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Positive Quality Intervention: Capivasertib (Truqap™) Patient Management

Description: This document will help in the identification and management of patients taking capivasertib.

Background: Capivasertib is a kinase inhibitor indicated in combination with fulvestrant for the treatment of adult patients with HR positive, HER2 negative, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations following progression on at least one endocrine-based regimen in the metastatic setting or recurrence ≤ 12 months of completing adjuvant therapy.[1] In the phase III CAPItello-291 study, the median progression-free survival (mPFS) was 7.2 months in the capivasertib–fulvestrant group, as compared with 3.6 months in the placebo–fulvestrant group (hazard ratio (HR), 0.60; 95% confidence interval (CI), 0.51-0.71; P<0.001). In the AKT pathway–altered population, the mPFS was 7.3 months in the capivasertib–fulvestrant group, as compared with 3.1 months in the placebo–fulvestrant group (HR 0.50; 95% CI, 0.38-0.65; P<0.001). The most frequent adverse events of ≥ Grade 3 in patients receiving capivasertib–fulvestrant were rash (12.1% vs. 0.3%) and diarrhea (9.3% vs. 0.3%). Adverse events leading to discontinuation were reported in 13% of the patients receiving capivasertib and in 2.3% with placebo.[2]

PQI Process:[3]

- For pre- and peri-menopausal patients, a luteinizing hormone-releasing hormone (LHRH) agonist (according to current clinical practice standards) should be administered; for males, consider administering an LHRH agonist (according to current clinical practice standards)
- Dosage guidance: Evaluate fasting blood glucose, HbA1c and then optimize blood glucose prior to capivasertib initiation
- Table 1. Dosing considerations for Capivasertib[3]

Dosage form	Tablet, Oral – 160 mg, 200 mg
Usual starting dose	400 mg twice daily (~12 hours apart) for 4 consecutive days, followed by 3 days off (administer capivasertib on days 1 to 4 of each week); in combination with fulvestrant*; continue until disease progression or unacceptable toxicity
Dose adjustments (renal/hepatic)	Capivasertib has not been studied in patients with severe hepatic or renal impairment
Dose reductions for toxicity	400 mg BID □ 320 mg BID □ 200 mg BID □ permanently discontinue if unable to tolerate the final dose reduction

* Refer to the fulvestrant Full Prescribing Information for recommended fulvestrant dosing information

- Once medication delivery is scheduled, ensure complete counseling on administration, proper handling, storage, missed dose management, side effect information, and all other pertinent information
- Assess the patient's understanding of the regimen complexity and provide tools to assist with adherence
- Monitor for signs/symptoms of cutaneous adverse reactions, diarrhea, and hyperglycemia; monitor for adverse reactions in patients with moderate hepatic impairment
- Monitor adherence

- Monitoring parameters [1]
  - FBG prior to treatment, at least every two weeks during the first month and at least every month starting from the second month of treatment
  - HbA1C prior to treatment and every 3 months of treatment

Patient-Centered Activities:[3]

- Administer with or without food, approximately every 12 hours on scheduled days; swallow whole; do not chew, crush, or split tablets
- If a dose is missed within 4 hours of the scheduled time, administer the missed dose; if a dose is missed by more than 4 hours of the scheduled time, skip the dose and administer the next dose at its usual scheduled time
- If a dose is vomited, do not administer an additional dose; administer the next dose at usual scheduled time
- Avoid grapefruit, star fruit, pomegranate and Seville oranges products
- This medication is considered hazardous - counsel on appropriate precautions for handling, administration, and disposal
    - Wash hands before and after handling; caregivers should wear gloves while handling
    - Do not dispose of any medication in trash or flush down sink or toilet – contact pharmacist for disposal locations
- Store in the original bottle at room temperature
- Check blood glucose levels more frequently as medication can cause high blood sugar
- Significant drug interactions exist, requiring dose/frequency adjustment or avoidance – let healthcare team know of any new medications
- Side effects to monitor
    - Skin changes that include inflammation, redness, rash, hives, itching, discoloration, sun sensitivity
    - Decreased appetite, diarrhea, nausea, vomiting, mouth sores
    - Signs of urinary tract infection (fever, burning or pain when passing urine, lower stomach, or pelvic pain)
    - Signs of hyperglycemia (confusion, fatigue, flushing, fast breathing, unusual thirst or hunger, urinating more frequently)
    - Fatigue, headache
- Ensure patient has access to supportive medications such as loperamide, moisturizing cream and antihistamine treatment
- Consider providing a blood glucose meter to the patient
- MyTRUQAP Support Program– patients can enroll to receive helpful resources, emails, and a starter kit[4]
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Truqap (capivasertib) Prescribing Information.
2. Turner NC, et al. Capivasertib in Hormone Receptor–Positive Advanced Breast Cancer. *New England Journal of Medicine*. 2023;388(22):2058-2070. doi:https://doi.org/10.1056/nejmoa2214131.
3. Lexicomp. *Capivasertib (Lexi-Drugs).*
4. Truqap website. https://www.truqap.com/.

Supplemental Information:[3]

Capivasertib Dose Reduction Levels	
Dose level	**Capivasertib dose and schedule**
Initial (usual) dose	400 mg twice daily for 4 days, followed by 3 days off
First dose reduction	320 mg twice daily for 4 days, followed by 3 days off
Second dose reduction	200 mg twice daily for 4 days, followed by 3 days off
Permanently discontinue if unable to tolerate the second dose reduction.	

Recommended Capivasertib Dosage Modifications		
Adverse reaction	**Severity**	**Capivasertib dosage modification[a]**
Dermatologic toxicity: Cutaneous adverse reactions	Any	Early consultation with a dermatologist is recommended. May require corticosteroids (topical or systemic, depending on the severity) to manage.
	Grade 2	Withhold capivasertib until recovery to ≤ Grade 1. Resume capivasertib at the same dose. *Persistent or recurrent Grade 2 toxicity:* Reduce capivasertib by one dose level.
	Grade 3	Withhold capivasertib until recovery to ≤ Grade 1. *Resolution ≤28 days after interruption*: Resume capivasertib at the same dose. *Resolution >28 days after interruption*: Resume capivasertib at one lower dose level. *Recurrent Grade 3 toxicity:* Permanently discontinue capivasertib.
	Grade 4	Permanently discontinue capivasertib.
GI toxicity: Diarrhea	Any	May require antidiarrheal medications to manage symptoms. Advise patients to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea.
	Grade 2	Withhold capivasertib until recovery to ≤ Grade 1. *Resolution ≤28 days after interruption*: Resume capivasertib at the same or at one lower dose level as clinically indicated.

Recommended Capivasertib Dosage Modifications		
Adverse reaction	**Severity**	**Capivasertib dosage modification[a]**
		Resolution >28 days after interruption: Resume capivasertib at one lower dose level as clinically indicated. *Recurrence:* Reduce capivasertib by one dose level.
	Grade 3	Withhold capivasertib until recovery to ≤ Grade 1. *Resolution ≤28 days after interruption*: Resume capivasertib at the same or at one lower dose level as clinically indicated. *Resolution >28 days after interruption*: Permanently discontinue capivasertib.
	Grade 4	Permanently discontinue capivasertib.
Hyperglycemia	Any	Consider consultation with a health care practitioner with expertise in hyperglycemia management. Counsel patients on lifestyle modifications.
	FBG[b] > ULN to 160 mg/dL or FBG > ULN to 8.9 mmol/L or HbA_{1c} >7%	Consider initiation or intensification of oral antidiabetic therapy.
	FBG 161 to 250 mg/dL or FBG 9 to 13.9 mmol/L	Withhold capivasertib until FBG decreases to ≤160 mg/dL (or ≤8.9 mmol/L). *Resolution ≤28 days after interruption*: Resume capivasertib at the same dose. *Resolution >28 days after interruption*: Resume capivasertib at one lower dose level.
	FBG 251 to 500 mg/dL or FBG 14 to 27.8 mmol/L	Withhold capivasertib until FBG decreases to ≤160 mg/dL (or ≤8.9 mmol/L). *Resolution ≤28 days after interruption*: Resume capivasertib at one lower dose level. *Resolution >28 days after interruption*: Permanently discontinue capivasertib.
	FBG >500 mg/dL or FBG >27.8 mmol/L or Life-threatening hyperglycemia sequelae at any FBG level	*If FBG is ≤500 mg/dL (or ≤27.8 mmol/L) within 24 hours:* Follow the guidance in this table for the relevant FBG. *Life-threatening hyperglycemia sequelae or if FBG persists at ≥500 mg/dL after 24 hours:* Permanently discontinue capivasertib.
Other adverse reactions [see	Grade 2	Withhold capivasertib until recovery to ≤ Grade 1. Resume capivasertib at the same dose.

Recommended Capivasertib Dosage Modifications		
Adverse reaction	**Severity**	**Capivasertib dosage modification[a]**
Adverse Reactions (6.1) in Package Insert][1]	Grade 3	Withhold capivasertib until recovery to ≤ Grade 1. *Resolution ≤28 days after interruption*: Resume capivasertib at the same dose. *Resolution >28 days after interruption*: Resume capivasertib at one lower dose level.
	Grade 4	Permanently discontinue capivasertib.

a. No dose adjustments in fulvestrant were permitted in the CAPItello-291 trial. Refer to the fulvestrant Full Prescribing Information for recommended fulvestrant dosing information.

b. FBG = fasting blood glucose.