Prostate

Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer

Matthew R Smith 1, Maha Hussain 1, Fred Saad 1, Karim Fizazi 1, Cora N Sternberg 1, E David Crawford 1, Evgeny Kopyltsov 1, Chandler H Park 1, Boris Alekseev et al, ARASENS Trial Investigators

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BACKGROUND

Darolutamide is a potent androgen-receptor inhibitor that has been associated with increased overall survival among patients with nonmetastatic, castration-resistant prostate cancer. Whether a combination of darolutamide, androgen-deprivation therapy, and docetaxel would increase survival among patients with metastatic, hormone-sensitive prostate cancer is unknown.

METHODS

In this international, phase III trial, we randomly assigned patients with metastatic, hormone-sensitive prostate cancer in a 1:1 ratio to receive darolutamide (at a dose of 600 mg [two 300-mg tablets] twice daily) or matching placebo, both in combination with androgen-deprivation therapy and docetaxel. The primary end point was overall survival.

RESULTS

The primary analysis involved 1306 patients (651 in the darolutamide group and 655 in the placebo group); 86.1% of the patients had disease that was metastatic at the time of the initial diagnosis. At the data cutoff date for the primary analysis (25 October 2021), the risk of death was significantly lower, by 32.5%, in the darolutamide group than in the placebo group (hazard ratio 0.68; 95% confidence interval, 0.57 to 0.80; P<0.001). Darolutamide was also associated with consistent benefits with respect to the secondary end points and prespecified subgroups. Adverse events were similar in the two groups, and the incidences of the most common adverse events (occurring in ≥10% of the patients) were highest during the overlapping docetaxel treatment period in both groups. The frequency of grade 3 or 4 adverse events was 66.1% in the darolutamide group and 63.5% in the placebo group; neutropenia was the most common grade 3 or 4 adverse event (in 33.7% and 34.2%, respectively).

CONCLUSIONS

In this trial involving patients with metastatic, hormone-sensitive prostate cancer, overall survival was significantly longer with the combination of darolutamide, androgen-deprivation therapy, and docetaxel than with placebo plus androgen-deprivation therapy and docetaxel, and the addition of darolutamide led to improvement in key secondary end points. The frequency of adverse events was similar in the two groups.