Kimmtrak® (tebentafusp-tebn) – New orphan drug approval

- On January 26, 2022, Immunocore announced the FDA approval of Kimmtrak (tebentafusp-tebn), for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma.

- Uveal melanoma is a rare and aggressive form of melanoma, which affects the eye. Although it is the most common primary intraocular malignancy in adults, the diagnosis is rare, and up to 50% of people with uveal melanoma will eventually develop metastatic disease.

- Kimmtrak is a novel bispecific protein comprised of a soluble T cell receptor fused to an anti-CD3 immune-effector function. Kimmtrak specifically targets gp100, a lineage antigen expressed in melanocytes and melanoma.

- The efficacy of Kimmtrak was established in IMCgp100-202, a randomized, open-label study in 378 patients with metastatic uveal melanoma. Patients were randomized to receive Kimmtrak or investigator's choice of Keytruda® (pembrolizumab), Yervoy® (ipilimumab), or dacarbazine. The major outcome was overall survival (OS). Additional efficacy outcomes were progression- free survival (PFS) and objective response rate (ORR).

    - Median OS was 21.7 months for Kimmtrak vs. 16 months for investigator's choice (hazard ratio [HR] 0.51, 95% CI: 0.37, 0.71; $p < 0.0001$).
    - Median PFS was 3.3 months for Kimmtrak vs. 2.9 months for investigator's choice (HR 0.73, 95% CI: 0.58, 0.94; $p = 0.0139$).
    - ORR was 9.1% (95% CI: 5.9, 13.4) and 4.8% (95% CI: 1.8, 10.1) for Kimmtrak and investigator's choice, respectively.

- Kimmtrak carries a boxed warning for cytokine release syndrome (CRS).

- Additional warnings and precautions for Kimmtrak include skin reactions, elevated liver enzymes, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 30%) with Kimmtrak use were CRS, rash, pyrexia, pruritus, fatigue, nausea, chills, abdominal pain, edema, hypotension, dry skin, headache, and vomiting. The most common laboratory abnormalities (≥ 50%) were decreased lymphocyte count, increased creatinine, increased glucose, increased aspartate aminotransferase, increased alanine aminotransferase, decreased hemoglobin, and decreased phosphate.

- The recommended intravenous dose of Kimmtrak is 20 mcg on day 1, 30 mcg on day 8, 68 mcg on day 15, and 68 mcg once every week thereafter. Treatment should continue until unacceptable toxicity or disease progression occur.

    - Patients should be selected for treatment based on a positive HLA-A*02:01 genotyping test. An FDA-approved test for the detection of HLA-A*02:01 genotyping is not currently available.

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- Immunocore plans to launch Kimmtrak within weeks. Kimmtrak will be available as a 100 mcg/0.5 mL single-dose vial.