IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

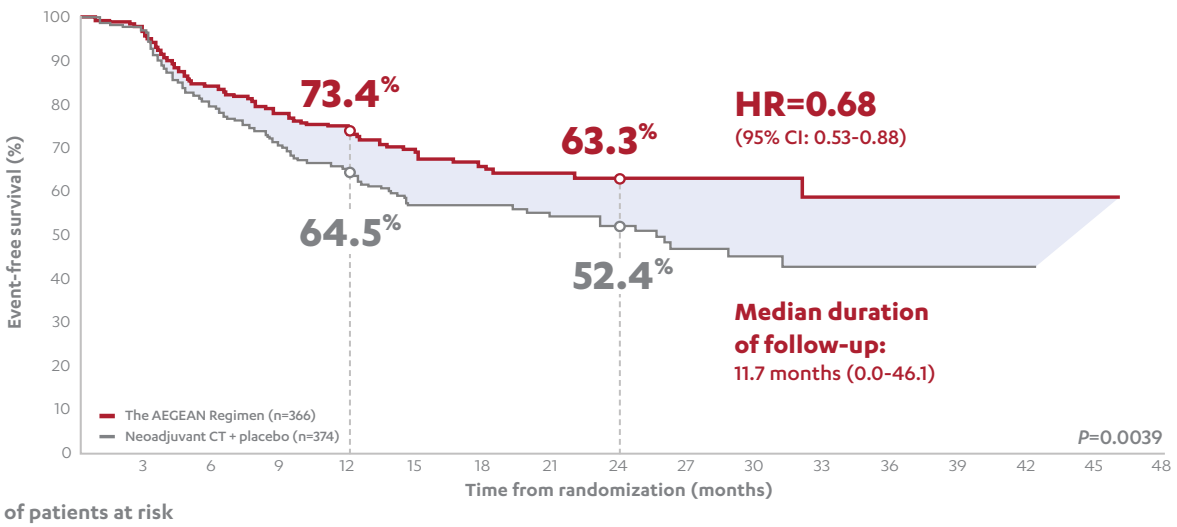
NOW AVAILABLE

FOR THE TREATMENT OF PATIENTS WITH RESECTABLE (TUMORS ≥4 CM AND/OR NODE POSITIVE) NSCLC AND NO KNOWN EGFR MUTATIONS OR ALK REARRANGEMENTS[1]

The AEGEAN Regimen* significantly improved event-free survival (EFS) in the modified ITT† (mITT) population vs neoadjuvant chemotherapy (CT) alone[1,2]

Median EFS was not reached with neoadjuvant IMFINZI + CT followed by adjuvant IMFINZI (95% CI: 31.9, NR) and was 25.9 months (95% CI: 18.9, NR) in the neoadjuvant CT + placebo arm (*P*=0.0039)[1,2]

EFS in mITT†: INTERIM ANALYSIS[1,2‡]



Number of patients at risk

The AEGEAN Regimen	366	336	271	194	140	90	78	50	49	31	30	14	11	3	1	1	0
Neoadjuvant CT + placebo	374	339	257	184	136	82	74	53	50	30	25	16	13	1	1	0	0

- Reduction in risk of disease progression, recurrence, or death vs placebo was 32% (HR=0.68; 95% CI, 0.53-0.88) with a log-rank test stratified by PD-L1 and disease stage[1]
- **The 12-month and 24-month EFS analyses were exploratory endpoints and not tested for statistical significance[2]**

4× pCR rate: 17.2% with the AEGEAN Regimen vs 4.3% with neoadjuvant CT alone at final analysis, *P*<0.0001[2§]

Indication:

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) non-small cell lung cancer (NSCLC) and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

IMPORTANT SAFETY INFORMATION

There are no contraindications for IMFINZI® (durvalumab).

Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue.

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

*The AEGEAN Regimen is defined as neoadjuvant IMFINZI + a choice of platinum-based CT followed by adjuvant IMFINZI after surgery.[1]
†The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]
‡At the interim analysis of EFS, the data maturity rate was 32%. Median duration of follow-up was 11.7 months (range: 0.0-46.1).[2]
§Based on a prespecified pCR interim analysis (January 14, 2022) in 402 patients, the pCR rate was statistically significant (*P*=0.000036) compared with significance level of 0.0082%.[1]
ALK=anaplastic lymphoma kinase; CI=confidence interval; EGFR=epidermal growth factor receptor; HR=hazard ratio; ITT=intent-to-treat; NR=not reached; NSCLC=non-small cell lung cancer; pCR=pathological complete response; PD-L1=programmed death-ligand 1.

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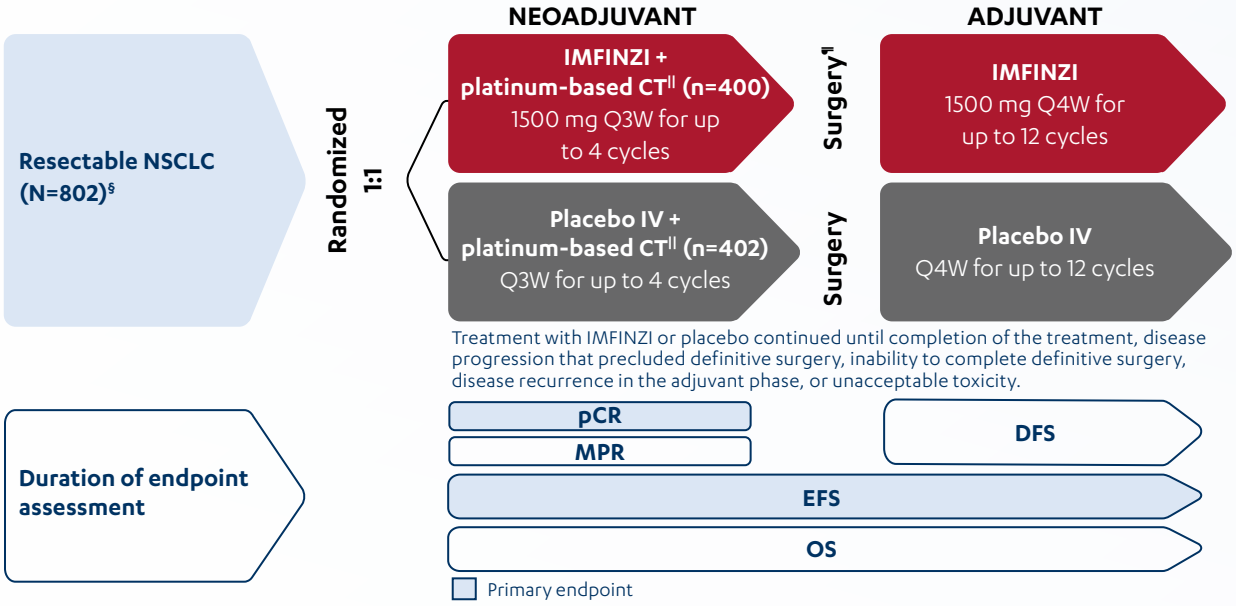
The AEGEAN study assessed perioperative IMFINZI-based treatment in Stage IIA to IIIB (N2) resectable NSCLC[1,2*]

Patients were randomized to receive either neoadjuvant IMFINZI + a choice of CT† followed by adjuvant IMFINZI or neoadjuvant placebo + CT followed by adjuvant placebo[1,2]

Primary endpoints included pCR evaluated after completion of neoadjuvant treatment and resection, and EFS based on perioperative therapy. Secondary endpoints included MPR, DFS, and OS.[1,2‡]



The trial was not designed to isolate the effect of IMFINZI in each phase (neoadjuvant or adjuvant) of treatment[1]

*The AEGEAN study enrollment was based on the 8th edition of the American Joint Committee on Cancer TNM staging system.[1] †Investigators were allowed the choice of platinum-based CT regimen for neoadjuvant treatment: Carboplatin/paclitaxel, cisplatin/gemcitabine, pemetrexed/cisplatin, and pemetrexed/carboplatin. In the event of unfavorable tolerability, patients in the study were able to switch from cisplatin to carboplatin therapy. In patients with comorbidities or unable to tolerate cisplatin per investigator's judgement, carboplatin AUC 5 can be administered from Cycle 1. The platinum-based CT regimen of cisplatin + paclitaxel may be considered; however, this therapy regimen was used outside of the per-protocol choice. Preoperative radiotherapy was not allowed in either arm.[2] ‡The primary endpoints were pCR by blinded central pathology review and EFS by BICR assessment. The key secondary endpoints were MPR by blinded central pathology review, DFS by BICR, and OS.[1] §In the intent-to-treat population, 802 eligible patients were randomized. Efficacy was evaluated in the mITT population (n=740), which excluded patients with documented EGFR or ALK alteration who were enrolled before a protocol amendment.[2] ‖For patients with squamous tumor histology: carboplatin AUC 6 and paclitaxel 200 mg/m^2 on Day 1 of each 3-week cycle, or cisplatin 75 mg/m^2 on Day 1 and gemcitabine 1250 mg/m^2 on Day 1 and Day 8 of each 3-week cycle, for 4 cycles. For patients with nonsquamous tumor histology: pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 on Day 1 of each 3-week cycle, for 4 cycles, or pemetrexed 500 mg/m^2 and carboplatin AUC 5 on Day 1 of each 3-week cycle, for 4 cycles.[1] ¶Surgery is expected within 40 days from the last immunotherapy dose. No more than 10 weeks may have elapsed between surgery and starting IMFINZI (except for patients receiving postoperative radiation therapy, which must be started within 8 weeks after surgery. IMFINZI must be given within 3 weeks from the end of postoperative radiation therapy).[2]

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Adverse Reactions (continued)

Immune-mediated adverse reactions can occur at any time after starting treatment or after discontinuation. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate. Withhold or permanently discontinue IMFINZI depending on severity. See USPI Dosing and Administration for specific details. In general, if IMFINZI requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less.

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AUC=area under the curve; BICR=blinded independent central review; DFS=disease-free survival; IV=intravenous; MPR=major pathological response; OS=overall survival; Q3W=every 3 weeks; Q4W=every 4 weeks; TNM=tumor, node, metastasis.

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Safety in AEGEAN study[1]

Neoadjuvant Phase

- Serious adverse reactions occurred in 21% of patients. The most frequent (≥1%) serious adverse reactions were pneumonia (2.7%), anemia (1.5%), 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%)
- Permanent discontinuation of IMFINZI due to an adverse reaction occurred in 6.7% of patients
- 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

Adjuvant Phase

- 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
- Permanent discontinuation of IMFINZI due to an adverse reaction occurred in 8% of patients

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Adverse Reactions (continued)
Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis
IMFINZI can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. In patients who did not receive recent prior radiation, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. In patients who received recent prior radiation, the incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 18.3% (87/475) in patients receiving IMFINZI and 12.8% (30/234) in patients receiving placebo. Of the patients who received IMFINZI (475), 1.1% were fatal and 2.7% were Grade 3 adverse reactions. The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC or BTC when given in combination with chemotherapy.

Immune-Mediated Colitis
IMFINZI can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions.

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

Immune-Mediated Endocrinopathies
- ***Adrenal Insufficiency***: IMFINZI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.

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IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Endocrinopathies (continued)

- ***Hypophysitis***: IMFINZI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated. Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
- ***Thyroid Disorders***: IMFINZI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.
- ***Thyroiditis***: Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Hyperthyroidism***: Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
- ***Hypothyroidism***: Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- ***Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis***: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.

Immune-Mediated Nephritis with Renal Dysfunction

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

Immune-Mediated Dermatology Reactions

IMFINZI can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/L-1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.

Other Immune-Mediated Adverse Reactions

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

- ***Cardiac/vascular***: Myocarditis, pericarditis, vasculitis.
- ***Nervous system***: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.
- ***Ocular***: Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.
- ***Gastrointestinal***: Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.
- ***Musculoskeletal and connective tissue disorders***: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.
- ***Endocrine***: Hypoparathyroidism.
- ***Other (hematologic/immune)***: Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection, other transplant (including corneal graft) rejection.

Infusion-Related Reactions

IMFINZI can cause severe or life-threatening infusion-related reactions. Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI based on the severity. See USPI Dosing and Administration for specific details. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses. Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.

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IMPORTANT SAFETY INFORMATION (continued)

Complications of Allogeneic HSCT after IMFINZI
Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity
Based on its mechanism of action and data from animal studies, IMFINZI can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. In females of reproductive potential, verify pregnancy status prior to initiating IMFINZI and advise them to use effective contraception during treatment with IMFINZI and for 3 months after the last dose of IMFINZI.

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

Adverse Reactions
- In patients with 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%), 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 adjuvant 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.

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

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

References:

1. IMFINZI® (durvalumab) [Prescribing Information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2024. **2.** Heymach JV, Harpole D, Mitsudomi T, et al. Perioperative durvalumab for resectable non-small-cell lung cancer. *N Engl J Med*. 2023;389(18):1672-1684 (including supplement and protocol).

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