# Report Imfinzi® – Durvalumab

| Product & Mechanism of action | Authorized indications Licensing status | Essential therapeutic features | NHS impact |
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| **Substance:** Durvalumab<br><br>**Brand Name:**Imfinzi®<br><br>**Originator/licensee:**AstraZeneca AB<br><br>**Classification:** NI<br><br>**ATC code:**L01XC28<br><br>**Orphan Status:**<br>**Eu:** No<br>**Us:** No<br><br>**Mechanism of action:**<br>Durvalumab is a fully human monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80. The blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation [1]. | **Authorized Indication:**<br><br>**EMA:** Durvalumab in combination with tremelimumab and platinum-based chemotherapy is indicated for the firstline treatment of adults with metastatic NSCLC with no sensitising EGFR mutations or ALK positive mutations [2].<br><br>**FDA:** Durvalumab in combination with tremelimumab and platinum-based chemotherapy is indicated for the treatment of adult pts with metastatic NSCLC with no sensitizing EGFR mutations or ALK genomic tumor aberrations [3].<br><br>**Route of administration:** IV<br><br>**Licensing status**:<br>**EU CHMP P.O. date:**15/12/2022<br>**FDA M.A. date:** 10/11/2022<br><br>**EU Speed Approval Pathway:** NO<br>**FDA Speed Approval Pathway:** NO<br>----------<br>**ABBREVIATIONS:**<br>**AEs:** Adverse events<br>**ALK**: anaplastic lymphoma kinase<br>**CHMP:** Committee for Medicinal Products for Human Use<br>**CTLA-4:** Cytotoxic T-Lymphocyte Antigen 4<br>**EGFR**: epidermal growth factor receptor<br>**EOCG**: Eastern Cooperative Oncology Group<br>**HR:** Hazard ratio<br>**M.A.:** Marketing Authorization<br>**NI:** New Indication<br>**NSCLC**: Non-small cell lung cancer<br>**OS**: overall survival<br>**PD-1**: Programmed Death<br>**PD-L1**: Programmed Death Ligand<br>**PFS**: progression-free survival<br>**P.O.:** Positive Opinion<br>**TC**: tumor cells | **Summary of clinical EFFICACY:** POSEIDON (NCT03164616) is a randomized, open-label, multi-center, phase III study to evaluate tremelimumab plus durvalumab and chemotherapy (T+D+CT) and durvalumab plus chemotherapy (D+CT) versus chemotherapy alone (CT) in firstline metastatic NSCLC. Chemotherapy options for all arms included carboplatin plus nab-paclitaxel regardless of histology, cisplatin or carboplatin plus gemcitabine for pts with squamous histology, and cisplatin or carboplatin plus pemetrexed for pts with non-squamous histology. Eligible pts had EGFR/ALK wild-type metastatic NSCLC with ECOG performance status of 0 or 1 and must have had no prior systemic therapy for metastatic NSCLC. Pts were randomly assigned (1:1:1) with stratification by PD-L1 expression (TC ≥50% vs TC <50%), disease stage (Stage IVA vs Stage IVB), and histology (non-squamous vs squamous) to: T+D+CT (T 75mg + D 1500mg + CT for up to four 21-day cycles, followed by D 1500mg once every 4 weeks, with one additional T dose after CT at week 16/cycle 6, i.e. fifth dose); D+CT (D 1500mg + CT for up to four 21-day cycles, followed by D 1500mg once every 4 weeks); or CT for up to six 21-day cycles. Pts continued treatment until disease progression or unacceptable toxicity.<br>The primary endpoints were PFS and OS for D+CT vs CT.Key alpha-controlled secondary endpoints were PFS and OS for T+D+CT vs CT. Initially, 1% alpha and 4% alpha were allocated to PFS and OS, respectively, for the D+CT vs CT comparison.Positivity for either primary endpoint enabled alpharecycling to the key secondary PFS and OS endpoints (T+D+CT vs CT). If either of the key secondary PFS or OS endpoints was met, the alpha could be recycled to the other key secondary endpoint.<br>PFS was significantly improved with D+CT vs CT (HR: 0.74; 95%CI: 0.62 to 0.89; P=0.0009). The median PFS was 5.5 (95%CI: 4.7to 6.5) vs 4.8 (95%CI: 4.6 to 5.8) months in the D+CTand CT arms, respectively, with 12-month PFS rates of24.4% vs 13.1%.<br>Although a trend forimprovement in OS was observed for D+CT vs CT, thiswas not statistically significant (HR: 0.86; 95%CI: 0.72 to 1.02; P=0.0758). The median OS was 13.3 (95% CI: 11.4 to 14.7) vs 11.7 (95%CI: 10.5 to 13.1) months with D+CT vs CT, respectively, and 24-month OS rates were29.6% vs 22.1%.<br>PFS for T+D+CT vs CT could be formally assessed, as the primary PFSendpoint for D+CT vs CT had been met. As this key secondary endpoint was also met, the comparison of OS forT+D+CT vs CT was also formally assessed.Both PFS (HR: 0.72; 95%CI: 0.60 to 0.86; P=0.0003) and OS (HR: 0.77; 95%CI: 0.65 to 0.92; P=0.0030) showed statistically significant improvement for T+D+CT vs CT. The median PFS was 6.2 months (95%CI: 5.0 to 6.5) vs 4.8 months (95%CI: 4.6 to 5.8), with12-month PFS rates of 26.6% vs 13.1%, in the T+D+CTarm vs CT arm, respectively. The median OS was 14.0 months (95%CI: 11.7 to 16.1) with T+D+CT vs 11.7 months (95%CI: 10.5 to 13.1) with CT; 24-month OS rates were 32.9% vs 22.1% [4].<br><br>**Summary of clinical SAFETY:**The safety analysis of the POSEIDON trial included 330, 334 and 333 pts in the T+D+CT, D+CT and CT arms, respectively. Any-grade AEs considered by the investigator to be treatment-related were reported in 306 (92.7%), 296 (88.6%), and 298 (89.5%) of pts treated with T+D+CT, D+ CT and CT, respectively. The incidence of treatment-related AEs with maximum grade 3/4 severity was numerically higher in the T+D+CT arm (51.8%) compared with the other arms (44.6% for D+CT and 44.4% for CT); a similar pattern was observed for treatment-related SAEs (27.6% vs 19.5% and 17.7%). The most common treatment-related AEs of maximum grade 3/4 were anemia and neutropenia. Treatment-related deaths occurred in 11 (3.3%), 7 (2.1%), and 8 (2.4%) pts treated with T+D+CT, D+ CT and CT, respectively [4].<br><br>**Ongoing studies:**<br>• ***For the same indication:*** Yes<br>• ***For other indications:*** Yes<br>**Discontinued studies (for the same indication):** Yes<br><br>**References:**<br>1.https://www.ema.europa.eu/en/documents/product-information/imfinzi-epar-product-information_en.pdf<br>2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/imfinzi-1<br>3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761069s033lbl.pdf<br>4. https://pubmed.ncbi.nlm.nih.gov/36327426/<br>5. https://gallery.farmadati.it/<br>6. https://www.aiom.it/wp-content/uploads/2020/10/2020_LG_AIOM_Polmone.pdf<br>7.https://www.cancer.org/cancer/lung-cancer/about/what-is.html<br>8. https://www.io.nihr.ac.uk/wp-content/uploads/2022/01/19355-Durvalumab-Tremelimumab-Chem-for-NSCLC-V1.0-MAY2018-NON-CONF.pdf<br>9. https://adisinsight.springer.com/drugs/800037095<br>10. https://clinicaltrials.gov/ | **Cost of therapy:**Considering the ex-factory price (2,631.59€ for Imfinzi® 50mg/mL 10mL, corresponding to 500mg of durvalumab), a single administration of 1500mg would cost 7,894.77€[5].<br><br>**Epidemiology:**In Italy, in 2020, a prevalence of more than 117,000 subjects with a previous diagnosis of lung cancer, and about 41,000 new cases of lung cancer were estimated [6]. About 85% of lung cancers are NSCLC [7-8], and the majority of pts with NSCLC have no EGFR or ALK mutations [8].<br><br>**POSSIBLE PLACE IN THERAPY:**<br>Durvalumab in combination with tremelimumabadded to standard chemotherapy has been approved as first line treatment[2].<br><br>**OTHER INDICATIONS IN DEVELOPMENT:** Bladder cancer; Cervical cancer; Endometrial cancer; Fallopian tube cancer; Gastric cancer; Head and neck cancer; Liver cancer; Pancreatic cancer; Mesothelioma; Oesophageal cancer; Ovarian cancer; Peritoneal cancer; Renal cell carcinoma; Solid tumours; Triple negative breast cancer [9].<br><br>**SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** -<br><br>**OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Datopotamabderuxtecan,penpulimab. [10]<br><br>*Service reorganization: No<br>*Possible off label use: Yes |

*Issued on:*