## Penpulimab-kcqx – New orphan drug approval

- On April 24, 2025, Akeso announced the FDA approval of penpulimab-kcqx:
    - **In combination with either cisplatin or carboplatin and gemcitabine, for the first-line treatment of adults with recurrent or metastatic non-keratinizing nasopharyngeal carcinoma (NPC)**
    - **As a single agent, for the treatment of adults with metastatic nonkeratinizing NPC and disease progression on or after platinum-based chemotherapy and at least one other prior line of therapy.**

- Penpulimab-kcqx is a programmed death receptor-1 (PD-1)-blocking antibody.

- The efficacy of penpulimab-kcqx for first-line treatment of recurrent or metastatic NPC was established in a randomized, double-blind study in a total of 291 patients. Patients were randomized to receive either: penpulimab-kcqx in combination with either cisplatin or carboplatin and gemcitabine, every 3 weeks, for up to 6 cycles, followed by single-agent penpulimab-kcqx every 3 weeks until disease progression or unacceptable toxicity or a maximum of 24 months; or placebo in combination with either cisplatin or carboplatin and gemcitabine, every 3 weeks for up to 6 cycles, followed by single-agent placebo every 3 weeks until disease progression or unacceptable toxicity or a maximum of 24 months. The major outcome measure was progression-free survival (PFS). The key secondary outcome measure was overall survival (OS).
    - Median PFS was 9.6 months in the penpulimab-kcqx arm vs. 7.0 months in the placebo arm (hazard ratio 0.45, 95% CI: 0.33, 0.62; $p < 0.0001$).
    - OS results were not mature with 70% of pre-specified OS events observed in the overall population.

- The efficacy of single-agent penpulimab-kcqx for treatment of recurrent metastatic nonkeratinizing NPC was established in an open-label, single-arm study in 125 patients. The major outcome measures were objective response rate (ORR) and duration of response (DOR).
    - **The ORR was 28%** (95% CI: 20, 37).
    - **The median DOR was not reached** (95% CI: 9.2, not estimable).

- Warnings and precautions for penpulimab-kcqx include severe and fatal immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic hematopoietic stem cell transplantation, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with penpulimab-kcqx in combination with either cisplatin or carboplatin and gemcitabine were nausea, vomiting, hypothyroidism, constipation, decreased appetite, decreased weight, cough, COVID-19 infection, fatigue, rash, and pyrexia.

- The most common adverse reactions (≥ 20%) with penpulimab-kcqx as a single-agent were anemia and hypothyroidism.

- For first-line treatment of recurrent or metastatic NPC, the recommended dosage of penpulimab-kcqx is 200 mg administered as an intravenous infusion over 60 minutes every 3 weeks until disease progression or unacceptable toxicity, for a maximum of 24 months. Refer to the drug label for cisplatin or carboplatin and gemcitabine dosing.

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- For recurrent metastatic nonkeratinizing NPC, the recommended dosage of penpulimab-kcqx is 200 mg administered as an intravenous infusion over 60 minutes every 2 weeks until disease progression or unacceptable toxicity, for a maximum of 24 months.

- Akeso's launch plans for penpulimab-kcqx are pending. Penpulimab-kcqx will be available as a 100 mg/10 mL (10 mg/mL) solution in a single-dose vial.

Optum