IMFINZI® durvalumab
Injection for Intravenous Use 50 mg/mL

+/-

IMJUDO® tremelimumab-actl
Injection for Intravenous Use 20 mg/mL

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. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic 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.

Lung Indications

UNRESECTABLE STAGE III NON-SMALL CELL LUNG CANCER (NSCLC)

IMFINZI, as a single agent, 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 (cCRT).

METASTATIC NSCLC (mNSCLC)

IMFINZI, in combination with IMJUDO and platinum-based chemotherapy, is indicated for the treatment of adult patients with metastatic NSCLC with no sensitizing EGFR mutations or ALK genomic tumor aberrations.

RESECTABLE NSCLC

IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by IMFINZI continued as a single agent as adjuvant treatment after surgery, is indicated for the treatment of adult patients with resectable (tumors ≥4 cm and/or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

LIMITED-STAGE SMALL CELL LUNG CANCER (LS-SCLC)

IMFINZI, as a single agent, is indicated for the treatment of adult patients with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy (cCRT).

EXTENSIVE-STAGE SMALL CELL LUNG CANCER (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).

Bladder Indications

CISPLATIN-ELIGIBLE MUSCLE-INVASIVE BLADDER CANCER (MIBC)

IMFINZI in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single-agent IMFINZI as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC).

Endometrial Indications

ADVANCED OR RECURRENT MISMATCH REPAIR DEFICIENT ENDOMETRIAL CANCER (dMMR EC)

IMFINZI in combination with carboplatin and paclitaxel followed by IMFINZI as a single agent is indicated for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR) as determined by an FDA-approved test.

IMPORTANT SAFETY INFORMATION (continued)

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.

HCC=hepatocellular carcinoma; SCLC=small cell lung cancer.

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 antibodies[1-3]
- Routine monitoring of patients, including periodic lab tests during and after treatment, is important[1,2]

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

- PD-L1 blocking antibody[1]
- Blocks the interaction of PD-L1 with PD-1 and CD80[1]
- 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]

IMJUDO®
tremelimumab-actl
Injection for Intravenous Use 20 mg/mL

- CTLA-4 blocking antibody[2]
- Binds to CTLA-4 and blocks the interaction with its ligands CD80 and CD86[2]
- Releases CTLA-4–mediated inhibition of T-cell activation[2]

For more indication-specific information, visit IMFINZIhcp.com

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Pneumonitis (continued)

- ***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.

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.

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

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 (page 66)
- imAR Quick Reference Guide (in pocket)

Management of imARs

General Guidance

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

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 reactions[1]
- IMJUDO is a monoclonal antibody that blocks T-cell inhibitory signals induced by the CTLA-4 pathway, thereby removing inhibition of the immune response[2]
- 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[1-3]

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, adrenocorticotropic 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 (continued)

Immune-Mediated Pneumonitis (continued)

- ***IMFINZI as a Single Agent* (continued)**
  - The incidence of pneumonitis (including radiation pneumonitis) in patients with LS-SCLC following chemoradiation within 42 days prior to initiation of IMFINZI in ADRIATIC was 14% (37/262) in patients receiving IMFINZI and 6% (16/265) in patients receiving placebo. Of the patients who received IMFINZI (262), 0.4% had a fatal adverse reaction and 2.7% had Grade 3 adverse reactions.
  - The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC or BTC when given in combination with chemotherapy.

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

General

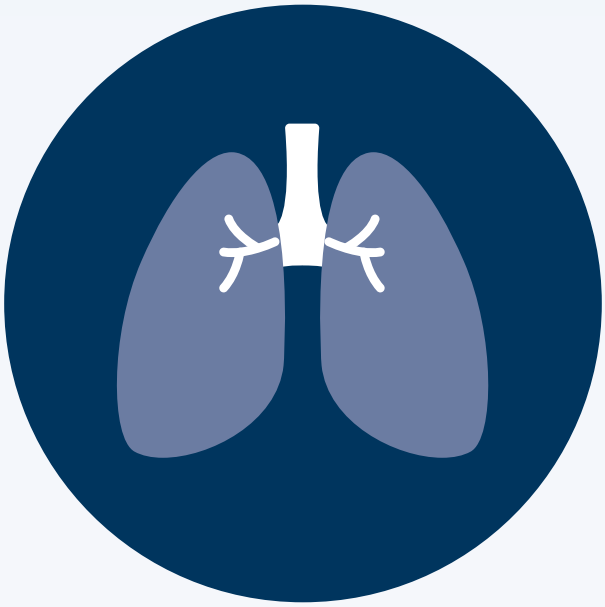
Management strategies[1,2]

- 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.

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

Management of imARs



Pulmonary

Pneumonitis

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Immune-mediated pneumonitis

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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 findings[1]

- 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
- The incidence of pneumonitis (including radiation pneumonitis) in patients with LS-SCLC following chemoradiation within 42 days prior to initiation of IMFINZI in ADRIATIC was 14% (37/262) in patients receiving IMFINZI and 6% (16/265) in patients receiving placebo. Of the patients who received IMFINZI (262), 0.4% had a fatal adverse reaction and 2.7% had Grade 3 adverse reactions. Events resolved in 19 of the 37 (51%) patients and resulted in permanent discontinuation in 18 of the 37 (49%) patients. Systemic corticosteroids were required in all patients, while 1 patient required use of infliximab with high-dose steroids

IMFINZI + IMJUDO[1,2]

- 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 findings[1]

- 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 chemotherapy[1,2]

- 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 patients with ES-SCLC 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]*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Symptomatic • Medical intervention indicated • Limiting instrumental ADL†	• Severe symptoms • Limiting self-care ADL‡ • Oxygen indicated	• Life-threatening consequences • 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		

*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 IMFINZI +/- IMJUDO 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

ADL=activities of daily living; CT=chemotherapy.

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
Pancreatitis

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Immune-mediated colitis

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 weeks

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.[1]

imAR findings[1]

- 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[1,2]

- 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	6%
Grade 3	3.6%

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[1,2]

- 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 patients with ES-SCLC 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	6.5%
Grade 3	2.5%
Grade 5	0.2%

imAR findings[1,2]

- IMFINZI with IMJUDO and platinum-based chemotherapy can cause immune-mediated colitis, which may be fatal
- 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. 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]*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Abdominal pain • Mucus or blood in stool	• Severe abdominal pain • Peritoneal signs	• 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 NCI CTCAE, v5.[4]
†Permanently discontinue IMFINZI for Grade 3 colitis when administered as part of a regimen containing IMJUDO.[1]

Additional withholding information[1,2]

- Resume IMFINZI +/- IMJUDO 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

IMFINZI + IMJUDO[1,2]

- IMFINZI in combination with IMJUDO can cause immune-mediated pancreatitis
- 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]*	–	• Enzyme elevation • Radiologic findings only	• Severe pain • Vomiting • Medical intervention indicated (eg, analgesia, nutritional support)	• 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 NCI CTCAE, v5.[4]

Additional withholding information[1,2]

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

Management of imARs

Hepatic

Hepatitis

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Immune-mediated hepatitis

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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 findings[1]

- 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

IMFINZI + IMJUDO[1,2]

- 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	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

Immune-mediated hepatitis (continued)

IMFINZI + IMJUDO + platinum-based chemotherapy[1,2]

- 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 patients with ES-SCLC 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 10 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

Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED HEPATITIS[1,2]

Hepatitis with no tumor involvement of the liver			
Severity*	–	• ALT or AST increases to >3 and up to 8 × ULN or total bilirubin increases >1.5 and up to 3 × ULN	• 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*	–	• AST or ALT is >1 and up to 3 × ULN at baseline and increases to >5 and up to 10 × ULN or: • AST or ALT is >3 and up to 5 × ULN at baseline and increases to >8 and up to 10 × ULN	• ALT or AST increases to >10 × 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	

*Toxicity grades were defined according to the 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 IMFINZI +/- IMJUDO 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

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

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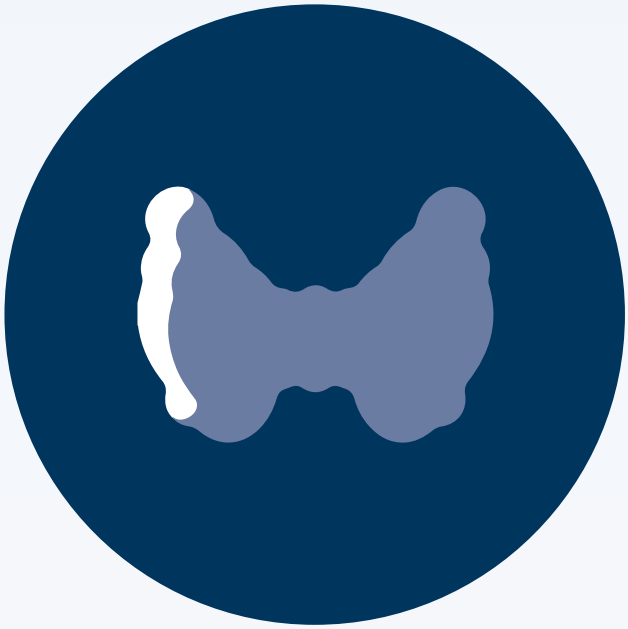
Please see additional Important Safety Information throughout and click here for Full Prescribing Information including Medication Guide for IMFINZI and IMJUDO.

Management of imARs



Endocrine

Adrenal insufficiency
Hypophysitis/hypopituitarism
Thyroid disorders
Type 1 diabetes mellitus

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

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

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

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 weeks

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 findings[1]

- 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**[1,2]

- 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

Immune-mediated adrenal insufficiency (continued)

IMFINZI + IMJUDO (continued)

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)

IMFINZI + IMJUDO + platinum-based chemotherapy[1,2]

- 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 patients with ES-SCLC 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 and platinum-based chemotherapy, 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]*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Moderate symptoms • Medical intervention indicated	• Severe symptoms • Hospitalization indicated	• 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 NCI CTCAE, v5.[4]

Additional withholding information[1,2]

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

Immune-mediated hypophysitis/hypopituitarism

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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.[1]

imAR findings[1]

- 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

IMFINZI + IMJUDO[1,2]

- 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%

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

Immune-mediated hypophysitis/hypopituitarism (continued)

IMFINZI + **IMJUDO** + platinum-based chemotherapy[1,2]

- 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 patients with ES-SCLC 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 and platinum-based chemotherapy, 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

Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED HYPOPHYSITIS/ HYPOPITUITARISM[1,2]

	Grade 1	Grade 2	Grade 3	Grade 4
Definition[4]*	• Asymptomatic or mild symptoms • Clinical or diagnostic observations only • Intervention not indicated	• Moderate • Minimal, local, or noninvasive intervention indicated • Limiting age-appropriate instrumental ADL†	• Severe or medically significant, but not immediately life threatening • Hospitalization or prolongation of hospitalization indicated • Limiting self-care ADL‡	• 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 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 +/- IMJUDO for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI +/- IMJUDO for recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI +/- IMJUDO for life-threatening (Grade 4) immune-mediated adverse reactions

Immune-mediated thyroid disorders

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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.[1]

imAR findings[1]

- 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

IMFINZI + IMJUDO[1,2]

- 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)

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Immune-mediated thyroid disorders (continued)

IMFINZI + IMJUDO + platinum-based chemotherapy[1,2]

- 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 patients with ES-SCLC 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 and platinum-based chemotherapy. 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 and platinum-based chemotherapy, 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 and platinum-based chemotherapy, including Grade 3 (0.5%) adverse reactions. Systemic corticosteroids were required in 2 patients (2/51) and all patients required endocrine therapy

IMFINZI + carboplatin + paclitaxel[1]

- The safety of IMFINZI in combination with carboplatin and paclitaxel followed by IMFINZI as a single agent was evaluated in 44 patients with dMMR advanced or recurrent endometrial cancer in DUO-E, a randomized, double-blind, placebo-controlled trial
- Patients received IMFINZI 1120 mg with carboplatin and paclitaxel every 3 weeks for up to six 21-day cycles followed by IMFINZI 1500 mg every 4 weeks or carboplatin and paclitaxel every 3 weeks for up to six 21-day cycles alone. The median duration of exposure to IMFINZI with carboplatin and paclitaxel was 14.8 months (range: 0.7 to 31.7)

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imAR findings[1]

- **Immune-mediated hypothyroidism** occurred in 14% (34/235) of patients receiving IMFINZI in combination with carboplatin and paclitaxel. Events resolved in 8 of the 34 patients. Endocrine therapy was required in 34 of the 34 patients

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]*	• Asymptomatic • Clinical or diagnostic observations only • Intervention not indicated	• Symptomatic • Limiting instrumental ADL† **Hyperthyroidism:** • Thyroid suppression therapy indicated **Hypothyroidism:** • Thyroid replacement therapy indicated	• Severe symptoms • Limiting self-care ADL‡ • Hospitalization indicated	• 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 hormone therapy for hypothyroidism as clinically indicated • Institute medical management of hyperthyroidism as clinically indicated		

*Toxicity grades were defined according to the 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 +/- IMJUDO for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue IMFINZI +/- IMJUDO for recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment
- Permanently discontinue IMFINZI +/- IMJUDO for life-threatening (Grade 4) immune-mediated adverse reactions

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Immune-mediated type 1 diabetes mellitus

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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.[1]

imAR findings[1]

- 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

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]

- 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	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[1,2]

- 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 patients with ES-SCLC 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	0.5%
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 and platinum-based chemotherapy, including Grade 3 (0.3%) adverse reactions
- All patients required endocrine therapy

Immune-mediated type 1 diabetes mellitus (continued)

Management strategies

IMFINZI +/- IMJUDO MANAGEMENT STRATEGIES FOR IMMUNE-MEDIATED TYPE 1 DIABETES MELLITUS[1,2]

	Grade 1	Grade 2	Grade 3	Grade 4
Definition[4]*	• Abnormal glucose above baseline with no medical intervention	• Change in daily management from baseline for a diabetic • Oral antiglycemic agent initiated • Workup for diabetes	• Insulin therapy initiated • Hospitalization indicated	• 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 NCI CTCAE, v5.[4]

Additional withholding information[1,2]

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

Management of imARs

Renal

Nephritis

Immune-mediated nephritis

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 weeks

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 findings[1]

- 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**[1,2]

- 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%
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)

IMFINZI + **IMJUDO** + platinum-based chemotherapy[1,2]

- 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 patients with ES-SCLC 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 and platinum-based chemotherapy, 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

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 IMMUNE-MEDIATED NEPHRITIS[1,2]

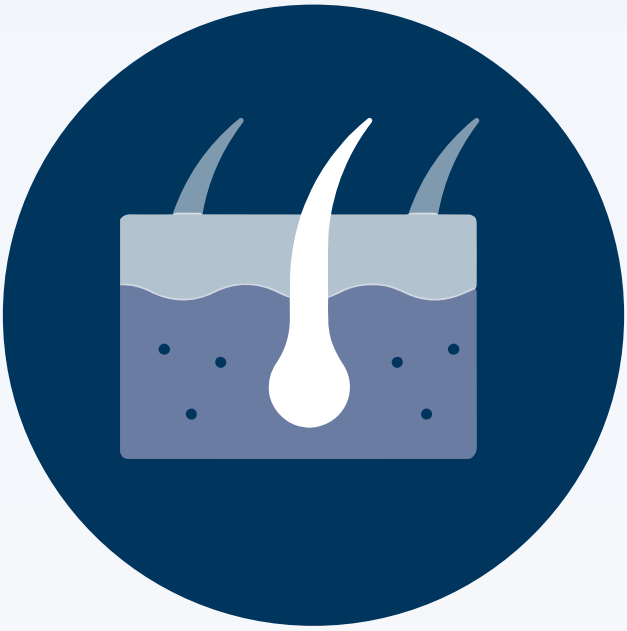
	Grade 1	Grade 2	Grade 3	Grade 4
Severity*	–	• Grade 2 or 3 increased blood creatinine		• Grade 4 increased blood creatinine
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Withhold IMFINZI +/- IMJUDO		Permanently discontinue IMFINZI +/- IMJUDO
Steroids	–	In general, if IMFINZI +/- IMJUDO 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 NCI CTCAE, v4.03.

Additional withholding information[1,2]

- Resume IMFINZI +/- IMJUDO 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

Management of imARs



Dermatologic

Rash or dermatitis

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Immune-mediated rash or dermatitis

IMFINZI as a single agent or in combination with chemotherapy[1]

- 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 (an open-label, single-arm, 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
- The data also reflect exposure to IMFINZI 1500 mg every 4 weeks as a single agent in 262 patients from the ADRIATIC study (a randomized, double-blind study in patients with LS-SCLC) and to IMFINZI in combination with chemotherapy in 265 patients from the CASPIAN study (a randomized, open-label study in patients with ES-SCLC) and in 338 patients from the TOPAZ-1 study (a randomized, double-blind study in patients with BTC). In the CASPIAN and TOPAZ-1 studies, IMFINZI was administered at a dose of 1500 mg every 3 or 4 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 findings[1]

- 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

IMFINZI + IMJUDO[1,2]

- 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]

- 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 patients with ES-SCLC 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 and platinum-based chemotherapy, 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	

*Toxicity grades were defined according to the NCI CTCAE, v4.03.

Additional withholding information[1,2]

- Resume IMFINZI +/- IMJUDO 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.

Other imARs

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

Other 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, other transplant (including corneal graft) 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

	Grade 1	Grade 2	Grade 3	Grade 4
Myocarditis				
Dosage modifications	Continue treatment with IMFINZI +/- IMJUDO	Permanently discontinue IMFINZI +/- IMJUDO		
Neurological toxicities				
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		

Infusion-related reactions

- 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 IMFINZI +/- IMJUDO 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

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

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 to >10 × ULN or total bilirubin increases to >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

*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-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 ≤Grade 1
- After improvement to ≤Grade 1, taper corticosteroid over at least 1 month
- Prescribing Information has additional information for dosage modification and management specific to adverse reactions

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Pneumonitis (continued)

- ***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.
- ***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***
    - Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
  - ***IMFINZI with IMJUDO***
    - 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***
    - 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***
    - Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
  - ***IMFINZI with IMJUDO***
    - Immune-mediated hypophysitis/hypopituitarism occurred in 1% (4/388) of patients receiving IMFINZI and IMJUDO.
  - ***IMFINZI with IMJUDO and Platinum-Based Chemotherapy***
    - 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.
  - ***IMFINZI as a Single Agent***
    - Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
    - Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
    - Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
  - ***IMFINZI with IMJUDO***
    - Immune-mediated thyroiditis occurred in 1.5% (6/388) of patients receiving IMFINZI and IMJUDO.
    - Immune-mediated hyperthyroidism occurred in 4.6% (18/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.3%) adverse reactions.
    - Immune-mediated hypothyroidism occurred in 11% (42/388) of patients receiving IMFINZI and IMJUDO.
  - ***IMFINZI with IMJUDO and Platinum-Based Chemotherapy***
    - Immune-mediated thyroiditis occurred in 1.2% (7/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy.
    - 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.
    - 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.
  - ***IMFINZI with Carboplatin and Paclitaxel***
    - Immune-mediated hypothyroidism occurred in 14% (34/235) of patients receiving IMFINZI in combination with carboplatin and paclitaxel.
- ***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***
    - Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.
  - ***IMFINZI with IMJUDO***
    - Two patients (0.5%, 2/388) had events of hyperglycemia requiring insulin therapy that had not resolved at last follow-up.

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Endocrinopathies (continued)

- ***Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis* (continued)**
  - ***IMFINZI with IMJUDO and Platinum-Based Chemotherapy***
    - 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/L-1 and CTLA-4 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

- ***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 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.

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

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

Infusion-Related Reactions

IMFINZI 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 2.6% (10/388) of 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.

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

Unresectable Stage III NSCLC

- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), the most common adverse reactions (≥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 (≥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 (≥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.

Resectable NSCLC

- In patients with resectable NSCLC in the AEGEAN study, the most common adverse reactions (occurring in ≥20% of patients) were anemia, nausea, constipation, fatigue, musculoskeletal pain, and rash.
- In patients with resectable NSCLC in the neoadjuvant phase of the AEGEAN study receiving IMFINZI in combination with platinum-containing chemotherapy (n=401), permanent discontinuation of IMFINZI due to an adverse reaction occurred in 6.7% of patients. Serious adverse reactions occurred in 21% of patients. The most frequent (≥1%) serious adverse reactions were pneumonia (2.7%), anemia (1.5%),

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

Resectable NSCLC (continued)

myelosuppression (1.5%), vomiting (1.2%), neutropenia (1%), and acute kidney injury (1%). Fatal adverse reactions occurred in 2% of patients, including death due to COVID-19 pneumonia (0.5%), sepsis (0.5%), myocarditis (0.2%), decreased appetite (0.2%), hemoptysis (0.2%), and death not otherwise specified (0.2%). Of the 401 IMFINZI treated patients who received neoadjuvant treatment and 398 placebo-treated patients who received neoadjuvant treatment, 1.7% (n=7) and 1% (n=4), respectively, did not receive surgery due to adverse reactions.

- In patients with resectable NSCLC in the adjuvant phase of the AEGEAN study receiving IMFINZI as a single agent (n=265), permanent discontinuation of IMFINZI due to an adverse reaction occurred in 8% of patients. Serious adverse reactions occurred in 13% of patients. The most frequent serious adverse reactions reported in >1% of patients were pneumonia (1.9%), pneumonitis (1.1%), and COVID-19 (1.1%). Four fatal adverse reactions occurred during the adjuvant phase of the study, including COVID-19 pneumonia, pneumonia aspiration, interstitial lung disease and aortic aneurysm.

Metastatic NSCLC

- 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 ≥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.

Limited-stage Small Cell Lung Cancer

- In patients with limited-stage SCLC in the ADRIATIC study receiving IMFINZI (n=262), the most common adverse reactions occurring in ≥20% of patients receiving IMFINZI were pneumonitis or radiation pneumonitis (38%), and fatigue (21%). The most common Grade 3 or 4 adverse reactions (≥3%) were pneumonitis or radiation pneumonitis and pneumonia.
- In patients with limited-stage SCLC in the ADRIATIC study receiving IMFINZI (n=262), IMFINZI was permanently discontinued due to adverse reactions in 16% of the patients receiving IMFINZI. Serious adverse reactions occurred in 30% of patients receiving IMFINZI. The most frequent serious adverse reactions reported in ≥1% of patients receiving IMFINZI were pneumonitis or radiation pneumonitis (12%), and pneumonia (5%). Fatal adverse reactions occurred in 2.7% of patients who received IMFINZI including pneumonia (1.5%), cardiac failure, encephalopathy and pneumonitis (0.4% each).

Extensive-stage Small Cell Lung Cancer

- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), the most common adverse reactions (≥20%) were nausea (34%), fatigue/asthenia (32%), and alopecia (31%). The most common Grade 3 or 4 adverse reaction (≥3%) was fatigue/asthenia (3.4%).
- In patients with extensive-stage SCLC in the CASPIAN study 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.

Locally Advanced or Metastatic Biliary Tract Cancers

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

Unresectable Hepatocellular Carcinoma

- In patients with unresectable HCC in the HIMALAYA study receiving IMFINZI and IMJUDO (n=388), the most common adverse reactions (occurring in ≥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 IMFINZI and IMJUDO, 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.

Primary advanced or Recurrent dMMR Endometrial Cancer

- In patients with advanced or recurrent dMMR endometrial cancer in the DUO-E study receiving IMFINZI in combination with carboplatin and paclitaxel followed by IMFINZI as a single-agent (n=44), the most common adverse reactions, including laboratory abnormalities (occurring in >20% of patients) were peripheral neuropathy (61%), musculoskeletal pain (59%), nausea (59%), alopecia (52%), fatigue (41%), abdominal pain (39%), constipation (39%), rash (39%), decreased magnesium (36%), increased ALT (32%), increased AST (30%), diarrhea (27%), vomiting (27%), cough (27%), decreased potassium (25%), dyspnea (25%), headache (23%), increased alkaline phosphatase (20%), and decreased appetite (18%). The most common Grade 3 or 4 adverse reactions (≥3%) were constipation (4.5%) and fatigue (4.5%).
- In patients with advanced or recurrent dMMR endometrial cancer in the DUO-E study receiving IMFINZI in combination with carboplatin and paclitaxel followed by IMFINZI as a single-agent (n=44), permanent discontinuation of IMFINZI due to adverse reactions occurred in 11% of patients. Serious adverse reactions occurred in 30% of patients who received IMFINZI with carboplatin and paclitaxel; the most common serious adverse reactions (≥4%) were constipation (4.5%) and rash (4.5%).

Muscle-Invasive Bladder Cancer (MIBC)

- In patients with muscle-invasive bladder cancer (MIBC), the most common adverse reactions, including laboratory abnormalities, in the overall study (occurring in ≥20% of patients) were decreased hemoglobin, decreased neutrophils, increased blood creatinine, decreased sodium, nausea, increased ALT, decreased calcium, decreased platelets, fatigue, increased potassium, decreased lymphocytes, increased AST, constipation, decreased magnesium, decreased appetite, increased alkaline phosphate, rash, pyrexia, diarrhea, vomiting and abdominal pain.
- In patients with MIBC in the neoadjuvant phase of the NIAGARA study receiving IMFINZI in combination with gemcitabine and cisplatin (n=530), permanent discontinuation of IMFINZI due to an adverse reaction occurred in 9% of patients. Serious adverse reactions occurred in 24% of patients; the most frequent (≥1%) serious adverse reactions were pulmonary embolism (1.9%), febrile neutropenia (1.5%), acute kidney injury (1.3%), thrombocytopenia (1.3%), urinary tract infection (1.3%), and pneumonia (1.3%). Fatal adverse reactions occurred in 1.1% of patients including sepsis, myocardial infarction, and pulmonary embolism (0.2% each). One fatal adverse reaction of pneumonia was reported in 1 (0.2%) patient in the post-surgery phase before adjuvant treatment started. Of the 530 patients in the IMFINZI treatment arm and 526 patients in the chemotherapy treatment arm who received neoadjuvant treatment, 1 (0.2%) patient in each treatment arm did not receive surgery due to adverse reactions. The adverse reaction that led to cancellation of surgery in the IMFINZI treatment arm was interstitial lung disease.
- In patients with MIBC in the adjuvant phase of the NIAGARA study receiving IMFINZI as a single agent (n=383), permanent discontinuation of adjuvant IMFINZI due to an adverse reaction occurred in 5% of patients. Serious adverse reactions occurred in 26% of patients. The most frequent serious adverse reactions (occurring in ≥1% of patients) were urinary tract infection (7%), acute kidney injury (3.7%), hydronephrosis (2.1%), pyelonephritis (2.1%), urosepsis (1.8%) and sepsis (1.6%). Fatal adverse reactions occurred in 1.8% of patients, including COVID-19, severe acute respiratory syndrome, cardiopulmonary failure, gastrointestinal hemorrhage, and chronic hepatic failure (0.3% each).

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

You may report side effects related to AstraZeneca products.

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL

IMPORTANT SAFETY INFORMATION (continued)

Indications:

IMFINZI, as a single agent, 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 (cCRT).

IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by IMFINZI continued as a single agent as adjuvant treatment after surgery, is indicated for the treatment of adult patients with resectable (tumors ≥4 cm and/or node positive) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

IMFINZI, in combination with IMJUDO and platinum-based chemotherapy, is indicated for the treatment of adult patients with metastatic NSCLC with no sensitizing EGFR mutations or ALK genomic tumor aberrations.

IMFINZI, as a single agent, is indicated for the treatment of adult patients with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy (cCRT).

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).

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

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

IMFINZI in combination with carboplatin and paclitaxel followed by IMFINZI as a single agent is indicated for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR) as determined by an FDA-approved test.

IMFINZI in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single-agent IMFINZI as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC).

IMFINZI® durvalumab
Injection for Intravenous Use 50 mg/mL

+/-

IMJUDO® tremelimumab-actl
Injection for Intravenous Use 20 mg/mL

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

AstraZeneca Access 360™ Helping patients access the care they need:

www.MyAccess360.com

1-844-ASK-A360
(1-844-275-2360)

1-844-FAX-A360
(1-844-329-2360)

Contact AstraZeneca Access 360™ Monday to Friday, 8 AM to 6 PM ET

If AstraZeneca medicines have been prescribed,
the Access 360 program provides personal support for*:

- Insurance coverage for AstraZeneca medicine
- Specialty Distributors or Pharmacies
- Out-of-pocket costs
- Affordability options

Description of the Access 360 program is for informational purposes only. Access 360 does not file claims or appeals on behalf of health care professionals or patients and makes no representation or guarantee concerning reimbursement or coverage for any service or item.

*Terms and conditions apply. See site for full eligibility and terms of use.

To learn more about the Access 360 program, please call **1-844-ASK-A360 (1-844-275-2360)** 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.azpatientsupport.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.

IMFINZI® durvalumab
Injection for Intravenous Use 50 mg/mL
+/-
IMJUDO® tremelimumab-actl
Injection for Intravenous Use 20 mg/mL

AstraZeneca offers resources and education for imAR management needs

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 1-800-236-9933

- Call to receive additional information about AstraZeneca products

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

Scan the QR code to see the resources available for IMFINZI and IMJUDO at IMFINZIhcp.com/resources

References: 1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025. **2.** IMJUDO® (tremelimumab-actl) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2024. **3.** Daniels GA, Guerrera 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 April 28, 2025. 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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IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL +/- IMJUDO® tremelimumab-actl Injection for Intravenous Use 20 mg/mL