RESECTABLE NSCLC

AEGEAN STUDY SURGICAL DATA COMPENDIUM

Data from the trial that evaluated neoadjuvant IMFINZI + platinum-based chemotherapy followed by adjuvant IMFINZI after surgical resection

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. 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. 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.

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

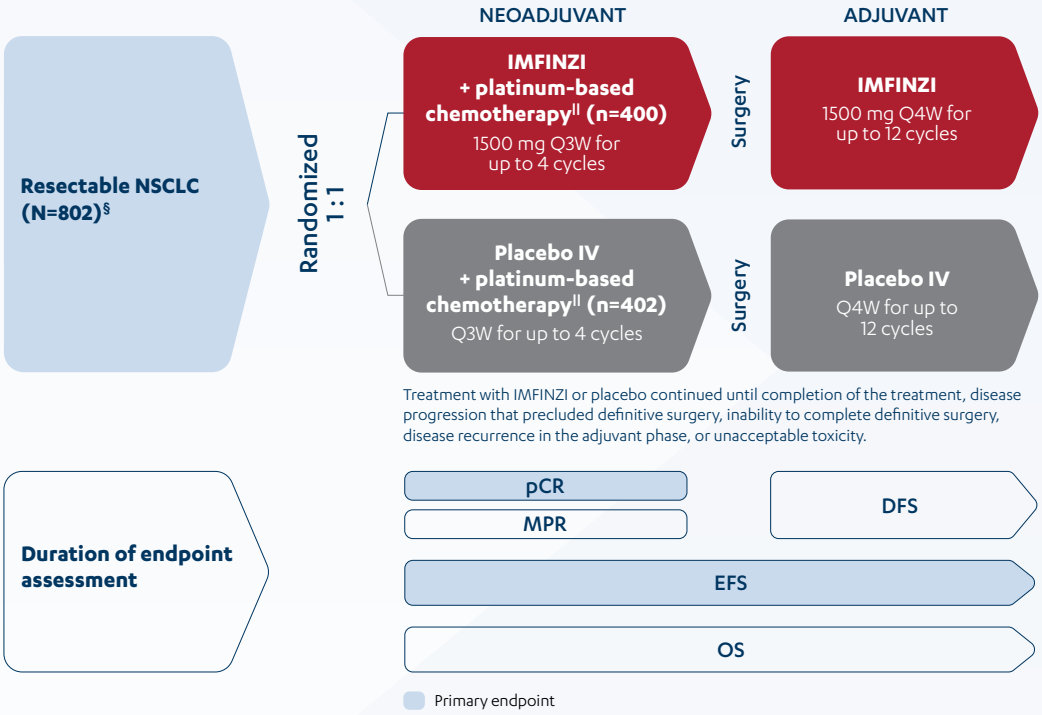
NSCLC=non-small cell lung cancer.

In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

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]**
- Within the study, a RECIST 1.1 tumor assessment was performed on a neoadjuvant follow-up scan acquired upon completion of the neoadjuvant period and prior to surgery[2]
- Surgery is expected within 40 days from the last IO 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]

The AEGEAN Regimen: Neoadjuvant IMFINZI + choice of platinum-based (cisplatin or carboplatin) doublet, followed by adjuvant IMFINZI[1,2]

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

AJCC=American Joint Committee on Cancer; ALK=anaplastic lymphoma kinase; AUC=area under the curve; BICR=blinded independent central review; CT=chemotherapy; DFS=disease-free survival; ECOG=Eastern Cooperative Oncology Group; EFS=event-free survival; EGFR=epidermal growth factor receptor; IO=immuno-oncology; ITT=intent to treat; IV=intravenous; MDT=multidisciplinary team; mITT=modified intent to treat; MPR=major pathological response; OS=overall survival; pCR=pathological complete response; Q3W=every 3 weeks; Q4W=every 4 weeks; RECIST=Response Evaluation Criteria in Solid Tumors; TNM=tumor, node, metastasis; WHO=World Health Organization.

A thoracic surgeon consulted with the MDT to determine if a complete resection (R0) was achievable for patients enrolled in the AEGEAN study[1,2]

Patients who were not intended for R0 were excluded[1,2]

AEGEAN was designed to identify appropriate patients for an IO-based perioperative treatment strategy and excluded[2¶]:

Planned pneumonectomies[#]:** Exclusion criteria included planned pneumonectomy or sublobar resections. Patients were required to be surgical candidates for lobectomy, sleeve resection, or bilobectomy

T4 invasions[#]: The study also excluded patients with T4 invasions, defined as T4 tumors adherent to the diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina

EGFR/ALK: Patients with EGFR mutations or ALK rearrangements were excluded from further enrollment and efficacy analysis following a protocol amendment

Your input within the MDT discussion prior to surgery is critical to deciding on a treatment regimen for your patients with resectable NSCLC[3,4]

*The AEGEAN study enrollment was based on the 8th edition of the AJCC 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 could be administered from Cycle 1. The platinum-based CT regimen of cisplatin + paclitaxel may be considered; however, this therapy regimen was used outside 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 ITT population, 802 eligible patients were randomized. Efficacy was evaluated in the mITT population (n=740), which excluded patients with documented EGFR or ALK alterations 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]

¶Inclusion criteria included: Previously untreated patients with documented NSCLC, no prior exposure to immune-mediated therapy, and WHO/ECOG performance status of 0 or 1. Patients with active or prior autoimmune disease or use of any immunosuppressive medication within 14 days of the first dose of IMFINZI were ineligible.[2]

#These characteristics were excluded after an amendment to the study protocol.[2]

**Surgical procedures did include unplanned pneumonectomies.[2]

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Pneumonitis

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

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Injection for Intravenous Use 50 mg/mL

In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

The AEGEAN Regimen significantly improved EFS for patients with Stage IIA to IIIB (N2) resectable NSCLC vs neoadjuvant CT alone[1,2]

- At the first 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]

FIRST INTERIM ANALYSIS OF **EFS IN mITT**[1*]

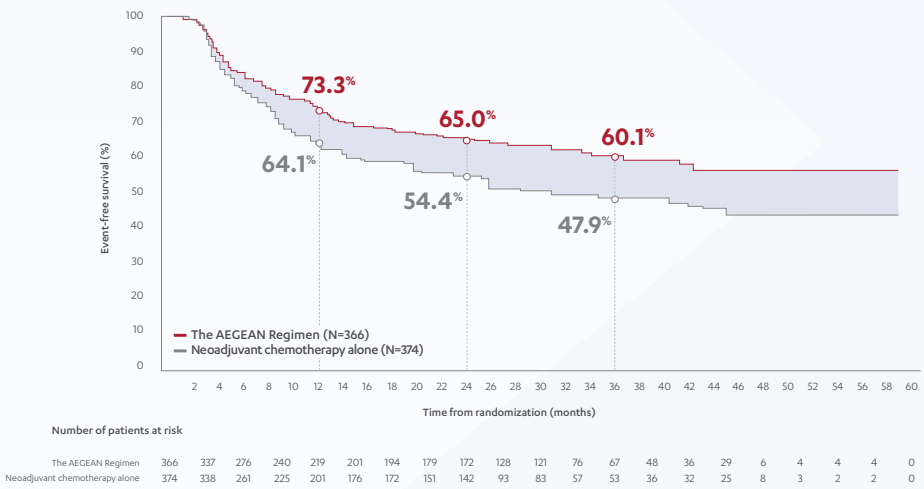
Median EFS not reached with neoadjuvant IMFINZI + CT followed by adjuvant IMFINZI (95% CI, 31.9-NR)

vs

25.9 months with neoadjuvant CT alone (95% CI, 18.9-NR)

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 (2-sided *P* value=0.0039)

EFS IN mITT: SECOND INTERIM ANALYSIS[5]



- **The 12-month, 24-month, and 36-month EFS analyses were exploratory endpoints and were not tested for statistical significance[2]**

Second interim analysis of EFS in mITT: Median EFS not reached (95% CI, 42.3-NR) with the AEGEAN Regimen and 30.0 months (95% CI, 20.6-NR) with neoadjuvant CT alone (HR=0.69; 95% CI, 0.55-0.88).[5]

At the second interim analysis of EFS, the data maturity rate was 39%. Median duration of follow-up was 25.9 months (range: 0.0-58.6).[5]

- **The second interim EFS analysis was not formally tested for statistical significance[2]**
- A final analysis is planned at ~50% maturity[2]

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4x more patients had no viable tumor cells in resected specimens with the AEGEAN Regimen vs neoadjuvant CT alone[1,2]

pCR IN mITT: FINAL ANALYSIS[1]

pCR[†‡§]	The AEGEAN Regimen (N=366)	Neoadjuvant CT alone (N=374)
Number of patients with a response	**63**	**16**
Response rate, % (95% CI)	**17.2 (13.5-21.5)**	**4.3 (2.5-6.8)**
P value	<0.0001	
Difference in proportions, % (95% CI)	13.0 (8.7-17.6)	

At the interim analysis, the trial demonstrated a statistically significant difference in MPR rate (34% vs 14%; *P*<0.0001).[1]

*The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]
†pCR results are based on final analysis (November 10, 2022), which occurred 46.3 months after study initiation.[1]
‡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]
§The 2-sided *P* value for pCR was calculated based on a stratified CMH test. Stratification factors include PD-L1 and disease stage.[1]

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Colitis

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

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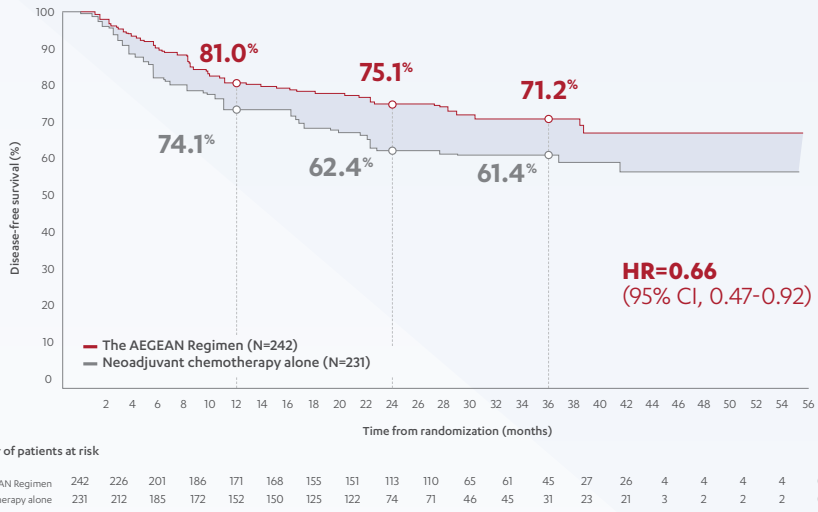
CI=confidence interval; CMH=Cochran-Mantel-Haenszel; HR=hazard ratio; NR=not reached; PD-L1=programmed death-ligand 1.

In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

After surgery: Disease-free survival within the AEGEAN study

DFS IN mITT*: SECOND INTERIM ANALYSIS AT ~3 YEARS[5]



Median follow-up in censored patients: 27.3 (0.8-55.7) months

DFS maturity: 29.8%

- Median DFS: NR (NR-NR) with the AEGEAN Regimen and NR (41.5-NR) with neoadjuvant CT alone[5]
- **Interim analysis was conducted at 30% DFS maturity and was not statistically significant.†** A final analysis will be conducted at 50% EFS maturity[2]
- DFS was evaluated in patients with R0/R1 margins and no evidence of progression in their first postsurgery scan[5]

Because DFS did not achieve statistical significance, a standard hierarchical process prevented formal testing of OS at the second interim analysis[5,6]

- OS at the second interim analysis (mITT): HR=0.89 (95% CI, 0.70-1.14)[5]
- Sensitivity analysis (censoring patients with cause of death due to COVID-19): HR=0.84 (95% CI, 0.66-1.08)[5]
- Lung cancer–specific survival (mITT); exploratory analysis: HR=0.70 (95% CI, 0.52-0.93)[5]

DFS: Time from the date of surgery until the first date of disease recurrence (local or distant), or date of death due to any cause, whichever occurs first.[2]

*The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]

†Following the multiple testing procedure, DFS did not reach statistical significance at the second planned interim analysis. Statistical significance was formally tested by a stratified log-rank test.[5]

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Hepatitis

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

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Consistent EFS results demonstrated across a majority of subgroups with the AEGEAN Regimen[5‡]

EFS SUBGROUP ANALYSIS IN mITT: SECOND INTERIM ANALYSIS[5]

Subgroup	No. of patients	Median EFS, months (95% CI)		Hazard ratio for disease progression, recurrence, or death (95% CI)
		AEGEAN Regimen	Neoadjuvant CT alone	
All patients	740	NR (42.3-NR)	30.0 (20.6-NR)	0.69 (0.55-0.88)
Age at randomization				
<65 years	358	NR (NR-NR)	34.4 (19.8-NR)	0.69 (0.48-0.97)
≥65 years	382	NR (31.9-NR)	25.9 (15.1-NR)	0.71 (0.52-0.97)
Sex				
Male	530	NR (41.2-NR)	25.9 (19.8-NR)	0.66 (0.50-0.88)
Female	210	NR (33.2-NR)	40.4 (15.1-NR)	0.80 (0.52-1.23)
ECOG PS				
0	506	NR (42.3-NR)	31.1 (19.5-NR)	0.66 (0.50-0.88)
1	234	NR (21.8-NR)	28.6 (18.9-NR)	0.79 (0.52-1.20)
Race[§]				
Asian	307	NR (42.3-NR)	25.9 (19.5-NR)	0.66 (0.45-0.95)
Non-Asian	433	NR (33.2-NR)	31.1 (15.7-NR)	0.73 (0.54-0.99)
Smoking				
Current	190	NR (33.2-NR)	20.4 (8.1-NR)	0.52 (0.32-0.82)
Former	443	NR (41.2-NR)	30.0 (20.7-NR)	0.75 (0.56-1.02)
Never	107	NR (13.0-NR)	34.4 (14.7-NR)	0.88 (0.47-1.61)
Histology				
Squamous	360	NR (41.2-NR)	40.4 (15.1-NR)	0.70 (0.49-0.98)
Nonsquamous	375	NR (36.6-NR)	28.6 (19.8-NR)	0.73 (0.53-1.00)
Disease stage (AJCC 8th ed)				
Stage II	214	NR (41.2-NR)	NR (34.4-NR)	0.82 (0.49-1.34)
Stage IIIA	338	NR (42.3-NR)	25.8 (11.7-45.0)	0.60 (0.42-0.84)
Stage IIIB	186	36.6 (12.7-NR)	19.8 (11.7-42.6)	0.81 (0.53-1.23)
Lymph node station				
N2 single	273	NR (NR-NR)	22.8 (13.9-42.6)	0.58 (0.39-0.85)
N2 multi	74	31.9 (9.3-NR)	12.2 (7.2-NR)	0.78 (0.40-1.49)
PD-L1 expression at baseline				
TC <1%	247	NR (24.7-NR)	20.6 (14.3-NR)	0.69 (0.46-1.02)
TC 1% to 49%	277	NR (31.9-NR)	25.9 (12.3-NR)	0.73 (0.50-1.05)
TC ≥50%	216	36.6 (41.2-NR)	NR (24.5-NR)	0.71 (0.44-1.12)
Planned neoadjuvant platinum agent				
Cisplatin	196	NR (NR-NR)	45.0 (13.9-NR)	0.58 (0.35-0.93)
Carboplatin	544	NR (36.6-NR)	16.2 (20.6-NR)	0.75 (0.57-0.97)

EFS subgroup analysis was not powered to show differences between or within individual subgroups and was not formally tested for statistical significance[2]

‡The AEGEAN Regimen included neoadjuvant IMFINZI + platinum-based CT and adjuvant IMFINZI after surgery.[1,2]
§Race was self-reported per the electronic case report form.[5]

IMPORTANT SAFETY INFORMATION (continued)

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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PS=performance status; TC=tumor cell.

In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

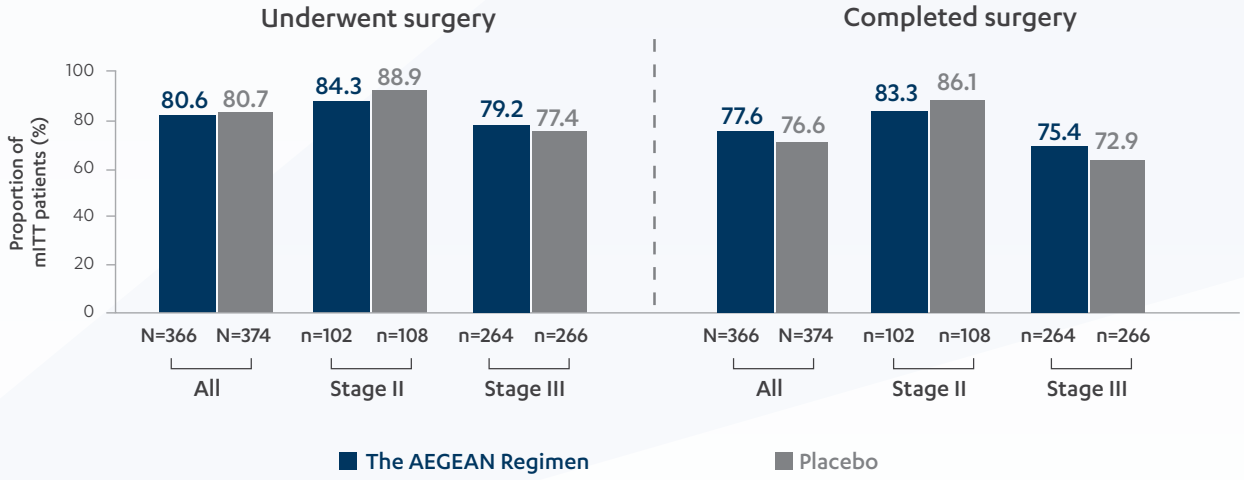
The AEGEAN study evaluated surgical outcomes

In the mITT population, ~78% of patients in the IMFINZI arm completed definitive surgery and ~77% of patients in the placebo arm[5]

TREATMENT SUMMARY IN mITT[5,7,8*]

Trial phase — no. (%)	The AEGEAN Regimen (N=366)	Neoadjuvant CT alone (N=374)	N2 disease	
			The AEGEAN Regimen (n=181)	Neoadjuvant CT alone (n=185)
Underwent randomization	**366 (100)**	374 (100)	**181 (100)**	185 (100)
Received CT plus IMFINZI or placebo	**366 (100)**	371 (99.2)	**181 (100)**	182 (98.4)
Completed 4 cycles of both CT agents	**310 (84.7)**	326 (87.2)	**151 (83.4)**	157 (84.9)
Completed 4 cycles of IMFINZI or placebo	**318 (86.9)**	331 (88.5)	**153 (84.5)**	159 (85.9)
Underwent surgery	**295 (80.6)**	302 (80.7)	**141 (77.9)**	144 (77.8)
Completed surgery	**284 (77.6)**	287 (76.7)	**133 (73.5)**	133 (71.9)
Days from last neoadjuvant treatment to surgery — median (range)†	**34.0 (12-91)**	34.0 (13-103)	**N/A**	N/A
Days from surgery to first dose of adjuvant treatment — median (range)‡	**50.0 (22-136)**	52.0 (21-141)	**N/A**	N/A

SURGERY COMPLETION BY STAGE IN mITT[2,7§]



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R0 was the surgical goal in the AEGEAN study

~95% of patients in the IMFINZI arm who completed surgery had a complete resection[2]

RESECTION STATUS BY DISEASE STAGE (PATIENTS IN mITT WHO COMPLETED SURGERY)[7]

R0:	The AEGEAN Regimen — % (n/N)	Neoadjuvant CT alone — % (n/N)
All	**94.7 (269/284)**	91.3 (262/287)
Stage II	**96.6 (84/87)**	93.5 (86/92)
Stage III	**93.9 (185/197)**	90.3 (176/195)

All: R1: 4.2% (12/284) and 7.7% (22/287); **R2:** 0.7% (2/284) and 0.7% (2/287)
Stage II: R1: 3.4% (3/87) and 5.4% (5/92); **R2:** 0.0% (0/87) and 1.1% (1/92)
Stage III: R1: 4.6% (9/197) and 8.7% (17/195); **R2:** 1.0% (2/197) and 0.5% (1/195)

RESECTION STATUS BY NODAL STATUS (PATIENTS IN mITT WHO COMPLETED SURGERY)[8]

R0:	The AEGEAN Regimen — % (n/N)	Neoadjuvant CT alone — % (n/N)
All	**94.7 (269/284)**	91.3 (262/287)
N2	**94.7 (126/133)**	91.7 (122/133)

Treatment completion data and surgical outcome data were not tested for statistical significance[7]

Data cutoff: May 10, 2024 (N=740).[5]
*The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]
†Based on the number of patients who underwent surgery (IMFINZI arm, n=295; placebo arm, n=302).[5]
‡Based on the number of patients in the mITT population who started adjuvant treatment (IMFINZI arm, n=318; placebo arm, n=331).[5]
§Surgery status was assessed by the investigator. Patients who underwent surgery were those for whom curative intent thoracic surgery was attempted, regardless of whether it was completed. Patients who completed surgery were those for whom curative intent thoracic surgery was completed.[2]

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.

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In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

Surgical approach in the AEGEAN study

SURGICAL APPROACH (PATIENTS IN mITT WHO UNDERWENT SURGERY)[7]*

Proportion of mITT patients (%)		Open procedure	Minimally invasive	Other†‡
All	**The AEGEAN Regimen (n=295)**	**49.2**	**49.2**	**1.6**
	Neoadjuvant CT alone (n=302)	50.7	47.0	2.3
Stage II	**The AEGEAN Regimen (n=86)**	**39.5**	**57.0**	**3.5**
	Neoadjuvant CT alone (n=96)	50.0	47.9	2.1
Stage III	**The AEGEAN Regimen (n=209)**	**53.1**	**45.9**	**1.0**
	Neoadjuvant CT alone (n=206)	51.0	46.6	2.4

SURGICAL APPROACH BY NODAL STATUS (PATIENTS IN mITT WHO UNDERWENT SURGERY)[8]

Proportion of mITT patients (%)		Open procedure	Minimally invasive	Other†‡
All	**The AEGEAN Regimen (n=295)**	**49.2**	**49.2**	**1.7**
	Neoadjuvant CT alone (n=302)	50.7	47.0	2.3
N2 disease	**The AEGEAN Regimen (n=141)**	**47.5**	**50.4**	**2.1**
	Neoadjuvant CT alone (n=144)	50.0	46.5	3.5

Minimally invasive surgery includes video-assisted thoracoscopic surgery (VATS) or robotic-assisted approaches[2]

*The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]
†Includes 4 patients in the IMFINZI arm and 6 patients in the placebo arm for whom the surgical approach was designated as "other" and 1 patient in each arm (both with Stage III disease) for whom the approach was missing.[7]
‡In the baseline N2 subgroup, includes 2 patients in the IMFINZI arm and 4 patients in the placebo arm for whom the surgical approach was designated as "other" and 1 patient in each arm for whom the approach was missing. In the mITT population, includes 4 patients in the IMFINZI arm and 6 patients in the placebo arm for whom the surgical approach was designated as "other" and 1 patient in each arm for whom the approach was missing.[8]

IMPORTANT SAFETY INFORMATION (continued)

Immune-Mediated Endocrinopathies (continued)

- ***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.

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TYPE OF SURGERY PROCEDURE PERFORMED (PATIENTS IN mITT WHO UNDERWENT SURGERY)[7]

Lobectomy[§]:	The AEGEAN Regimen — % (n/N)	Neoadjuvant CT alone — % (n/N)
All	**88.1 (260/295)**	85.4 (258/302)
Stage II	**87.2 (75/86)**	89.6 (86/96)
Stage III	**88.5 (185/209)**	83.5 (172/206)
Pneumonectomy:		
All	**9.2 (27/295)**	9.6 (29/302)
Stage II	**9.3 (8/86)**	7.3 (7/96)
Stage III	**9.1 (19/209)**	10.7 (22/206)
Other:		
All	**2.7 (8/295)**	5.0 (15/302)
Stage II	**3.5 (3/86)**	3.1 (3/96)
Stage III	**2.4 (5/209)**	5.8 (12/206)

TYPE OF SURGERY PROCEDURE BY NODAL STATUS (PATIENTS IN mITT WHO UNDERWENT SURGERY)[8]

Lobectomy[§]:	The AEGEAN Regimen — % (n/N)	Neoadjuvant CT alone — % (n/N)
All	**88.1 (260/295)**	85.4 (258/302)
N2	**89.4 (126/141)**	84 (121/144)
Pneumonectomy:		
All	**9.2 (27/295)**	9.6 (29/302)
N2	**9.2 (13/141)**	11.1 (16/144)
Other:		
All	**2.7 (8/295)**	5.0 (15/302)
N2	**1.4 (2/141)**	4.9 (7/144)

- Lobectomy proportion included patients who had a sleeve resection (including bronchial and arterial) and bilobectomy[7]
- Other types of surgery included wedge resection (IMFINZI arm, n=1; placebo arm, n=2) and other not otherwise specified (IMFINZI arm, n=1; placebo arm, n=2)[7]
- **Treatment completion data and surgical outcome data were not tested for statistical significance[7]**

[§]Includes sleeve resection (including bronchial or arterial) and bilobectomy.[7,8]

IMPORTANT SAFETY INFORMATION (continued)

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.

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In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

More than 80% of patients within the IMFINZI arm did not have surgical delays[7]

SUMMARY OF SURGERY DELAYS (PATIENTS IN mITT WHO UNDERWENT SURGERY)[7]*

	The AEGEAN Regimen (N=295)	Neoadjuvant CT alone (N=302)
No surgical delay† — no. (%)	**244 (82.7)**	235 (77.8)
Any surgical delay — no. (%)	**51 (17.3)**	67 (22.2)
Duration of delay‡ — no. (%)		
<2 weeks	**28 (9.5)**	38 (12.6)
2 to <4 weeks	**12 (4.1)**	22 (7.3)
4 to <6 weeks	**7 (2.4)**	3 (1.0)
≥6 weeks	**4 (1.4)**	4 (1.3)
Reason for surgical delay§ — no. (%)		
Logistical reasons	**28 (9.5)**	37 (12.3)
Adverse events	**9 (3.1)**	13 (4.3)
Unresolved toxicity from previous study treatments	**3 (1.0)**	4 (1.3)
IMFINZI or placebo	**1 (0.3)**	2 (0.7)
CT standard of care	**2 (0.7)**	2 (0.7)
Other	**13 (4.4)**	13 (4.3)

IMPORTANT SAFETY INFORMATION (continued)

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.

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

REASONS FOR NOT UNDERGOING OR COMPLETING SURGERY (mITT)[7]

	The AEGEAN Regimen (N=366)	Neoadjuvant CT alone (N=374)
Patients who did not undergo surgery — no. (%)	**71 (19.4)**	72 (19.3)
Disease progression	**27 (7.3)**	30 (8.0)
Unfit for surgery[‖]	**15 (4.1)**	10 (2.7)
Patient decision	**12 (3.3)**	17 (4.5)
Death	**9 (2.5)**	2 (0.5)
Adverse event	**7 (1.9)**	5 (1.3)
Surgical resection with curative intent performed outside of protocol	**1 (0.3)**	5 (1.3)
Investigator decision	**2 (0.5)**	2 (0.5)
Other/missing	**2 (0.5)**	3 (0.8)
Patients who completed surgery[¶] — no. (%)	**284 (77.6)**	287 (76.7)

Treatment completion data and surgical outcome data were not tested for statistical significance[7]

Patients with delayed surgery[†‡]: 17.3% with the AEGEAN Regimen and 22.2% with neoadjuvant CT alone, with logistical reasons as the leading cause of delay[7#]

*The mITT population excluded patients with documented EGFR or ALK alterations who were enrolled before a protocol amendment.[2]
†A surgical delay is defined as surgery occurring more than 40 days after the last dose of the study treatment in the neoadjuvant period.[7]
‡The length of delay is the time beyond the per-protocol window of 40 days after the last dose of study treatment to the date of surgery.[7]
§Reasons for surgical delay are not mutually exclusive for patients with multiple reasons per delay or patients with multiple delays (although a patient can only be counted once per category).[7]
‖Includes responses of "unfit for surgery," "inadequate lung function," and "inadequate cardiac function."[2]
¶Surgery status was assessed by the investigator. Patients who underwent surgery were those for whom curative intent thoracic surgery was attempted, regardless of whether it was completed. Patients who completed surgery were those for whom curative intent thoracic surgery was completed.[2]
#9.5% of patients had delays due to logistical reasons with the AEGEAN Regimen and 12.3% with neoadjuvant CT alone.[7]

IMPORTANT SAFETY INFORMATION (continued)

Other Immune-Mediated Adverse Reactions (continued)

- ***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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In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

Surgery-related safety summary in the AEGEAN study

ADVERSE EVENTS POSSIBLY RELATED TO SURGERY AND SURGICAL COMPLICATIONS (PATIENTS IN MODIFIED SAFETY ANALYSIS SET WHO UNDERWENT SURGERY)[7]

Postsurgery period*	The AEGEAN Regimen (N=296)	Neoadjuvant CT alone (N=301)
Any-grade AEs possibly related to surgery† — no. (%)	**119 (40.2)**	118 (39.2)
Maximum Grade 3 or 4	**25 (8.4)**	28 (9.3)
Severe adverse event	**33 (11.1)**	33 (11.0)
Outcome of death†‡	**6 (2.0)**	4 (1.3)
Patients with any surgical complication — no. (%)	**175 (59.1)**	181 (60.1)
Maximum reported by Clavien-Dindo classification grade		
1	**125 (42.2)**	131 (43.5)
2	**32 (10.8)**	25 (8.3)
≥3	**18 (6.1)**	25 (8.3)

Data cutoff: November 10, 2022.[7]

*This includes AEs between the date of surgery (including day of surgery) and the earliest of the date of surgery + 90 days or first dose of subsequent anticancer therapy; this also includes AEs with an onset date during this period and AEs with an onset date prior to dosing that worsen during this period. The summary of AEs possibly related to surgery and surgical complications summary reflect data collected for all patients in the modified safety analysis set who underwent surgery (including 1 patient assigned to the placebo arm who erroneously received a single cycle of IMFINZI and was therefore included in the IMFINZI arm for safety assessment), with AEs graded using the NCI CTCAE, version 5.0.[7]

†Included infectious pleural effusion (placebo arm, n=1), pneumonia (IMFINZI arm, n=2; placebo arm, n=1), septic shock (IMFINZI arm, n=1), acute respiratory failure (placebo arm, n=1), bronchopleural fistula (IMFINZI arm, n=1), interstitial lung disease (IMFINZI arm, n=1; also possibly related to IMFINZI), pneumonitis (IMFINZI arm, n=1; also possibly related to IMFINZI), pulmonary hemorrhage (placebo arm, n=1), and post-procedural pulmonary embolism (IMFINZI arm, n=1).[7]

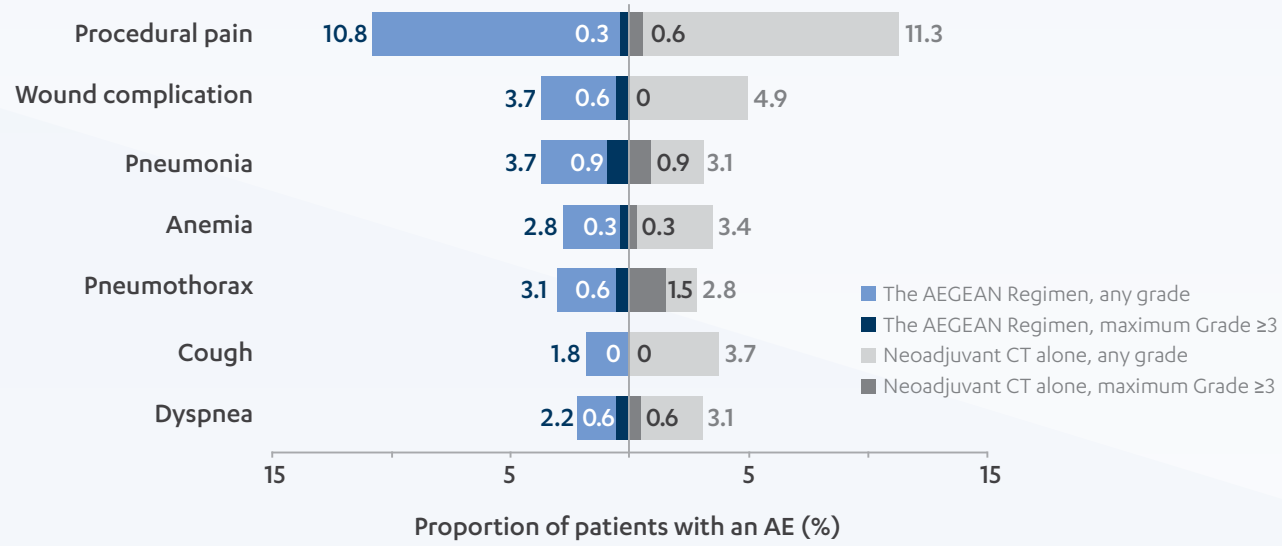
‡There were no AEs with outcome of death, possibly related to surgery, within 1 day of surgery in either arm. Note: All deaths regardless of any causality within 30 days of surgery=12 (IMFINZI arm, n=4; placebo arm, n=8).[7]

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

AEs=adverse events; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

Surgery-related adverse reactions in the AEGEAN study

MOST COMMON AEs POSSIBLY RELATED TO SURGERY (≥3% OF PATIENTS WHO UNDERWENT SURGERY; SAFETY ANALYSIS SET)[7§]



Data cutoff: November 10, 2022 (N=740).[7]

[§]Displayed are AEs reported with a frequency of ≥3% in either arm during the postsurgery period in the safety analysis set (IMFINZI arm, n=325; placebo arm, n=326), which includes all randomized patients who received ≥1 dose of study treatment and underwent surgery (includes 1 patient assigned to the placebo arm who erroneously received a single cycle of IMFINZI and was therefore included in the IMFINZI arm for the safety assessment). This includes AEs between the date of surgery (including day of surgery) and the earliest of the date of the surgery + 90 days or first dose of subsequent anticancer therapy; this also includes AEs with an onset date during this period and AEs with an onset date prior to dosing that worsen during this period.[7]

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Demonstrated safety profile with perioperative IMFINZI-based treatment[1,2]

Safety was evaluated from the start of neoadjuvant treatment (4 cycles) through resection and for up to 1 year of adjuvant therapy[1,2]

ADVERSE REACTIONS OCCURRING IN ≥10% OF PATIENTS IN THE AEGEAN STUDY[1]

	IMFINZI with CT (N=401)		Placebo with CT (N=398)	
Adverse reaction	**All Grades (%)**	**Grade 3 or 4 (%)**	All Grades (%)	Grade 3 or 4 (%)
Gastrointestinal disorders				
Nausea	**25**	**0.2**	29	0.3
Constipation	**25**	**0.2**	21	0
Diarrhea*	**14**	**1**	13	1.3
Vomiting	**11**	**0.7**	11	1
General disorders and administration site conditions				
Fatigue†	**25**	**0**	25	1.5
Skin and subcutaneous tissue disorders				
Rash‡	**22**	**0.5**	14	0.3
Pruritus	**12**	**0.2**	6	0
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain§	**24**	**1**	29	0.5
Metabolism and nutrition disorders				
Decreased appetite	**18**	**0.2**	18	0.3
Nervous system disorders				
Peripheral neuropathy‖	**16**	**0.5**	22	0.8
Endocrine disorders				
Hypothyroidism¶	**11**	**0**	3.8	0
Respiratory, thoracic, and mediastinal disorders				
Cough/productive cough	**11**	**0**	13	0
Pneumonia#**	**11**	**3.5**	10	3
COVID-19††	**11**	**0.2**	9	0.8
Psychiatric disorders				
Insomnia	**10**	**0**	12	0

The most common adverse reactions (occurring in ≥20% of patients) were anemia, nausea, constipation, fatigue, musculoskeletal pain, and rash[1]

INCIDENCE OF TREATMENT-RELATED MAXIMUM GRADE 3 OR 4 AEs AT FIRST INTERIM ANALYSIS[2]

32.4% with the AEGEAN Regimen

32.9% with neoadjuvant CT alone

*Includes colitis, diarrhea, enteritis, and proctitis.[1]
†Includes fatigue and asthenia.[1]
‡Includes dermatitis, dermatitis acneiform, drug eruption, eczema, eczema asteatotic, erythema, palmar-erythrodysesthesia syndrome, pemphigoid, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, skin exfoliation, and urticarial dermatitis.[1]
§Includes arthralgia, arthritis, back pain, bone pain, chest pain, musculoskeletal chest pain, musculoskeletal pain, musculoskeletal discomfort, musculoskeletal stiffness, myalgia, neck pain, noncardiac chest pain, pain in extremity, and spinal pain.[1]
‖Includes dysesthesia, hypoesthesia, neuralgia, neuropathy peripheral, paresthesia, peripheral sensory neuropathy, and polyneuropathy.[1]
¶Includes blood thyroid-stimulating hormone increased and hypothyroidism.[1]
#Includes lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia aspiration, pneumonia bacterial, pneumonia chlamydial, pneumonia cryptococcal, pneumonia fungal, pneumonia pseudomonal, pneumonia streptococcal, pneumonia viral, and post-procedural pneumonia.[1]
**Five Grade 5 events in the IMFINZI arm and four Grade 5 events in the placebo arm.[1]
††Includes COVID-19 and COVID-19 pneumonia. Five Grade 5 events in the IMFINZI arm and one Grade 5 event in the placebo arm.[1]
‡‡Graded per NCI CTCAE, version 5.[1]
§§The denominator used to calculate the rate varied from 349 to 399 based on the number of patients with a baseline value and at least 1 post-treatment value.[1]
‖‖The denominator used to calculate the rate varied from 333 to 398 based on the number of patients with a baseline value and at least 1 post-treatment value.[1]

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Laboratory abnormalities worsening from baseline occurring in ≥20% of patients in the AEGEAN study[1]

SELECT LABORATORY ABNORMALITIES[1]

Laboratory abnormality[‡‡]	IMFINZI with CT[§§]		Placebo with CT[‖‖]	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Hematology				
Hemoglobin decreased	**78**	**10**	75	9
Leukocytes decreased	**63**	**12**	64	11
Neutrophils decreased	**52**	**24**	56	27
Platelets decreased	**46**	**7**	44	8
Lymphocytes decreased	**41**	**11**	37	9
Chemistry				
Calcium corrected, decreased	**51**	**3.3**	52	4.5
Alanine aminotransferase increased	**49**	**6**	42	2
Aspartate aminotransferase increased	**47**	**3.5**	37	1.8
Potassium increased	**33**	**1.5**	29	2
Sodium decreased	**35**	**5**	33	6
Gamma glutamyl transferase increased	**36**	**4.7**	35	2.1
Creatinine increased	**32**	**2.3**	27	3.3
Amylase increased	**25**	**4.7**	24	3.6
Magnesium decreased	**22**	**2.8**	20	3.6
Lipase increased	**23**	**4.9**	24	7

Discontinuation rate of IMFINZI or placebo due to adverse events of any grade: 12% in the IMFINZI arm and 6% in the placebo arm[2]

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Safety by phase in the AEGEAN study[1]

Neoadjuvant phase of AEGEAN

A total of 401 patients received at least 1 dose of IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment, and 398 patients received at least 1 dose of placebo in combination with platinum-containing chemotherapy as neoadjuvant treatment.

Serious adverse reactions occurred in 21% of patients who received IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment; 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 any study drug due to an adverse reaction occurred in 14% of patients who received IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment; the most frequent (>0.5%) adverse reactions that led to permanent discontinuation of any study drug were anemia (1.5%), neutropenia (0.7%), myelosuppression (0.7%), and periphery sensory neuropathy (0.7%). Permanent discontinuation of IMFINZI due to an adverse reaction occurred in 6.7% of patients who received IMFINZI in combination with platinum-containing chemotherapy as neoadjuvant treatment; the most frequent (≥0.5%) adverse reactions that led to permanent discontinuation of IMFINZI were peripheral sensory neuropathy (0.7%) and pneumonitis (0.5%).

Of the 401 IMFINZI-treated patients 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. Adverse reactions that led to cancellation of surgery in the IMFINZI arm were COVID-19 pneumonia, HIV infection, pneumonitis, prostate cancer, colon cancer, pruritus, and colitis.

Of the 325 IMFINZI-treated patients who received surgery, 4% (n=15) experienced delay of surgery (a surgical delay is defined as on-study surgery occurring more than 40 days after the last dose of study treatment in the neoadjuvant period) due to adverse reactions. Of the 326 placebo-treated patients who received surgery, 4% (n=16) experienced delay of surgery due to adverse reactions.

Of the 325 IMFINZI-treated patients who received surgery, 6.5% (n=21) did not receive adjuvant treatment due to adverse reactions. Of the 326 placebo-treated patients who received surgery, 5.8% (n=19) did not receive adjuvant treatment due to adverse reactions.

Adjuvant phase of AEGEAN

A total of 265 patients in the IMFINZI arm and 254 patients in the placebo arm received at least 1 dose of adjuvant treatment.

Of the patients who received single-agent IMFINZI as adjuvant treatment, 13% experienced serious adverse reactions. 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 adjuvant IMFINZI due to an adverse reaction occurred in 8% of patients. The most frequent (≥0.5%) adverse reactions that led to permanent discontinuation of adjuvant IMFINZI were pneumonitis (1.1%) and rash (0.8%).

ADVERSE EVENT SUMMARY FROM SECOND INTERIM ANALYSIS[5]

	Overall study period (including neoadjuvant, surgical, and adjuvant treatment phases)	
AEs	**AEGEAN Regimen (N=401)**	**Neoadjuvant CT alone (N=398)**
Any-grade all-causality AEs, n (%)	**387 (96.5)**	379 (95.2)
Serious AEs	**157 (39.2)**	126 (31.7)
Fatal AEs	**23 (5.7)**	15 (3.8)
Leading to discontinuation	**51 (12.7)**	25 (6.3)
Leading to cancellation of surgery	**7 (1.7)**	4 (1.0)
Max. Grade 3 or 4	**175 (43.6)**	172 (43.2)

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

Treatment modifications for IMFINZI: General guidance[1]

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

TREATMENT MODIFICATIONS FOR IMFINZI[1]

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

*Based on NCI CTCAE, version 4.03.[1]

†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.[1]

‡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.[1]

ALT=alanine aminotransferase; AST=aspartate aminotransferase; DRESS=Drug Rash with Eosinophilia and Systemic Symptoms; HIV=human immunodeficiency virus; imARs=immune-mediated adverse reactions; SJS=Stevens-Johnson Syndrome; TEN=toxic epidermal necrolysis; ULN=upper limit of normal.

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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 click here for Full Prescribing Information including Medication Guide for IMFINZI.

You may report side effects related to AstraZeneca products.

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). **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer. V.3.2025. ©National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed January 15, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** Salgia R, Boehmer LM, Celestin C, Yu H, Spigel DR. Improving care for patients with stage III or IV NSCLC: learnings for multidisciplinary teams from the ACCC National Quality Survey. *JCO Oncol Pract*. 2021;17(8):e1120-e1130. **5.** Heymach JV, Harpole D, Mitsudomi T, et al. Perioperative durvalumab for resectable NSCLC: updated outcomes from the phase 3 AEGEAN trial. Presented at: IASLC 2024 World Conference on Lung Cancer; September 7-10, 2024; San Diego, CA. **6.** AstraZeneca and US Food and Drug Administration. Combined FDA and Applicant ODAC Briefing Document. BLA# 761069/Supplement 43. Published July 25, 2024. Accessed November 15, 2024. https://www.fda.gov/media/180242/download. **7.** Mitsudomi T, Heymach JV, Reck M, et al. Surgical outcomes with neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in resectable NSCLC (AEGEAN). Presented at: IASLC 2023 World Conference on Lung Cancer; September 9-12, 2023; Singapore. **8.** Heymach JV, Reck M, Mitsudomi T, et al. Outcomes with perioperative durvalumab in patients with resectable NSCLC and baseline N2 lymph node involvement (N2 R-NSCLC). Presented at: ASCO 2024 Annual Meeting; June 2, 2024; Chicago, IL. Abstract 8011.

IMFINZI®
durvalumab
Injection for Intravenous Use 50 mg/mL

In resectable Stage IIA to IIIB (tumors ≥4 cm and/or node positive [N1, N2]) NSCLC with no known EGFR mutations or ALK rearrangements

Choose the AEGEAN Regimen—for your patients with resectable NSCLC[1,3,7]

PROVEN RESULTS[1]:

Median EFS not reached
with the AEGEAN Regimen
vs 25.9 months with neoadjuvant CT alone
at first planned interim analysis
(**HR=0.68**; 95% CI, 0.53-0.88; 2-sided *P* value=0.0039)

4× pCR rate
17.2% with the AEGEAN Regimen vs 4.3%
with neoadjuvant CT alone at final analysis;
P<0.0001*

Patients without surgical delays: 82.7% of patients within the IMFINZI arm and 77.8% of patients within the placebo arm had no surgical delays[7]

R0 was the goal: Of the patients who completed surgery, 94.7% within the IMFINZI arm and 91.3% of patients within the placebo arm achieved a complete resection[2]

Treatment completion data and surgical outcome data were not tested for statistical significance[7]

NCCN CATEGORY 1

Perioperative durvalumab (IMFINZI®) in combination with neoadjuvant platinum-based chemotherapy (carboplatin or cisplatin) is an **NCCN Category 1 recommendation** for patients with resectable NSCLC[3†‡]

Consider IMFINZI for all your appropriate Stage II and Stage III patients and learn more at IMFINZIhcp.com

*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]
†See the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for detailed recommendations, including other treatment options for resectable NSCLC.[3]
‡Neoadjuvant durvalumab (IMFINZI®) in combination with platinum-based CT, followed by durvalumab (IMFINZI®) continued as a single agent as adjuvant treatment after surgery, is a recommended option for patients with resectable (tumors ≥4 cm and/or node positive) NSCLC and no known EGFR mutations or ALK rearrangements.[3]

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).

You may report side effects related to AstraZeneca products.

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NCCN=National Comprehensive Cancer Network® (NCCN®).

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