

Phase III, randomized, double-blind, multicenter trial comparing orteronel (TAK-700) plus prednisone with placebo plus prednisone in patients with metastatic castration-resistant prostate cancer that has progressed during or after docetaxel-based therapy: ELM-PC 5.

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Abstract

PURPOSE:

Orteronel (TAK-700) is an investigational, nonsteroidal, reversible, selective 17,20-lyase inhibitor. This study examined orteronel in patients with metastatic castration-resistant prostate cancer that progressed after docetaxel therapy.

PATIENTS AND METHODS:

In our study, 1,099 men were randomly assigned in a 2:1 schedule to receive orteronel 400 mg plus prednisone 5 mg twice daily or placebo plus prednisone 5 mg twice daily, stratified by region (Europe, North America [NA], and non-Europe/NA) and Brief Pain Inventory-Short Form worst pain score. Primary end point was overall survival (OS). Key secondary end points (radiographic progression-free survival [rPFS], $\geq 50\%$ decrease of prostate-specific antigen [PSA50], and pain response at 12 weeks) were to undergo statistical testing only if the primary end point analysis was significant.

RESULTS:

The study was unblinded after crossing a prespecified OS futility boundary. The median OS was 17.0 months versus 15.2 months with orteronel-prednisone versus placebo-prednisone (hazard ratio [HR], 0.886; 95% CI, 0.739 to 1.062; $P = .190$). Improved rPFS was observed with orteronel-prednisone (median, 8.3 v 5.7 months; HR, 0.760; 95% CI, 0.653 to 0.885; $P < .001$). Orteronel-prednisone showed advantages over placebo-prednisone in PSA50 rate (25% v 10%, $P < .001$) and time to PSA progression (median, 5.5 v 2.9 months, $P < .001$) but not pain response rate (12% v 9%; $P = .128$). Adverse events (all grades) were generally more frequent with orteronel-prednisone, including nausea (42% v 26%), vomiting (36% v 17%), fatigue (29% v 23%), and increased amylase (14% v 2%).

CONCLUSION:

Our study did not meet the primary end point of OS. Longer rPFS and a higher PSA50 rate with orteronel-prednisone indicate antitumor activity.