**Report Imfinzi® - durvalumab**

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| **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, a type of protein designed to attach to a protein called 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 slow down the progression of the disease [1]. | **Authorized Indication:**  **EMA:** durvalumab in combination with GemCis is indicated for the first‑line treatment of adults with unresectable or metastatic BTC [2].  **FDA:** durvalumabin combination with GemCis, as treatment of adult patients with locally advanced or metastatic BTC [3].  **Route of administration:** iv  **Licensing status**  **EU CHMP P.O. date:**10/11/2022 **FDA M.A. date:** 02/09/2022  **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:** No  **----- ABBREVIATIONS:**  **AE**: Adverse Event  **BTC**: biliary tract cancer  **CHMP**: The Committee for Medicinal Products for Human Use  **CI**: confidence interval  **GemCis**: gemcitabine and cisplatin  **HS:** hazard ratio  **M.A.**: Marketing Authorization  **OS**: Overall Survival  **P**: p-value  **Pbo**: placebo  **P.O.**: Positive Opinion  **Pts**: patients  **TEAE**: treatment-emergent adverse event | **Summary of clinical EFFICACY:**  TOPAZ-1 (NCT03875235) is a randomized, double-blind, pbo controlled, phase III study to evaluate efficacy and safety of durvalumab plus GemCis for pts with advanced BTC.  The primary end-point is OS, defined as the time between randomization and death due to any cause.  Eligible pts was >18 years with previously untreated unresectable or metastatic BTC or with recurrent disease.  Pts (N=685) were randomly assigned in a 1:1 ratio to receive durvalumab (N=338) (1,500mg) or pbo (N=342) on day 1 of each cycle in combination with gemcitabine (100mg/m2) and cisplatin (25mg/m2), which were administered on days 1 and 8 of each cycle, for up to eight cycles. After completion of GemCis, durvalumab or pbo monotherapy was administered every four weeks until clinical disease progression or unacceptable toxicity.  TheRCT met the primary end-point: Durvalumab plus chemotherapy demonstrated statistically significant prolonged OS vs pbo plus chemotherapy [4].   |  |  |  | | --- | --- | --- | |  | **Durvalumab + GemCis** | **Pbo + GemCis** | | **Median OS (months)** | 12.8  (95% CI, 11.1 to 14.0) | 11.5  (95% CI, 10.1 to 12.5) | | **HR** | 0.80  (95% CI, 0.66 to 0.97; P=0.021) | | | **Pts who died (N; %)** | 198 (58.1%) | 226 (65.7%) |   **Summary of clinical SAFETY:**  The safety profiles of the two treatments were similar. The safety analysis set included 680 pts who received one or more doses of durvalumab (n=338) or pbo (n=342).  The most common AE were anemia (48%), nausea (40%), constipation (32%) and neutropenia (32%) in the durvalumab group and anemia (45%), nausea (34%), and decreased neutrophil count (31%) in the pbo group [4].   |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **AE (%)** | **Any grade** | **Serious** | **grade 3 or 4** | **leading to discontinuation** | **leading to death** | | **Durvalumab** | 336 (99) | 160 (47) | 256 (76) | 44 (13) | 12 (4) | | **Pbo** | 338 (99) | 149 (44) | 266 (78) | 52 (15) | 14 (4) |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | **TEAE (N%)** | **Any grade** | **Serious** | **grade 3 or 4** | **leading to discontinuation** | **Leading to death** | | **Durvalumab** | 314 (99) | 53 (16) | 212 (63) | 30 (9) | 2 (1) | | **Pbo** | 308 (90) | 59 (17) | 222 (65) | 39 (11) | 1 (>1) |   **Ongoing studies:**[5].   * ***For the same indication:***Yes * ***For other indications:***Yes   **Discontinued studies (for the same indication):**No  -----  **References:**  [1]. <https://www.ema.europa.eu/en/medicines/human/EPAR/imfinzi>  [2]. <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/imfinzi-0>  [3]. <https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761069s035lbl.pdf>  [4]. Oh DY et al. Gemcitabine and cisplatin plus durvalumab with or without tremelimumab in chemotherapy-naive patients with advanced biliary tract cancer: an open-label, single-centre, phase 2 study. Lancet Gastroenterol Hepatol. 2022 Jun;7(6):522-532. doi: 10.1016/S2468-1253(22)00043-7. Epub 2022 Mar 9. PMID: 35278356.  [5]. [**https://adisinsight.springer.com/drugs/800037095**](https://adisinsight.springer.com/drugs/800037095)  **[6].** <https://gallery.farmadati.it/>  **[7].**  https://www.aiom.it/wp-content/uploads/2021/10/2021\_NumeriCancro\_web.pdf  **[8].** <https://clinicaltrials.gov/ct2/show/NCT04003636?recrs=abdf&type=Intr&cond=Biliary+Tract+Cancer&phase=2&draw=2&rank=15> | **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 1,500 mg would cost 7,894.77€ [6].  **Epidemiology:**  The incidence of new cases of biliary tract cancer in Italy in 2020 was around 5,400 subjects (2,400 man and 3,000 women) [7].  -----  **POSSIBLE PLACE IN THERAPY**  Durvalumab added to the first-line standard of care, gemcitambine and cisplatin, for the treatment of unresectable or metastatic BTC.  **OTHER INDICATIONS IN DEVELOPMENT**: Bladder cancer; Cervical cancer; Endometrial cancer; Fallopian tube cancer; Gastric cancer; Head and neck cancer; Liver cancer; Mesothelioma; Oesophageal cancer; Ovarian cancer; Peritoneal cancer; Renal cell carcinoma; Solid tumours; Triple negative breast cancer [5].  **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**No  **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION**: Pembrolizumab [8].  \*Service reorganization: No  \*Possible off label use: Yes |