



Positive Quality Intervention: Management of Alpelisib (Piqray®) Induced Hyperglycemia

Description: This PQI is intended to address effective practices for the management of alpelisib induced hyperglycemia by focusing on a multidisciplinary approach.

Background: Alpelisib (in combination with fulvestrant) is indicated for the treatment of HR-positive, HER2-negative, PIK3CA-mutated, advanced or metastatic breast cancer in males and postmenopausal females following progression on or after an endocrine-based regimen. PIK3CA mutations are present in up to 40% of HR-positive, HER2-negative, primary and metastatic breast cancers. Hyperglycemia is an expected on-target effect of PI3K inhibition. The phase 3 SOLAR-1 trial evaluated the combination of alpelisib and fulvestrant versus fulvestrant alone in patients with HR-positive, PIK3CA-mutated, advanced breast cancer who had received prior endocrine therapy. Hyperglycemia was reported in 63.7% of patients treated with alpelisib including 33% with Grade 3 (FPG>250- 500 mg/dL) and 3.9% with Grade 4 (Fasting Blood Glucose (FBG) >500 mg/dL) events. Increases in fasting blood glucose and hemoglobin A1C were more pronounced in patients who were diabetic or prediabetic at baseline, with 83% and 74% of these patients experiencing hyperglycemia when treated with alpelisib, respectively.

PQI Process: Upon receipt of alpelisib prescription:

- Verify recommended starting dose for alpelisib in combination with fulvestrant: 300 mg (2x150 mg tabs) by mouth once daily with food
- Evaluate patient medical history of diabetes and other risk factors that may contribute to treatment induced hyperglycemia (high BMI, age, concurrent medications)
- Ensure baseline labs including HbA1C and FBG ⁶
 - Repeat weekly for two weeks, then monthly, and as needed
 - If blood glucose is elevated it is recommended to optimize blood glucose prior to initiation
 - If hyperglycemia develops, discuss initiation of metformin dosing with the provider as well as dose interruption and reductions (see supplemental information)

Patient Centered Activities:

- Provide [Oral Chemotherapy Education \(OCE\) sheet](#)
- Provide and discuss with the patient a Patient Pocket-size Card from the manufacturer. Patients can show this card to any health care provider involved in the care of this individual, for educational purposes (ex. primary care physician, endocrinologist, emergency room, hospitalist, dermatologist)
- Consider developing a dietitian-based recommendations/handout for patients with hyperglycemia^{3,4}
- Recommend a use of glucometer for patients who cannot travel to weekly lab appointments

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed the Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



Supplemental Information:

Metformin Dosing Guidance from SOLAR 1 Trial

1. Initiate metformin at 500 mg once a day with food
2. Increase to 500 mg twice a day if tolerated
3. Increase to 500 mg in am and 1000 mg in pm if tolerated
4. Increase to 1000 mg twice a day if needed and tolerated. Do not exceed 2000 mg per day

*Evaluate a patient for renal and hepatic impairment prior to the start of metformin

**In SOLAR-1, 87% of patients who developed hyperglycemia were initially started on metformin followed by insulin sensitizers and DPP-4 inhibitors, in accordance with ADA recommendation

Dose Modifications: Based on Monitoring of Fasting Plasma Glucose (FPG)

- Grade 1 (FPG > ULN – 160 mg/dL): No dose adjustment; Initiate metformin
- Grade 2 (FPG > 160 – 250 mg/dL): Intensify antidiabetic therapy. Reduce by 1 level if no resolution of FPG ≤ 160 within 21 Days
- Grade 3 (FPG > 250 – 500 mg/dL): Suspend alpelisib therapy. Intensify antidiabetic therapy and consider IV hydration and/or electrolyte replacement. Reduce by 1 level if no resolution of FPG ≤ 160 within 5 Days. Discontinue treatment if no resolution of FPG ≤ 160 within 21 Days
- Grade 4 (FPG > 500 mg/dL): Suspend alpelisib therapy. Intensify antidiabetic therapy and consider IV hydration and/or electrolyte replacement. If FPG decreases to ≤ 500 mg/dL after 24 hours, follow Grade 3 guidelines. If no resolution after 24 hours, discontinue therapy

Alpelisib Dose Adjustment Levels:

- Recommended starting dose: 300 mg (2x150) by mouth once daily with food
- If 300 mg reduce to 250 mg once daily with food
- If 250 mg reduce to 200 mg once daily with food

Proposed Enhancements in EMR Protocol for Alpelisib - Collaborate with your providers

1. When possible, add a baseline 7-day window in EMR regimen to alert the prescriber to schedule Fasting Blood Glucose and HbA1C tests
2. Consider providing the patient with the prescription for a home glucometer to be purchased through retail drug store. The clinic can arrange teaching of a patient and/or caregiver on the use of glucometer and strips. May utilize Telehealth services. **The new ICD-10 Code R09.65** was adopted in October of 2019 to cover Drug and Chemical induced diabetes mellitus with hyperglycemia (Ref. ICD10Data.com) (To note: Recommend prescribing generic glucometer and strips to ensure better insurance coverage)
3. Add a dietitian consult at the start of the treatment if service is available or supply the patient with Internally developed patient handout discussing “Diet for Hyperglycemia”
4. Add endocrinology referral note to alpelisib regimen which can be initiated at the point of need

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed the Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



Diet for Hyperglycemia

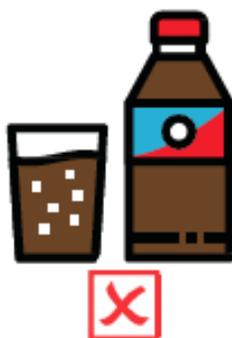
Hyperglycemia occurs when your blood sugar is high. High blood sugar can occur when you have diabetes, pre-diabetes or when you are taking certain medications like steroids or Alpelisib (PIQRAY®).

You may need to limit the amount of carbohydrates in your diet. At mealtimes, limit carbohydrates to 1 serving or ¼ of your plate.

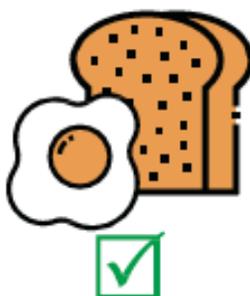
Breads, crackers and cereals	1 slice bread 4-6 small crackers ½ cup cooked cereal
Pasta, rice and grains	⅓ cup pasta or rice or quinoa
Starchy vegetables	¼ large baked potato (3 ounces) ½ cup corn or mashed potatoes
Beans and legumes	½ cup beans or peas
Milk, soymilk and yogurt	1 cup milk or soymilk ⅔ cup (6 ounces) unsweetened yogurt or sweetened with a sugar-free sweetener
Fruits and fruit juices	1 cup or 1 small piece of fresh fruit ½ cup canned fruit (no sugar added) 17 small grapes 1 cup melon or berries 2 tablespoons dried fruit (no added sugar)
Sweets (cakes, cookies, candies, ice cream, jam or jelly)	2-inch square cake (unfrosted) ½ cup ice cream or frozen yogurt 2 small cookies (⅔ ounce) 1 tablespoon syrup, jam, jelly, table sugar or honey

Serving Size

Other quick tips to keep your blood sugar down



- Do not drink sugar sweetened beverages, including juices. Drink sugar-free beverages such as water, unsweetened tea and unsweetened coffee.



- Always include a protein food when you eat carbohydrates for better blood sugar control. Foods that contain protein are meats (chicken, turkey, fish, beef and pork) that are not breaded or fried, eggs, nuts, nut butters (without sugar added), cheese and cottage cheese.



- Choose higher quality carbohydrates that contain fiber like beans, whole grain breads and pastas, brown rice, quinoa etc.

Authors: Amy Ladendecker, MS, RD, CSO, LDN & Dana Ingoglia, RD, CSO, LDN of Florida Cancer Specialists & Research Institute

References:

1. Academy of Nutrition and Dietetics. Carbohydrate Counting for People with Diabetes. [Leaflet]
2. Hopkins, B. D. et al. Suppression of insulin feedback enhances the efficacy of PI3K inhibitors. *Nature*. 2018; 560:499-



Reference:

1. PIQRAY® Package Insert. (n.d.). Retrieved April 07, 2021, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212526s000lbl.pdf.
2. Goncalves MD, Hopkins BD, Cantley LC. Phosphatidylinositol 3-Kinase, Growth Disorders, and cancer. N. ENgl J Med. 2018;379(21):2052-2062).
3. Academy of Nutrition and Dietetics. Carbohydrate Counting for People with Diabetes.
4. Link -<https://www.eatright.org/health/diseases-and-conditions/diabetes/carbohydrates-part-of-a-healthy-diabetes-diet>.
5. Nature. 2018 Aug;560(7719):499-503. doi: 10.1038/s41586-018-0343-4. Epub 2018 Jul 4. Suppression of insulin feedback enhances the efficacy of PI3K inhibitors.
6. Alpelisib Patient Management Guide for Clinicians. Novartis.
7. Fabrice A, et.al. Alpelisib for PIK3CA-Mutated, Hormone Receptor -positive Advance Breast Cancer. N. ENg. J Med. 2019; 380:1929-1940.
8. Schwartzberg L, Vidal G. Targeting PIK3CA Alterations in Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor-2-negative Advanced Breast Cancer.
9. Early intervention for and management of alpelisib (ALP)-induced hyperglycemia: case studies from the Phase III SOLAR trial. Mayer,I et al. Poster presentation.

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed the Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.