Evaluate Vantage

January 04, 2023

No Blys for Vera

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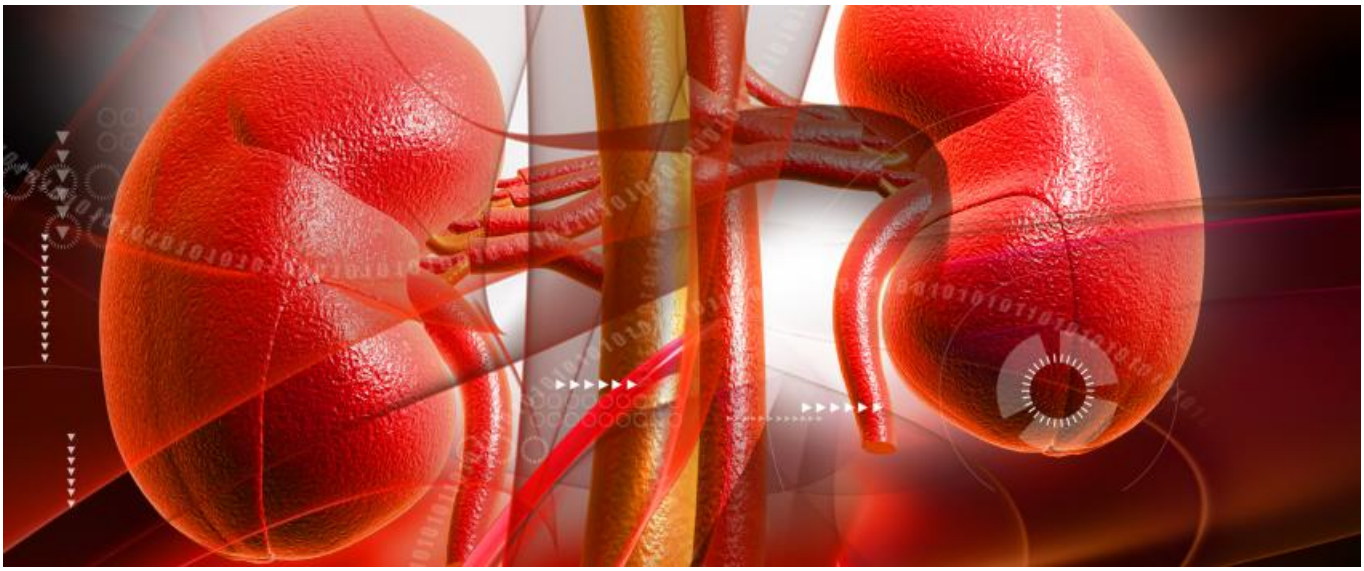

Atacicept hits in phase 2, but uncompetitive data are seen as good news for its IgAN rivals.

With the immunoglobulin A nephropathy (IgAN) pipeline getting crowded, contenders not only have to succeed in clinical trials but must also look competitive. Vera Therapeutics found this out today with its stock opening down 56% despite ostensibly positive results with its lead candidate, atacicept, in a mid-stage trial.

The Origin study met its primary endpoint, change in proteinuria, but the reduction did not match numbers previously reported by the likes of Travere and Chinook – although, as ever, such cross-trial comparisons should be treated with caution.

Investors in Chinook who sent that group's shares up 4% this morning should note that this company's projects have not yet been tested in placebo-controlled studies. The first such test will come in the third quarter of this year, when the phase 3 Align study of atrasentan is set to read out.

Meanwhile, there are concerns about liver toxicity with Travere's sparsentan. An FDA decision on approval has been delayed until February, after the agency requested an updated risk evaluation mitigation strategy (REMS) to include liver monitoring.

While sparsentan and atrasentan are endothelin A inhibitors, Vera's atacicept works differently, targeting two cytokines known as April and Blys. But, on a cross-trial basis, it does not appear as good as other projects with this dual mechanism, or those inhibiting April alone. The project to beat here looks like Chinook's anti-April project BION-1301 – but again, impressive proteinuria reductions came from an uncontrolled study in a small number of patients. Chinook plans to start a phase 3 trial this year.

Cross-trial comparison of selected IgAN projects					
Project	**Company**	**Description**	**Trial**	**Time point**	**Reduction in proteinuria**
Atrasentan	Chinook	Oral endothelin A receptor inhibitor	Interim data from Ph2 Affinity (NCT04573920)	24wk	55% (no control arm)
BION-1301	Chinook	SC anti-April antibody	Ph1/2 (NCT03945318)	24wk	54% cohort 2 (no control arm)
Sparsentan	Travere	Oral endothelin A & angiotensin II type 1 inhibitor	Ph3 Protect (NCT03762850)	36wk	50% (35 points adjusted for irbesartan control)
Telitacicept	Remegen	SC anti-April/Blys fusion protein	Ph2 China study (NCT04291781)	24wk	49% (~49 points pbo-adjusted*)
Sibeprenlimab (VIS649)	Otsuka	SC anti-April antibody	Ph2 interim analysis (NCT04287985)	36wk	43% pbo-adjusted**
Cemdisiran	Alnylam	SC anti-complement C5 RNAi	Ph2 (NCT03841448)	32wk	37% pbo-adjusted
Tarpeyo	Calliditas	Oral formulation of budesonide	Ph3 Nefigard (NCT03643965)	36wk	34% (31% pbo-adjusted)
Atacicept	Vera Therapeutics	SC anti-April/Blys fusion protein	Ph2 Origin (NCT04716231)	24wk	33% (28% pbo-adjusted^)
*240mg arm; **pooled data with IV doses 2mg, 4mg & 8mg monthly; ^result with 150mg dose selected for ph3. Source: clinicaltrials.gov & company releases.*					

Vera's chief executive, Marshall Fordyce, noted the placebo-controlled design of Origin several times during a conference call today, and contended that cross-trial comparisons were particularly difficult here.

Still, he added that the 33% proteinuria reduction seen with a 150mg weekly dose of atacicept at 24 weeks stacked up favourably to the 18% reduction seen with Calliditas's approved IgAN drug, Tarpeyo, at the same time point.

When asked about the company's response to concerns that atacicept had "missed the mark", Dr Jonathan Barratt, an IgAN expert at the University of Leicester, said long-term data would be important – adding that he expects proteinuria to decline further over time. Initial 36-week data released today, showing a 36% proteinuria reduction among 38% of patients in the study, seem to support this – full 36-week results are due in the second quarter.

Safety will also be an important factor in how this market shakes out. Atacicept looked relatively clean in Origin, although one patient in the 150mg arm discontinued due to injection site reaction.

As well as showing proteinuria reductions, IgAN players will also have to demonstrate an impact on estimated glomerular filtration rate (eGFR), a harder endpoint. Vera's phase 3 trial of atacicept, slated to start in the first half, will test the 150mg dose, with a primary endpoint of proteinuria at 36 weeks, and a key secondary of two-year eGFR.

Perhaps data in the next couple of years will give a better idea of how the anti-April agents compare. But with even this subset of the IgAN space getting busy it is no wonder that investors are already trying to gauge which groups might eventually prevail.

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