent.

Biomarker testing is not required to start IMFINZI + gem-cis

IV=intravenous.

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Adverse Reactions (continued)

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

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.

Safety and tolerability profile for IMFINZI + gem-cis

Similar rates of Grades 3-4 adverse reactions were reported for IMFINZI + gem-cis (75.7%) and placebo + gem-cis (77.8%)[2]

ADVERSE REACTIONS OCCURRING IN ≥10% OF PATIENTS[1‡]

	IMFINZI + gem-cis (n=338)		Placebo + gem-cis (n=342)	
	All grades[§] (%)	Grades 3-4[§] (%)	All grades[§] (%)	Grades 3-4[§] (%)
General disorders and administration site conditions				
Fatigue[‖]	42	6	43	6
Pyrexia	20	1.5	16	0.6
Gastrointestinal disorders				
Nausea	40	1.5	34	1.8
Constipation	32	0.6	29	0.3
Abdominal pain[¶]	24	0.6	23	2.9
Vomiting	18	1.5	18	2.0
Diarrhea	17	1.2	15	1.8
Metabolism and nutrition disorders				
Decreased appetite	26	2.1	23	0.9
Skin and subcutaneous tissue disorders				
Rash[#]	23	0.9	14	0
Pruritus	11	0	8	0
Psychiatric disorders				
Insomnia	10	0	11	0

‡Table summarizes the ARs that occurred in ≥10% of patients treated with IMFINZI + gem-cis.

§Graded according to NCI CTCAE version 5.0.

‖Includes fatigue, malaise, cancer fatigue, and asthenia.

¶Includes abdominal pain, abdominal pain lower, abdominal pain upper, and flank pain.

#Includes rash macular, rash maculopapular, rash morbilliform, rash papular, rash pruritic, rash pustular, rash erythematous, dermatitis acneiform, dermatitis bullous, drug eruption, eczema, erythema, dermatitis, and rash.

- Safety data are available for the 680 patients who received at least 1 dose of IMFINZI + gem-cis (n=338) or placebo + gem-cis (n=342)[1,2]
- Serious adverse reactions occurred in 47% of patients receiving IMFINZI + gem-cis. The most frequent serious adverse reactions (≥2% of patients) were cholangitis (7%), pyrexia (3.8%), anemia (3.6%), sepsis (3.3%), and acute kidney injury (2.4%)[1]
- Fatal adverse reactions occurred in 3.6% of patients receiving IMFINZI + gem-cis. These include ischemic or hemorrhagic stroke (4 patients), sepsis (2 patients), and upper gastrointestinal hemorrhage (2 patients)[1]
- The most common adverse reactions (occurring in ≥20% of patients) with IMFINZI + gem-cis were fatigue, nausea, constipation, decreased appetite, abdominal pain, rash, and pyrexia[1]
- The safety profile observed at the 3-year analysis (post-hoc analysis; data cutoff: October 23, 2023) was consistent with the safety profile observed at the primary analysis[3]

ARs=adverse reactions; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

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Immune-mediated ARs with IMFINZI + gem-cis[2]

Most imARs in the safety analysis population were Grade 1 or 2

imARs REPORTED IN TOPAZ-1[2]

	IMFINZI + gem-cis (n=338)		Placebo + gem-cis (n=342)	
	Any grade (%)	Grades 3-4 (%)	Any grade (%)	Grades 3-4 (%)
Any imAR*	12.7	2.4	4.7	1.5
Hypothyroid events	5.9	0	1.5	0
Dermatitis/rash	3.6	0.9	0.3	0
Pneumonitis	0.9	0.3	0.6	0.3
Hepatic events	1.2	0.6	0.6	0.3
Adrenal insufficiency	1.2	0	0.3	0
Diarrhea/colitis	0.6	0.3	0.3	0.3
Hyperthyroid events	0.6	0	0	0
Type 1 diabetes mellitus	0.3	0.3	0	0
Pancreatic events	0.3	0	0.6	0.3
Hypophysitis	0.3	0	0	0
Thyroiditis	0.3	0	0	0
Renal events	0	0	0.6	0
Myositis	0	0	0.3	0
Other rare/miscellaneous†	0.3	0.3	0.3	0.3

*An imAR is defined as a reaction that is associated with drug exposure and consistent with an immune-mediated mechanism of action and where there is no clear alternate etiology.
†The events in the "other rare/miscellaneous" category were immune-mediated arthritis in the IMFINZI group and arthritis in the placebo group.

- The most common Grade 3 or 4 imARs with IMFINZI + gem-cis were dermatitis/rash (0.9%) and hepatic events (0.6%)[2]

IMFINZI is associated with imARs. Routine monitoring of patients for signs and symptoms is advised.[1]

imARs=immune-mediated adverse reactions.

IMPORTANT SAFETY INFORMATION (continued)

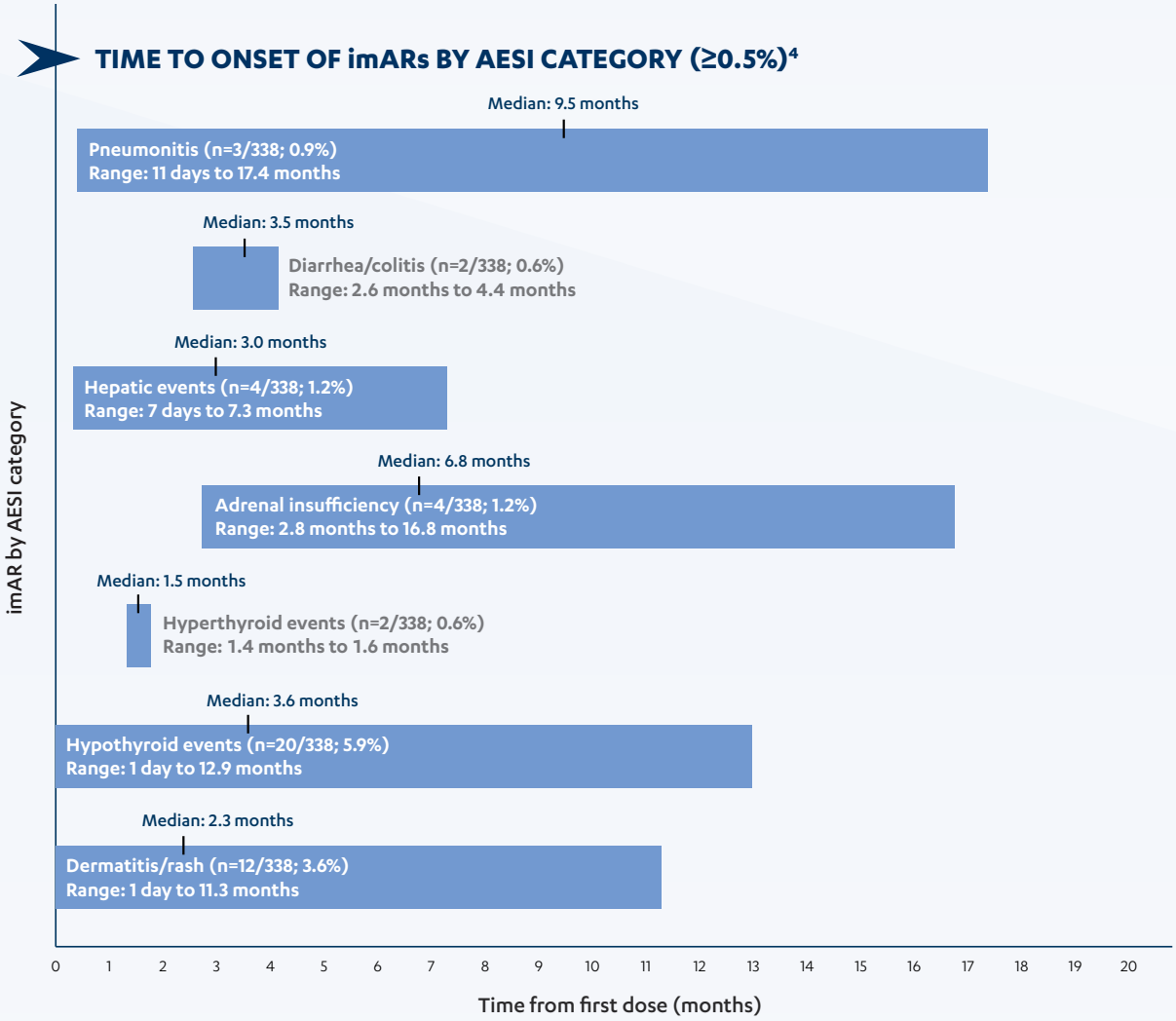
Immune-Mediated Pneumonitis

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, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. 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 18.3% (87/475) in patients receiving IMFINZI and 12.8% (30/234) in patients receiving placebo. Of the patients who received IMFINZI (475), 1.1% were fatal and 2.7% were Grade 3 adverse reactions. The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC or BTC when given in combination with chemotherapy.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.

Time to onset of imARs with IMFINZI + gem-cis[4]

Immune-mediated ARs can occur at any time after starting treatment or after discontinuation[1]



Discontinuation due to treatment-related ARs was 8.9% with IMFINZI + gem-cis and 11.4% with placebo + gem-cis[2]

AESI=adverse event of special interest.

IMPORTANT SAFETY INFORMATION (continued)

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 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions.

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General imAR management strategies[1]

General guidance

No dose reduction of IMFINZI is recommended. Withholding or permanently discontinuing IMFINZI due to adverse reactions may be required

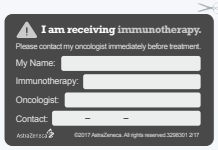
- No dose reduction of IMFINZI is recommended
- Withhold IMFINZI for severe (Grade 3) imARs
- If IMFINZI requires interruption or permanent discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade ≤1. After improvement to Grade ≤1, initiate corticosteroid taper and continue to taper over at least 1 month
- Resume IMFINZI in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) imARs that require systemic immunosuppressive treatment, if no complete or partial resolution within 12 weeks of initiating corticosteroids, or an inability to reduce corticosteroid dose to ≤10 mg prednisone or equivalent per day within 12 weeks of initiating corticosteroids
- Permanently discontinue IMFINZI for life-threatening (Grade 4) imARs

Routine monitoring for potential imARs

Patients being treated with IMFINZI should be monitored at baseline and periodically during and after treatment

- Patients should also be monitored for signs and symptoms of other adverse reactions, including infusion-related reactions
- imARs can occur at any time during treatment and after discontinuation of therapy with IMFINZI
- Important imARs described here may not include all possible severe and fatal imARs. imARs can occur in any organ system or tissue

An IMFINZI Immunotherapy Wallet Card is available for your patients. Available for download at IMFINZIhcp.com in the Support & Resources section



IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Hepatitis

IMFINZI can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2.8% (52/1889) of patients receiving IMFINZI, including fatal (0.2%), Grade 4 (0.3%) and Grade 3 (1.4%) adverse reactions.

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. Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.

Please see additional Important Safety Information throughout and Full Prescribing Information including Medication Guide for IMFINZI.

Treatment modifications for IMFINZI[1]

No dose reduction of IMFINZI is recommended. Withholding or permanently discontinuing IMFINZI due to adverse reactions may be required

Adverse reaction	Severity*	Treatment modification
Immune-mediated adverse reactions		
Pneumonitis	Grade 2	Withhold†
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2 or 3	Withhold†
	Grade 4	Permanently discontinue
Intestinal perforation	Any grade	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT increases to >3 and up to 8 × ULN or total bilirubin increases to >1.5 and up to 3 × ULN	Withhold†
	AST or ALT increases to >8 × ULN or total bilirubin increases to >3 × ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver‡	AST or ALT is >1 and up to 3 × ULN at baseline and increases to >5 and up to 10 × ULN or AST or ALT is >3 and up to 5 × ULN at baseline and increases to >8 and up to 10 × ULN	Withhold†
	AST or ALT increases to >10 × ULN or total bilirubin increases to >3 × 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†
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold†
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold†
	Grade 3 or 4	Permanently discontinue
Other adverse reactions		
Infusion-related reactions	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

*Based on NCI CTCAE version 4.03.

†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 corticosteroids or an inability to reduce corticosteroid dose to 10 mg of prednisone or less per day (or equivalent) within 12 weeks of initiating corticosteroids.

‡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.

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 of normal.

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IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Endocrinopathies (continued)

- ***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. Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received 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.
- ***Thyroiditis***: Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Hyperthyroidism***: Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
- ***Hypothyroidism***: Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***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. Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.5% (10/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.

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. Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.

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.
- ***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, other transplant (including corneal graft) rejection.

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 USPI Dosing and Administration for specific details. 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.

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.

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. Advise pregnant women of the potential risk to a fetus. In females of reproductive potential, verify pregnancy status prior to initiating IMFINZI and advise them to use effective contraception during treatment with IMFINZI and for 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 3 months after the last dose.

Adverse Reactions

- In patients with locally advanced or metastatic BTC in the TOPAZ-1 study receiving IMFINZI (n=338), the most common adverse reactions (occurring in ≥20% of patients) were fatigue (42%), nausea (40%), constipation (32%), decreased appetite (26%), abdominal pain (24%), rash (23%), and pyrexia (20%).
- In patients with locally advanced or metastatic BTC in the TOPAZ-1 study receiving IMFINZI (n=338), discontinuation due to adverse reactions occurred in 6% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 47% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 2% of patients were cholangitis (7%), pyrexia (3.8%), anemia (3.6%), sepsis (3.3%) and acute kidney injury (2.4%). Fatal adverse reactions occurred in 3.6% of patients receiving IMFINZI plus chemotherapy. These include ischemic or hemorrhagic stroke (4 patients), sepsis (2 patients), and upper gastrointestinal hemorrhage (2 patients).

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

Please see additional Important Safety Information throughout and Full Prescribing Information for IMFINZI.

You may report side effects related to AstraZeneca products.

References: 1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2024. **2.** Oh DY, He AR, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. *NEJM Evid*. 2022;1(8). doi:10.1056/EVIDoa2200015. **3.** Oh DY, He AR, Qin S, et al. Three-year survival and safety update from the phase 3 TOPAZ-1 study of durvalumab plus chemotherapy in biliary tract cancer. Poster presented at: 2024 CCF Conference; April 17-19, 2024; Salt Lake City, UT. **4.** Antonuzzo L, Takahashi H, Oh Park J, et al. Immune-mediated adverse event incidence, timing and association with efficacy in the phase 3 TOPAZ-1 study of durvalumab or placebo plus gemcitabine and cisplatin in advanced biliary tract cancer. Presented at: 2022 ESMO Congress; September 9-13, 2022; Paris, France.

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Check patients for immune-mediated adverse reactions at each visit[1]

Monitoring your patients who are being treated with IMFINZI at every infusion and office visit can aid early identification of and intervention for imARs. This is important to help ensure the safety of your patients as they continue treatment with IMFINZI.

Consult with the care team right away if patients present any new or worsening signs or symptoms, including the below.

Pulmonary
- Cough
- Shortness of breath
- Chest pain

Gastrointestinal
- Diarrhea (loose stools) or more frequent bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe abdominal pain or tenderness

Pancreas
- Pain in your upper stomach area (abdomen)
- Severe nausea or vomiting
- Loss of appetite

Hepatic
- Yellowing of the skin or whites of the eyes
- Severe nausea or vomiting
- Pain on the right side of abdomen
- Dark urine (tea colored)
- Bleeding or bruising more easily than normal

Renal
- Decrease in amount of urine
- Blood in urine
- Swelling of ankles
- Loss of appetite

Skin
- 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

Endocrine
- Headaches that will not go away or unusual headaches
- Eye sensitivity to light
- Eye problems
- Rapid heartbeat
- Increased 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
- Voice gets deeper
- Dizziness or fainting
- Changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Other
- 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, numbness, or weakness of the arms or legs
- Double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- Persistent or severe muscle pain or weakness, muscle cramps, joint pain, joint stiffness or swelling
- Low red blood cells, bruising

Learn more about how IMFINZI may help patients with advanced BTCs, including cholangiocarcinoma and gallbladder cancer, at IMFINZIhcp.com/BTCs

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