# Report KIMMTRAK® tebentafusp

| Product & Mechanism of action | Authorized indications Licensing status | Essential therapeutic features | NHS impact |
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| **Substance:**tebentafusp<br><br>**Brand Name:**Kimmtrak<br><br>**Originator/licensee:**Immunocore Ireland Limited<br><br>**Classification:** NCE<br><br>**ATC code:** L01<br><br>**OrphanStatus:**<br>**Eu:** Yes<br>**Us:** Yes<br><br>**Mechanism of action:**<br>Tebentafusp is an antineoplastic agent with bispecific affinity, targeting the CD3 T cells and a gp100 peptide on the surface of uveal melanoma tumour cells. Thisredirects and activates T cells and results in direct lysis of uveal melanoma tumour cells [1]. | **Authorized Indication:**<br>**EMA**: tebentafusp is indicated as monotherapy for the treatment of HLA-A*02:01 positive adult pts with unresectable or metastatic uveal melanoma [1].<br>**FDA**: tebentafusp is a bispecific gp100 peptide-HLA-directed CD3 T cell engager<br>indicated for the treatment of HLA-A*02:01-positive adult pts with unresectable or metastatic uveal melanoma [2].<br><br>**Route of administration:** IV<br><br>**Licensing status**<br>**EU CHMP P.O. date:** 24/02/2022<br>**FDA M.A. date:** 25/01/2022<br><br>**EU Speed Approval Pathway:** No<br>**FDA Speed Approval Pathway:** No<br>**-----**<br><br>**ABBREVIATIONS:**<br>**AEs:** Adverse events<br>**CHMP**: Committee for Medicinal Product for Human Use<br>**CI**: Confidence Interval<br>**HLA**: human leukocyte antigen<br>**HR**: Hazard Ratio<br>**IFN:** Interferon<br>**MA**: Marketing Authorization<br>**OS**: Overall Survival<br>**PO**: Positive Opinion<br>**PI**: Principal Investigator<br>**Pts**: patients<br>**TRAEs**: treatment-related adverse events<br>**vs**.: versus | **Summary of clinical EFFICACY:**<br>**IMCgp100-202 (NCT03070392):** open-label, phase III trial where previously untreated HLA-A*02:01-positive adult pts (n=378) with metastatic uveal melanoma were randomized in a 2:1 ratio to receive tebentafusp (n=252) or the PI choice of therapy (n=126) with single-agent pembrolizumab, ipilimumab, or dacarbazine (control group) for three weeks.<br>- Pts received IV tabentafuspat a dose of 20 µg on day 1, 30 µg on day 8 and 68 µg weekly thereafter;<br>- Pembrolizumab was administered intravenously at a dose of 2 mg/kg to a maximum of 200 mg per dose or at a fixed dose of 200 mg on day 1 of each 21-day cycle;<br>- Ipilimumab was administered intravenously at a dose of 3 mg/kg on day 1 of each 21-day cycle for a maximum of four doses;<br>- Dacarbazine was administered intravenously at a dose of 1,000 mg per square meter of body-surface area on day 1 of each 21-day cycle.<br>The primary endpoint was OS.<br>The estimated OS at one year was 73% (95% CI, 66 to 79) in the tebentafusp group and 59% (95% CI, 48 to 67) in the control group (HR for death, 0.51; 95% CI, 0.37 to 0.71; p<0.001).The estimated median duration of OS was 21.7 months (95% CI, 18.6 to 28.6) with tebentafuspand 16.0 months (95% CI, 9.7 to 18.4) with the control drug, respectively [3].<br><br>**Summary of clinical SAFETY:**<br>Any-grade TRAEs occurred in 99% of pts in the tabentafusp arm vs. 91% in the control group. The most common any-grade TRAEswere cytokine-related AEs, such as pyrexia (76% vs. 3%), chills (47% vs. 3%), and hypotension (38% vs. 0%), and skin-related AEs, such as rash (83% vs. 24%), pruritus (69% vs. 21%), and erythema (23% vs. 1%). Treatment-related AEs of grade 3 or 4 were reported in 109 pts (44%) in the tebentafusp group and in 19 pts (17%) in the control group. No treatment-related deaths were reported in either group [3].<br><br>**Ongoing studies:**<br>● ***For the same indication:***No<br>● ***For other indications:***Yes<br>**Discontinued studies (for the same indication):**No<br><br>**References:**<br>1. https://www.ema.europa.eu/en/documents/smop-initial/chmp-summary-opinion-kimmtrak_en.pdf<br>2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761228s000lbl.pdf<br>3. https://pubmed.ncbi.nlm.nih.gov/34551229/<br>4. https://www.aiom.it/wp-content/uploads/2020/10/2020_LG_AIOM_Melanoma.pdf<br>5. https://ichgcp.net/it/clinical-trials-registry/NCT02626962<br>6. https://jnccn.org/view/journals/jnccn/16/5S/article-p646.xml<br>7. https://adisinsight.springer.com/drugs/800033036<br>8. https://clinicaltrials.gov/ct2/results?cond=Metastatic+Uveal+Melanoma&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= | **Cost of therapy:**<br>Not yet available.<br><br>**Epidemiology:**<br>In Italy, uveal melanoma has an incidence of about 0.7 per 100,000 person-years among females and 0.5among males [4]. Metastases in uveal melanoma appear in 6.5-35% of pts during the first decade [5].<br><br>**POSSIBLE PLACE IN THERAPY**<br>For distant metastasis, no single systemic therapy has proven to be effective for uveal melanoma. If approved, tebentafusp would be the first major pharmacological treatment [6].<br><br>**OTHER INDICATIONS IN DEVELOPMENT:** Yes (Malignant melanoma) [7].<br><br>**SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**-<br><br>**OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Yes (Nivolumab + Relatlimab, Binimetinib + Belinostat, Defactinib Hydrochloride + Raf/MEK Inhibitor VS-6766) [8].<br><br>*Service reorganization Y/N: Yes<br>*Possible off label use Y/N: Yes |

*Issued on: March 2022*