

# The Medical Letter<sup>®</sup>

## on Drugs and Therapeutics

Volume 65

Published online April 17, 2023

Online  
Article

### IN THIS ISSUE

In Brief: In Brief: Retifanimab (Zynyz) for Merkel Cell Carcinoma

## Important Copyright Message

### FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying, or any distribution of this material without permission to a nonsubscriber is prohibited.

Sharing a password with a nonsubscriber or otherwise making the contents of this site available to third parties is prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)  
or call customer service at: 800-211-2769

# The Medical Letter<sup>®</sup>

## on Drugs and Therapeutics

Volume 65

Published online April 17, 2023

Online  
Article

### IN THIS ISSUE

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  $\geq 12$  years old and avelumab (*Bavencio*), a programmed death ligand-1 (PD-L1) blocking antibody, is approved for treatment of metastatic MCC in patients  $\geq 12$  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.<sup>1</sup>

**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.<sup>2</sup> About 76% of patients who achieved a response had a response of  $\geq 6$  months and 62% had a response of  $\geq 12$  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 cost of Zynyz is not yet available. ■

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.

**PRESIDENT:** Mark Abramowicz, M.D.; **VICE PRESIDENT, EDITOR IN CHIEF:** Jean-Marie Pflomm, Pharm.D.; **ASSOCIATE EDITORS:** Susan M. Daron, Pharm.D., Amy Faucard, MLS, Michael P. Viscusi, Pharm.D. **CONSULTING EDITORS:** Joanna Esterow, PA-C, Mordechai Sacks, DMSc, PA-C, Brinda M. Shah, Pharm.D., F. Peter Swanson, M.D.

**CONTRIBUTING EDITORS:** Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons; Ericka L. Crouse, Pharm.D., B.C.P.P., C.G.P., F.A.S.H.P., F.A.S.C.P., Virginia Commonwealth University; Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School; Eric J. Epstein, M.D., Albert Einstein College of Medicine; David N. Juurlink, BPhm, M.D., Ph.D., Sunnybrook Health Sciences Centre; Richard B. Kim, M.D., University of Western Ontario; Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine; Dan M. Roden, M.D., Vanderbilt University School of Medicine; Esperance A.K. Schaefer, M.D., M.P.H., Harvard Medical School; Neal H. Steigbigel, M.D., New York University School of Medicine; Arthur M. F. Yee, M.D., Ph.D., F.A.C.R., Weill Medical College of Cornell University

**MANAGING EDITOR AND DIRECTOR OF CONTENT OPERATIONS:** Susie Wong; **EDITORIAL ASSISTANT:** Karrie Ferrara

**FULFILLMENT AND SYSTEMS MANAGER:** Cristine Romatowski; **EXECUTIVE DIRECTOR OF SALES:** Elaine Reaney-Tomaselli  
**EXECUTIVE DIRECTOR OF MARKETING AND COMMUNICATIONS:** Joanne F. Valentino; **INTERIM PUBLISHER:** Jean-Marie Pflomm, Pharm.D.

Founded in 1959 by Arthur Kallet and Harold Aaron, M.D.

**Copyright and Disclaimer:** The Medical Letter, Inc. is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter, Inc. does not sell advertising or receive any commercial support. No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The Medical Letter, Inc. does not warrant that all the material in this publication is accurate and complete in every respect. The Medical Letter, Inc. and its editors shall not be held responsible for any damage resulting from any error, inaccuracy, or omission.

#### Subscription Services

#### Address:

The Medical Letter, Inc.  
 145 Huguenot St. Ste. 312  
 New Rochelle, NY 10801-7537  
[www.medicalletter.org](http://www.medicalletter.org)

#### Customer Service:

Call: 800-211-2769 or 914-235-0500  
 Fax: 914-632-1733  
 E-mail: [custserv@medicalletter.org](mailto:custserv@medicalletter.org)

#### Permissions:

To reproduce any portion of this issue,  
 please e-mail your request to:  
[permissions@medicalletter.org](mailto:permissions@medicalletter.org)

#### Subscriptions (US):

1 year - \$159; 2 years - \$298;  
 3 years - \$398. \$65 per year  
 for students, interns, residents,  
 and fellows in the US and Canada.  
 Reprints - \$45 per issue or article

#### Site License Inquiries:

E-mail: [SubQuote@medicalletter.org](mailto:SubQuote@medicalletter.org)  
 Call: 800-211-2769  
 Special rates available for bulk  
 subscriptions.