

Report KEYTRUDA® pembrolizumab - EC

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
<p>Substance: pembrolizumab</p> <p>Brand Name: Keytruda</p> <p>Originator/licensee: Merck Sharp & Dohme B.V.</p> <p>Classification: NI</p> <p>ATC code: L01XC18</p> <p>Orphan Status: Eu: No Us: No</p> <p>Mechanism of action: Pembrolizumab is a humanized monoclonal antibody which binds to the PD-1 receptor and blocks its interaction with ligands PD-L1 and PD-L2 [1].</p>	<p>Authorized Indication: EMA: pembrolizumab, in combination with lenvatinib, is indicated for the treatment of advanced or recurrent EC in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation [2]. FDA: pembrolizumab, in combination with lenvatinib, is indicated for the treatment of pts with advanced EC that is not MSI-H or dMMR, who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation [3].</p> <p>Route of administration: IV</p> <p>Licensing status EU CHMP P.O. date: 14/10/2021 FDA M.A. date: 19/09/2019</p> <p>EU Speed Approval Pathway: No FDA Speed Approval Pathway: Yes -----</p> <p>ABBREVIATIONS: CHMP: Committee for Medicinal Products for Human Use dMMR: Deficient Mismatch Repair EC: Endometrial Carcinoma IV: Intravenous MA: Marketing Authorization MSI-H: Microsatellite Instable OS: Overall Survival PD-1: Programmed Cell Death-1 PD-L1: Programmed Cell Death-Ligand1 PFS: Progression Free Survival PO: Positive Opinion pts: Patients QD: Every Day Q3W: Every Three Weeks TPC: Treatment of Physician's Choice vs: Versus</p>	<p>Summary of clinical EFFICACY: Study KEYNOTE-775/Study 309 (NCT03517449): multicenter, randomized, open-label, active-controlled phase III trial designed to evaluate the investigational use of pembrolizumab in combination with lenvatinib for the treatment of advanced EC, following at least one prior platinum-based regimen. Pts (n=827) were randomized 1:1 to receive either pembrolizumab 200 mg by IV infusion on Day one of each 21-day cycle plus lenvatinib 20 mg orally QD during each 21-day cycle for up to 35 cycles (n=411), or TPC of either doxorubicin at 60 mg/m² dose by IV every three weeks for up to a maximum cumulative dose of 500 mg/m² or paclitaxel at a 80 mg/m² dose by IV on a 28-day cycle (n=416). The dual primary endpoints were OS and PFS. Pembrolizumab and lenvatinib reduced the risk of disease progression or death by 44% (HR=0.56 [95% CI: 0.47-0.66]; p<0.0001), with a median PFS of 7.2 months (95% CI: 5.7-7.6; number of events=281) vs. 3.8 months (95% CI: 3.6-4.2; number of events=286) for pts who received TPC. Additionally, pembrolizumab and lenvatinib reduced the risk of death by 38% (HR=0.62 [95% CI: 0.51-0.75]; p<0.0001), with a median OS of 18.3 months (95% CI: 15.2-20.5; number of events=188) vs. 11.4 months (95% CI: 10.5-12.9; n. of events=245) for pts who received TPC [4].</p> <p>Summary of clinical SAFETY: Any-grade TEAEs occurred in all pts in the experimental arm vs. 98% in the comparator arm. The most common (≥25% of pts) TEAEs of any grade in the pembrolizumab + lenvatinib arm were: hypertension (64% vs. 5%), hypothyroidism (57% vs. 1%), diarrhoea (54% vs. 19%), nausea (50% vs. 46%), decreased appetite (45% vs. 21%), vomiting (37% vs. 20%), weight decrease (34% vs. 6%), fatigue (33% vs. 28%), arthralgia (31% vs. 8%), proteinuria (29% vs. 3%), anemia (26% vs. 47%), constipation (26% vs. 25%) and urinary tract infections (26% vs. 10%). Grade 3 TRAEs occurred in 89% of pts in the pembrolizumab + lenvatinib arm vs. 73% of pts in the TPC arm. Grade 5 TEAEs of any cause occurred in 6% of pts in the experimental vs. 5% in the TPC arm. Death occurred in 184 (45%) pts in the experimental arm vs. 236 (61%) in the TPC arm [4].</p> <p>Ongoing studies:</p> <ul style="list-style-type: none"> ● For the same indication: Yes ● For other indications: Yes <p>Discontinued studies (for the same indication): No</p> <p>References:</p> <ol style="list-style-type: none"> 1. https://www.ema.europa.eu/en/documents/product-information/keytruda-epar-product-information_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/keytruda-5 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/125514s065lbl.pdf 4. https://clinicaltrials.gov/ct2/show/results/NCT03517449?term=NCT03517449&draw=2&rank=1&view=results 5. https://gallery.farmadati.it/Home.aspx 6. https://www.aiom.it/i-numeri-del-cancro-in-italia/ 7. https://clinicaltrials.gov/ct2/home 	<p>Cost of therapy: The Italian price for a three-week cycle with pembrolizumab is 11,315 €* [5]. *Retail price including VAT.</p> <p>Epidemiology: In Italy, there were an estimated 8,300 new cases of EC in 2020 (slightly less than 5% of all female cancers). It is the third most common malignancy in women in the 50-69 age group [6].</p> <p>POSSIBLE PLACE IN THERAPY The first-line treatment for advanced/metastatic EC is represented by the combination of carboplatin and paclitaxel. In pts progressing to the first-line there is no defined standard of second-line: the most active drugs are represented by doxorubicin and weekly paclitaxel. The combination of lenvatinib and pembrolizumab has recently been shown to increase PFS and OS compared with chemotherapy in the second-line treatment after platinum of endometrial cancers without MSI [6].</p> <p>OTHER INDICATIONS IN DEVELOPMENT: Yes (Prostate Cancer, Ovarian Cancer, Multiple Myeloma) [7].</p> <p>SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: Yes (NCT03914612) [7].</p> <p>OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: Yes (Atezolizumab, Abemaciclib + Letrozolo) [7].</p> <p>*Service reorganization Y/N: No *Possible off label use Y/N: Yes</p>