Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

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BACKGROUND

Apalutamide is an inhibitor of the ligand-binding domain of the androgen receptor. Whether the addition of apalutamide to androgen-deprivation therapy (ADT) would prolong radiographic progression-free survival and overall survival as compared with placebo plus ADT among patients with metastatic, castration-sensitive prostate cancer has not been determined.

METHODS

In this double-blind, phase 3 trial, we randomly assigned patients with metastatic, castration-sensitive prostate cancer to receive apalutamide (240 mg per day) or placebo, added to ADT. Previous treatment for localised disease and previous docetaxel therapy were allowed. The primary end points were radiographic progression-free survival and overall survival.

RESULTS

A total of 525 patients were assigned to receive apalutamide plus ADT and 527 to receive placebo plus ADT. The median age was 68 years. A total of 16.4% of the patients had undergone prostatectomy or had received radiotherapy for localised disease, and 10.7% had received previous docetaxel therapy; 62.7% had high-volume disease, and 37.3% had low-volume disease. At the first interim analysis, with a median of 22.7 months of follow-up, the percentage of patients with radiographic progression-free survival at 24 months was 68.2% in the apalutamide group and 47.5% in the placebo group (hazard ratio for radiographic progression or death, 0.48; 95% confidence interval [CI], 0.39 to 0.60; P<0.001). Overall survival at 24 months was also greater with apalutamide than with placebo (82.4% in the apalutamide group vs. 73.5% in the placebo group; hazard ratio for death, 0.67; 95% CI, 0.51 to 0.89; P = 0.005). The frequency of grade 3 or 4 adverse events was 42.2% in the apalutamide group and 40.8% in the placebo group; rash was more common in the apalutamide group.

CONCLUSIONS

In this trial involving patients with metastatic, castration-sensitive prostate cancer, overall survival and radiographic progression-free survival were significantly longer with the addition of apalutamide to ADT than with placebo plus ADT, and the side-effect profile did not differ substantially between the two groups.