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In Brief: Retifanlimab *(Zynyz)* for Merkel Cell Carcinoma

IN BRIEF

Retifanlimab *(Zynyz)* for Merkel Cell Carcinoma

Retifanlimab-dlwr (*Zynyz* – Incyte), a programmed death receptor-1 (PD-1) blocking antibody, has received accelerated approval from the FDA for treatment of metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) in adults. Accelerated approval of the drug was based on the response rate and duration of response. Retifanlimab is the third drug to be approved in the US for treatment of MCC; pembrolizumab *(Keytruda)*, a PD-1 blocking antibody, is approved for the same indication as retifanlimab in patients ≥12 years old and avelumab *(Bavencio)*, a programmed death ligand-1 (PD-L1) blocking antibody, is approved for treatment of metastatic MCC in patients ≥12 years old.

Pronunciation Key

Retifanlimab-dlwr: re" ti fan' li mab *Zynyz*: zye' niz

The four-letter suffix -dlwr has no pronunciation or meaning; such suffixes are added to biologic drugs to distinguish reference products from their biosimilars.

MCC — MCC is a rare, aggressive neuroendocrine carcinoma of the skin. It is more common in men, particularly elderly, fair-skinned men with chronic sun exposure.[1]

MECHANISM OF ACTION — Binding of PD-L1 and PD-L2 to PD-1 on T cells suppresses T-cell proliferation and cytokine production. Retifanlimab binds to PD-1 on T cells, blocking its interaction with PD-L1 and PD-L2 and restoring T cell antitumor immune responses.

CLINICAL STUDIES — FDA approval of retifanlimab was based on the results of a single-arm trial (PODIUM-201) in 65 patients with metastatic or recurrent locally advanced MCC who had not received prior systemic therapy for advanced disease. Patients received retifanlimab 500 mg IV once every 4 weeks for up to 2 years. At the time of the primary efficacy analysis, about 42% of patients had discontinued treatment. The objective response rate was 46.2%, of which 12.3% were complete responses.[2] About 76% of patients who achieved a response had a response of ≥6 months and 62% had a response of ≥12 months.

ADVERSE EFFECTS — Retifanlimab can cause fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea. Infusion-related reactions and severe and fatal immune-mediated reactions, including pneumonitis, colitis, hepatitis, endocrinopathies, and nephritis with renal dysfunction, can occur. Liver enzyme levels, serum creatinine levels, and thyroid function should be assessed before starting treatment and periodically during treatment. Potentially fatal complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody.

PREGNANCY AND LACTATION — Inhibition of the PD-1/PD-L1 pathway can result in immune-mediated rejection of the developing fetus and fetal death. Women of reproductive potential should use effective contraception during treatment with retifanlimab and for 4 months after the last dose. Women should not breastfeed during treatment with retifanlimab and for 4 months after the last dose.

DOSAGE, ADMINISTRATION, AND COST — *Zynyz* is supplied in 500 mg/20 mL single-dose vials. The recommended dosage is 500 mg administered intravenously over 30 minutes every 4 weeks until disease progression or unacceptable toxicity occurs or for up to 24 months. The label contains dosage adjustments that should be made if adverse effects occur. The wholesale acquisition cost (WAC) for one 500-mg dose of *Zynyz* is $14,454.[3] ■

1. E Dellambra et al. Merkel cell carcinoma. Biomedicines 2021; 9:718.
2. G Grignani et al. 545 A phase 2 study of retifanlimab in patients with advanced or metastatic merkel cell carcinoma (MCC) (POD1UM-201). J ImmunoTher Cancer 2021; 9(Suppl 2):A574.
3. Approximate WAC or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. November 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.