Adding Docetaxel to Androgen-Deprivation Therapy in Newly Diagnosed Metastatic Prostate Cancer

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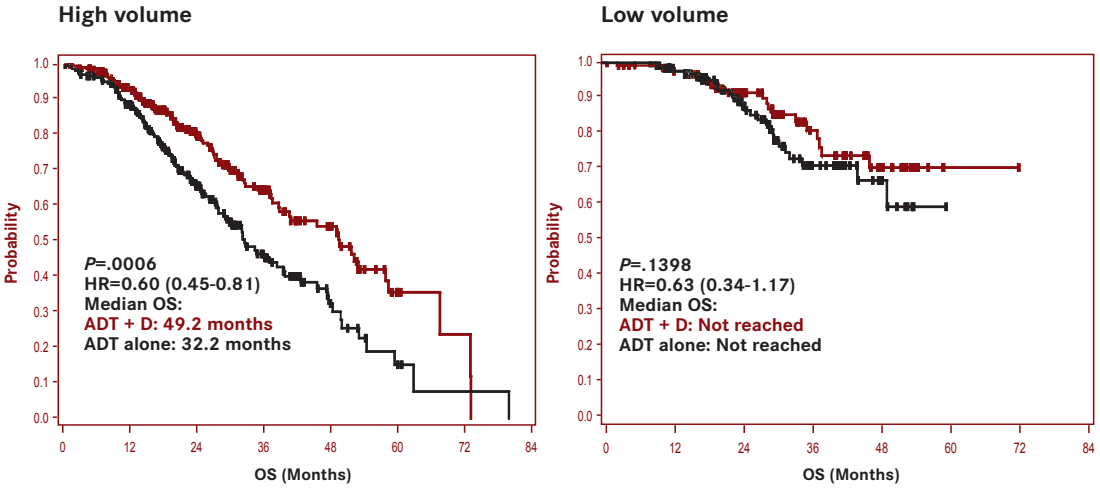
Adding docetaxel to androgen-deprivation therapy (ADT) improved survival in men with newly diagnosed, hormone-sensitive prostate cancer in the phase III, E3805 CHAART-ED study (ChemoHormonal Therapy versus Androgen Ablation Randomized Trial for Extensive Disease in Prostate Cancer). The results may represent the biggest advance in the treatment of metastatic prostate cancer since surgical castration.

The study was presented at the 2014 Annual Meeting of the American Society of Clinical Oncology (ASCO) and was led by the Eastern Cooperative Oncology Group and funded by the National Cancer Institute.

In the 8-year trial, 790 men with newly diagnosed metastatic prostate cancer were randomly assigned 1:1 to receive either ADT alone or ADT with docetaxel, dosed at 75mg/m^2 every 3 weeks for 6 cycles within 4 months of starting ADT. After the combination cohort completed 6 courses of docetaxel, all patients continued on ADT alone. Approximately two-thirds of patients had high-extent disease. The primary endpoint was overall survival (OS).

At a median follow-up of 29 months, median OS was 44 months in the ADT group versus 57.6 months in the ADT-

FIGURE. OS by Extent of Metastatic Disease at Start of ADT



In patients with high-volume metastatic disease, there is a 17-month improvement in median overall survival from 32.2 months to 49.2 months.
We projected 33 months in ADT-alone arm with collaboration of SWOG9346 team.

ADT, androgen-deprivation therapy; D, docetaxel; HR, hazard ratio; OS, overall survival.

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docetaxel group, or a 39% higher likelihood of survival in the combination arm at any time point during the study (hazard ratio 0.61, *P* = .0003).

Among 520 patients with high-volume disease (visceral metastases and/or 4 or more bone metastases), adding docetaxel to ADT improved median OS by 17 months (32.2 months in the ADT-only group vs 49.2 months in the combination group). The median OS in patients with low-volume disease has not yet been reached.

Combination therapy favored all subgroups. Patients were stratified according to age, volume of disease, bone and visceral metastases, race, Gleason score, prior local therapy, use of anti-androgen therapy beyond 30 days, and skeletal-related events.

Docetaxel also delayed disease progression. At 1 year, the percentage of patients with prostate-specific antigen (PSA) levels less than 0.2 ng/mL was 11.7% in the ADT group versus 22.7% in the combination group. The median time to clinical progression was 19.8 months in the ADT group versus 32.7 months in the combination group. The median time to castration-resistant prostate cancer (determined by a rise in PSA, new symptoms, or scan) was 14.7 months in the ADT group and 20.7 months in the combination group.

Adverse events in the combination group included neutropenic fever (4% grade 3, 2% grade 4), 1% grade 3 sensory neuropathy, and 1% grade 3 motor neuropathy. There was 1 death due to treatment in this group.

At this point in time, 6 cycles of docetaxel in addition to ADT (within 4 months of starting ADT) represents an appropriate option for men with metastatic prostate cancer commencing ADT who are suitable for docetaxel therapy. The benefit in patients with a high volume of metastases is clear and justifies the treatment burden. However, longer follow-up is required for patients with low-volume metastatic disease, and studies are needed in order to optimize the distinction between patients who benefit from upfront chemotherapy and those who don't.

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REFERENCE

Sweeney C, Chen Y-H, Carducci MA, et al. Impact on overall survival (OS) with chemohormonal therapy versus hormonal therapy for hormone-sensitive newly metastatic prostate cancer (mPRCa): An ECOG-led phase III randomized trial. *J Clin Oncol*. 2014;32(suppl; abstr LBA2).