

Retifanlimab-dlwr (Zynyz) in Combination with CARBOplatin + PACLitaxel for the First-Line Treatment of Inoperable Locally Recurrent or Metastatic Squamous Cell Carcinoma of the Anal Canal

Description:

- The purpose of this PQI is to review clinical considerations and general management of retifanlimab-dlwr in combination with chemotherapy for squamous cell carcinoma of the anal canal (SCAC).

Background:

- Retifanlimab is a programmed death receptor-1 (PD-1) antibody that blocks interaction with its ligands and potentiates T-cell activity.^{1,2}
- Retifanlimab in combination with CARBOplatin and PACLitaxel is indicated for the first-line treatment of adults with inoperable locally recurrent or metastatic SCAC based on data from the POD1UM-303 trial.^{3,4}
 - See prescribing information for additional indications.
- Most common adverse reactions occurring in $\geq 20\%$ in SCAC first-line therapy:¹
 - Fatigue, peripheral neuropathy, nausea, alopecia, diarrhea, musculoskeletal pain, constipation, hemorrhage, rash, vomiting, decreased appetite, pruritus, and abdominal pain
- Other warnings and precautions that warrant monitoring include:¹
 - Immune-mediated reactions (including pneumonitis, colitis, hepatitis, adrenal insufficiency, and dermatitis)
 - See prescribing information for additional immune-mediated reactions.
 - Infusion-related reactions
 - Complications of allogeneic hematopoietic stem cell transplantation (HSCT)
 - Embryo-fetal toxicity

PQI Process:

- Confirm squamous cell histology and assess patient's kidney function for CARBOplatin dosing.
- Verify dose and frequency:
 - Administer retifanlimab IV over 30 minutes via 0.2-5 micron in-line or add-on filter or 15 micron mesh in-line or add-on filter until disease progression, unacceptable toxicity, or up to 12 months.¹

Dosing	Frequency
Retifanlimab 500mg IV	every 4 weeks
Retifanlimab 375mg IV	every 3 weeks

- Administer retifanlimab in combination with CARBOplatin + PACLitaxel
 - Refer to the Prescribing Information for the agents administered in combination with retifanlimab for recommended dosing information and pre-medications, as appropriate.
- Administer retifanlimab prior to chemotherapy.⁴

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- Monitor labs and for immune-mediated adverse reactions
 - Per the retifanlimab prescribing information (PI):¹
 - Verify pregnancy status in females of reproductive potential prior to initiating retifanlimab.
 - Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.
 - Monitor for hyperglycemia or other signs and symptoms of diabetes and initiate treatment with insulin as clinically indicated.
 - Additional practical monitoring considerations:
The following may be considered based on patient-specific factors, clinical judgment, and institutional practice:
 - Obtain TSH at baseline and periodically during treatment to support thyroid function monitoring.
 - Obtain baseline cortisol, with repeat testing as clinically appropriate, to support ongoing monitoring for potential immune-mediated adrenal insufficiency.
 - Obtain CBC and CMP prior to each dose to support broader safety monitoring of the overall treatment regimen.
 - Perform repeat pregnancy testing during treatment in females of reproductive potential.
- Adverse reaction management¹
 - No dose reduction of retifanlimab is recommended.
 - Withhold or permanently discontinue retifanlimab based on the type and severity of the immune-mediated adverse reaction.
 - For immune-mediated adverse reactions requiring interruption or discontinuation of retifanlimab, administer systemic corticosteroid therapy (prednisone 1–2 mg/kg/day or equivalent) until improvement to Grade 1 or less, then taper over at least 1 month. Consider other systemic immunosuppressants if the reaction is not controlled with corticosteroid therapy.
 - Permanently discontinue for life-threatening Grade 4 or recurrent severe Grade 3 events that require systemic immunosuppressive treatment, or inability to reduce corticosteroid dose to ≤10mg of prednisone equivalent per day within 12 weeks.

Adverse Effect ¹	Management & Monitoring ¹
Pneumonitis	• Withhold for Grade 2 • Permanently discontinue for Grade 3-4
Colitis	• Withhold for Grade 2-3 • Permanently discontinue for Grade 4
Hepatitis with no tumor involvement of the liver	• Withhold for AST/ALT >3 to ≤8x ULN OR Tbili >1.5 to ≤3x ULN • Permanently discontinue AST/ALT >8x ULN • Tbili >3x ULN
Hepatitis with tumor involvement of the liver	• Withhold for baseline AST/ALT >1 to ≤3x ULN and increases >5 to ≤10x ULN • Withhold for baseline AST/ALT >3 to ≤5x ULN and increased >8 to ≤10x ULN • Permanently discontinue for AST/ALT >10x ULN • Permanently discontinue Tbili >3x ULN

Endocrinopathies	Withhold until clinically stable or permanently discontinue based on severity for Grade 3-4
Nephritis with renal dysfunction	- Withhold for Grade 2-3 increase in SCr - Permanently discontinue for Grade 4 increase in SCr
Exfoliative dermatologic conditions	- Withhold for Grade 3 or suspected Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), or drug rash with eosinophilia and systemic symptoms (DRESS) - Permanently discontinue for Grade 4 or confirmed SJS, TEN, or DRESS
Myocarditis	Permanently discontinue for Grade 2, 3, or 4
Neurological toxicities	- Withhold for Grade 2 - Permanently discontinue for Grade 3-4
Infusion-related reaction	- Interrupt or slow rate of infusion for Grade 1-2 - Permanently discontinue for Grade 3-4

Patient-Centered Activities:

- Provide [retifanlimab NCODA Patient Education Sheet](#).
- Provide appropriate anti-emetics for chemotherapy portion of regimen.
- Monitor patient for infusion-related reactions during the infusion.
- Advise women of reproductive potential to use effective contraception during treatment and for 4 months after the last dose of retifanlimab.
- Educate on common side effects and proactive symptom management.
 - [Fatigue](#)
 - [Nausea and Vomiting](#)
 - [Diarrhea](#)
 - Peripheral Neuropathy
- Report any new or worsening symptoms, such as changes in breathing, diarrhea, or rash.
 - Please see [Immune-Related Adverse Event \(irAE\) Management Tool – NCODA](#)

References:

1. ZYNYZ (retifanlimab-dlwr) [prescribing information]. Incyte Corporation; 2026.
2. Han Y, Liu D, Li L. PD-1/PD-L1 pathway: current researches in cancer. Am J Cancer Res. 2020;10(3):727-742.
3. US Food and Drug Administration. FDA approves retifanlimab-dlwr with carboplatin and paclitaxel and as a single agent for squamous cell carcinoma of the anal canal. Published May 15, 2025. Accessed August 7, 2026.
4. Rao S, Samalin-Scalzi E, Evesque L, et al. Survival outcomes in POD1UM-303/InterAACT-2: a phase III study of retifanlimab plus carboplatin-paclitaxel in first-line advanced squamous anal cancer. Ann Oncol. 2026;37(8):1157-1166. doi:10.1016/j.annonc.2026.04.016.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Antiemesis. Version 2.2026. Published June 24, 2026. Accessed August 7, 2026.