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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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Introduction & Objectives: PREVAIL was a phase 3 trial of enzalutamide vs placebo in asymptomatic or mildly symptomatic chemotherapy-naïve men with mCRPC. Overall survival (OS) was first evaluated after 784 (45.7%) deaths and median follow-up of 31 months. Here we report OS and safety after an additional 3 years of follow-up.

Materials & Methods: Men with chemotherapy-naïve mCRPC were randomized 1:1 to enzalutamide 160 mg/day or placebo. OS and radiographic progression-free survival were coprimary endpoints in PREVAIL, which was halted after a preplanned interim analysis revealed superiority with enzalutamide. Eligible placebo patients could crossover to enzalutamide (n=234) in an open-label extension; these patients were included in the placebo group for the final analysis of OS.

Results: 1717 men were randomized (1715 treated) to PREVAIL between September 2010 and September 2012. At the 5-year OS analysis reported here (data cutoff 30 September 2017; 5 years after the last patient was randomized) there were 1382 deaths (689 in the enzalutamide arm and 693 in the placebo arm). Survival probabilities at 2, 3, and 5 years favored enzalutamide (Table). Enzalutamide reduced the risk of death by 17% (HR, 0.83; 95% CI, 0.75-0.93; P=0.0008). Median OS was 35.5 months (95% CI, 33.5-38.0) in the enzalutamide arm vs 31.4 months (95% CI, 28.9-33.8) in the placebo arm, with a median follow-up time of 69 months. The treatment effect was consistent across all baseline disease specific subgroups. At the data cutoff, 70% of patients in the enzalutamide arm and 80% in the placebo arm had received ≥1 postbaseline antineoplastic therapy. The most common subsequent therapy was docetaxel (55% in the enzalutamide arm and 62% in the placebo arm), followed by abiraterone acetate (42% and 51%, respectively). Treatment-emergent adverse event (TEAE) was reported as the primary reason for discontinuation in 9.1% of patients in the enzalutamide arm and 6.0% in the placebo arm; 6.9% and 3.8% of patients had a TEAE that led to death. The most common (≥20%) AEs were fatigue (38.2% vs 26.1%), back pain (32.5% vs 22.4%), constipation (25.6% vs 17.4%), nausea (24.5% vs 22.7%), arthralgia (23.5% vs 16.2%), and decreased appetite (21.0% vs 16.6%) in the enzalutamide vs placebo arms, respectively.

	Enzalutamide 160 mg (n=872)	Placebo (n=845)
2-Year survival rate (95% CI)	71% (68%-74%)	62% (58%-65%)

3-Year survival rate (95% CI)	49% (46%-53%)	44% (40%-47%)
5-Year survival rate (95% CI)	26% (23%-29%)	21% (18%-24%)

Conclusions: With >5 years of follow-up, enzalutamide continued to demonstrate benefit vs placebo in OS in men with asymptomatic or mildly symptomatic mCRPC despite crossover in the placebo arm and multiple subsequent therapies. The safety profile was consistent with that reported previously.