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Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy

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BACKGROUND

Enzalutamide (formerly called MDV3100) targets multiple steps in the androgen-receptor–signaling pathway, the major driver of prostate-cancer growth. We aimed to evaluate whether enzalutamide prolongs survival in men with castration-resistant prostate cancer after chemotherapy.

METHODS

In our phase 3, double-blind, placebo-controlled trial, we stratified 1199 men with castration-resistant prostate cancer after chemotherapy according to the Eastern Cooperative Oncology Group performance-status score and pain intensity. We randomly assigned them, in a 2:1 ratio, to receive oral enzalutamide at a dose of 160 mg per day (800 patients) or placebo (399 patients). The primary end point was overall survival.

RESULTS

The study was stopped after a planned interim analysis at the time of 520 deaths. The median overall survival was 18.4 months (95% confidence interval [CI], 17.3 to not yet reached) in the enzalutamide group versus 13.6 months (95% CI, 11.3 to 15.8) in the placebo group (hazard ratio for death in the enzalutamide group, 0.63; 95% CI, 0.53 to 0.75; P<0.001). The superiority of enzalutamide over placebo was shown with respect to all secondary end points: the proportion of patients with a reduction in the prostate-specific antigen (PSA) level by 50% or more (54% vs. 2%, P<0.001), the soft-tissue response rate (29% vs. 4%, P<0.001), the quality-of-life response rate (43% vs. 18%, P<0.001), the time to PSA progression (8.3 vs. 3.0 months; hazard ratio, 0.25; P<0.001), radiographic progression-free survival (8.3 vs. 2.9 months; hazard ratio, 0.40; P<0.001), and the time to the first skeletal-related event (16.7 vs. 13.3 months; hazard ratio, 0.69; P<0.001). Rates of fatigue, diarrhea, and hot flashes were higher in the enzalutamide group. Seizures were reported in five patients (0.6%) receiving enzalutamide.

CONCLUSIONS

Enzalutamide significantly prolonged the survival of men with metastatic castration-resistant prostate cancer after chemotherapy. (Funded by Medivation and Astellas Pharma Global Development; AFFIRM ClinicalTrials.gov number, NCT00974311.)

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SOURCE INFORMATION

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The AFFIRM (A Study Evaluating the Efficacy and Safety of the Investigational Drug MDV3100) investigators are listed in the Supplementary Appendix, available at NEJM.org.

APPENDIX

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