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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Agonists vs Antagonists: Evaluating ADT Efficacy as Monotherapy and Combination Therapy in Hormone-Sensitive Prostate Cancer

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. McKay:
This is CME on ReachMD, and I'm Rana McKay, a genitourinary medical oncologist at the University of California in San Diego. Today, we're going to be discussing agonists and antagonists, evaluating ADT efficacy as monotherapy and combination therapy in hormone-sensitive prostate cancer.

So the first thing to think about is thinking about androgen deprivation therapy. There are many different forms of androgen deprivation therapy. There are GnRH agonists that basically work to suppress testosterone production from the testicles, but they initially work through continuous activity on the GnRH receptor. And that continuous, as opposed to pulsatile, activity ends up resulting in blockage of testosterone production, whereas the antagonist, the way that they work is they immediately disrupt the signal from the brain to the testicles, telling the testicles to make more testosterone. And so there are differences between the agonist and antagonist pharmacologically with regards to how exactly they work.

Currently most of these therapies are given as injectables. Whether that be intramuscular or subcutaneous injectables, most are given as injections. And with the antagonists, currently there are 2 antagonists that are approved for utilization. One is a once-monthly injectable called degarelix that's a subcutaneous injection in the abdomen. The other is an oral pill called relugolix. And historically, more traditionally the injectables have been utilized, but the advent of the oral relugolix medication has really opened up the door with regards to different sorts of treatment administration for patients with prostate cancer.

So with the oral formulation, patients take that orally as opposed to an injection. They take it daily for the intended duration of time that they are to be on treatment, and it results in immediate decline in testosterone levels and more sustained testosterone levels over time.

The activity of relugolix was really demonstrated in the phase 3 HERO study, and this study looked at the comparison of relugolix versus leuprolide for patients with advanced prostate cancer that were intended to receive therapy with androgen deprivation therapy for greater than a year. And what we saw in the context of that trial was more immediate and sustained declines in testosterone with relugolix compared to leuprolide. Additionally, we also saw that at the time of therapy discontinuation, there was a more rapid normalization of testosterone post-discontinuation of treatment.

There's been very heterogenous data around the cardiovascular profile of antagonist versus agonist, and I think that the number one thing to consider with regards to antagonists, or really in general rather, is that cardiovascular prevention is really key across the board for all patients initiating androgen deprivation therapy or on androgen deprivation therapy. This will have a tremendous impact in regards to mitigating cardiovascular risk. But nonetheless, in a post hoc exploratory analysis in the context of the HERO trial, there were

demonstration of decreased cardiovascular events that were seen.

So I think, in summary, there are 2 forms of agents that can be utilized to decrease testosterone in the clinic. Historically, agonists have been utilized, specifically injectable form, and antagonists, now we have two forms, an injectable and an oral version called relugolix.

Thank you so much for your attention today. Lots of opportunities for utilization of these agents in the clinic.

Announcer:
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