# Skip the injection, go straight to abiraterone

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a day ago · 28 Replies

I was discussing abiraterone acetate (brand name Zytiga) with my MO and asked why it was always given with ADT.

"I don't know, it's just always been done that way."

This seemed odd to me. ADT usually involves a drug like Leuprorelin (Lupron) to trick the hormone system into shutting down testosterone production in the testicles. But men and women make testosterone in their adrenal glands, so the levels never fall to zero.

Abiraterone acetate (AA) works more directly, by interfering with Cytochrome P450 17A1, an enzyme that is used in testosterone production in the testicles, adrenals, and some prostate cancer cells. It is called an anti-androgen.

Since AA shuts down testosterone production pretty much everywhere, at a molecular level, it seemed to me that ADT wasn't really necessary.

It turns out it isn't. Two abstracts from ACCO 2019 discuss small trials where they compared AA alone versus ADT + AA (AA is almost always given with prednisone.)

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This paper describes a randomized trial with 67 patients with mCRPC. Half received continued androgen-deprivation therapy (ADT) plus abiraterone acetate plus prednisone (AA+P) or AA+P alone. In all patients, median testosterone levels remained below castrate levels throughout treatment. Unlike ADT, with AA+P alone testosterone production recovered rapidly, within 28 days of stopping treatment.

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This paper describes a similar trial, retrospective rather than randomized, of 57 consecutive patients with mCRPC. 36 were treated with AA+ADT, 10 received AA alone, and 11 initially received AA+ADT and transitioned to AA alone.

Castrate levels of testosterone were maintained with all groups. The authors discussed the cost savings; in the US Lupron is roughly $1000 for a monthly dose. I found this curious, as Zytiga brand AA is about $10,000 a month. There are savings, but they are at most 9% or so.

So the combination of AA + ADT has been given to hundreds of thousands of men over the past 8 years because that's how it was done in the original clinical trials. A huge waste of time and money for lack of will or ability to think clearly about the issue.

These findings will take a while to find their way into the clinic, but I intend to discuss it with my MO at our next meeting. There are implications for those interested in integrating evolutionary dynamics into prostate cancer treatments. We can start and stop testosterone production much faster and without the need for an injection.

nature.com/articles/s41467-...