Evaluate Vantage

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Chemocentryx soars on superior avacopan

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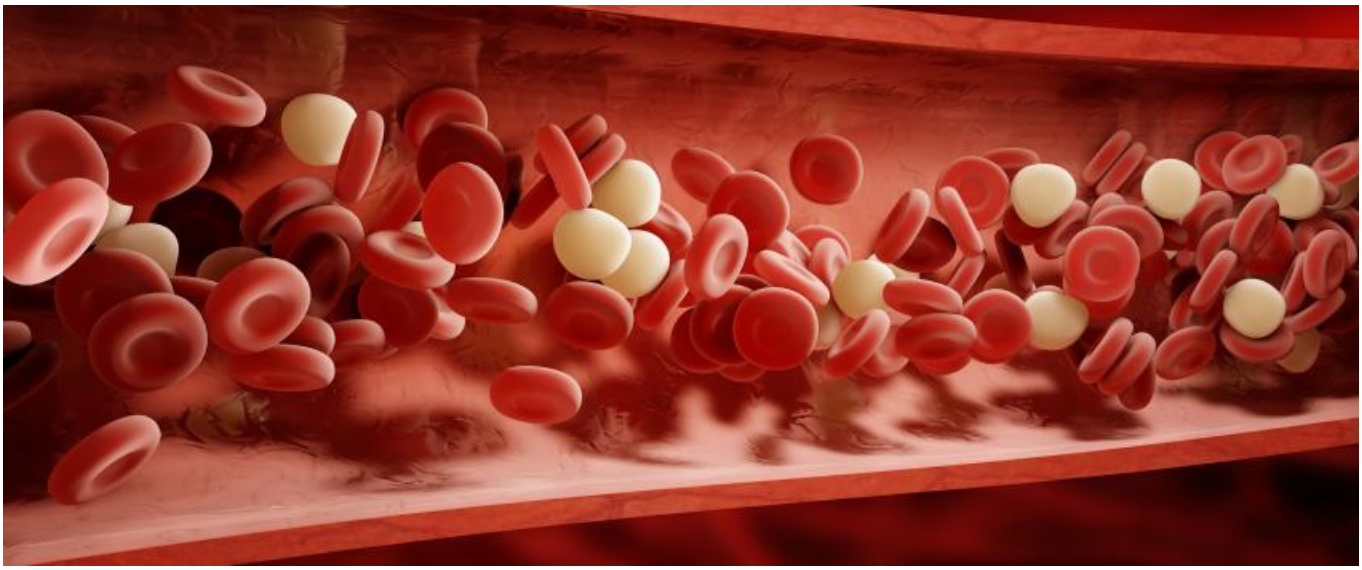

With data showing superiority over glucocorticoids, Chemocentryx could have a new standard of care for vasculitis in avacopan.

It is fair to say that topline data from the phase III Advocate trial of avacopan have come as a surprise. Sentiment had turned against the complement factor C5a inhibitor after the failure of Inflarx's similarly acting IFX-1 in hidradenitis suppurativa in May, as investors feared a class effect.

But the highly positive results – Advocate was designed to show noninferiority to standard of care, but avacopan was found to be actually superior – position the project as the therapy of choice in the rare disease anti-neutrophil cytoplasmic antibody-associated vasculitis. Some analysts peg the value of this market at $3bn, and Chemocentryx's stock is up 300% today, giving the company a weighty $1.7bn valuation.

The trial enrolled 331 patients with acute Anca vasculitis, a condition in which overactivation of the complement pathway boosts neutrophil activity, causing inflammation and destruction of small blood vessels. Subjects took either avacopan or the steroid prednisone (the current standard of care), plus either Rituxan or cyclophosphamide.

At six months avacopan was noninferior to control on remission rates, as assessed by the Birmingham vasculitis activity score. At a year, however, Chemocentryx's project was statistically superior to the steroid cohort on the same measure. These two measures, the co-primary endpoints of the trial, were tested sequentially.

Selected phase III Advocate trial data				
	Avacopan + Rituxan or cyclophosphamide	**Glucocorticoid-based SoC**	**P for noninferiority**	**P for superiority**
Remission at 26 weeks (%)	72.3	70.1	<0.0001	
Remission at 52 weeks (%)	65.7	54.9		0.0066
GTI cumulative worsening score	39.7	56.6		0.0002
GTI aggregate improvement score	11.2	23.4		0.0082
Mean increase from baseline to week 26 in eGFR (ml/min/1.732)	5.8	2.8	0.0413	
Mean increase from baseline to week 52 in eGFR (ml/min/1.732)	7.3	4.0	0.0259	
Serious adverse events (%)	42.0	45.0		
GTI=glucocorticoid toxicity index; eGFR=estimated glomerular filtration rate. Source: company press release.				

The avacopan arm showed a significant reduction in glucocorticoid-related toxicity, as might be expected for a steroid-sparing regimen. Significant improvements in kidney function in patients with renal disease were seen with the avacopan regimen, and Chemocentryx said that the project was better on quality of life measures, too.

That said, safety could not be described as anything better than “acceptable”, though numerically fewer subjects had serious adverse events in the avacopan group than with control.

Approval applications in the US and Europe will come next year; avacopan is licensed to Vifor Pharma outside the US, and Vifor has sublicensed it to Kissei for Japan.

Weighing Anca

Investor reaction to this data seems to reflect an expectation that avacopan could become the new standard of care for the initial treatment of Anca vasculitis. This is a remarkable turnaround since Chemocentryx withdrew an EU marketing application seeking early approval for avacopan in Anca vasculitis, in June.

Regulators might require studies in the maintenance setting before broadening its label to include this use, but patients will presumably be open to options that avoid the chronic high-dose steroids with which they are lumbered today.

The drug’s European composition of matter patent expires in 2029, but its US IP should cover it until 2031, and some analysts are forecasting peak sales in the early 2030s well into blockbuster territory.

Chemocentryx’s success has lifted Inflarx’s shares, with investors in the latter clearly hoping that the Advocate data provides positive read-across to the phase II Anca vasculitis trial of its anti-C5a asset IFX-1. IFX-1 is the only other project in mid or late-stage development for the condition.

Avacopan is not only at a later stage of development than IFX-1, though, it is also orally administered; Inflarx’s antibody is intravenous. Even if IFX-1 matches avacopan in phase III – it is doubtful whether it will even make it that far given the hidradenitis suppurativa debacle – avacopan’s convenience should give it an edge in the market.