Evaluate Vantage

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Yes, Pfizer is taking the threats to Xtandi seriously

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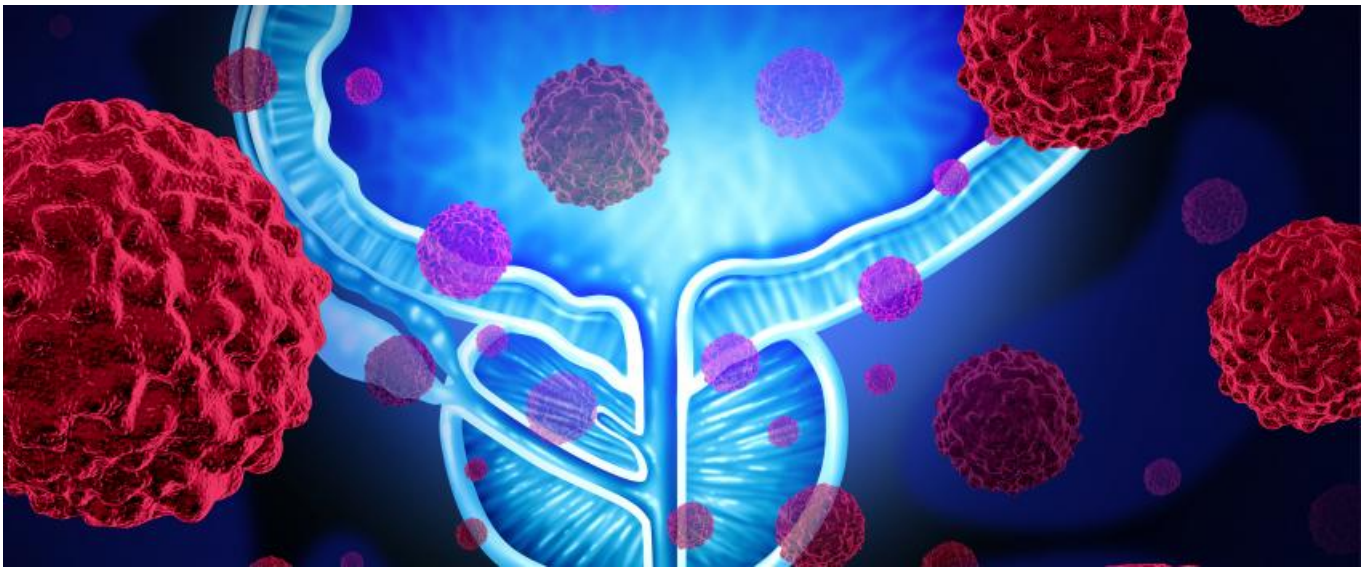

Having recently neutralised Erleada, Pfizer moves to challenge earlier use of Zytiga.

As if any more evidence were needed of the threat Zytiga poses to the fast-changing prostate cancer market, Pfizer yesterday accelerated readout of two key trials to give itself more time to make the case for early use of Xtandi.

The Xtandi setting in question is hormone-sensitive disease, the use in which the UK academic consortium-sponsored Stampede trial delivered stunning data backing Johnson & Johnson's Zytiga. Pfizer's problem is that this battle is not just versus J&J; it could soon encompass generics players, given that Zytiga's key US patent expired this year.

Pfizer's decision to amend the protocols for Xtandi's Arches and Embark trials mirrors last year's acceleration of the Prosper trial, in non-metastatic castration-resistant disease. The Prosper data allowed Xtandi to be approved in this early disease in July, just five months after J&J's Zytiga follow-on, Erleada, got the nod in this, its first use.

Blockbusters

The battle reflects the changing nature of treating prostate cancer, whose castration-resistant, metastatic form represents a setting in which Zytiga and Xtandi have become blockbusters.

It was already clear that Zytiga was set to be used earlier in the treatment cascade, and the stunning success of the Stampede trial, presented at last year's Esmo meeting, confirmed the drug's potential in hormone-sensitive disease (*Asco-GU – J&J's Zytiga follow-on strategy crumbles on Spartan, February 5, 2018*).

This was followed by approval in this setting, based on J&J's own Latitude trial. The company needed to move quickly with its follow-on, Erleada, and cleverly positioned this in the brand-new, non-metastatic setting, where it was approved in February.

The key movers in early prostate cancer treatment				
		Prostate cancer setting		
Drug	**Company**	**Metastatic, castration-resistant**	**Hormone-sensitive**	**Non-metastatic, castration-resistant**
Zytiga	J&J	Approved, established use	Approved Feb 2018 Latitude (NCT01715285) Stampede (NCT00268476)	NA
Xtandi	Pfizer/Astellas	Approved, established use	Phase III Arches (NCT02677896) Embark (NCT02319837)	Approved Jul 2018 Prosper (NCT02003924)
Erleada	J&J	NA	Phase III Titan (NCT02489318)	Approved Feb 2018 Spartan (NCT01946204)

With Xtandi Pfizer and its partner Astellas are taking on both early-stage prostate cancer uses. Prosper, whose enrolment size was cut from 1,560 to 1,440 subjects to enable it to read out over a year early, led to approval in pre-metastatic prostate cancer in July.

Now the companies are trying to repeat the trick in hormone-sensitive disease, the subject of the Arches and Embark trials. The former, whose primary measure is radiographic progression-free survival, has had its protocol revised to reduce the number of events required to trigger primary endpoint analysis to 262, Astellas told *Vantage*. This should enable readout late this year, rather than in April 2020.

Embark, meanwhile, has metastasis-free survival as its primary endpoint, and its analyses are being changed to reduce the target hazard ratio and thus focus on a smaller sample size. The target readout for this trial is now mid-2020, Pfizer says, rather than March 2021.

Astellas said the companies were comfortable with needing fewer events to demonstrate a treatment effect. They will of course have noted Xtandi's efficacy in other settings, and know that there is no time to lose.

J&J is also testing Erleada in hormone-sensitive prostate cancer, but its phase III study, Titan, is at present not expected to yield data until November 2020; notably, this now falls after Pfizer's trials.

Still, the threat of Erleada is probably now of secondary importance to Pfizer. With Zytiga fast establishing itself as the standard of care in hormone-sensitive patients – and perhaps being used off label in non-metastatic disease too – for Pfizer every second counts.

It might be little solace, but with Zytiga generics waiting around the corner this drug's move earlier in the treatment cascade will give J&J just as big a headache as it will Pfizer.

This story has been updated to add comments from Astellas about study powering assumptions.