Association of Survival Benefit With Docetaxel in Prostate Cancer and Total Number of Cycles Administered: A Post hoc Analysis of the Mainsail Study.


Abstract

IMPORTANCE: The optimal total number of docetaxel cycles in patients with metastatic castration resistant prostate cancer (mCPRC) has not been investigated yet. It is unknown whether it is beneficial for patients to continue treatment upon 6 cycles.

OBJECTIVE: To investigate whether the number of docetaxel cycles administered to patients deriving clinical benefit was an independent prognostic factor for overall survival (OS) in a post hoc analysis of the Mainsail trial.

DESIGN, SETTING, AND PARTICIPANTS: The Mainsail trial was a multinational randomized phase 3 study of 1059 patients with mCRPC receiving docetaxel, prednisone, and lenalidomide (DPL) or docetaxel, prednisone, and a placebo (DP). Study patients were treated until progressive disease or unacceptable adverse effects occurred. Median OS was found to be inferior in the DPL arm compared with the DP arm. As a result of increased toxic effects with the DPL combination, patients on DPL received fewer docetaxel cycles (median, 6) vs 8 cycles in the control group. As the dose intensity was comparable in both treatment arms, we investigated whether the number of docetaxel cycles administered to patients deriving clinical benefit on Mainsail was an independent prognostic factor for OS. We conducted primary univariate and multivariate analyses for the intention-to-treat population. Additional sensitivity analyses were done, excluding patients who stopped treatment for reasons of disease progression and those who received 4 or fewer cycles of docetaxel for other reasons, minimizing the effect of confounding factors.

MAIN OUTCOMES AND MEASURES: Total number of docetaxel cycles delivered as an independent factor for OS.

RESULTS: Overall, all 1059 patients from the Mainsail trial were included (mean [SD] age, 68.7 [7.89] years). Treatment with 8 or more cycles of docetaxel was associated with superior OS (hazard ratio [HR], 1.909; 95% CI, 1.660-2.194; P < .001), irrespective of lenalidomide treatment (HR, 1.060; 95% CI, 0.924-1.215; P = .41). Likewise, in the sensitivity analysis, patients who received a greater number of docetaxel cycles had superior OS; patients who received more than 10 cycles had a median OS of 33.0 months compared with 26.9 months in patients treated with 8 to 10 cycles; and patients who received 5 to 7 cycles had a median OS of 22.8 months (P < .001).
CONCLUSIONS AND RELEVANCE: These findings suggest that continuation of docetaxel chemotherapy contributes to the survival benefit. Prospective validation is warranted.

PMID: 27560549   DOI: 10.1001/jamaoncol.2016.3000

[PubMed - as supplied by publisher]