FDA Approves Erleada for Hormone-Sensitive Prostate Cancer

Two androgen receptor inhibitors improved survival by 33% in men with metastatic prostate cancer that responds to hormone therapy.

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The Food and Drug Administration (FDA) has approved Erleada (apalutamide) for the treatment of men with prostate cancer that has spread to the bones or elsewhere in the body but still responds to hormone therapy.

Studies presented at the recent American Society of Clinical Oncology (ASCO) annual meeting showed that both Erleada and a similar drug, Xtandi (enzalutamide), extended progression-free survival and overall survival for this population when added to medications that suppress testosterone.

Testosterone and other androgens—known as male hormones, although females produce small amounts too—can stimulate prostate cancer growth. Treatment for localized prostate cancer typically involves surgery or radiation therapy, often followed by androgen deprivation therapy (ADT). This type of treatment deprives tumors of hormones that promote their growth by stopping testosterone production; this is referred to as castration, though today it is usually done with medications rather than surgical removal of the testicles. Metastatic prostate cancer that has spread to the bones, internal organs or elsewhere in the body is more difficult to treat.

Prostate cancer that still responds to ADT is known as castration-sensitive, while cancer that develops the ability to grow despite a low testosterone level is known as castration-resistant. An estimated 40,000 men are diagnosed with metastatic castration-sensitive prostate cancer (mCSPC) each year.

Erleada, from Janssen, and Xtandi, from Pfizer and Astellas, are next-generation androgen receptor inhibitors that block the activity of male hormones by interfering with chemical signals relayed through androgen receptors on cells. Both are already approved for the treatment of castration-resistant prostate cancer that no longer responds to ADT. But new study findings suggest that starting more intensive treatment for metastatic cancer sooner may be beneficial.

The additional approval of Erleada for metastatic castration-sensitive prostate cancer is based on findings from the Phase III TITAN study, a randomized, controlled trial that included 1,052 men

with mCSPC in more than 20 countries. The median age was 68. About 16% had previously undergone prostate removal surgery or received radiation therapy for localized disease and about 10% had used chemotherapy. Participants were randomly assigned to take either Erleada or placebo pills once daily, both in combination with ADT using drugs such as Lupron (leuprolide) or Zoladex (goserelin).

As described in The New England Journal of Medicine, the first interim analysis, after a median 24 months of follow-up, showed that 68% of men taking Erleada and 48% of those taking the placebo were still alive without evidence of progression on radiographic scans (known as progression-free survival, or PFS), representing a 52% improvement. Overall survival at 24 months was 82% in the Erleada group versus 74% in the placebo group—a 33% improvement.

Men taking Erleada were also more likely to see a drop in their prostate specific antigen (PSA) levels and went longer before they needed to start chemotherapy. Responses to Erleada were seen in men with high- and low-volume disease and did not differ according to prior treatment.

Treatment was generally safe, though over 40% of participants in both groups experienced severe (Grade 3 or 4) adverse events; 8% of Erleada recipients and 5% of placebo recipients stopped treatment for this reason. Although the study authors concluded that "the side-effect profile did not differ substantially between the two groups," Janssen reported that in this and another trial, people taking Erleada were more likely to experience skin rash, fatigue, hot flushes, high blood pressure, decreased appetite, weight loss, diarrhea, joint pain, falls and fractures.

"Prostate cancer is more difficult to treat once it spreads, and for patients with castration-sensitive disease, it is clear that androgen deprivation therapy alone, is often not enough," TITAN lead investigator Kim Chi, MD, of BC Cancer in Vancouver said in a Janssen press release. "Results from the TITAN study showed that, regardless of the extent of disease, patients with metastatic castration-sensitive prostate cancer have the potential to benefit from treatment with apalutamide in addition to ADT."

Another study, also reported at ASCO and in The New England Journal of Medicine, saw comparable results with Xtandi.

The Phase III ENZAMET trial included 1,125 men with mCSPC. The median age was 69. They were randomly assigned to take either once-daily Xtandi pills or a first-generation nonsteroidal anti-androgen medication (bicalutamide, flutamide or nilutamide), both with ADT. About 45% in both groups planned to use concurrent early docetaxel chemotherapy.

After a median follow-up period of 34 months, men taking Xtandi were less likely to experience disease progression as indicated by rising PSA levels (a 61% improvement) or clinical outcomes (a 60% improvement). Overall survival rates at three years were 80% in the Xtandi group versus 72% in the control group—again a 33% reduction in the risk of death. In this study, the overall survival advantage was most pronounced in men who did not receive docetaxel (83% versus 70%, respectively) and in those with low-volume disease.

Here, too, treatment was generally safe but side effects were common. Serious adverse events were reported by 42% of men taking Xtandi and 34% of those taking the older anti-androgen drugs. Participants taking Xtandi more frequently experienced fatigue and seizures and were more likely to stop treatment because of adverse events.

“Physicians and patients with prostate cancer now have a new treatment option with enzalutamide, and this is especially relevant for men who cannot tolerate chemotherapy and have a lower burden of disease seen on scans,” study cochair Christopher Sweeney, MBBS, of Dana-Farber Cancer Institute in Boston, said in an ASCO press release.

Given these findings, there’s a good chance the FDA may also approve Xtandi for men with metastatic castration-sensitive prostate cancer. Since both medications extend survival to a similar degree, this would offer patients and their providers more options to choose among for intensified upfront treatment of metastatic prostate cancer, based on factors such as side effects and cost.

Click here to see the full prescribing information for Erleada.

Click here to see the full prescribing information for Xtandi.

Click here to learn more about prostate cancer.
