NEW INDICATION APPROVED IN SEPTEMBER 2022

IMFINZI® durvalumab
Injection for Intravenous Use 50 mg/mL

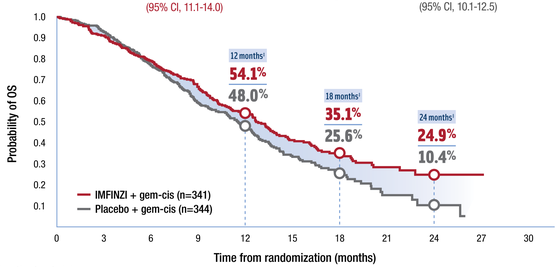
IMFINZI® (durvalumab) in combination with gemcitabine plus cisplatin (gem-cis) is the first and only FDA-approved regimen for the 1L treatment of patients with locally advanced or metastatic biliary tract cancer (BTC)[1,2]★

IMFINZI + gem-cis significantly improved OS vs gem-cis in the TOPAZ-1 trial[1,2]

20% reduction in the risk of death with IMFINZI + gem-cis vs gem-cis

HR=0.80 (95% CI, 0.66-0.97; *P*=0.021)†

12.8 months median OS with IMFINZI + gem-cis (95% CI, 11.1-14.0) vs 11.5 months median OS with gem-cis (95% CI, 10.1-12.5)



Number of patients at risk

IMFINZI + gem-cis	341	331	324	309	294	278	268	252	238	208	174	151	135	118	93	79	74	57	49	39	29	24	15	12	9	8	4	1	0
Placebo + gem-cis	344	337	329	317	299	283	261	242	220	183	159	143	125	97	78	65	52	40	29	21	15	10	8	4	4	3	0	0	0

- Median duration of follow-up was 16.8 months (95% CI: 14.8-17.7) with IMFINZI + gem-cis and 15.9 months (95% CI: 14.9-16.9) with gem-cis[2]
- OS at 12, 18, and 24 months were descriptive endpoints and were not formally tested for statistical significance[2]
- At the prespecified interim analysis (DCO: August 11, 2021), 424 events (198 in the IMFINZI group and 226 in the placebo group) had occurred[1,2]

Tumor assessments were conducted every 6 weeks for the first 24 weeks after the date of randomization and then every 8 weeks until confirmed objective disease progression.[1]

★BTCs include intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, and gallbladder cancer.[1]
†HR based on Cox proportional hazards model stratified by disease status and primary tumor location, 2-sided *P* value based on a stratified log rank test compared with alpha boundary of 0.030.[1]
‡OS for IMFINZI + gem-cis and gem-cis were: 54.1% (95% CI: 48.4-59.4) and 48.0% (95% CI: 42.4-53.4) at 12 months, 35.1% (95% CI: 29.1-41.2) and 25.6% (95% CI: 19.9-31.7) at 18 months, and 24.9% (95% CI: 17.9-32.5) and 10.4% (95% CI: 4.7-18.8) at 24 months.[1]

Please scroll to the right to see additional Important Safety Information throughout and complete Prescribing Information including Medication Guide.

TOPAZ-1: A randomized, double-blind, placebo-controlled, multicenter, global Phase III study[1,2]

Key eligibility criteria

- Histologically confirmed locally advanced or metastatic BTCs*
- Previously untreated if unresectable or metastatic at initial diagnosis§
- ECOG PS 0 or 1
- ≥1 target lesion by RECIST v1.1
- Patients with ampullary carcinoma; active or prior documented autoimmune or inflammatory disorders, HIV infection or active infections, or current or prior use of immunosuppressive medications within 14 days before the first dose of IMFINZI were ineligible to participate in the TOPAZ-1 study‖

R 1:1 (N=685)

- **IMFINZI 1500 mg + gem-cis¶** Q3W for up to 8 cycles (n=341) → **IMFINZI 1500 mg Q4W** until disease progression or unacceptable toxicity¶
- **Placebo + gem-cis¶** Q3W for up to 8 cycles (n=344) → **Placebo Q4W** until disease progression or unacceptable toxicity¶

Stratification factors

- Disease status (initially unresectable vs recurrent)
- Primary tumor location (iCCA vs eCCA vs GBC)

Primary endpoint

- OS

Key secondary endpoints

- PFS#
- DoR#
- ORR#
- Safety

Safety and tolerability profile from TOPAZ-1[1,2]

- Serious adverse reactions occurred in 47% of patients receiving IMFINZI + gem-cis. The most frequent (≥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 + gem-cis, and included ischemic or hemorrhagic stroke (reported in 4 patients), sepsis, and upper gastrointestinal hemorrhage (reported in 2 patients each)
- The most common adverse reactions (≥20% of patients) with IMFINZI + gem-cis and gem-cis were fatigue (42% vs 43%), nausea (40% vs 34%), constipation (32% vs 29%), decreased appetite (26% vs 23%), abdominal pain (24% vs 23%), rash (23% vs 14%), and pyrexia (20% vs 16%)
- Similar rates of Grade 3-4 adverse reactions were reported for IMFINZI + gem-cis (75.7%) and gem-cis (77.8%)

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

NCCN RECOMMENDATION

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend durvalumab (IMFINZI®) in combination with gemcitabine + cisplatin as a Category 1, preferred systemic therapy option for primary treatment of patients with unresectable or metastatic BTCs.3††**

BACK TO BEGINNING

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,

‖Patients who developed recurrent disease >6 months after surgery and/or completion of adjuvant therapy were eligible.[1]
¶IMFINZI 1500 mg or placebo administered on Day 1 + gemcitabine 1000 mg/m^2 and cisplatin 25 mg/m^2 (each administered on Days 1 and 8) Q3W (21 days) for up to 8 cycles.[1]
¶IMFINZI 1500 mg or placebo Q4W until disease progression or unacceptable toxicity (treatment was permitted beyond disease progression if the patient was clinically stable and deriving clinical benefit as determined by the investigator).[1]
§Investigator assessed according to RECIST v1.1.[1]
**See the NCCN Guidelines® for Hepatobiliary Cancers for detailed recommendations, including other treatment options.
††BTCs: Gallbladder cancer, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma.[3]

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Important Safety Information (cont'd)

Immune-Mediated Adverse Reactions (cont'd)

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 Dosing and Administration for specific details. 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.

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

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.
- ***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), have 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.

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 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 at least 3 months after the last dose of IMFINZI.

Lactation

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

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, nausea, constipation, decreased appetite, abdominal pain, rash, and pyrexia
- 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), upper gastrointestinal hemorrhage (2 patients)

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

BACK TO BEGINNING

Please see complete Prescribing Information including Medication Guide.
You may report side effects related to AstraZeneca products by clicking here.

1L=first-line; AR=adverse reaction; CI=confidence interval; DCO=data cutoff; DoR=duration of response; eCCA=extrahepatic cholangiocarcinoma; ECOG=Eastern Cooperative Oncology Group; FDA=US Food and Drug Administration; GBC=gallbladder cancer; HR=hazard ratio; iCCA=intrahepatic cholangiocarcinoma; NCCN=National Comprehensive Cancer Network; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PS=performance status; Q3W=every 3 weeks; Q4W=every 4 weeks; R=randomized; RECIST=Response Evaluation Criteria in Solid Tumors.

References: 1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **2.** Oh DY, He AR, Qin S, et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer. *NEJM Evidence*. 2022;1(8). doi:10.1056/EVIDoa2200015 **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers. V.2.2022 © 2022 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed September 1, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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AstraZeneca