

Darolutamide for non-metastatic, castration-resistant prostate cancer



Darolutamide significantly improves metastasis-free survival in men with non-metastatic, castration-resistant prostate cancer, according to a randomised, double-blind, placebo-controlled, phase 3 trial. The trial population comprised 1509 men with non-metastatic, castration-resistant prostate cancer with a prostate-specific antigen (PSA) doubling time of 10 months or less. Patients were randomly assigned to receive either the androgen-receptor antagonist darolutamide (n=955) or placebo (n=554). The primary endpoint was metastasis-free survival.

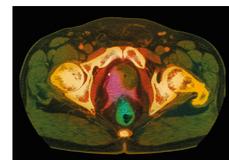
Median follow-up was 17.9 months. Median metastasis-free survival was 40.4 months in the darolutamide group and 18.4 months in the placebo group (hazard ratio 0.41, 95% CI 0.34–0.50; $p < 0.001$). Metastasis-free

survival was favourable for patients with a PSA doubling time of 6 months or less or more than 6 months who received darolutamide. Serious adverse events occurred in 237 (25%) of 954 patients in the darolutamide group and 111 (20%) of 554 patients in the placebo group. Co-author Karim Fizazi (Institut Gustave Roussy, Villejuif, France) noted that, in terms of metastasis-free survival, darolutamide is similar to other androgen-receptor inhibitors, apalutamide and enzalutamide. Although cross-trial comparisons should be made with caution, the darolutamide group did not see an excess of falls (4.2%), fractures (4.2%), or heart failure (1.9%) compared with trials of other agents. When asked if studies comparing darolutamide with apalutamide were likely,

Fizazi explained, "It would be more interesting to focus on other stages of the disease and see what kind of results we get with darolutamide".

Nicholas James (University of Birmingham, Birmingham, UK) said that keeping patients on hormone therapy might be problematic. "You have circulating androgen for a reason. Long-term toxicity follow-up is going to be very important for these men. Are they going to end up with brittle bones, weak muscles, and a poor quality of life? We still have to work out what drivers relapse in patients on androgen-receptor targeting drugs," said James. "The really pressing question is, what do you do when the drugs stop working?"

Talha Burki



Science Photo Library

Published Online
February 21, 2019
[http://dx.doi.org/10.1016/S1470-2045\(19\)30102-0](http://dx.doi.org/10.1016/S1470-2045(19)30102-0)
For more on the **darolutamide study** see *N Engl J Med* 2019; published online Feb 14.
DOI:10.1056/NEJMoa1815671