Report IMFINZI® - Durvalumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
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, durvalumab increases the ability of the immune system to attack the cancer cells and thereby slows down the progression of the disease [1].	**Authorized Indication:** **EMA**: Durvalumab in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by Durvalumab as monotherapy adjuvant treatment after radical cystectomy, is indicated for the treatment of adults with resectable MIBC [1]. **FDA:** Durvalumab in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by single agent Durvalumab as adjuvant treatment following radical cystectomy, is indicated for the treatment of adults with MIBC [2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 22/05/2025 **FDA M.A. date:** 28/03/2025 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AE**: Adverse Event **AJCC:** American Joint Committee on Cancer **BICR:** Blinded independent central review **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **EFS:** Event-free survival **HR**: Hazard Ratio **IV**: Intravenously **ITT:** Intention to treat **M.A.:** Marketing Authorization **MIBC**: Muscle invasive bladder cancer **PFS**: Progression-Free Survival **PI**: Proteasome inhibitor **P.O.**: Positive Opinion **PS**: Performance Status **Pts**: Patients **RR**:Risk Ratio **SAE**: Serious adverse events **TRAE**: Treatment related AEs **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **NIAGARA (NCT03732677)** is global, open-label, randomized trial phase 3. Eligible pts were >18 years of age, with histologically or cytologically documented MIBC (clinical tumour stage of T2, T3, or T4a, N0 or N1, and M0 according to the 8th AJCC Cancer Staging Manual). Pts. were candidates for radical cystectomy and had not received prior systemic chemotherapy or immune-mediated therapy for the treatment of NMIBC or MIBC. Pts. with pure nonurothelial histology, any small cell histology and primary non-bladder cancer of the urothelium were excluded. Pts (n=1,060) were randomized in a 1:1 ratio to the durvalumab (n=530) or comparison (n=530) group. Pts. received: • Durvalumab group: four cycles of neoadjuvant durvalumab 1,500 mg with gemcitabine 1,000 mg/m2 and cisplatin 70 mg/m2 administered intravenously every three weeks, followed by radical cystectomy and then up to eight cycles of adjuvant durvalumab 1500 mg administered intravenously every four weeks; • Comparison group: the same neoadjuvant regimen of gemcitabine–cisplatin followed by radical cystectomy alone. The dual primary end points were pathological complete response and EFS as assessed by BICR or by central pathology review, if a biopsy was needed for analysis of a suspected new lesion in the ITT population. Randomization was stratified on the basis of clinical tumour stage, renal function and tumour PD-L1 expression level. According to the primary analysis, a pathological complete response occurred in 33.8% (95% CI, 29.8 to 38.0) of the pts. in the durvalumab group and in 25.8% (95% CI, 22.2 to 29.8) of those in the comparison group (RR, 1.30; 95% CI, 1.09 to 1.56; P = 0.004). In the reanalysis (including the results for the 59 samples omitted from the primary analysis), a pathological complete response occurred in 37.3% (95% CI, 33.2 to 41.6) of the pts. in the durvalumab group and in 27.5% (95% CI, 23.8 to 31.6) of those in the comparison group (RR, 1.34; 95% CI, 1.13 to 1.60) The estimated EFS at 24 months was 67.8% (95% CI, 63.6 to 71.7) in the durvalumab group and 59.8% (95% CI, 55.4 to 64.0) in the comparison group (HR for progression, recurrence, not undergoing radical cystectomy, or death from any cause, 0.68; 95% CI, 0.56 to 0.82; P<0.001 by stratified log-rank test). **Summary of clinical SAFETY:** AEs of any cause occurred in 99.4% of those in the durvalumab group and in 99.8% of those in the comparison group, with grade ≥3 AEs occurring in 69.4% and 67.5% of the pts, respectively. The most common AEs of any cause were nausea, anaemia, and constipation. Grade ≥3 TRAEs occurred in 40.6% and 40.9% of the pts., respectively. TRAEs leading to death occurred in three pts. (0.6%) in each group. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** Yes --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/imfinzi [2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761069s050lbl.pdf [3] https://www.nejm.org/doi/full/10.1056/NEJMoa2408154 [4] https://gallery.farmadati.it/ [5] https://pmc.ncbi.nlm.nih.gov/articles/PMC7151633/ [6] https://www.sciencedirect.com/topics/medicine-and-dentistry/muscle-invasive-bladder-cancer [7] https://uroweb.org/guidelines/muscle-invasive-and-metastatic-bladder-cancer/chapter/disease-management	**Cost of therapy:** In Italy, 50mg/mL 10mL, corresponding to 500mg of durvalumab, cost 2,631.59 € (ex-factory price). A single injection of 1,500 mg would cost 7.894,77 € [4]. **Epidemiology:** Bladder cancer is the 10th most common cancer in the world, accounting for 3% of global cancer diagnoses and it is especially prevalent in the developed world. Southern Europe has the highest incidence of bladder cancer with an estimated 26.5 cases per 100,000 men and 5.5 cases per 100,000 women diagnosed annually [5]. MIBC represents 25% of newly diagnosed bladder cancer [6]. --- **POSSIBLE PLACE IN THERAPY**: For pts. who present with MIBC, cisplatin-based neoadjuvant or adjuvant chemotherapy is considered the standard to lower the risk of recurrence, and radical cystectomy is the mainstay surgical treatment. External beam radiation may also be used [5,7]. The addition of Durvalumab to these regimens could represent a further opportunity for these pts. **OTHER INDICATIONS IN DEVELOPMENT:** Advanced Solid Malignancies (NCT03084471); Head and Neck Cancer (NCT02369874); Unresectable Biliary Tract Cancers (NCT05924880); Hepatocellular Carcinoma (NCT05883644); Advanced Biliary Tract Cancer (NCT03875235); **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Pembrolizumab (NCT03924895); Durvalumab + Tremelimumab + Enfortumab vedotin (NCT04960709); Atezolizumab (NCT04660344); Bempegaldesleukin (NCT04209114) *Service reorganization: No *Possible off label use: Yes

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