



IMMUNE-MEDIATED ADVERSE REACTIONS MANAGEMENT HANDBOOK



Addressing immune-mediated adverse reactions
associated with IMFINZI, with or without IMJUDO

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab) or IMJUDO® (tremelimumab-actl).

Severe and Fatal 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.

Please see additional Important Safety Information throughout and click here for Full Prescribing Information including Medication Guide for [IMFINZI](#) and [IMJUDO](#).

Lung Indications



STAGE III NSCLC

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.



METASTATIC NSCLC

IMFINZI, in combination with IMJUDO and platinum-based chemotherapy, is indicated for the treatment of adult patients with metastatic NSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.



ES-SCLC

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).

Hepatobiliary Indications



LOCALLY ADVANCED OR METASTATIC BILIARY TRACT CANCERS (BTCs)

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



UNRESECTABLE HEPATOCELLULAR CARCINOMA (uHCC)

IMFINZI in combination with IMJUDO is indicated for the treatment of adult patients with unresectable hepatocellular carcinoma (uHCC).



**For more indication-specific information,
visit [IMFINZIhcp.com](https://www.imfinzihcp.com)**



IMPORTANT SAFETY INFORMATION

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotrophic hormone (ACTH) level, and thyroid function at baseline and before each dose. 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 and IMJUDO depending on severity. See USPI Dosing and Administration for specific details. In general, if IMFINZI and IMJUDO 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 click here for Full Prescribing Information including Medication Guide for [IMFINZI](#) and [IMJUDO](#).

Your source for imAR risk management

Dear Healthcare Professional,

There are known serious immune-mediated safety risks associated with Immune Checkpoint Inhibitors (ICIs), including IMFINZI and IMJUDO. Through proper knowledge and practice, you can manage your patients' immune-mediated adverse reactions (imARs).^{1,2}

- Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 and/or CTLA-4 blocking antibodies¹⁻³
- Routine monitoring of patients, including periodic lab tests during and after treatment, is important^{1,2}



- PD-L1 blocking antibody¹
- Blocks the interaction of PD-L1 with PD-1 and CD80¹
- Blockade of PD-L1/PD-1 and PD-L1/CD80 interactions releases the inhibition of immune responses, without inducing antibody dependent cell-mediated cytotoxicity (ADCC)¹



- CTLA-4 blocking antibody²
- Binds to CTLA-4 and blocks the interaction with its ligands CD80 and CD86²
- Releases CTLA-4-mediated inhibition of T-cell activation²

CD80=cluster of differentiation 80; CD86=cluster of differentiation 86; CTLA-4=cytotoxic T-lymphocyte-associated protein 4; PD-1=programmed cell death protein 1; PD-L1=programmed death-ligand 1.

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

How to use this handbook

This handbook was created to inform you about the imARs associated with IMFINZI and IMJUDO and their management. It is important to recognize and address signs and symptoms early. Management information for imARs included in this handbook:

- Incidence of imARs
- Signs and symptoms to recognize
- Management and dosage modification information
- Follow-up instructions

The sections in this handbook are:



General Guidance



Pulmonary



Gastrointestinal



Hepatic



Endocrine



Renal



Dermatologic



Other

Additional resources included in this handbook:

- Financial assistance details
- imAR Quick Reference Guide

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information](#) including Medication Guide for IMFINZI and IMJUDO.

Management of imARs



General Guidance

General guidance for IMFINZI and IMJUDO imARs^{1,2}

- IMFINZI is a monoclonal antibody that belongs to a class of drugs that bind to either PD-1 or 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 reactions¹
- IMJUDO is a monoclonal antibody that blocks T-cell inhibitory signals induced by the CTLA-4 pathway, thereby removing inhibition of the immune response²
- The reactions described in this handbook 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 and/or CTLA-4 blocking antibody. While they usually manifest during treatment, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 and/or CTLA-4 blocking antibodies

Identification of imARs^{1,2}

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, or in combination with IMJUDO with or without platinum-based chemotherapy, unless otherwise noted within this handbook.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 and/or CTLA-4 blocking antibodies.

- Evaluate liver enzymes, creatinine, adrenocorticotrophic hormone (ACTH), 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

➤ **Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions^{1,2}**

IMPORTANT SAFETY INFORMATION

Immune-Mediated Pneumonitis

IMFINZI and IMJUDO can cause immune-mediated pneumonitis, which may be fatal. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

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

General



General
Guidance

Management Strategies^{1,2}

- No dose reductions for IMFINZI or IMJUDO are recommended
- In general, withhold IMFINZI/IMJUDO for severe (Grade 3) immune-mediated adverse reactions
- In general, if IMFINZI +/- IMJUDO 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
- Permanently discontinue IMFINZI and IMJUDO for:
 - Life-threatening (Grade 4) immune-mediated adverse reactions
 - Recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
 - An inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating corticosteroids

These are general guidelines. Please refer to individual sections within this handbook regarding specific imAR management guidelines.

Management of imARs



Pulmonary

Pneumonitis

Immune-mediated pneumonitis

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety population (N=1889) reflects exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108, (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

	Without prior radiation (n=1414)	With prior radiation (n=475)
All Grades	2.4%	18.3%
Grade 3 or 4	0.4%	2.7%*
Grade 5	<0.1%	1.1%

*Only Grade 3 reported.

The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiotherapy 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 or BTC when given in combination with chemotherapy.^{1†}

imAR findings¹

- IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation
- In patients who received IMFINZI without recent prior radiation therapy, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3 to 4 (0.4%) adverse reactions. Events resolved in 19 of the 34 patients and resulted in permanent discontinuation in 5 patients. Systemic corticosteroids were required in 19 patients (19/34) with pneumonitis who did not receive chemoradiation prior to initiation of IMFINZI
- 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. Events resolved in 50 of the 87 patients and resulted in permanent discontinuation in 27 patients. Systemic corticosteroids were required in 64 patients (64/87) with pneumonitis who had received chemoradiation prior to initiation of IMFINZI, while 2 patients required use of infliximab with high-dose steroids

[†]In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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

IMFINZI + IMJUDO^{1,2}

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	1.3%
Grade 3	0.2%
Grade 5	0.3%

imAR findings¹

- Immune-mediated pneumonitis occurred in 1.3% (5/388) of patients receiving IMFINZI in combination with IMJUDO, including fatal (0.3%) and Grade 3 (0.2%) adverse reactions. Events resolved in 3 of the 5 patients and resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in all patients; of these, 4 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). One patient (1/5) required other immunosuppressants

Immune-mediated pneumonitis (continued)

IMFINZI + **IMJUDO** + platinum-based therapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades	3.5%
Grade 3	1%
Grade 5	0.5%

imAR findings^{1,2}

- Immune-mediated pneumonitis occurred in 3.5% (21/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.5%), and Grade 3 (1%) adverse reactions. Events resolved in 11 of the 21 patients and resulted in permanent discontinuation in 7 patients. Systemic corticosteroids were required in all patients with immune-mediated pneumonitis, while 1 patient (1/21) required other immunosuppressants

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information](#) including Medication Guide for **IMFINZI** and **IMJUDO**.

Signs and symptoms of pneumonitis^{1,2}

- Cough
- Shortness of breath
- Chest pain

Management strategies

➤ **IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED PNEUMONITIS^{1,2}**

	Grade 1	Grade 2	Grade 3	Grade 4
Definition^{4*}	<ul style="list-style-type: none">• Asymptomatic• Clinical or diagnostic observations only• Intervention not indicated	<ul style="list-style-type: none">• Symptomatic• Medical intervention indicated• Limiting instrumental ADL[†]	<ul style="list-style-type: none">• Severe symptoms• Limiting self-care ADL[‡]• Oxygen indicated	<ul style="list-style-type: none">• Life-threatening compromise• Urgent intervention indicated (eg, tracheotomy or intubation)
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		

ADL=activities of daily living; CT=chemotherapy; mNSCLC=metastatic non-small cell lung cancer.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

[†]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.⁴

[‡]Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.⁴

Additional withholding information^{1,2}

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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

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

Management of imARs



Gastrointestinal

Colitis
Diarrhea
Pancreatitis

Immune-mediated colitis

IMFINZI as a single agent or in combination with chemotherapy

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more¹
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks¹

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades	2%
Grade 3	0.4%
Grade 4	<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.^{i*}

imAR findings^{1,2}

- IMFINZI with IMJUDO and platinum-based chemotherapy can cause immune-mediated colitis, which may be fatal
- 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. Events resolved in 27 of the 37 patients and resulted in permanent discontinuation in 8 patients. Systemic corticosteroids were required in all patients with immune-mediated colitis, while 2 patients (2/37) required other immunosuppressants (eg, infliximab, mycophenolate)

IMFINZI + IMJUDO

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study^{1,2}
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	6%
Grade 3	3.6%

ⁱIn the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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



imAR findings^{1,2}

- Immune-mediated colitis or diarrhea occurred in 6% (23/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (3.6%) adverse reactions. Events resolved in 22 of the 23 patients and resulted in permanent discontinuation in 5 patients. All patients received systemic corticosteroids, and 20 of the 23 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Three patients also received other immunosuppressants. Intestinal perforation has been observed in other studies of IMFINZI in combination with IMJUDO

IMFINZI + IMJUDO + platinum-based chemotherapy

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study, and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)^{1,2}
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades	6.5%
Grade 3	2.5%
Grade 5	0.2%

imAR findings^{1,2}

- Immune-mediated colitis occurred in 6.5% (39/596) of patients receiving IMFINZI in combination with IMJUDO including fatal (0.2%) and Grade 3 (2.5%) adverse reactions. Events resolved in 33 of 39 patients and resulted in permanent discontinuation in 11 patients. Systemic corticosteroids were required in all patients with immune-mediated colitis, while 4 patients (4/39) required other corticosteroids
- Intestinal perforation and large intestine perforation were reported in 0.1% of patients receiving IMFINZI in combination with IMJUDO

Immune-mediated colitis (continued)

Signs and symptoms of colitis^{1,2}

- Diarrhea or more bowel movements than usual
- Stools that are black, tarry, sticky, or have blood or mucus
- Severe abdominal pain or tenderness

Management strategies



IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED COLITIS^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Definition^{4*}	<ul style="list-style-type: none">• Asymptomatic• Clinical or diagnostic observations only• Intervention not indicated	<ul style="list-style-type: none">• Abdominal pain• Mucus or blood in stool	<ul style="list-style-type: none">• Severe abdominal pain• Peritoneal signs	<ul style="list-style-type: none">• Life-threatening consequences• Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Withhold or permanently discontinue [†] IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

[†]Permanently discontinue IMFINZI for Grade 3 colitis when administered as part of a regimen containing IMJUDO® (tremelimumab-actl).¹

Additional withholding information^{1,2}

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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
- Permanently discontinue IMFINZI +/- IMJUDO if immune-mediated intestinal perforation occurs at any grade

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



Immune-mediated pancreatitis^{1,2}

IMFINZI in combination with IMJUDO can cause immune-mediated pancreatitis.

IMFINZI + IMJUDO

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	2.3%
Grade 3	1.5%
Grade 4	0.3%

imAR findings^{1,2}

- Immune-mediated pancreatitis occurred in 2.3% (9/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions. Events resolved in 6 of the 9 patients. Systemic corticosteroids were required in all 9 patients, and of these, 7 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)

Signs and symptoms of pancreatitis^{1,2}

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

Immune-mediated pancreatitis (continued)

Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED PANCREATITIS^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Definition^{4*}	–	<ul style="list-style-type: none"> • Enzyme elevation • Radiologic findings only 	<ul style="list-style-type: none"> • Severe pain • Vomiting • Medical intervention indicated (eg, analgesia, nutritional support) 	<ul style="list-style-type: none"> • Life-threatening consequences • Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Withhold or permanently discontinue IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

Additional withholding information^{1,2}

- In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions

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

Management of imARs



Hepatic

Hepatitis

Immune-mediated hepatitis

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades	2.8%
Grade 3	1.4%
Grade 4	0.3%
Grade 5	0.2%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.^{1*}

imAR findings¹

- 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. Events resolved in 21 of the 52 patients and resulted in permanent discontinuation of IMFINZI in 6 patients. Systemic corticosteroids were required in all patients with immune-mediated hepatitis, while 2 patients (2/52) required use of mycophenolate with high-dose steroids

¹In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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



Hepatic

IMFINZI + IMJUDO^{1,2}

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study^{1,2}
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	7.5%
Grade 3	4.1%
Grade 4	0.3%
Grade 5	0.8%

imAR findings^{1,2}

- Immune-mediated hepatitis occurred in 7.5% (29/388) of patients receiving IMFINZI in combination with IMJUDO, including fatal (0.8%), Grade 4 (0.3%), and Grade 3 (4.1%) adverse reactions. Events resolved in 12 of the 29 patients and resulted in permanent discontinuation in 9 patients. Systemic corticosteroids were required in all 29 patients and all 29 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Eight patients (8/29) required other immunosuppressants

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

Immune-mediated hepatitis (continued)

IMFINZI + IMJUDO + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades	3.9%
Grade 3	2%
Grade 4	0.5%
Grade 5	0.3%

imAR findings^{1,2}

- Immune-mediated hepatitis occurred in 3.9% (23/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.3%), Grade 4 (0.5%), and Grade 3 (2%) adverse reactions. Events resolved in 12 of the 23 patients and resulted in permanent discontinuation in 27 patients. Systemic corticosteroids were required in all patients with immune-mediated hepatitis, while 2 patients (2/23) required use of other immunosuppressants

Signs and symptoms of hepatitis^{1,2}

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

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO.](#)



Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED HEPATITIS^{1,2}

Hepatitis with no tumor involvement of the liver			
Severity*	–	<ul style="list-style-type: none">• ALT or AST increases to >3 and up to 8 × ULN or total bilirubin increases >1.5 and up to 3 × ULN	<ul style="list-style-type: none">• ALT or AST increases to >8 × ULN or total bilirubin increases to >3 × ULN
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month	
Hepatitis with tumor involvement of the liver†			
Severity*	–	<ul style="list-style-type: none">• AST or ALT is >1 and up to 3 × ULN at baseline and increases to >5 and up to 10 × ULNor:• AST or ALT is >3 and up to 5 × ULN at baseline and increases to >8 and up to 10 × ULN	<ul style="list-style-type: none">• ALT or AST increases to >10 × ULNor:• Total bilirubin increases to >3 × ULN
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month	

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.

[†]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.

Additional withholding information^{1,2}

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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

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

Management of imARs



Endocrine

Adrenal insufficiency
Hypophysitis/hypopituitarism
Thyroid disorders
Type 1 diabetes mellitus

Immune-mediated endocrinopathies

Signs and symptoms of endocrinopathies^{1,2}

- 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

Immune-mediated adrenal insufficiency



IMFINZI as a single agent or in combination with chemotherapy

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more¹
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks¹

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades	0.5%
Grade 3	<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.^{1*}

imAR findings¹

- 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
- Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 1 of the 9 patients and 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

IMFINZI + IMJUDO

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study^{1,2}
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	1.5%
Grade 3	0.3%

imAR findings^{1,2}

- Immune-mediated adrenal insufficiency occurred in 1.5% (6/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.3%) adverse reactions. Events resolved in 2 of the 6 patients. Systemic corticosteroids were required in all 6 patients, and of these, 1 patient required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)

*In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

Please see additional Important Safety Information throughout and click here for Full Prescribing Information including Medication Guide for [IMFINZI](#) and [IMJUDO](#).

Immune-mediated adrenal insufficiency (continued)

IMFINZI + **IMJUDO** + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

➤ **imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}**

All Grades	2.2%
Grade 3	0.8%

imAR findings^{1,2}

- Immune-mediated adrenal insufficiency occurred in 2.2% (13/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.8%) adverse reactions. Events resolved in 2 of the 13 patients and resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in all patients with adrenal insufficiency. One patient also required endocrine therapy



Management strategies



IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED ADRENAL INSUFFICIENCY^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Definition ^{4*}	<ul style="list-style-type: none">• Asymptomatic• Clinical or diagnostic observations only• Intervention not indicated	<ul style="list-style-type: none">• Moderate symptoms• Medical intervention indicated	<ul style="list-style-type: none">• Severe symptoms• Hospitalization indicated	<ul style="list-style-type: none">• Life-threatening consequences• Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO		Withhold IMFINZI +/- IMJUDO until clinically stable or permanently discontinue depending on severity	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		
Clinical Management	–	Initiate symptomatic treatment, including hormone replacement as clinically indicated		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

Additional withholding information^{1,2}

- In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions

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

Immune-mediated hypophysitis/hypopituitarism

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades

<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.^{1*}

imAR findings¹

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

^{*}In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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



Endocrine

IMFINZI + IMJUDO^{1,2}

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

Grade 3

1%

imAR findings^{1,2}

- Immune-mediated hypophysitis/hypopituitarism occurred in 1% (4/388) of patients receiving IMFINZI in combination with IMJUDO. Events resolved in 2 of the 4 patients. Systemic corticosteroids were required in 3 patients, and of these, 1 patient received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)
- Two patients also required endocrine therapy

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

Immune-mediated hypophysitis/hypopituitarism (continued)

IMFINZI + **IMJUDO** + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

➤ **imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}**

All Grades	1.3%
Grade 3	0.5%

imAR findings^{1,2}

- Immune-mediated hypophysitis occurred in 1.3% (8/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.5%) adverse reactions. Events resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in 6 patients with immune-mediated hypophysitis; of these, 2 of the 8 patients received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)
- Four patients also required endocrine therapy

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for **IMFINZI** and **IMJUDO**.](#)



Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR HYPOPHYSITIS/HYPOPITUITARISM^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Definition ^{4**}	<ul style="list-style-type: none">• Asymptomatic• Clinical or diagnostic observations only• Intervention not indicated	<ul style="list-style-type: none">• Moderate• Minimal, local, or noninvasive intervention indicated• Limiting age-appropriate instrumental ADL[†]	<ul style="list-style-type: none">• Severe or medically significant, but not immediately life threatening• Hospitalization or prolongation of hospitalization indicated• Limiting self-care ADL[‡]	<ul style="list-style-type: none">• Life-threatening consequences• Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO		Withhold IMFINZI +/- IMJUDO until clinically stable or permanently discontinue depending on severity	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		
Clinical Management	–	Initiate symptomatic treatment, including hormone replacement as clinically indicated		

ADL=activities of daily living.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

[†]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.⁴

[‡]Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.⁴

Additional withholding information^{1,2}

- In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions

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

Immune-mediated thyroid disorders

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

Thyroiditis	
All Grades	0.5%
Grade 3	<0.1%
Hyperthyroidism	
All Grades	2.1%
Hypothyroidism	
All Grades	8.3%
Grade 3	<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.*

imAR findings¹

- 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
- **Immune-mediated thyroiditis** occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 4 of the 9 patients and resulted in permanent discontinuation in 1 patient. Systemic corticosteroids were required in 3 patients (3/9) with immune-mediated thyroiditis, while 8 patients (8/9) required endocrine therapy
- **Immune-mediated hyperthyroidism** occurred in 2.1% (39/1889) of patients receiving IMFINZI. Events resolved in 30 of the 39 patients and did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in 9 patients (9/39) with immune-mediated hyperthyroidism, while 35 patients (35/39) required endocrine therapy
- **Immune-mediated hypothyroidism** occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions. Events resolved in 31 of the 156 patients and did not lead to permanent discontinuation of IMFINZI in any patients. Systemic corticosteroids were required in 11 patients (11/156) and the majority of patients (152/156) required long-term thyroid hormone replacement

*In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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

**IMFINZI + IMJUDO^{1,2}****uHCC**

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

Thyroiditis	
All Grades	1.5%
Hyperthyroidism	
All Grades	4.6%
Grade 3	0.3%
Hypothyroidism	
All Grades	11%

imAR findings^{1,2}

- **Immune-mediated thyroiditis** occurred in 1.5% (6/388) of patients receiving IMFINZI in combination with IMJUDO. Events resolved in 2 of the 6 patients. Systemic corticosteroids were required in 2 patients (2/6) with immune-mediated thyroiditis; of these, 1 patient required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). All patients required other therapy including hormone replacement therapy, thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker
- **Immune-mediated hyperthyroidism** occurred in 4.6% (18/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.3%) adverse reactions. Events resolved in 15 of the 18 patients. Two patients (2/18) required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). Seventeen patients required other therapy (thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker)
- **Immune-mediated hypothyroidism** occurred in 11% (42/388) of patients receiving IMFINZI in combination with IMJUDO. Events resolved in 5 of the 42 patients. One patient received high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day). All patients required other therapy (thiamazole, carbimazole, propylthiouracil, perchlorate, calcium channel blocker, or beta-blocker)

Immune-mediated thyroid disorders (continued)

IMFINZI + IMJUDO + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

Thyroiditis	
All Grades	1.2%
Hyperthyroidism	
All Grades	5%
Grade 3	0.2%
Hypothyroidism	
All Grades	8.6%
Grade 3	0.5%

imAR findings^{1,2}

- **Immune-mediated thyroiditis** occurred in 1.2% (7/596) of patients receiving IMFINZI in combination with IMJUDO. Events resolved in 2 of the 7 patients and 1 resulted in permanent discontinuation. Systemic corticosteroids were required in 2 patients (2/7) with immune-mediated thyroiditis, while all patients required endocrine therapy
- **Immune-mediated hyperthyroidism** occurred in 5% (30/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.2%) adverse reactions. Events resolved in 21 of the 30 patients. Systemic corticosteroids were required in 5 patients (5/30) with immune-mediated hyperthyroidism, while 28 patients (28/30) required endocrine therapy
- **Immune-mediated hypothyroidism** occurred in 8.6% (51/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.5%) adverse reactions. Systemic corticosteroids were required in 2 patients (2/51) and all patients required endocrine therapy

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for **IMFINZI** and **IMJUDO**.](#)



Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED THYROID DISORDERS^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Thyroiditis, hyperthyroidism, hypothyroidism				
Definition ^{4*}	<ul style="list-style-type: none">• Asymptomatic• Clinical or diagnostic observations only• Intervention not indicated	<ul style="list-style-type: none">• Symptomatic• Limiting instrumental ADL[†] Hyperthyroidism: <ul style="list-style-type: none">• Thyroid suppression therapy indicated Hypothyroidism: <ul style="list-style-type: none">• Thyroid replacement therapy indicated	<ul style="list-style-type: none">• Severe symptoms• Limiting self-care ADL[‡]• Hospitalization indicated	<ul style="list-style-type: none">• Life-threatening consequences• Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO		Withhold IMFINZI +/- IMJUDO until clinically stable or permanently discontinue depending on severity	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		
Clinical Management	–	<ul style="list-style-type: none">• Initiate hormone therapy for hypothyroidism or as clinically indicated• Institute medical management of hyperthyroidism as clinically indicated		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

[†]Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.⁴

[‡]Self-care ADL refer to bathing, dressing and undressing, self-feeding, using the toilet, taking medications, and not being bedridden.⁴

Additional withholding information^{1,2}

- In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions

Please see additional Important Safety Information throughout and click here for Full Prescribing Information including Medication Guide for [IMFINZI](#) and [IMJUDO](#).

Immune-mediated type 1 diabetes mellitus

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks



imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

Grade 3

<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.*

imAR findings¹

- 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
- 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
- Two additional patients (0.1%, 2/1889) had events of hyperglycemia requiring insulin therapy that did not resolve at the time of reporting

*In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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



Endocrine

IMFINZI + IMJUDO

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study^{1,2}
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades

0.5%

imAR findings^{1,2}

- Two patients (0.5%, 2/388) had events of hyperglycemia requiring insulin therapy that had not resolved at last follow-up

IMFINZI + IMJUDO + platinum-based chemotherapy

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)^{1,2}
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 dose^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades

0.5%

Grade 3

0.3%

imAR findings^{1,2}

- Immune-mediated type 1 diabetes mellitus occurred in 0.5% (3/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.3%) adverse reactions
- All patients required endocrine therapy

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



Immune-mediated type 1 diabetes mellitus (continued)

Management strategies



IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR TYPE 1 DIABETES MELLITUS^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Definition ^{4*}	<ul style="list-style-type: none">• Abnormal glucose above baseline with no medical intervention	<ul style="list-style-type: none">• Change in daily management from baseline for a diabetic• Oral antiglycemic agent initiated• Workup for diabetes	<ul style="list-style-type: none">• Insulin therapy initiated• Hospitalization indicated	<ul style="list-style-type: none">• Life-threatening consequences• Urgent intervention indicated
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO		Withhold IMFINZI +/- IMJUDO until clinically stable or permanently discontinue depending on severity	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		
Clinical Management	–	Monitor patients for hyperglycemia or other signs or symptoms of diabetes. Initiate treatment with insulin as clinically indicated		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v5.⁴

Additional withholding information^{1,2}

- In general, withhold IMFINZI for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI for recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI for life-threatening (Grade 4) immune-mediated adverse reactions

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

Management of imARs



Renal

Nephritis

Immune-mediated nephritis

IMFINZI as a single agent or in combination with chemotherapy

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more¹
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks¹

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades	0.5%
Grade 3	<0.1%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.*

imAR findings¹

- 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. Events resolved in 5 of the 10 patients and resulted in permanent discontinuation in 3 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis

IMFINZI + IMJUDO

uHCC

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study^{1,2}
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks^{1,2}

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	1%
Grade 3	0.5%

imAR findings^{1,2}

- Immune-mediated nephritis occurred in 1% (4/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.5%) adverse reactions. Events resolved in 3 of the 4 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis; of these, 3 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)

*In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.¹

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



Renal

IMFINZI + IMJUDO + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades	0.7%
Grade 3	0.2%

imAR findings^{1,2}

- Immune-mediated nephritis occurred in 0.7% (4/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.2%) adverse reactions. Events resolved in 1 of the 4 patients and resulted in permanent discontinuation in 3 patients. Systemic corticosteroids were required in all patients with immune-mediated nephritis

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO.](#)



Renal

Immune-mediated nephritis (continued)

Signs and symptoms of nephritis^{1,2}

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

Management strategies



IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR NEPHRITIS^{1,2}

	Grade 1	Grade 2	Grade 3	Grade 4
Severity*	–	• Grade 2 or 3 increased blood creatinine		• Grade 4 increased blood creatinine
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO		Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.^{1,2}

Additional withholding information^{1,2}

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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

Please see additional Important Safety Information throughout and click here for Full Prescribing Information including Medication Guide for [IMFINZI](#) and [IMJUDO](#).

Management of imARs



Dermatologic

Rash or dermatitis

Immune-mediated rash or dermatitis

IMFINZI as a single agent or in combination with chemotherapy¹

Unresectable Stage III NSCLC

ES-SCLC

BTCs

- The combined safety data (N=1889) reflect exposure to IMFINZI as a single agent in the PACIFIC study (a randomized, placebo-controlled study of 475 patients with Stage III NSCLC), Study 1108 (a multicohort study of 970 patients with advanced solid tumors), and the ATLANTIC study (an open-label, single-arm trial of 444 patients with advanced solid tumors, including NSCLC). Among the 1889 patients, 38% were exposed for 6 months or more and 18% were exposed for 12 months or more
- In these trials, IMFINZI was administered at a dose of 10 mg/kg every 2 weeks

imAR INCIDENCE WITH IMFINZI AS A SINGLE AGENT (N=1889)¹

All Grades	1.8%
Grade 3	0.4%

The incidence and severity of immune-mediated adverse reactions were similar when IMFINZI was administered as a single agent or in combination with chemotherapy, unless otherwise noted.^{1*}

imAR findings¹

- 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/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate nonexfoliative rashes. Withhold or permanently discontinue IMFINZI depending on severity
- Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions. Events resolved in 19 of the 34 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis

¹In the CASPIAN and TOPAZ-1 studies, 265 and 338 patients, respectively, received IMFINZI in combination with chemotherapy.

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

**IMFINZI + IMJUDO^{1,2}****uHCC**

- The safety of IMFINZI + IMJUDO was evaluated in a total of 388 patients in HIMALAYA, a randomized, open-label, multicenter study
- Study patients received IMFINZI 1500 mg administered as a single intravenous infusion with IMJUDO 300 mg, followed by IMFINZI 1500 mg every 4 weeks

imAR INCIDENCE WITH IMFINZI + IMJUDO (N=388)^{1,2}

All Grades	4.9%
Grade 3	1.5%
Grade 4	0.3%

imAR findings^{1,2}

- Immune-mediated rash or dermatitis occurred in 4.9% (19/388) of patients receiving IMFINZI in combination with IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions. Events resolved in 13 of the 19 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis; of these, 12 patients required high-dose corticosteroid treatment (at least 40 mg prednisone or equivalent per day)
- One patient received other immunosuppressants

Immune-mediated rash or dermatitis (continued)

IMFINZI + **IMJUDO** + platinum-based chemotherapy^{1,2}

mNSCLC

- The pooled safety population (N=596) reflects exposure to IMFINZI 1500 mg in combination with IMJUDO 75 mg and histology-based platinum chemotherapy regimens in 330 patients in the POSEIDON study and 266 ES-SCLC patients in the CASPIAN study who received platinum-etoposide plus IMFINZI 1500 mg with IMJUDO 75 mg followed by IMFINZI 1500 mg (an unapproved regimen for ES-SCLC)
- Fifty-five percent were exposed to IMFINZI for 6 months or more and 24% were exposed to IMFINZI for 12 months or more. Of the 330 patients who received IMFINZI and IMJUDO plus platinum-based chemotherapy in the POSEIDON study, 66% received the maximum of 5 doses of IMJUDO and 79% received at least 4 doses

imAR INCIDENCE WITH IMFINZI + IMJUDO + PLATINUM-BASED CT (N=596)^{1,2}

All Grades	7.2%
Grade 3	0.3%

imAR findings^{1,2}

- Immune-mediated rash or dermatitis occurred in 7.2% (43/596) of patients receiving IMFINZI in combination with IMJUDO, including Grade 3 (0.3%) adverse reactions. Events resolved in 32 of the 43 patients and resulted in permanent discontinuation in 2 patients. Systemic corticosteroids were required in all patients with immune-mediated rash or dermatitis



Signs and symptoms of rash or dermatitis^{1,2}

- Rash
- Itching
- Skin blistering or peeling
- Painful sores or ulcers in mouth, nose, throat, or genital area
- Fever or flu-like symptoms
- Swollen lymph nodes

Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED EXFOLIATIVE DERMATOLOGIC CONDITIONS^{1,2}

Severity*	–	Suspected SJS, TEN, or DRESS	Confirmed SJS, TEN, or DRESS
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month	

DRESS=Drug Rash with Eosinophilia and Systemic Symptoms; SJS=Stevens-Johnson Syndrome; TEN=toxic epidermal necrolysis.

*Toxicity grades were defined according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), v4.03.^{1,2}

Additional withholding information^{1,2}

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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

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

Management of imARs



Other imARs

Class-wide imARs and imARs with an incidence of <1%^{1,2}

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI or IMFINZI in combination with IMJUDO, or were reported with the use of other PD-1/PD-L1 and CTLA-4 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

Monitor patients for the following signs and symptoms of other imARs^{1,2}

- 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 eyesight
- Persistent or severe muscle pain or weakness, muscle cramps
- Low red blood cells, bruising

Management strategies



IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR MYOCARDITIS AND NEUROLOGICAL TOXICITIES

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR MYOCARDITIS AND NEUROLOGICAL TOXICITIES

	Grade 1	Grade 2	Grade 3	Grade 4
Myocarditis				
Dosage modifications	May continue treatment with IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO		
Neurological Toxicities				
Dosage modifications	May continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO	
Steroids	–	In general, if IMFINZI +/- IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to ≤Grade 1. Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue to taper over at least 1 month		

Infusion-related reaction

- For Grade 1 or 2, interrupt or slow the rate of infusion
- For Grade 3 or 4, permanently discontinue

Additional withholding information for neurological toxicities

- Resume in patients with complete or partial resolution (Grade 0-1) after corticosteroid taper
- Permanently discontinue IMFINZI +/- IMJUDO 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

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO](#).

Summary: Treatment modifications^{1,2}



TREATMENT MODIFICATIONS FOR IMFINZI +/- IMJUDO

Adverse reaction	Severity*	Treatment modification
imARs		
Pulmonary Pneumonitis	Grade 2	Withhold [†]
	Grade 3 or 4	Permanently discontinue
Gastrointestinal Colitis	Grade 2	Withhold [†]
	Grade 3	Withhold [†] or permanently discontinue [‡]
	Grade 4	Permanently discontinue
Gastrointestinal Intestinal perforation	Any grade	Permanently discontinue
Hepatic Hepatitis with no tumor involvement of the liver	AST or ALT increases >3 and up to 8 × ULN or Total bilirubin increases >1.5 and up to 3 × ULN	Withhold [†]
	AST or ALT increases >8 × ULN or Total bilirubin increases >3 × ULN	Permanently discontinue
Hepatic 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 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 >10 × ULN or Total bilirubin increases >3 × ULN	Permanently discontinue
Endocrine Endocrinopathies	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Renal 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
Cardiac 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

ALT=alanine aminotransferase; DRESS=Drug Reaction with Eosinophilia and Systemic Symptoms; SJS=Stevens-Johnson Syndrome; TEN=toxic epidermal necrolysis; ULN=upper limit of normal.

*Based on NCI CTCAE, v4.03.

[†]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.

[‡]Permanently discontinue IMFINZI for Grade 3 colitis when administered as part of an IMJUDO® (tremelimumab-actl) containing regimen.

[§]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.

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

- Dose reduction of IMFINZI or IMJUDO is not recommended. Withholding or permanently discontinuing IMFINZI +/- IMJUDO due to adverse reactions may be required
- Withhold IMFINZI +/- IMJUDO for severe (Grade 3) imARs
- Permanently discontinue IMFINZI +/- IMJUDO for recurrent severe (Grade 3) imARs that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to ≤ 10 mg prednisone or equivalent per day within 12 weeks of initiating corticosteroids
- Permanently discontinue IMFINZI +/- IMJUDO for life-threatening (Grade 4) imARs
- If IMFINZI +/- IMJUDO requires withholding or permanent discontinuation, administer systemic corticosteroid therapy (1 mg-2 mg/kg/day prednisone or equivalent) until improvement to \leq Grade 1
- After improvement to \leq Grade 1, taper corticosteroid over at least 1 month
- Prescribing Information has additional information for dosage modification and management specific to adverse reactions

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

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab) or IMJUDO® (tremelimumab-actl).

Severe and Fatal 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 clinical chemistries including liver enzymes, creatinine, adrenocorticotrophic hormone (ACTH) level, and thyroid function at baseline and before each dose. 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 and IMJUDO depending on severity. See USPI Dosing and Administration for specific details. In general, if IMFINZI and IMJUDO 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 and IMJUDO can cause immune-mediated pneumonitis, which may be fatal. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

• IMFINZI as a Single Agent

- 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.

• IMFINZI with IMJUDO

- Immune-mediated pneumonitis occurred in 1.3% (5/388) of patients receiving IMFINZI and IMJUDO, including fatal (0.3%) and Grade 3 (0.2%) adverse reactions.

• IMFINZI with IMJUDO and Platinum-Based Chemotherapy

- Immune-mediated pneumonitis occurred in 3.5% (21/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.5%), and Grade 3 (1%) adverse reactions.

Immune-Mediated Colitis

IMFINZI with IMJUDO and platinum-based chemotherapy can cause immune-mediated colitis, which may be fatal.

IMFINZI and IMJUDO 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.

• IMFINZI as a Single Agent

- Immune-mediated colitis occurred in 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions.

• IMFINZI with IMJUDO

- Immune-mediated colitis or diarrhea occurred in 6% (23/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (3.6%) adverse reactions. Intestinal perforation has been observed in other studies of IMFINZI and IMJUDO.

Please see additional Important Safety Information throughout and [click here for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO](#).

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- Immune-mediated colitis occurred in 6.5% (39/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy including fatal (0.2%) and Grade 3 (2.5%) adverse reactions. Intestinal perforation and large intestine perforation were reported in 0.1% of patients.

Immune-Mediated Hepatitis

IMFINZI and IMJUDO can cause immune-mediated hepatitis, which may be fatal.

- **IMFINZI as a Single Agent**

- 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.

- **IMFINZI with IMJUDO**

- Immune-mediated hepatitis occurred in 7.5% (29/388) of patients receiving IMFINZI and IMJUDO, including fatal (0.8%), Grade 4 (0.3%) and Grade 3 (4.1%) adverse reactions.

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- Immune-mediated hepatitis occurred in 3.9% (23/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.3%), Grade 4 (0.5%), and Grade 3 (2%) adverse reactions.

Immune-Mediated Endocrinopathies

- **Adrenal Insufficiency:** IMFINZI and IMJUDO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated.

- **IMFINZI as a Single Agent**

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

- **IMFINZI with IMJUDO**

- o Immune-mediated adrenal insufficiency occurred in 1.5% (6/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.3%) adverse reactions.

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- o Immune-mediated adrenal insufficiency occurred in 2.2% (13/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.8%) adverse reactions.

- **Hypophysitis:** IMFINZI and IMJUDO 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.

- **IMFINZI as a Single Agent**

- o Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.

- **IMFINZI with IMJUDO**

- o Immune-mediated hypophysitis/hypopituitarism occurred in 1% (4/388) of patients receiving IMFINZI and IMJUDO.

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- o Immune-mediated hypophysitis occurred in 1.3% (8/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.5%) adverse reactions.

- **Thyroid Disorders (Thyroiditis, Hyperthyroidism, and Hypothyroidism):** IMFINZI and IMJUDO 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.

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

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Endocrinopathies (continued)

– IMFINZI as a Single Agent

- o Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- o Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
- o Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.

– IMFINZI with IMJUDO

- o Immune-mediated thyroiditis occurred in 1.5% (6/388) of patients receiving IMFINZI and IMJUDO.
- o Immune-mediated hyperthyroidism occurred in 4.6% (18/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.3%) adverse reactions.
- o Immune-mediated hypothyroidism occurred in 11% (42/388) of patients receiving IMFINZI and IMJUDO.

– IMFINZI with IMJUDO and Platinum-Based Chemotherapy

- o Immune-mediated thyroiditis occurred in 1.2% (7/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy.
- o Immune-mediated hyperthyroidism occurred in 5% (30/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.2%) adverse reactions.
- o Immune-mediated hypothyroidism occurred in 8.6% (51/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.5%) 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.

– IMFINZI as a Single Agent

- o Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

– IMFINZI with IMJUDO

- o Two patients (0.5%, 2/388) had events of hyperglycemia requiring insulin therapy that had not resolved at last follow-up.

– IMFINZI with IMJUDO and Platinum-Based Chemotherapy

- o Immune-mediated Type 1 diabetes mellitus occurred in 0.5% (3/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy including Grade 3 (0.3%) adverse reactions.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI and IMJUDO can cause immune-mediated nephritis.

• IMFINZI as a Single Agent

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

• IMFINZI with IMJUDO

- Immune-mediated nephritis occurred in 1% (4/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.5%) adverse reactions.

• IMFINZI with IMJUDO and Platinum-Based Chemotherapy

- Immune-mediated nephritis occurred in 0.7% (4/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.2%) adverse reactions.

Immune-Mediated Dermatology Reactions

IMFINZI and IMJUDO 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/L1 and CTLA-4 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

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

- **IMFINZI as a Single Agent**

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

- **IMFINZI with IMJUDO**

- Immune-mediated rash or dermatitis occurred in 4.9% (19/388) of patients receiving IMFINZI and IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions.

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- Immune-mediated rash or dermatitis occurred in 7.2% (43/596) of patients receiving IMFINZI in combination with IMJUDO and with platinum-based chemotherapy, including Grade 3 (0.3%) adverse reactions.

Immune-Mediated Pancreatitis

IMFINZI in combination with IMJUDO can cause immune-mediated pancreatitis. Immune-mediated pancreatitis occurred in 2.3% (9/388) of patients receiving IMFINZI and IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) 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 and IMJUDO or were reported with the use of other immune-checkpoint inhibitors.

- **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 and IMJUDO 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 and IMJUDO 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.

- **IMFINZI as a Single Agent**

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

- **IMFINZI with IMJUDO**

- Infusion-related reactions occurred in 10 (2.6%) patients receiving IMFINZI and IMJUDO.

- **IMFINZI with IMJUDO and Platinum-Based Chemotherapy**

- Infusion-related reactions occurred in 2.9% (17/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.3%) adverse reactions.

Please see additional Important Safety Information throughout and click [here](#) for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO.

IMPORTANT SAFETY INFORMATION (continued)

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 their mechanism of action and data from animal studies, IMFINZI and IMJUDO 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 IMJUDO and advise them to use effective contraception during treatment with IMFINZI and IMJUDO and for 3 months after the last dose of IMFINZI and IMJUDO.

Lactation

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

Adverse Reactions

- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), the most common adverse reactions ($\geq 20\%$) were cough (40%), fatigue (34%), pneumonitis or radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The most common Grade 3 or 4 adverse reactions ($\geq 3\%$) were pneumonia (7%) and pneumonitis/radiation pneumonitis (3.4%).
- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), discontinuation due to adverse reactions occurred in 15% of patients in the IMFINZI arm. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions ($\geq 2\%$) 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.
- In patients with mNSCLC in the POSEIDON study receiving IMFINZI and IMJUDO plus platinum-based chemotherapy (n=330), the most common adverse reactions (occurring in $\geq 20\%$ of patients) were nausea (42%), fatigue (36%), musculoskeletal pain (29%), decreased appetite (28%), rash (27%), and diarrhea (22%).
- In patients with mNSCLC in the POSEIDON study receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy (n=330), permanent discontinuation of IMFINZI or IMJUDO due to an adverse reaction occurred in 17% of patients. Serious adverse reactions occurred in 44% of patients, with the most frequent serious adverse reactions reported in at least 2% of patients being pneumonia (11%), anemia (5%), diarrhea (2.4%), thrombocytopenia (2.4%), pyrexia (2.4%), and febrile neutropenia (2.1%). Fatal adverse reactions occurred in a total of 4.2% of patients.
- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), the most common adverse reactions ($\geq 20\%$) were nausea (34%), fatigue/asthenia (32%), and alopecia (31%). The most common Grade 3 or 4 adverse reaction ($\geq 3\%$) was fatigue/asthenia (3.4%).
- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy.
- In patients with locally advanced or metastatic BTC in the TOPAZ-1 study receiving IMFINZI (n=338), the most common adverse reactions (occurring in $\geq 20\%$ of patients) were fatigue (42%), nausea (40%), constipation (32%), decreased appetite (26%), abdominal pain (24%), rash (23%), and pyrexia (20%).

Please see additional Important Safety Information throughout and click [here](#) for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO.

- 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).
- In patients with unresectable HCC in the HIMALAYA study receiving IMFINZI and IMJUDO (n=388), the most common adverse reactions (occurring in $\geq 20\%$ of patients) were rash (32%), diarrhea (27%), fatigue (26%), pruritus (23%), musculoskeletal pain (22%), and abdominal pain (20%).
- In patients with unresectable HCC in the HIMALAYA study receiving IMFINZI and IMJUDO (n=388), serious adverse reactions occurred in 41% of patients. Serious adverse reactions in $>1\%$ of patients included hemorrhage (6%), diarrhea (4%), sepsis (2.1%), pneumonia (2.1%), rash (1.5%), vomiting (1.3%), acute kidney injury (1.3%), and anemia (1.3%). Fatal adverse reactions occurred in 8% of patients who received IMJUDO in combination with durvalumab, including death (1%), hemorrhage intracranial (0.5%), cardiac arrest (0.5%), pneumonitis (0.5%), hepatic failure (0.5%), and immune-mediated hepatitis (0.5%). Permanent discontinuation of treatment regimen due to an adverse reaction occurred in 14% of patients.

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

You may [report side effects related to AstraZeneca products](#) .

AstraZeneca strives to make treatment with IMFINZI and IMJUDO accessible and affordable



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or Pharmacies



Out-of-pocket costs



Affordability options

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Monday through Friday, 8 AM - 6 PM ET or visit **www.MyAccess360.com**.

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



IMFINZI and IMJUDO Patient Savings Programs*

The IMFINZI and IMJUDO Patient Savings Programs* are available to assist eligible, commercially insured patients with their out-of-pocket costs for IMFINZI and IMJUDO.

- The IMFINZI and IMJUDO Patient Savings Programs cover out-of-pocket costs for both the medication and administration
 - Eligible patients with commercial insurance may pay as little as \$0 per infusion for IMFINZI and IMJUDO
 - Eligible patients can receive up to \$100 per infusion of IMFINZI and IMJUDO to help cover the costs of administration.**
- There are no income requirements to participate

For more information, including full Eligibility Requirements for the program and Terms of Use, visit **www.astrazenecaspecialtysavings.com** or **call 1-844-ASK-A360 (1-844-275-2360)** for more information.

*To be eligible, patients must be a resident of the United States or Puerto Rico and have commercial health insurance that covers medication costs for IMFINZI and IMJUDO, but not the full cost to the patient. Patients are ineligible if prescriptions are paid by any state or other federally funded programs, including, but not limited to, Medicare Part B, Medicare Part D, Medicaid, Medigap, VA or TRICARE, or where prohibited by law. Additional restrictions may apply. The IMFINZI and IMJUDO Patient Savings Programs cover the cost of IMFINZI and IMJUDO and up to \$100 administration cost per infusion, per drug, and does not cover costs for office visits, or any other associated costs. Offer is invalid for claims and transactions more than 365 days from the date of service. Individual costs and benefit design may vary by plan. Costs to patients may vary by plan. Please consult with individual plan for specific information.

†Patients who are residents of Massachusetts and Rhode Island are not eligible for infusion administration assistance.

*Patients are responsible for any cost associated with the infusion above the \$100 per infusion assistance provided by the program.

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

AstraZeneca offers resources and education for imAR management needs

imAR Quick Reference Guide

- Use the Quick Reference Guide to help monitor your patients' imARs

IMFINZIhcp.com

- Learn more about IMFINZI +/- IMJUDO and download additional resources

IMFINZI.com

- Find information about IMFINZI +/- IMJUDO from the patient site

IMFINZIhcp.com/nurse-center

- Learn more about IMFINZI +/- IMJUDO and download additional resources for nurses

AstraZeneca Information Center at 800-236-9933

- Call to receive additional information about AstraZeneca products

Ask your AZ Sales Representative about connecting with an Oncology Nurse Educator for education and training.

Please see the imAR Quick Reference Guide to aid in identification of imARs.

➤ **Scan the QR code to see the resources available for IMFINZI and IMJUDO**



References: 1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2023. 2. IMJUDO® (tremelimumab-actl) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2023. 3. Daniels GA, Guerrero AD, Katz D, Viets-Upchurch J. Challenge of immune-mediated adverse reactions in the emergency department. *Emerg Med J.* 2019;36(6):369-377. 4. US Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE), version 5. Accessed May 18, 2023. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf.

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



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