Report TEVIMBRA® - Tislelizumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Tislelizumab **Brand Name:** Tevimbra **Originator/licensee:** BeiGene Ireland Ltd **Classification:** NI **ATC code:** L01FF09 **Orphan Status:** **Eu:** Yes **Us:** / **Mechanism of action:** Tislelizumab is a monoclonal antibody that blocks PD-1 receptor on specific cells of the immune system. Some cancers can produce proteins (PD-L1 and PD-L2) that combine with PD-1 to switch off the activity of the immune cells, preventing them from attacking the cancer. By blocking PD-1, tislelizumab stops the cancer switching off these immune cells, thereby increasing the ability of the immune system to kill the cancer cells [1].	**Authorized Indication:** **EMA**: Tislelizumab, in combination with gemcitabine and cisplatin, is indicated for the first-line treatment of adults with recurrent, not amenable to curative surgery or radiotherapy, or metastatic NPC [1]. **FDA:** / **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 22/05/2025 **FDA M.A. date:** / **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** / --- **ABBREVIATIONS:** **AE**: Adverse Event **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **HR**: Hazard Ratio **IV**: Intravenously **IRC**: independent review committee **M.A.**: Marketing Authorization **MM**: Multiple myeloma **NPC**: Nasopharyngeal carcinoma **OS**: Oral administration **PFS**: Progression-Free Survival **P.O.**: Positive Opinion **PS**: Performance Status **Pts**: Patients **Q3W**: every 3 weeks **R/M**: Recurrent or metastatic **RECIST**: Response Evaluation Criteria in Solid Tumors **TEAE:** Treatment-emergent adverse event **TRAE**: Treatment related AEs **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **RATIONALE-309 (NCT03924986)** is a multicentre, randomized, double-blind, placebo-controlled phase III conducted at 42 sites in Asia. Eligible pts. aged 18–75 years, with treatment-naive histologically or cytologically confirmed R/M NPC, regardless of PD-L1 expression level, with R1 measurable lesion per RECIST v1.1, an ECOG PS of ≥1, a life expectancy of ≥12 weeks, and adequate organ function. Pts. with prior curative neoadjuvant/adjuvant therapy for non-metastatic disease required ≥6-month treatment-free interval before randomization; pts., who have received ≤4 cycles of prior neoadjuvant chemotherapy were allowed. Prior treatment with anti-PD-1/PD-L1 therapy, previous systemic anticancer therapy within 28 days prior to initiation of study treatment or immunotherapy or investigational therapies within 14 days or five half-lives of randomization were not permitted. Pts. (n=263) were randomized in a 1:1 ratio to receive either tislelizumab 200 mg IV (n=131) or matching placebo (n=132) Q3W, plus the chemotherapy regimen gemcitabine and cisplatin. The chemotherapy regimen was administered Q3W for four to six cycles, at the investigators' discretion. The chemoradiotherapy regimen included gemcitabine 1 g/m2 IV, given on day one and day eight, and cisplatin 80 mg/m^2 on day one. Randomization was stratified by gender and liver metastatic status. The primary endpoint was PFS, as assessed by IRC, according to RECIST v1.1 in the ITT population. At the interim analysis, IRC-assessed PFS was 9.2 months with tislelizumab-chemotherapy vs 7.4 months with placebo-chemotherapy (HR 0.52; 95% CI: 0.38, 0.73; p < 0.0001). At a median follow-up of 15.5 months, IRC-assessed PFS was consistent with the interim analysis (HR 0.50 [95% CI: 0.37, 0.68]; nominal p < 0.0001; PFS: 9.6 and 7.4 months, respectively) [2]. **Summary of clinical SAFETY:** All pts. in the tislelizumab-chemotherapy arm and 99.2% of pts. in the placebo-chemotherapy arm experienced ≥1 TEAE; grade ≥3 TEAE occurred in 106 (80.9%) pts. and in 108 (81.8%) pts., respectively. TEAEs leading to death were reported in five (3.8%) pts. in the tislelizumab-chemotherapy arm and two (1.5%) pts. in the placebo-chemotherapy arm. One pt. (0.8%) in the tislelizumab-chemotherapy arm experienced myelodysplastic syndrome leading to death considered related to tislelizumab [2]. **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/medicines/human/EPAR/tevimbra [2] https://www.sciencedirect.com/science/article/pii/S153561082300140X?via%3Dihub [3] https://www.orpha.net/en/disease/detail/150 [4] https://www.tumoritestaecollo.it/tumori/tumore-rinofaringe/ [5] https://www.esmo.org/guidelines/esmo-euracan-clinical-practice-guideline-nasopharyngeal-carcinoma	**Cost of therapy:** The price is not available yet. **Epidemiology:** NPC is a rare type of head and neck cancer. It has an annual incidence of approximately 1 case per 100,000 individuals in Western countries [3]. In Italy, NPC is very rare, with an annual incidence of 0.5 case per 100,000 people, showing higher rates in pts. aged over 65 years [4]. --- **POSSIBLE PLACE IN THERAPY**: Radiotherapy and intensity-modulated radiotherapy represent the current standard of care for pts with NPC. For advanced or metastatic disease, a combination approach with platinum-based regimens is required. No standard second-line treatment exists. Immunotherapy is a promising approach in this context, though its precise therapeutic role remains to be established [5]. The addition of tislelizumab to these regimens could represent a further opportunity for these pts. **OTHER INDICATIONS IN DEVELOPMENT:** Hepatocellular carcinoma (NCT03412773); Classical Hodgkin Lymphoma (NCT04486391); Colorectal Cancer (NCT05116085); Urothelial cancer (NCT04004221O) **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Cadonilimab (NCT05587374); Penplulimab (NCT04974398). *Service reorganization: No *Possible off label use: Yes

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