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Positive Quality Intervention: Abiraterone acetate (Yonsa®) Patient Selection and Management

Description: The purpose of this PQI is to discuss the clinical considerations around the use of abiraterone acetate fine particle formulation (Yonsa®) to optimize outcomes for patients with metastatic castration-resistant prostate cancer (mCRPC).

Background: Abiraterone acetate (AA), a prodrug of abiraterone, functions as an inhibitor of CYP17 and androgen biosynthesis. By inhibiting CYP17, AA effectively suppresses androgen production in both extragonadal and testicular tissues, leading to a reduction in serum testosterone levels.[1]Abiraterone acetate fine-particle formulation (AAFP) was approved for the treatment of patients with mCRPC in 2018.[2] Micronization of abiraterone in AAFP increases bioavailability and improves absorption in the gastrointestinal tract allowing for more reliable dosing with lower amounts of the drug.[3] The fine particle formulation also allows for administration with or without food and doesn't necessitate taking the dose on an empty stomach.[2] The STAAR clinical trial, a randomized, open-label, phase II trial involving 53 men with mCRPC (mean age of 75.1 years; 54.7% with a Gleason score greater than 7), aimed to evaluate the therapeutic equivalence of once daily AAFP 500 mg combined with methylprednisolone compared to the original formulation of abiraterone acetate (OAA) 1000 mg once daily combined with prednisone.[4] The primary endpoint was comparison of combined average serum testosterone level in both groups on days 9 and 10 after starting treatment. The least squares mean difference in serum testosterone levels, measured on the planned days, between AAFP and OAA was 0.04 ng/dl (95% CI: −0.063 to 0.135) with no statistically significant difference between the groups (P = 0.4703). Average serum testosterone levels for each group were also measured on days 28, 56, and 84 and no statistically significant differences were observed. LS means difference in trough plasma concentrations between the treatment groups were not statistically significant at any time points. Additionally, a decrease of ≥ 50% in PSA level from baseline was seen in > 65% of patients in both groups consistently on days 28, 56, and 84. Adverse events (AE) of any grade occurred in 18 AAFP patients (75.0%) vs 24 OAA patients (82.8%), with most common AE in the AAFP group being infection (n = 7, 29.2% vs n = 6, 20.7% in the OAA group) and in the OAA group being musculoskeletal disorders (n = 11, 37.9% vs. n = 3, 12.5% in the AAFP group). [4] Common adverse events seen with AAFP are fatigue, joint swelling and discomfort, muscle discomfort, hypertension, edema, flushing, diarrhea, constipation, hypertriglyceridemia, increase in AST, hypokalemia, and hypophosphatemia.[2]

PQI Process:

Upon receipt of an order for abiraterone acetate:[2]

- Ensure patient is a candidate for treatment based on indication
  - AAFP formulation is only approved in patients w/ mCRPC
  - Review if patient was previously on abiraterone (AAFP is not interchangeable with other abiraterone acetate products)
  - Patient should be on a gonadotropin-releasing hormone analog concurrently or have received a bilateral orchiectomy
  - Not appropriate for patients with baseline severe hepatic impairment (Child-Pugh Class C)
- Ensure patient was also prescribed methylprednisolone 4 mg twice daily
- Recommended dosing: 500 mg (four 125 mg tablets) by mouth daily with methylprednisolone
- Dose adjustments for moderate hepatic impairment (Child-Pugh Class B): 125 mg (one tablet) by mouth daily with methylprednisolone
- Can be taken with or without food

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Table 1. Recommended Monitoring	
ALT, AST, bilirubin	• At baseline • Every 2 weeks for 3 months • Monthly thereafter
	If patient has moderate hepatic impairment • At baseline • Every week for the first month • Every 2 weeks for the following two months • Monthly thereafter
Potassium	• At baseline • Monthly
Signs/symptoms of adrenocorticoid insufficiency	• Monthly
Blood pressure and fluid retention	• At baseline • Monthly

Table 2. Dose Modifications While on Treatment	
ALT and/or AST > 5X ULN or Total Bilirubin > 3X ULN	• Hold treatment • Restart at lower dose (reduce by 125 mg or 1 tablet) when ALT/AST returns to baseline or ≤ to 2.5X ULN and total bilirubin ≤ to 1.5X ULN • Recommend monitoring serum transaminases and bilirubin every 2 weeks for 3 months and monthly thereafter
If hepatotoxicity recurs at reduced dose of 250 mg	**Discontinue treatment**
Dose Modifications While on Treatment w/ Baseline Hepatic Impairment	
ALT and/or AST > 5X ULN or Total Bilirubin > 3X ULN	**Discontinue treatment** **Do not re-treat patients**

Patient-Centered Activities:[2, 4]

- Provide Oral Chemotherapy Education (OCE) sheet
- Counsel patient to administer once a day with or without food
- Remind patient importance of taking methylprednisolone 4 mg twice daily while on therapy
- Review medication history (prescribed, OTC, herbal, and supplements) for drug interactions, especially CYP3A4
- Counsel on adverse events especially those highlighted in OCE sheet
- Discuss risk of hypoglycemia in diabetic patients on treatment for diabetes
- Recommend correction of hypokalemia and control of hypertension prior to start of treatment

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4. Stein CA, Levin R, Given R, et al. Randomized phase 2 therapeutic equivalence study of abiraterone acetate fine particle formulation vs. originator abiraterone acetate in patients with metastatic castration-resistant prostate cancer: The STAAR study. Urol Oncol. 2018;36(2):81.