NCODA Positive Quality Interventions

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Tivozanib (Fotivda) for Relapsed or Refractory Advanced Renal Cell Carcinoma

Description:

- The purpose of this PQI is to review the clinical considerations around the use of tivozanib (Fotivda) for patients with relapsed or refractory advanced renal cell carcinoma.

Background:

- Tivozanib is a small molecule that inhibits the phosphorylation of vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, and VEGFR-3.[1,2]
- Tivozanib is FDA approved for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.[1]
- Most common adverse reactions (≥20%): fatigue, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis

PQI Process:

- Verify dosage: The recommended starting dose of tivozanib is 1.34 mg by mouth once daily, with or without food, for 21 days on treatment followed by 7 days off treatment for a 28-day cycle[1]
- Dose interruptions and/or dose reduction may be needed to manage adverse reactions (see below)
    - First and only dose reduction: tivozanib 0.89 mg daily by mouth once daily for 21 days on treatment followed by 7 days off treatment for a 28-day cycle[1]
- Dose reductions are recommended for patients with moderate hepatic impairment (Tbili >1.5-3 times ULN with any AST)
- Monitor thyroid levels at baseline and every 2-3 months
- Ensure blood pressure is controlled prior to initiation and monitor throughout treatment
- Closely monitor patients at increased risk for venous thromboembolic events
- Check pregnancy status in females of reproductive potential
- Review patient medication list for possible drug-drug interactions/allergies
    - Strong CYP3A4 inducer: avoid concomitant use
    - Contains RD&C Yellow No.5 (tartrazine)
- Hold for at least 24 days before elective surgery; do not administer for 2 weeks following major surgery

Dose Modifications for Adverse Reactions[1]

Adverse Reaction	Severity	Dose Modifications
Hypertension	Grade 3	• Hold for Grade 3 that persists despite optimal antihypertensive therapy • Resume at reduced dose when hypertension is controlled at less than or equal to Grade 2
	Grade 4 or Hypertensive Crisis	• Permanently discontinue
Cardiac Failure	Grade 3	• Hold until improves to Grade 0 to 1 or baseline • Resume at a reduced dose or discontinue depending on the severity and persistence of adverse reaction
	Grade 4	• Permanently discontinue
Thromboembolic Events	Any Grade	• Permanently discontinue
Hemorrhagic Events	Grade 3 or 4	• Permanently discontinue
Proteinuria	2 grams or greater proteinuria in 24 hours	• Hold until ≤ to 2 grams of proteinuria per 24 hours • Resume at a reduced dose • Permanently discontinue for nephrotic syndrome
Reverse Posterior Leukoencephalopathy Syndrome	Any Grade	• Permanently discontinue
Other Adverse Reactions	Persistent or intolerable Grade 2 or 3 adverse reaction Grade 4 laboratory abnormality	• Withhold until improves to Grade 0 to 1 or baseline • Resume at reduced dose
	Grade 4 adverse reaction	• Permanently discontinue

Dose Modifications and Timing of Adverse Events:[3]

Tivozanib-Emergent Adverse Event	Dose Modification Rate, %	Median Time to Onset, days (range)	Median Duration, days (range)
Hypertension	20	17 (11-35)	29 (7-66)
Diarrhea	18	58 (27-127)	15 (3-57)
Asthenia/Fatigue	24	29 (11-74)	90 (28-...)
Nausea/Vomiting	25	54 (14-107)	15 (3-71)
Rash	18	110 (39-294)	51 (14-...)
Hand-foot syndrome	14	40 (29-71)	62 (26-...)

Patient-Centered Activities:

- Provide Patient Education Sheet and review with patient

- Consider providing Treatment Support Kit (TSK)
- Instruct patient to monitor blood pressure at home and report any increases from baseline
- Ensure that the patient has access to loperamide to use as needed for diarrhea and to call the provider if loperamide does not control diarrhea
- Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment and for one month after the last dose
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Fotivda® (tivozanib) [prescribing information].
2. Eskens, Ferry ALM, et al. "Biologic and clinical activity of tivozanib (AV-951, KRN-951), a selective inhibitor of VEGF receptor-1,-2, and-3 tyrosine kinases, in a 4-week-on, 2-week-off schedule in patients with advanced solid tumors." Clinical Cancer Research 17.22 (2011): 7156-7163.
3. Zengin ZB, Pal SK, McDermott DF, et al. Temporal Characteristics of Adverse Events of Tivozanib and Sorafenib in Previously Treated Kidney Cancer. Clin Genitourin Cancer. 2022;20(6):553-557.