Diethylstilbestrol (DES) retains activity and is a reasonable option in patients previously treated with docetaxel for castration-resistant prostate cancer

Docetaxel-based chemotherapy is currently the standard treatment for metastatic castration-resistant prostate cancer (CRPC). Two large randomized studies demonstrated that this treatment prolongs survival and also improves time-to-disease progression, pain control and prostate-specific antigen (PSA) response, as compared with mitoxantrone and prednisone [1, 2]. However, patients eventually experience cancer progression within several months and there is currently no established standard treatment after failure of front-line docetaxel-based chemotherapy. Many data indicate that CRPC continues to depend on androgen-receptor signaling even after failure of docetaxel-based chemotherapy [3, 4]. Evidence has also been provided that combining an estrogen-containing drug, estramustine, with chemotherapy may improve overall survival in patients with CRPC [5]. Diethylstilbestrol (DES) is a synthetic ethynil estrogen often used in CRPC as salvage therapy after several hormone manipulations [6]. The activity of DES in patients exhibiting progression after docetaxel-based chemotherapy has not previously been reported. We carried out an analysis to evaluate DES as salvage therapy after first-line docetaxel-based chemotherapy in patients with progressive CRPC. Twenty patients (median age 65.7 years) were treated with DES, given orally at an initial dose of 1 mg daily. None of these patients had received DES before docetaxel. The median duration of prior sensitivity to androgen deprivation therapy was 23 months (range 5–95 months). The median baseline serum PSA value was 45 ng/ml (range 4–680). A PSA response as defined as a PSA decline ≥30% and ≥50% was observed in five (25%) and three (15%) patients, respectively. Among the two patients who had progressive disease while receiving docetaxel, one had a 67% decline in serum PSA. Median progression-free survival was 3.7 months [95% confidence interval (CI) 2.7–4.7 months] and median overall survival was 20.7 months (95% CI 13.4–28.0 months). The cause of DES discontinuation was progressive cancer in all patients. Ten patients have received a preventive anticoagulation by low-dose aspirin. DES was well tolerated overall and only one thromboembolic complication was reported.

These results add to the compelling data indicating that CRPC is hormone sensitive in a significant proportion of cases, even when pretreated with docetaxel-based chemotherapy. Since there is no standard of care when progression occurs after docetaxel-based chemotherapy in patients with CRPC, DES appears as a reasonable option worth considering in this setting.

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