

# Docetaxel, Prednisone and Mitoxantrone in Patients with Hormone-refractory Prostate Cancer

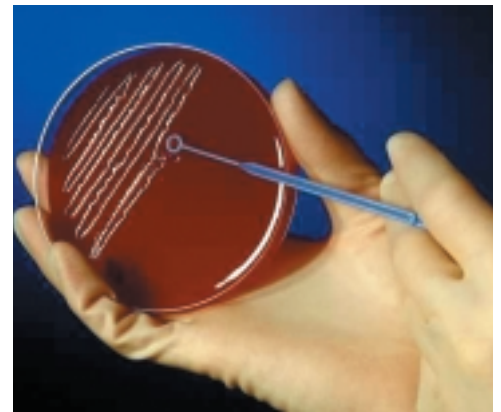
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## Background

Docetaxel-based regimens have shown encouraging anti-tumor activity in phase II trials in HRPC. This study compared two schedules of D+P to MTZ+P, an accepted standard in HRPC.

## Methods

Patients (pts) with histologically-proven metastatic HRPC, testosterone <50 ng/ml, adequate hematologic and organ function, clinical and/or biochemical (PSA) progression, and no antiandrogens within 6 wk, were stratified by pain and KPS and randomized to daily prednisone (5mg po bid) plus D (**ARM A**-75mg/m<sup>2</sup> q3wk x 10 cycles; **ARM B**-30mg/m<sup>2</sup>/wk x 5 of 6 wk x 5 cycles) or MTZ (**ARM C**-12mg/m<sup>2</sup> q3wk x 10 cycles). Primary endpoint was survival; secondary endpoints included PSA response (≥50% decrease for at least 4 wk), pain response, and toxicity. A modified Bonferroni method was used to adjust for multiple comparisons.



## Results

1,006 pts were randomized. Median follow up was 20.7 mo. Pts in all arms had similar baseline characteristics. Planned treatment was delivered to 98%, 96% and 99% pts in A, B, and C, respectively. Grade 3/4 toxicities (% pts A, B, C): overall (45.8%, 43.0%, 34.6%), including bone pain (7.8%, 7.3%, 9.9%), infection (5.7%, 5.5%, 4.2%), fatigue (4.5%, 5.5%, 5.1%), and diarrhea (2.1%, 4.8%, 1.2%). The most common laboratory grade 3/4 toxicity was neutropenia (32.0%, 1.5%, 21.7%).

## Conclusions

The D q3wk +P schedule improved overall survival and increased pain response and PSA response vs MTZ+P. It was well tolerated, but with more grade 3/4 neutropenia than MTZ+P. This is the first phase III study to show a significant survival benefit in HRPC. (Supported by Aventis.) **OA**

### Efficacy Analysis (intent-to-treat; p-values and hazard ratios vs Arm C):

	Arm A (D q3wk+P) N=335	Arm B (D qwk+P) N=334	Arms A+B N=669	Arm C (MTZ+P) N=337
<b>Median Survival</b>	18.9 mo	17.4 mo	18.3 mo	16.5 mo
<b>Hazard Ratio (95% CI)</b>	0.76 (0.62-0.94) p=0.0094	0.91 (0.75-1.11) p=0.36	0.83 (0.70-0.99) p=0.04	NA
<b>Pain Response*</b>	35% p=0.011	31% p=0.08	33% p=0.015	22%
<b>PSA Response**</b>	45% p=0.0005	48% p<0.0001	47% p<0.0001	32%

\* Pts with baseline present pain intensity ≥ 2 (A/153; B/154; C/157).

\*\* Pts with baseline PSA ≥ 20ng/ml (Arm/pts: A/291; B/282; C/300).