Androgen priming and chemotherapy in advanced prostate cancer: evaluation of determinants of clinical outcome.


Abstract
We conducted a randomized clinical trial in men with stage D2 prostate cancer to test whether androgen priming potentiates the efficacy of cytotoxic chemotherapy. Eighty-five men with progressive prostate cancer refractory to orchiectomy were treated continuously with aminoglutethimide and hydrocortisone to lower adrenal androgen secretion and were administered cyclic intravenous (IV) chemotherapy. The patients were randomized to receive either androgen priming or no additional treatment for three days before and on the day of chemotherapy. Median duration of follow-up was 43 months. Response rate (remission plus disease stabilization) was not significantly different between the stimulation and control arm when the analysis was restricted to evaluable patients (79% vs 73%, respectively) or when it was extended to all patients (46% vs 61%). Median duration of response was similar for the stimulation and control arm (9 and 10 months, respectively). Median survival was 10 months in the stimulation and 15 months in the control group (P = .0047). The androgen sensitivity of the tumors was supported by the greater toxicity in the stimulation arm associated with androgen administration. Factors found to be independently associated with improved clinical outcome included a high Karnofsky score and hematocrit, long duration of response to the initial castration, and normalization of an elevated serum acid phosphatase on treatment. We conclude that in this group of patients with advanced disease, androgen priming does not potentiate the efficacy of chemotherapy and is actually associated with a worse outcome. Furthermore, our data emphasize the heterogeneity of biologic behavior of prostate cancer.

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