Written By: Collin Dempsey PharmD, BCPS
SUNY Upstate Medical University

Positive Quality Intervention: Androgen Deprivation Therapy with Relugolix (Orgovyx®)

Description: The purpose of this PQI is to provide awareness of an oral androgen deprivation therapy (ADT) option for patients undergoing treatment for prostate cancer and to discuss counseling, monitoring parameters, and patient management strategies to maximize medication adherence and improve patient outcomes.

Background: Relugolix is an orally available luteinizing hormone-releasing hormone (LHRH) antagonist. It is a nonpeptide gonadotropin-releasing hormone (GnRH) antagonist that competitively binds to pituitary GnRH receptors, decreasing luteinizing hormone (LH), follicle stimulating hormone (FSH), and subsequent testosterone levels.[1] Relugolix received FDA approval for the treatment of advanced prostate cancer as a result of the HERO trial, a phase III, randomized, prospective trial comparing relugolix (120 mg orally once daily) and leuprolide (22.5 mg injections every 3 months) for 48 weeks.[2] The primary endpoint, sustained castrate levels of testosterone (<50 ng/dL) through 48 weeks, showed noninferiority and superiority of relugolix over leuprolide (96.7% vs. 88.8%). In addition, reduction of testosterone to castrate levels was quicker, with 56% of relugolix patients achieving at day 4 vs. 0% in the leuprolide patients. Subgroup analysis revealed a higher percentage of patients with testosterone levels recovering to normal range (≥280 ng/dL) in the relugolix group 90 days after treatment discontinuation, 54% vs 3%. There were significantly less cardiovascular events in patients treated with relugolix compared to leuprolide (2.9% vs 6.2%). The most common adverse events were similar between the relugolix and the leuprolide group (any grade): Hot flash (54.3% vs 51.6%), fatigue (21.5% vs 18.5%), constipation (12.2% vs 9.7%), diarrhea (12.2% vs 6.8%) and arthralgia (12.1% vs 9.1%).
Trial data may be limited to certain patient populations as patients with curative-intent were not included. In addition, adherence to oral therapy during the 48 weeks was >99%, highlighting the importance of patient management programs to best achieve stated outcomes.[3]

PQI Process: Upon receipt of an order for relugolix

- Ensure patient is an appropriate candidate for relugolix based on indication
  - Relugolix may be preferred in history of needle phobia or cardiovascular disease
  - Assess for any history of poor medication adherence
  - Relugolix may be used with or without antiandrogen therapy
- Dose of relugolix: 360 mg (3x 120 mg tab) on day 1, followed by 120 mg by mouth once daily
- Increase dose accordingly if co-administered with
  - Strong CYP3A4/PGP inducers – consider alternative or increase to 240 mg/daily
  - PGP Inhibitors – take relugolix first and separate by at least 6 hours
  - Monitor for sustained suppression of testosterone
- Verify monitoring parameters
  - Monitor baseline PSA, testosterone, EKG, CMP, lipid panel and reassess periodically throughout duration of therapy
  - Caution for QTc prolongation with other agents known to prolong QTc
    - Consider EKG if clinically indicated

Patient-Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel to administer orally once daily, with first day loading dose
    - Take at approximately the same time each day with or without food
    - Missed dose can be taken within 12 hours of the next scheduled dose
    - Dose interruptions >7 days will require repeating the loading dose
- Proper sign/symptom monitoring
- Evaluate patient adherence at follow-up assessment and provide adherence aids as needed
    - Poor adherence may make injectable ADT preferential
- Provide symptom management techniques to minimize treatment toxicities
    - Assess need for clinical intervention/mediation with treatment team
    - Consider pharmacologic options for severe hot flashes not responding to lifestyle or dietary modifications
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Orgovyx (relugolix) [package insert].
2. Shore ND, Saad F, Cookson MS, et al. Oral relugolix for androgen deprivation therapy in advanced prostate cancer. N Engl J Med 2020;382:2187-2196.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN guidelines®) prostate cancer. All rights reserved.