ZYNYZ® (retifanlimab-dlwr)

Prescribing Information and Data Review in MCC

MSL-RET-US-0033 06/25

Notice

- Some information contained in this presentation may not be included in the approved Prescribing Information for ZYNYZ (retifanlimab-dlwr). This presentation is not intended to offer recommendations for any administration, indication, dosage, or other use for ZYNYZ in a manner inconsistent with the approved Prescribing Information

Indication and Usage

- ZYNYZ is a programmed death receptor-1 (PD-1)-blocking antibody indicated:
  - Squamous Cell Carcinoma of the Anal Canal (SCAC)
    - In combination with carboplatin and paclitaxel for the first-line treatment of adult patients with inoperable locally recurrent or metastatic 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
  - Merkel Cell Carcinoma (MCC)
    - For the treatment of adult patients with metastatic or recurrent locally advanced MCC
      - This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials

- **Please see the Full Prescribing Information, including Warnings & Precautions, and Medication Guide for ZYNYZ**

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ZYNYZ (retifanlimab-dlwr). Prescribing Information. Incyte Corporation; May 2025.

Prescribing Information

- Indication, Dosing, and Administration
- Dosage Modifications for Adverse Reactions
- Clinical Data Review
- Safety Overview
- Warnings & Precautions

Indication, Dosing, and Administration

Indication and Recommended Dosing and Administration in MCC

Indication

Retifanlimab-dlwr is indicated for the treatment of adult patients with metastatic or recurrent locally advanced MCC. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials

Recommended Dosing and Administration

Administer as an intravenous infusion after dilution, over 30 minutes, as recommended

Indication	Recommended Dosage	Duration of Treatment
Monotherapy		
Adult patients with metastatic or recurrent locally advanced MCC	500 mg every 4 weeks	Until disease progression, unacceptable toxicity, or up to 24 months

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Dosage Modifications for Adverse Reactions

Dosage Modifications for Adverse Reactions

- No dose reduction of retifanlimab-dlwr is recommended. In general, withhold retifanlimab-dlwr for severe (Grade 3) immune-mediated adverse reactions
- Permanently discontinue retifanlimab-dlwr for life threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids

Select for dosage modifications for adverse reactions that require management different from these general guidelines

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Clinical Data Review

POD1UM-201

POD1UM-201: Study Design[1-3]

Study Design: Phase 2, open-label, single-arm study (ClinicalTrials.gov, NCT03599713) evaluating the safety, tolerability, and pharmacokinetics of retifanlimab-dlwr in adult patients with advanced/metastatic MCC

N=107 (enrollment closed, study ongoing)

Key Eligibility Criteria:
- Patients ≥18 years old
- MCC with distant metastatic disease or recurrent, advanced locoregional disease not amenable to surgery or radiation
- ECOG PS 0 or 1
- HIV-positive patients eligible: CD4+ count ≥300/μL, undetectable viral load, and receiving HAART

Retifanlimab-dlwr 500 mg IV q4w[a]

Treatment for up to 2 years in 28-day cycles

No premedication required

Primary endpoint
- ORR (per RECIST v1.1, determined by ICR)

Secondary objectives
- DOR, DCR, PFS, OS, safety, PK

Exploratory objectives
- Biomarkers, immunogenicity, efficacy per immune-related response criteria, HRQOL

- A protocol amendment limited the study population to chemotherapy-naïve patients owing to changes in the standard of care for first-line treatment of MCC
- The predefined primary analysis in POD1UM-201 was ORR by ICR (RECIST v1.1) on chemotherapy-naïve patients, based on the protocol amendment

[a] Whereas retifanlimab was administered as an infusion over 60 min in this study, the recommended dosing is a 30-min infusion based on data from the POD1UM-203 study.[4]

DCR, disease control rate; DOR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; HAART, highly active antiviral therapy; HIV, human immunodeficiency virus; HRQOL, health-related quality of life; ICR, independent central review; iv, intravenous; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

1. Grignani G, et al. SITC 2021. Poster P545. 2. Grignani G, et al. ASCO 2025. Poster 9536. 3. ClinicalTrials.gov. Accessed June 2025. Available at: https://clinicaltrials.gov/study/NCT03599713. 3. ZYNYZ (retifanlimab-dlwr). Prescribing Information. Incyte Corporation; May 2025.

POD1UM-201: Baseline Demographics and Characteristics

65 patients were evaluated in the POD1UM-201 clinical study

Demographics

- **Median age:** 71 (44-90) years
  - ≥75: 37%
- **Sex:** Male: 65%
- **Race:**
  - White: 78%
  - Unknown/not reported: 20%
  - Asian: 2%

Characteristics

- **ECOG PS:**
  - Score of 0: 74%
  - Score of 1: 26%
- **HIV status:**
  - Negative: 98%
- **Prior surgery:** 72%
- **Prior radiotherapy:** 38%
- **Metastatic disease at BL:** 88%
- **Merkel Cell Polyomavirus**
  - Positive: 71%
  - Negative: 23%
  - Equivocal: 2%
  - Missing: 5%

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POD1UM-201: Efficacy Results

Endpoint	N=65
Objective Response Rate (95% CI)	52% (40, 65)
Complete responses, n (%)	12 (18)
Partial responses, n (%)	22 (34)
Duration of Response	**N=34**
Range, months	1.1 to 24.9+
Patients with DOR ≥ 6 months, n (%)	26 (76)
Patients with DOR ≥ 12 months, n (%)	21 (62)

Tumor response assessments were performed every 8 weeks for the first year of therapy and 12 weeks thereafter

+ denotes ongoing response.

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Safety Overview

POD1UM-201

POD1UM-201: Safety Overview

- Serious adverse reactions occurred in 22% of patients receiving retifanlimab-dlwr
- The most frequent serious adverse reactions (≥2% of patients) were:
  - Fatigue
  - Arrythmia
  - Pneumonitis
- Retifanlimab-dlwr was permanently discontinued in 11% of patients due to an adverse reaction which included asthenia, atrial fibrillation, concomitant disease progression of chronic lymphocytic leukemia, demyelinating polyneuropathy, eosinophilic fasciitis, increased transaminases, infusion-related reaction, lung disorder, pancreatitis, polyarthritis, and radiculopathy (1 patient each)
- Dosage interruptions due to an adverse reaction occurred in 25% of patients who received retifanlimab-dlwr
  - Adverse reactions that resulted in dosage interruptions in ≥ 2% of patients were increased transaminases, increased lipase, increased amylase, pneumonitis, and pyrexia
- The most common (≥10%) adverse reactions were fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea

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Adverse Reactions Occurring in ≥10% of Patients with Metastatic or Recurrent Locally Advanced MCC

Adverse Reaction	Retifanlimab-dlwr (N=105)	
	All Grades (%)	Grade 3-4 (%)
General disorders and administration site conditions		
Fatigue[a]	28	1
Pyrexia	10	0
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain[b]	22	2.9
Skin and subcutaneous tissue disorders		
Pruritis	18	0
Rash[c]	11	1
Gastrointestinal disorders		
Diarrhea	15	0
Nausea	10	0

Graded according to NCI CTCAE v5.0.

[a] Includes fatigue and asthenia. [b] Includes arthralgia, back pain, bone pain, pain in extremity, neck pain, and myalgia. [c] Includes rash, dermatitis, dermatitis bullous, rash erythematous, rash maculo-papular, rash papular, and rash pruritic.

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Laboratory Abnormalities that Worsened from BL to Grade 3 or 4 in ≥1% of Patients with Metastatic or Recurrent Locally Advanced MCC

Adverse Reaction	Retifanlimab-dlwr (N=105)	
	All Grades (%)[a]	Grade 3-4 (%)[a]
Hematology		
Decreased hemoglobin	38	1.1
Decreased lymphocytes	29	10
Decreased neutrophils	13	3.3
Decreased leukocytes	12	1.1
Chemistry		
Increased lipase	30	3.4
Decreased sodium	23	3.3
Increased AST	23	2.2
Increased ALT	21	3.3
Increased alkaline phosphatase	20	1.1
Increased amylase	19	1.2
Decrease potassium	9	1.1
Increased calcium	8	1.1

Graded according to NCI CTCAE v5.0.
BL, baseline.
[a] The denominator used to calculate the rate varied from 86 to 92 based on the number of patients with a BL value and at least one post-treatment value.
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Warnings & Precautions

Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions

- Retifanlimab-dlwr is a monoclonal antibody that belongs to a class of drugs that binds to either the programmed death receptor-1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response with the potential for breaking of peripheral tolerance and induction of immune-mediated adverse reactions. Important immune mediated adverse reactions listed under Warnings and Precautions may not be inclusive of all possible severe and fatal immune-mediated reactions
- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1–blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1–blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1–blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously
- Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1–blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

- Withhold or permanently discontinue retifanlimab-dlwr depending on severity. In general, if retifanlimab-dlwr requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids
- Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below

Immune-Mediated Pneumonitis

- Retifanlimab-dlwr can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation
- Immune-mediated pneumonitis occurred in 3% (13/440) of patients receiving retifanlimab-dlwr, including 1 (0.2%) patient with fatal pneumonitis, Grade 3 (0.9%), and Grade 2 (1.4%). Pneumonitis led to permanent discontinuation of retifanlimab-dlwr in 1 patient and withholding of retifanlimab-dlwr in 0.9% of patients
- Systemic corticosteroids were required in 77% (10/13) of patients with pneumonitis. Pneumonitis resolved in 10 of the 13 patients. Of the 4 patients in whom retifanlimab-dlwr was withheld for pneumonitis, 3 reinitiated retifanlimab-dlwr after symptom improvement; of these, 1 had recurrence of pneumonitis

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Colitis

- Retifanlimab-dlwr can cause immune-mediated colitis. Cytomegalovirus infection/reactivation have occurred in patients with corticosteroid-refractory immune-mediated colitis treated with PD 1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies
- *Retifanlimab-dlwr as a Single Agent*: Immune-mediated colitis occurred in 1.6% (7/440) of patients receiving retifanlimab-dlwr, including Grade 4 (0.2%), Grade 3 (0.2%), and Grade 2 (0.7%). Colitis led to permanent discontinuation of retifanlimab-dlwr in 1 patient and withholding of retifanlimab-dlwr in 0.9% of patients. Systemic corticosteroids were required in 71% (5/7) of patients. Colitis resolved in 4 of the 7 patients. Of the 4 patients in whom retifanlimab-dlwr was withheld for colitis, 1 reinitiated retifanlimab-dlwr after symptom improvement; this patient did not have recurrence of colitis
- *Retifanlimab-dlwr in Combination with Carboplatin and Paclitaxel*: Immune-mediated colitis occurred in 10% (16/154) of patients receiving retifanlimab-dlwr in combination with carboplatin and paclitaxel, including Grade 4 (0.6%), Grade 3 (2.6%), and Grade 2 (3.2%). Colitis led to permanent discontinuation of retifanlimab-dlwr in 2 patients and withholding of retifanlimab-dlwr in 2 patients. Systemic corticosteroids were required in 94% (15/16) of patients. Colitis resolved in 15 of the 16 patients. Of the 2 patients in whom retifanlimab-dlwr was withheld for colitis, both reinitiated retifanlimab-dlwr after symptom improvement; neither patient had a recurrence of colitis

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Hepatitis

- Retifanlimab-dlwr can cause immune-mediated hepatitis.
- Immune-mediated hepatitis occurred in 3% (13/440) of patients receiving retifanlimab-dlwr, including Grade 4 (0.2%), Grade 3 (2.3%), and Grade 2 (0.5%). Hepatitis led to permanent discontinuation of retifanlimab-dlwr in 1.4% of patients and withholding of retifanlimab-dlwr in 0.9% of patients.
- Systemic corticosteroids were required in 85% (11/13) of patients. Hepatitis resolved in 6 of the 13 patients. Of the 4 patients in whom retifanlimab-dlwr was withheld for hepatitis, 2 reinitiated retifanlimab-dlwr after symptom improvement; of these, 1 had recurrence of hepatitis

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

- Retifanlimab-dlwr can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment per institutional guidelines, including hormone replacement as clinically indicated. Withhold or permanently discontinue retifanlimab-dlwr depending on severity
- *Retifanlimab-dlwr as a Single Agent*: Adrenal insufficiency occurred in 0.7% (3/440) of patients receiving retifanlimab-dlwr, including Grade 3 (0.5%) and Grade 2 (0.2%). Adrenal insufficiency did not lead to permanent discontinuation of retifanlimab-dlwr. retifanlimab-dlwr was withheld for 1 patient with adrenal insufficiency. All patients required systemic corticosteroids. Adrenal insufficiency resolved in 1 of the 3 patients

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Endocrinopathies (cont)

Adrenal Insufficiency (cont)

- *Retifanlimab-dlwr in Combination with Carboplatin and Paclitaxel*: Adrenal insufficiency occurred in 5.8% (9/154) of patients receiving retifanlimab-dlwr in combination with carboplatin and paclitaxel, including Grade 3 and Grade 2 (1.9% each). Adrenal insufficiency led to permanent discontinuation of retifanlimab-dlwr in 1 patient and withholding of retifanlimab-dlwr in 3 patients. All patients required systemic corticosteroids. Adrenal insufficiency resolved in 4 of the 9 patients

Hypophysitis

- Retifanlimab-dlwr can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue retifanlimab-dlwr depending on severity
- Hypophysitis occurred in 0.5% (2/440, both Grade 2) of patients receiving retifanlimab-dlwr. No patients discontinued or withheld retifanlimab-dlwr due to hypophysitis. All patients required systemic steroids. Hypophysitis resolved in 1 of the 2 patients

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Endocrinopathies (cont)

Thyroid Disorders

- Retifanlimab-dlwr can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue retifanlimab-dlwr depending on
- Thyroiditis occurred in 0.7% (3/440, all Grade 1) of patients receiving retifanlimab-dlwr. No patients discontinued or withheld retifanlimab-dlwr due to thyroiditis. Thyroiditis resolved in 1 of the 3 patients

Hypothyroidism

- Hypothyroidism occurred in 10% (42/440) of patients receiving retifanlimab-dlwr, including Grade 2 (4.8%). No patients discontinued retifanlimab-dlwr due to hypothyroidism. Hypothyroidism led to withholding of retifanlimab-dlwr in 0.5% of patients. Systemic corticosteroids were required for 1 patient and 79% (33/42) of patients received endocrine therapy

Hyperthyroidism

- Hyperthyroidism occurred in 6% (24/440) of patients receiving retifanlimab-dlwr, including Grade 2 (2.5%). No patients discontinued retifanlimab-dlwr due to hyperthyroidism. Hyperthyroidism led to withholding of retifanlimab-dlwr in 1 patient. Systemic corticosteroids were required for 13% (3/24) of patients and 46% (11/24) of patients received endocrine therapy

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Endocrinopathies (cont)

Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis

- Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold retifanlimab-dlwr depending on severity
- Type 1 diabetes mellitus occurred in 0.2% (1/440) of patients receiving retifanlimab-dlwr, including Grade 3 (0.2%) adverse reactions. Type 1 diabetes mellitus led to withholding of retifanlimab-dlwr in 1 patient. This event led to retifanlimab-dlwr being withheld and did not lead to permanent discontinuation of retifanlimab-dlwr. The patient received insulin

Immune-Mediated Nephritis with Renal Dysfunction

- Retifanlimab-dlwr can cause immune-mediated nephritis
- Immune-mediated nephritis occurred in 1.6% (7/440) of patients receiving retifanlimab-dlwr, including Grade 4 (0.5%), Grade 3 (0.7%), and Grade 2 (0.5%). Nephritis led to permanent discontinuation of retifanlimab-dlwr in 0.9% of patients and withholding of retifanlimab-dlwr in 1 patient
- Systemic corticosteroids were required in 57% (4/7) of patients. Nephritis resolved in 3 of the 7 patients. The 1 patient in whom retifanlimab-dlwr was withheld for immune-mediated nephritis had retifanlimab-dlwr reinitiated after symptom improvement and did not have recurrence of immune mediated nephritis

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Immune-Mediated Dermatologic Adverse Reactions

- Retifanlimab-dlwr can cause immune-mediated rash or dermatitis. Bullous and exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1–blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue retifanlimab-dlwr depending on severity
- Immune-mediated skin reactions occurred in 8% (36/440) of patients receiving retifanlimab-dlwr, including Grade 3 (1.1%) and Grade 2 (7%). Immune mediated dermatologic adverse reactions led to permanent discontinuation of retifanlimab-dlwr in 1 patient and withholding of retifanlimab-dlwr in 2.3% of patients
- Systemic corticosteroids were required in 25% (9/36) of patients. Immune-mediated dermatologic adverse reactions resolved in 75% (27/36) of patients. Of the 10 patients in whom retifanlimab-dlwr was withheld for immune-mediated dermatologic adverse reactions, 7 reinitiated retifanlimab-dlwr after symptom improvement; of these, 1 had recurrence of immune-mediated dermatologic adverse reactions

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Warnings & Precautions

Severe and Fatal Immune-Mediated Adverse Reactions (cont)

Other Immune-Mediated Adverse Reactions

- The following clinically significant immune-mediated adverse reactions occurred at an incidence of < 1% in 440 patients who received retifanlimab-dlwr or were reported with the use of other PD-1/PD-L1–blocking antibodies, including severe or fatal cases
  - *Cardiac/vascular:* myocarditis, pericarditis, vasculitis
  - *Gastrointestinal:* pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis
  - *Musculoskeletal:* myositis/polymyositis, rhabdomyolysis (and associated sequelae, including renal failure), arthritis, polymyalgia rheumatica
  - *Neurological:* meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy
  - *Ocular:* uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss
  - *Endocrine:* hypoparathyroidism
  - *Other (Hematologic/Immune):* hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection, other transplant (including corneal graft) rejection

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Warnings & Precautions

Infusion-Related Reactions

- A severe infusion-related reaction (Grade 3) occurred in 4 (0.7%) of 594 patients receiving retifanlimab-dlwr. Monitor patients for signs and symptoms of infusion related reactions. Interrupt or slow the rate of infusion or permanently discontinue retifanlimab-dlwr based on severity of reaction. Consider premedication with an antipyretic and/or an antihistamine for patients who have had previous systemic reactions to infusions of therapeutic proteins

Complications of Allogeneic HSCT

- Fatal and other serious 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. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT
- Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT

Embryo-Fetal Toxicity

- Based on its mechanism of action, retifanlimab-dlwr can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus, resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with retifanlimab-dlwr and for 4 months after the last dose

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Recommended Dosage Modifications for Adverse Reactions (1 of 2)

BACK

Adverse Reaction	Severity[a]	Dosage Modifications
Immune-Mediated Adverse Reactions		
Pneumonitis	Grade 2	Withhold[b]
	Grade 3 or 4	Permanently discontinue
Colitis	Grade 2 or 3	Withhold[b]
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT >3 but no more than 8 times ULN ***or*** TBIL increases to >1.5 and up to 3 times ULN	Withhold[b]
	AST or ALT increases to >8 times ULN ***or*** TBIL >3 times ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver[c]	Baseline AST or ALT is >1 and up to 3 times ULN and increases >5 and up to 10 times ULN ***or*** Baseline AST or ALT is >3 and up to 5 times ULN and increases >8 and up to 10 times ULN	Withhold[b]
	AST or ALT increases to >10 times ULN ***or*** TBIL increases to >3 times ULN	Permanently discontinue

[a] Toxicity graded per National Cancer Institute CTCAE v5. [b] Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg/day (or equivalent) within 12 weeks of initiating steroids. [c] If AST and ALT are less than or equal to ULN at baseline in patients with liver involvement, withhold or permanently discontinue retifanlimab-dlwr based on recommendations for hepatitis with no liver involvement.
CTCAE, Common Terminology Criteria for Adverse Events; TBIL, total bilirubin; ULN, upper limit of normal.
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Recommended Dosage Modifications for Adverse Reactions (2 of 2)

BACK

Adverse Reaction	Severity[a]	Dosage Modifications
Immune-Mediated Adverse Reactions (cont'd)		
Endocrinopathies[b]	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[b]
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Grade 3 or suspected SJS, TEN, or DRESS	Withhold[c]
	Grade 4 or confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold[c]
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

[a] Toxicity graded per National Cancer Institute CTCAE v5. [b] Depending on clinical severity, consider withholding for Grade 2 endocrinopathy until symptom improvement with hormone replacement. Resume once acute symptoms have resolved. [c] Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg/day (or equivalent) within 12 weeks of initiating steroids.
DRESS, drug rash with eosinophilia and systemic symptoms; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.
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