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# MOA Deep Dive: The MRA Spectrum

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**Dr. McMurray:**
Hello, my name is John McMurray. I'm professor of medical cardiology at the University of Glasgow in Scotland in the United Kingdom.

**Dr. Heerspink:**
Hello, my name is Hiddo Heerspink. I'm professor of clinical pharmacology at the University Medical Center Groningen in the Netherlands.

**Dr. McMurray:**
So, Hiddo, we're here to talk about mineralocorticoid receptor antagonists today. And spironolactone and eplerenone have been around for a long time, and us cardiologists have used these for many years. Now, there's this new agent, finerenone. What's the difference between finerenone and the older mineralocorticoid receptor antagonists?

**Dr. Heerspink:**
Yeah, indeed, John, there has been quite some development in the area of the mineralocorticoid receptor antagonists, and finerenone is indeed the first nonsteroidal mineralocorticoid receptor antagonist. It's a little different than spironolactone and eplerenone. It's still very selective for the mineralocorticoid receptor itself, but it has different characteristics. The chemical structure is different; it's much larger than spironolactone and eplerenone. The half-life is much shorter, it doesn't have active metabolites, and it binds specifically to the gene-responsive element of the hormone in the DNA. Thereby it activates different cofactors and may have differential pharmacodynamic effects compared to eplerenone and spironolactone.

**Dr. McMurray:**
And, Hiddo, one of the problems that we as cardiologists encounter with spironolactone in our patients with heart failure is that in men, we sometimes see, for example, gynecomastia, these antiandrogen or estrogenic adverse effects. What about finerenone? Do you get that sort of problem with finerenone?

**Dr. Heerspink:**
Well, it's always difficult to compare different trials because there were different patients included. But the trials that have been done with finerenone don't see these side effects as much as older mineralocorticoid receptor antagonists. So the evidence suggests that, indeed, these drugs are more tolerable for male individuals and have less androgen side effects.

**Dr. McMurray:**
And, Hiddo, one of the other things that we see in cardiological practice is that physicians often avoid using the older MRAs in patients with impaired kidney function, and, indeed, those patients were excluded from the cardiovascular trials with the nonsteroidal MRAs. Is

there any experience in using finerenone in people with reduced kidney function?

**Dr. Heerspink:**
Two trials have been done in type 2 diabetes, FIDELIO and FIGARO, and these trials were done in patients with impaired kidney function. The efficacy is consistent across the spectrum of GFR. Safety was consistent also in people with a very low GFR. So there's a lot of evidence now, at least in type 2 diabetes, and a nondiabetic CKD trial is ongoing and will be finishing at the end of next year.

**Dr. McMurray:**
Okay. Well, very interesting. Hopefully we'll learn more about that potential additional use of finerenone, and hopefully we'll hear more about the effects of finerenone in patients with heart failure.

**Dr. Heerspink:**
Yes, indeed. We'll look forward to it.

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