Enzalutamide for the treatment of prostate cancer: results and implications of the AFFIRM trial.

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Abstract
Enzalutamide is a second-generation androgen receptor signaling inhibitor that was approved by the US FDA in 2012 for the treatment of metastatic docetaxel-pretreated castrate-resistant prostate cancer. In preclinical studies, enzalutamide demonstrated higher affinity to the androgen receptor compared with the first-generation androgen receptor inhibitors. In the well-designed Phase III AFFIRM study, enzalutamide treatment showed improved overall survival compared with placebo in addition to improvement of all preplanned secondary parameters. Overall, enzalutamide seemed to be very well tolerated with a favorable side-effect profile, with a lower incidence of grade 3-4 adverse events. A potentially concerning adverse effect was the occurrence of seizures that were reported in approximately 1% of the patients receiving enzalutamide (compared with 0% in the placebo arm). This review will summarize the mechanism of action of enzalutamide, the preclinical and clinical development that led to its approval focusing on the AFFIRM trial results, its safety and efficacy and the ongoing trials, as well as patterns of resistance to this drug in the context of five new drugs approved for the treatment of metastatic castration-resistant prostate cancer. With a changing landscape for these patients, treatment sequencing and best treatment for individual patients remains challenging.

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