# Report IMFINZI® - Durvalumab

## Product & Mechanism of action

**Substance:** Durvalumab

**Brand Name:** Imfinzi

**Originator/licensee:** AstraZeneca AB

**Classification:** NI

**ATC code:** L01XC28

**Orphan Status:**
**Eu:** No
**Us:** No

**Mechanism of action:**
Durvalumab is a monoclonal antibody designed to attach to PD-L1, which is present on the surface of many cancer cells. PD-L1 acts to switch off immune cells that would otherwise attack the cancer cells. By attaching to PD-L1 and blocking its effects, Duravlumab increases the ability of the immune system to attack the cancer cells and thereby slows down the progression of the disease [1].

## Authorized indications Licensing status

**Authorized Indication:**
**EMA**: Durvalumab in combination with platinum-based chemotherapy as neoadjuvant treatment, followed by Durvalumab as monotherapy as adjuvant treatment, is indicated for the treatment of adults with resectable NSCLC at high risk of recurrence and no EGFR mutations or ALK rearrangements [1].

**FDA:** Durvalumab in combination with platinum-containing chemotherapy as neoadjuvant treatment, followed by Durvalumab continued as a single agent as adjuvant treatment after surgery, is indicated for the treatment of adults with resectable (tumors ≥ 4 cm and/or node positive) NSCLC and no known EGFR mutations or ALK rearrangements [2].

**Route of administration:** IV

**Licensing status**
**EU CHMP P.O. date:** 27/02/2025
**FDA M.A. date:** 04/12/2024

**EU Speed Approval Pathway:** No
**FDA Speed Approval Pathway:** No

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**ABBREVIATIONS:**
**AE:** Adverse Event
**ALK**: Anaplastic lymphoma kinase
**BICR**: Blinded independent central review
**CHMP:** Committee for Medicinal Products for Human Use
**CI:** Confidential Interval
**pCR**: pathological complete response
**ECOG:** Eastern Cooperative Oncology Group
**EGFR:** Epidermal growth factor receptor
**HR**: hazard ratio
**ITT:** Intention-to-treat
**IV**: Intravenously
**M.A.:** Marketing Authorization
**NSCLC:** Non-Small Cell Lung Cancer
**P.O.:** Positive Opinion
**PS:** Performance Status
**Pts:** patients
**RECIST:** Response Evaluation Criteria in Solid Tumors

## Essential therapeutic features

**Summary of clinical EFFICACY:**
**AEGEAN Study (NCT03800134)** was a randomized, double-blind, placebo-controlled, multicentre, phase III trial.
Adults ≥18 years of age, with newly diagnosed, previously untreated, stage IIa to stage IIIb (according to the anatomic classification in the AJCC Cancer Staging Manual, 8th edition), resectable NSCLC and ECOG-PS of 0 or 1 were enrolled. Pts. must be candidates for planned surgical treatment, no prior exposure to immune-mediated therapy and at least one RECIST v.1.1 target lesion. Pts. were enrolled regardless of tumour PD-L1 expression.

Pts. (n=802) were randomized 1:1 to receive four cycles of platinum-based chemotherapy plus durvalumab 1,500 mg (n=400) or placebo (n=402) administered IV, followed by adjuvant Durvalumab 1,500 mg as a single agent or placebo every four weeks for up to 12 cycles post-surgery. Randomization was stratified according to disease stage (II or III) and PD-L1 expression (<1% or ≥1%).

The primary end points were event-free survival by BICR and pCR in the modified ITT population, which excluded pts. with documented EGFR or ALK alterations.

At the first interim analysis, the HR in terms of disease progression, recurrence, or death for durvalumab vs. placebo was 0.68 [95% CI, 0.53 to 0.88; P=0.004]. At the 12-month landmark analysis, event-free survival was observed in 73.4% of the pts., who received durvalumab (95% CI, 67.9 to 78.1), as compared with 64.5% of the pts., who received placebo (95% CI, 58.8 to 69.6).

Data on the pCR endpoint are reported in the table below [3]:

| | pCR | Durvalumab arm (n=400) | Placebo arm |
|---|---|---|---|
| Base on final analysis | pCR rate, % (95% CI) | 17.2 (13.5 to 21.5) | 4.3 (2.5 to 6.8) |
| Based on interim analysis (data from 402 pts) | Difference in proportions, % (95% CI) | 13.0 (8.7 to 17.6) | |
| | p-value | < 0.0001 | |

**Summary of clinical SAFETY:**
Safety was assessed in all the pts. who had undergone randomization and received at least one dose of any trial treatments (i.e., durvalumab or chemotherapy) or placebo.
AEs of any cause occurred in 96.5% of the pts., who received durvalumab and 94.7% of those, who received placebo. The incidence of grade 3 or 4 AEs of any cause was similar in the two groups (42.4% in the durvalumab group and 43.2% in the placebo group, respectively).
Grade 3 or 4 immune mediated AEs reported in 4.2% and 2.5%, respectively.
AEs that led to death possibly related to any trial treatment or placebo occurred in 1.7% of pts. in the durvalumab group and 0.5% of those in the placebo group, respectively [3].

**Ongoing studies:**
- ***For the same indication:*** *Yes*
- ***For other indications:*** Yes

**Discontinued studies (for the same indication):** No

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**References:**
[1] https://www.ema.europa.eu/en/medicines/human/EPAR/imfinzi
[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761069s049lbl.pdf
[3] https://www.nejm.org/doi/full/10.1056/NEJMoa2304875
[4] https://gallery.farmadati.it/
[5] https://www.oncologiatoracica.it/public/A%20Epidemiologia.pdf
[6] https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.20107
[7] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8474201/
[8] https://www.esmo.org/content/download/87433/1608958/1/IT-Cancro-del-Polmone-non-a-Piccole-Cellule-NSCLC-Guida-per-il-Paziente.pdf


## NHS impact

**Cost of therapy:**
In Italy, 500 mg of IMFINZI® concentrate for infusion cost € 2,631.59 [4].

**Epidemiology:**
Lung cancer is the leading cause of death from cancer in industrialised countries.
In Italy the number of new cases per year is around 35-40,000 [5]. NSCLC accounts for 80%-90% of lung cancers [6].
Currently, about two-thirds of pts with NSCLC are diagnosed with locally advanced or metastatic disease (stage III or IV) [7].

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**POSSIBLE PLACE IN THERAPY**:
For pts with NSCLC without any types of mutations there are limited treatment options.
First-line therapy for squamous NSCLC is represented by platinum-based chemotherapy (cisplatin/carboplatin + gemcitabine/vinorelbina/paclitaxel).

First-line therapy for non-squamous NSCLC is based on platinum-based chemotherapy plus bevacizumab or pembrolizumab, or cisplatin/ carboplatin plus pemetrexed [8].

The addition of durvalumab to these regimens could represent a new opportunity for these pts.

**OTHER INDICATIONS IN DEVELOPMENT:** Advanced Solid Malignancies (NCT03084471); Unresectable or Advanced Biliary Tract Cancers (NCT05924880, NCT03875235); Head and Neck Cancer (NCT02369874); Non-muscle Invasive Bladder Cancer (NCT03528694, NCT05943106); Papillary Renal Cell Carcinoma (NCT05043090); Hepatocellular carcinoma (NCT03847428, NCT03298451).

**SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: -

**OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Nivolumab (NCT01642004); Atezolizumab (NCT04513925); Sacituzumab Govitecan (NCT05089734).

*Service reorganization: No
*Possible off label use: Yes

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