Report TECENTRIQ® Atezolizumab

Product Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: atezolizumab **Brand Name:** Tecentriq® **Originator/licensee:**Roche Registration GmbH **Classification:** NI **ATC code:**L01XC32 **Orphan Status:** **Eu:**No **Us:**No **Mechanism of action:** atezolizumab is a monoclonal antibody designed to recognise and attach to PD-L1. PD-L1 acts to switch off immune cells that would otherwise attack the cancer cells. By attaching to PD-L1 and reducing its effects, atezolizumab 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:** atezolizumab as monotherapy is indicated for the first-line treatment of adult pts with metastatic NSCLC whose tumors have a PD-L1 expression ≥ 50% TC or ≥ 10% tumor-infiltrating IC and who do not have EGFR mutant or ALK-positive NSCLC [2]. **FDA:** atezolizumab is indicated for the first-line treatment of adult pts with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of TC [TC ≥ 50%] or PD-L1 stained tumor-infiltrating IC covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations [3]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:**25/03/2021 **FDA M.A. date:**18/05/2020 **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:**No --- **ABBREVIATIONS:** **AE:** adverse event **AUC:** area under the concentration−time Curve; **BSC:** best supportive care; **CHMP:** Committee for Medicinal Products for Human Use; **DLBCL:** Diffuse Large B-Cell Lymphoma; **IC:** immune cells; **IV:** intravenous; **M.A.:** Marketing Authorization; **NHL:** non-Hodgkin lymphoma; **NSCLC:** non-small cell lung cancer; **OS:** Overall Survival; **PD-L1:** programmed death-ligand1; **P.O.:** Positive Opinion; **Pts:** patients; **SCLC:** small cell lung cancer; **TC:** tumor cells	**Summary of clinical EFFICACY:** **IMpower110 (NCT02409342):** a multicenter, international, randomized, open-label, Phase 3 trial evaluating the efficacy of atezolizumab in 572 adult pts with stage IV non-squamous or squamous NSCLC who had not previously received chemotherapy and who had PD-L1 expression on at least 1% of TC or at least 1% of tumor-infiltrating IC.Pts were randomly assigned in a 1:1 ratio to receive either atezolizumab 1200 mg IV (n=285) once every 3 weeks or platinum-based chemotherapy (n=287). Platinum-based chemotherapy regimens consisted in: - for non-squamous NSCLC, cisplatin (75 mg/m²) and pemetrexed (500 mg/m²) or carboplatin (AUC 6 mg/mL/min) and pemetrexed (500 mg/m²) every 3 weeks for a maximum of 4 or 6 cycles followed by pemetrexed 500 mg/m² until disease progression or unacceptable toxicity; - for squamous NSCLC, cisplatin (75 mg/m²) on Day 1 with gemcitabine (1250 mg/m^2) on Days 1 and 8 of each 21-day cycle or carboplatin (AUC 5 mg/mL/min) on Day 1 with gemcitabine (1000 mg/m^2) on Days 1 and 8 of each 21-day cycle for a maximum of 4 or 6 cycles followed by BSC until disease progression or unacceptable toxicity. The primary endpoint was OS in the PD-L1–selected population that excluded pts with EGFR mutations or ALK translocations.According to the results of the interim analysis,among pts with EGFR and ALK wild-type tumours who had high PD-L1 expression, the median OS was significantly longer - by 7.1 months - in the atezolizumab group than in the chemotherapy group (20.2 months vs. 13.1 months)[3][4][5] **Summary of clinical SAFETY:** Among all the pts who could be evaluated for safety, AEs occurred in 90.2% of the pts in the atezolizumab group and in 94.7%of those in the chemotherapy group; grade 3 or 4 AEs occurred in 30.1%and 52.5% of the pts in the respective groups.The most frequent grade 3 or 4 AEs occurring in the atezolizumab group were pneumonia (2.4%), hyperkalemia (2.1%), hyponatremia (2.1%) and anemia (1.7%)[4]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***Yes **Discontinued studies (for the same indication):** No --- **References:** **[1].**https://www.ema.europa.eu/en/documents/product-information/tecentriq-epar-product-information_en.pdf **[2].**https://www.ema.europa.eu/en/medicines/human/summaries-opinion/tecentriq-3 **[3].** https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761034s031s032lbl.pdf **[4].**Herbst RS, Giaccone G, de Marinis F, et al. Atezolizumab for First-Line Treatment of PD-L1-Selected Patients with NSCLC. N Engl J Med. 2020;383(14):1328-1339. doi:10.1056/NEJMoa1917346 **[5].**https://clinicaltrials.gov/ct2/show/NCT02409342 **[6].**https://gallery.farmadati.it/Home.aspx **[7].** IARC. Cancer Incidence, Mortality and Prevalence Worldwide GLOBOCAN 2012. http://gco.iarc.fr/ **[8].** Neoplasie del polmone. Linee Guida AIOM 2020 **[9].** Jemal A, Bray F, Center MM et al. Global cancer statistics. CA Cancer J Clin 2011; 61: 69–90. **[10].**Herbst RS, Baas P, Kim DW, et al.Pembrolizumab versus docetaxel for previouslytreated, PD-L1-positive, advanced nonsmall-cell lung cancer (KEYNOTE-010): arandomised controlled trial. Lancet 2016;387: 1540-50. **[11].**Garon EB, Rizvi NA, Hui R, et al. Pembrolizumab for the treatment of non–small-cell lung cancer.N Engl J Med 2015;372: 2018-28. **[12].**D. Planchard et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.Ann Oncol (2018) 29(Suppl 4): iv192–iv237 (Updated version published 15 September 2020) **[13].**https://www.clinicaltrials.gov/	**Cost of therapy:** 7,596.38€* for one IV vial1.200 mg 20 ml[6] Price for one cycle: 7,596.38€ **retail price including VAT* **Epidemiology:** primary lung cancer remains the most common malignancy after non-melanocytic skin cancer, and deaths from lung cancer exceed those from any other malignancy worldwide[7].In 2020, about 41,000 new cases of lung cancer were estimated in Italy (27,550 in men and 13,300 in women): it is the second most frequent malignancy in men (14%) and the third in women (7%) [8].NSCLC accounts for 80%-90% of lung cancers[9]. Approximately 23 to 28% of pts with advanced NSCLC have a high level of PD-L1 expression[10][11]. --- **POSSIBLE PLACE IN THERAPY:** for pts with advanced NSCLC and PD-L1 expression ≥ 50%, with no EGFR or ALK genomic tumor aberrations and who do not have contraindications to use of immunotherapy, pembrolizumab is considered a standard first-line option.Atezolizumab represents a promising first-line treatment option in pts with PD-L1-high[12]. **OTHER INDICATIONS IN DEVELOPMENT:** SCLC, Malignant Pleural Mesothelioma, Thymic Carcinoma, Urinary Tract Cancer, DLBCL, NHL,Cutaneous T-cell lymphoma, Rectal Cancer, Breast Cancer, Bladder Cancer, other[13]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**No **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** No [if it is..] *Service reorganization: Yes *Possible off label use: No

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