Zynyz® (retifanlimab-dlwr) – New indication

- On May 15, 2025, Incyte announced the FDA approval of Zynyz (retifanlimab-dlwr):
    - **In combination with carboplatin and paclitaxel, for the first-line treatment of adult patients with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC)**
    - **As a single agent, for the treatment of adult patients with locally recurrent or metastatic SCAC with disease progression on or intolerance to platinum-based chemotherapy.**

- Zynyz is also approved via accelerated approval for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC).

- The approval of Zynyz for the new indication was based on POD1UM-303/InterAACT 2, a randomized, double-blind study in 308 patients with chemotherapy-naïve inoperable locally recurrent or metastatic SCAC. Patients were randomized to receive either Zynyz or placebo, in combination with carboplatin and paclitaxel. The major outcomes were progression-free survival (PFS) and overall survival (OS). Additional outcome measures included objective response rate (ORR) and duration of response (DOR).
    - Median PFS was 9.3 months in the Zynyz arm vs. 7.4 months in the placebo arm (hazard ratio [HR] 0.63, 95% CI: 0.47, 0.84; p = 0.0006).
    - **Median OS was 29.2 months in the Zynyz arm vs. 23 months in the placebo arm** (HR 0.70, 95% CI: 0.49, 1.01). OS results were not statistically significant at this interim analysis.
    - The ORR was 56% (95% CI: 48, 64) in the Zynyz arm vs. 44% (95% CI: 36, 62) in the placebo arm.
    - The median DOR was 14.0 months (95% CI: 8.6, 22.2) in the Zynyz arm vs. 7.2 months (95% CI: 5.6, 9.3) in the placebo arm.

- The efficacy of Zynyz for the new indication was also evaluated in POD1UM-202, an open-label, single-arm study in 94 patients with locally recurrent or metastatic SCAC who progressed on or were intolerant of platinum-based chemotherapy. The major outcomes were ORR and DOR.
    - **The ORR was 14%** (95% CI: 8, 23).
    - **The median DOR was 9.5 months** (95% CI: 4.4, not evaluable).

- The most common adverse reactions (≥ 20%) with Zynyz use, in combination with carboplatin and paclitaxel (for SCAC) were fatigue, peripheral neuropathy, nausea, alopecia, diarrhea, musculoskeletal pain, constipation, hemorrhage, rash, vomiting, decreased appetite, pruritis, and abdominal pain.

- The most common adverse reactions (≥ 10%) with Zynyz use as a single agent (for SCAC) were fatigue, musculoskeletal pain, diarrhea, non-urinary tract infections, perineal pain, hemorrhage, urinary tract infection, rash, nausea, decreased appetite, constipation, abdominal pain, dyspnea, pyrexia, vomiting, cough, pruritus, hypothyroidism, headache, and decreased weight.

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- The recommended dose of Zynyz is **500 mg intravenously every 4 weeks**. The treatment duration is until disease progression, unacceptable toxicity, or up to 12 months (when used in combination therapy) or up to 24 months (when used as monotherapy).