Enzalutamide in Men With Chemotherapy-Naïve Metastatic Castration-Resistant Prostate Cancer (mCRPC): Long-term Overall Survival and Safety Analyses of the Phase 3 PREVAIL Study

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BACKGROUND

• The oral androgen receptor inhibitor enzalutamide reduced the risk of death and radiographic progression versus placebo in the PREVAIL study, of patients with asymptomatic or minimally symptomatic chemotherapy-naïve castration-resistant prostate cancer (mCRPC).1

• The magnitude of prostate-specific antigen (PSA) decline at 3 months was strongly associated with improved clinical and patient reported outcomes in patients with mCRPC treated with enzalutamide in the PREVAIL study.1

• Overall survival (OS) benefit of enzalutamide in these patients was confirmed in an analysis of the PREVAIL study after an additional 9 months of follow-up.1

• A validated prognostic model incorporating variables routinely collected in PREVAIL patients with chemotherapy-naïve mCRPC treated with enzalutamide, identifying a subset of patients with widely different survival outcomes to help inform external validation, patient care, and clinical trial design.2

Here we evaluated long-term OS and safety in patients from the PREVAIL study with >5 years of follow-up.

METHODS

Study Design

• The PREVAIL study design is presented in Figure 1. PREVAIL was halted after a preplanned interim analysis revealed the superiority of enzalutamide over placebo.3-5 Eligible patients could cross over to enzalutamide (n = 234) in an open-label extension after >5 years of follow-up.2 These patients were included in the placebo group for the final analysis of OS after >5 years of follow-up.

Statistical Analyses

• This preplanned final OS analysis was performed in the intention-to-treat population.

• Comparisons were made between enzalutamide and placebo treatment arms.

• Hazard ratios (HRs) were based on Cox regression models with treatment as the only covariate.

RESULTS

Baseline Characteristics

1,171 men were randomized (1171 treated) to PREVAIL between September 2010 and September 2012.

• At the extended OS data cutoff (September 30, 2017), 455 patients (50% of the original enzalutamide arm and 43% of the placebo arm) had entered the open-label extension or were in long-term follow-up.

• Of these, 485 patients continued to receive enzalutamide in the open-label extension and 480 patients discontinued study drug but were monitored in the long-term follow-up.

• The enzalutamide treatment effect was generally consistent across all baseline disease-specific subgroups (Figure 3). In patients with liver metastasis at baseline, OS benefit was not observed with enzalutamide compared with placebo (HR = 1.12 ± 0.08) but there were relatively few patients in this subgroup with a wide CI.

• Overall survival (OS) of patients treated with enzalutamide (n = 845) was 73.5 ± 3.8 months, versus 62.7 ± 3.5 among patients treated with placebo (HR = 0.87 ± 0.05; P = 0.0001). A statistically significant OS benefit was observed across all patient subgroups (Table 1).

— The 5-year OS analysis (data cutoff December 20, 2017) 5 years after the last patient was randomized, revealed 1,382 deaths (enzalutamide arm, n = 688; placebo arm, n = 693).

— Survival probabilities at 2, 5, and 7 years for enzalutamide were 92.9%, 87.6%, and 81.9%, respectively

— At the 5-year OS analysis, enzalutamide reduced the risk of death by 17% (HR: 0.83; 95% confidence interval [CI], 0.75-0.92; P = 0.0001). At a median follow-up of 49 months, median OS was 35.5 months (95% CI, 33.5-33.6) in the enzalutamide arm versus 31.4 months (95% CI, 28.9-33.8) in the placebo arm.

— Although OS benefit was observed across all subsequent therapy subgroups, OS was 34.2 months with subsequent docetaxel (enzalutamide arm, n = 445) versus 25.4 months with subsequent abiraterone acetate (enzalutamide arm, n = 452) (HR = 0.73, 95% CI 0.61-0.88, P = 0.0008).

— Subsequent Therapy

• At the data cutoff, 67% of patients in the enzalutamide arm and 62% in the placebo arm had received ≥1 postbaseline antineoplastic therapy (Table 2).

• The most common subsequent therapy was docetaxel (enzalutamide arm, 55%; placebo arm, 46%). The following were also used: abiraterone acetate (30%; 20%), cabazitaxel (8%; 5%), or other therapies (17%; 15%).

• Enzalutamide OS benefit was observed across all patient subgroups studied, aside from the liver metastasis subgroup which had relatively few patients.

• The safety profile with enzalutamide was consistent with that reported previously.

CONCLUSIONS

• With >5 years of follow-up, enzalutamide continued to demonstrate benefit compared with placebo in OS for patients with asymptomatic or mildly symptomatic mCRPC despite crossover in the placebo arm and multiple subsequent therapies.

• Enzalutamide OS benefit was observed across all patient subgroups studied, aside from the liver metastasis subgroup which had relatively few patients.

• The safety profile with enzalutamide was consistent with that reported previously.

ACKNOWLEDGMENTS

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REFERENCES


