5-ARIs. The Gleason sum scores for the cancers were similar in the two groups.

The association of the higher incidence of higher Gleason score prostate cancer in men receiving 5-alpha-reductase inhibitors was first noted in 2003 for men receiving finasteride as part of the Prostate Cancer Prevention Trial (PCPT). This observational study with a 14-year follow-up does not show any excess high-grade cancer for men with benign prostatic hyperplasia (BPH) who received finasteride as part of therapy for BPH. These data may support the idea that the excess high Gleason score cancers occurring with 5-alpha-reductase inhibitors in randomized trials such as the PCPT may be caused by biases in the study design rather than clinically meaningful endpoints.

G. L. Andriole, Jr, MD

Abiraterone and Increased Survival in Metastatic Prostate Cancer
de Bono JS, for the COU-AA-301 Investigators (Inst of Cancer Res and Royal Marsden Hosp, Sutton, Surrey, UK; et al)


Background.—Biosynthesis of extragonadal androgen may contribute to the progression of castration-resistant prostate cancer. We evaluated whether abiraterone acetate, an inhibitor of androgen biosynthesis, prolongs overall survival among patients with metastatic castration-resistant prostate cancer who have received chemotherapy.

Methods.—We randomly assigned, in a 2:1 ratio, 1195 patients who had previously received docetaxel to receive 5 mg of prednisone twice daily with either 1000 mg of abiraterone acetate (797 patients) or placebo (398 patients). The primary end point was overall survival. The secondary end points included time to prostate-specific antigen (PSA) progression (elevation in the PSA level according to prespecified criteria), progression-free survival according to radiologic findings based on prespecified criteria, and the PSA response rate.

Results.—After a median follow-up of 12.8 months, overall survival was longer in the abiraterone acetate—prednisone group than in the placebo—prednisone group (14.8 months vs. 10.9 months; hazard ratio, 0.65; 95% confidence interval, 0.54 to 0.77; \( P < 0.001 \)). Data were unblinded at the interim analysis, since these results exceeded the preplanned criteria for study termination. All secondary end points, including time to PSA progression (10.2 vs. 6.6 months; \( P < 0.001 \)), progression-free survival (5.6 months vs. 3.6 months; \( P < 0.001 \)), and PSA response rate (29% vs. 6%, \( P < 0.001 \)), favored the treatment group. Mineralocorticoid-related adverse events, including fluid retention, hypertension, and hypokalemia, were more frequently reported in the abiraterone acetate—prednisone group than in the placebo—prednisone group.

Conclusions.—The inhibition of androgen biosynthesis by abiraterone acetate prolonged overall survival among patients with metastatic
castration-resistant prostate cancer who previously received chemotherapy. (Funded by Cougar Biotechnology; COU-AA-301 ClinicalTrials.gov number, NCT00638690.)

This much-anticipated study shows that inhibition of androgen biosynthesis by abiraterone acetate, which blocks cytochrome P450 c17 (CYP17), a critical enzyme in testosterone synthesis, improves survival of men with metastatic castrate-resistant prostate cancer who previously received docetaxel chemotherapy. The difference in survival between the placebo and treated groups was 14.8 months versus 10 months. Both treatment arms received prednisone because of abiraterone’s potential effect on inhibition of mineralocorticoid synthesis. As can be seen in Fig 2 in the original article, this effect was noted in virtually every subgroup. This will add to the armamentarium of the treatment for men with advanced prostate cancer.\(^1\) Hopefully, soon there will be other agents (alpha particles and selective androgen receptor inhibitors) that can also be applied to men with metastatic castrate-resistant prostate cancer.

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Reference


Safety and Immunological Efficacy of a DNA Vaccine Encoding Prostatic Acid Phosphatase in Patients With Stage D0 Prostate Cancer


*Purpose.*—Prostatic acid phosphatase (PAP) is a prostate tumor antigen. We have previously demonstrated that a DNA vaccine encoding PAP can elicit antigen-specific CD8+ T cells in rodents. We report here the results of a phase I/IIa trial conducted with a DNA vaccine encoding human PAP in patients with stage D0 prostate cancer.

*Patients and Methods.*—Twenty-two patients were treated in a dose-escalation trial with 100 μg, 500 μg, or 1,500 μg plasmid DNA, coadministered intradermally with 200 μg granulocyte-macrophage colony-stimulating factor as a vaccine adjuvant, six times at 14-day intervals. All patients were observed for 1 year after treatment.

*Results.*—No significant adverse events were observed. Three (14%) of 22 patients developed PAP-specific IFNγ-secreting CD8+ T-cells immediately after the treatment course, as determined by enzyme-linked immunospot. Nine (41%) of 22 patients developed PAP-specific CD4+ and/or CD8+ T-cell proliferation. Antibody responses to PAP were not detected. Overall, the prostate-specific antigen (PSA) doubling time was observed...