For men with mCRPC who have progressed on ADT

LETS DO THIS

STRONG TOGETHER

ZYTIGA® & PREDNISONE

mCRPC = metastatic castration-resistant prostate cancer; ADT = androgen-deprivation therapy.

INDICATION
ZYTIGA® (abiraterone acetate) in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC).

IMPORTANT SAFETY INFORMATION
Contraindications—ZYTIGA® is not indicated for use in women. ZYTIGA® can cause fetal harm (Pregnancy Category X) when administered to a pregnant woman and is contraindicated in women who are or may become pregnant.

Please see full Important Safety Information on pages 6 and 7. Click here for full Prescribing Information.
In a SEER analysis, 62% of patients with metastatic prostate cancer were aged 71 years and older*1

SEER = Surveillance, Epidemiology, and End Results.
*1998-2003 data for age-adjusted stage IV prostate cancer from a SEER population-based cancer registry.

IMPORTANT SAFETY INFORMATION
Hypertension, Hypokalemia, and Fluid Retention Due to Mineralocorticoid Excess—Use with caution in patients with a history of cardiovascular disease or with medical conditions that might be compromised by increases in blood pressure, hypokalemia, or fluid retention. ZYTIGA® may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Safety has not been established in patients with LVEF <50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) because these patients were excluded from these randomized clinical trials. Control hypertension and correct hypokalemia before and during treatment. Monitor blood pressure, serum potassium, and symptoms of fluid retention at least monthly.

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In the final analysis of OS from the pivotal phase 3 study... 

**ZYTIGA® + prednisone** achieved a median OS of almost 3 years (34.7 months) after a median 4 years (49 months) of follow-up†‡

- **Co-primary end point**—4.4 months improvement in median OS: 34.7 months with ZYTIGA® + prednisone vs **30.3 months** with placebo + prednisone (active compound)§; HR=0.81; 95% CI: 0.70, 0.93; *P* = 0.0033

- **Co-primary end point**—rPFS: at the prespecified rPFS analysis, median not reached for ZYTIGA® + prednisone vs a median of 8.28 months for placebo + prednisone; HR=0.425; 95% CI: 0.347, 0.522; *P*<0.0001§¶

OS = overall survival; ITT = intent-to-treat; HR = hazard ratio; rPFS = radiographic progression-free survival.

*For the ITT population.

**Study Design:** ZYTIGA®, in combination with prednisone, was evaluated in a phase 3, randomized, double-blind, placebo-controlled, multicenter trial in patients with mCRPC who had not received prior chemotherapy (N=1,088). Patients were using a luteinizing hormone-releasing hormone (LHRH) agonist or were previously treated with orchiectomy. In the ZYTIGA® arm, patients received ZYTIGA® 1,000 mg orally once daily + prednisone 5 mg orally twice daily. In the placebo arm, patients received placebo orally once daily + prednisone 5 mg orally twice daily. Patient demographics were balanced between the treatment arms. The median age was 70 years. In this study, the co–primary efficacy end points were OS and rPFS. Select exclusion criteria included aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) ≥ 2.5X upper limit of normal (ULN), liver metastases, moderate or severe pain, opiate use for cancer pain, prior ketoconazole treatment for prostate cancer, a history of adrenal gland or pituitary disorders, and visceral organ metastases. Concurrent use of spironolactone was not allowed during the study period.

†At a prespecified final analysis for OS, 65% (354/546) of patients treated with ZYTIGA® + prednisone compared with 71% (387/542) of patients treated with placebo + prednisone had died.

§Prednisone, as a single agent, is not approved for the treatment of prostate cancer.

¶At the prespecified rPFS analysis, 150 (28%) of patients treated with ZYTIGA® + prednisone and 251 (46%) of patients treated with placebo + prednisone had radiographic progression.

49 MONTHS REPRESENTS ONE OF THE LONGEST MEDIAN FOLLOW-UP PERIODS AMONG STUDIES OF PATIENTS WITH mCRPC²

**IMPORTANT SAFETY INFORMATION**

**Adrenocortical Insufficiency (AI)**—AI was reported in patients receiving ZYTIGA® in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Please see full Important Safety Information on pages 6 and 7. Click here for full Prescribing Information.
Contraindicated in women who are or may become pregnant; Warnings and Precautions include Mineralocorticoid Excess, Adrenocortical Insufficiency, and Hepatotoxicity

The most common adverse reactions (≥10%) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection, and contusion

The most common laboratory abnormalities (>20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT, and hypokalemia

IMPORTANT SAFETY INFORMATION

Hepatotoxicity—In postmarketing experience, there have been ZYTIGA®-associated severe hepatic toxicities, including fulminant hepatitis, acute liver failure and deaths. Monitor liver function and modify, withhold, or discontinue ZYTIGA® dosing as recommended (see Prescribing Information for more information). Measure serum transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] and bilirubin levels prior to starting treatment with ZYTIGA®, every two weeks for the first three months of treatment, and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient’s baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA® treatment and closely monitor liver function. Re-treatment with ZYTIGA® at a reduced dose level may take place only after return of liver function tests to the patient’s baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

Permanently discontinue ZYTIGA® for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

Please see full Important Safety Information on pages 6 and 7. Click here for full Prescribing Information.
>70% OF MEDICARE PATIENTS are covered by a plan that requires prior failure with or intolerance to ZYTIGA® before they will authorize Xtandi® (enzalutamide)² 

**IMPORTANT SAFETY INFORMATION**

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**Important Safety Information**

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Hepatotoxicity (continued)
or bilirubin from the patient’s baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA® treatment and closely monitor liver function. Re-treatment with ZYTIGA® at a reduced dose level may take place only after return of liver function tests to the patient’s baseline or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN. Permanently discontinue ZYTIGA® for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

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Drug Interactions—Based on in vitro data, ZYTIGA® is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency only during the co-administration period [see Dosage and Administration (2.3)]. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA®. Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations—Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).
LET’S DO THIS WITH ZYTIGA® FIRST (ABIRATERONE ACETATE)

ZYTIGA® IN GERIATRIC PATIENTS
Of the total number of patients receiving ZYTIGA® in phase 3 trials, 73% of patients were aged 65 years and over and 30% were aged 75 years and over

- No overall differences in safety or effectiveness were observed between these elderly patients and younger patients
- Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out

IMPORTANT SAFETY INFORMATION
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For more information, please visit www.zytigahcp.com/geriatrics.