Evaluate Vantage

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Aclaris MK2 bears fruit

Madeleine Armstrong

Aclaris takes a step towards an oral rheumatoid arthritis therapy.

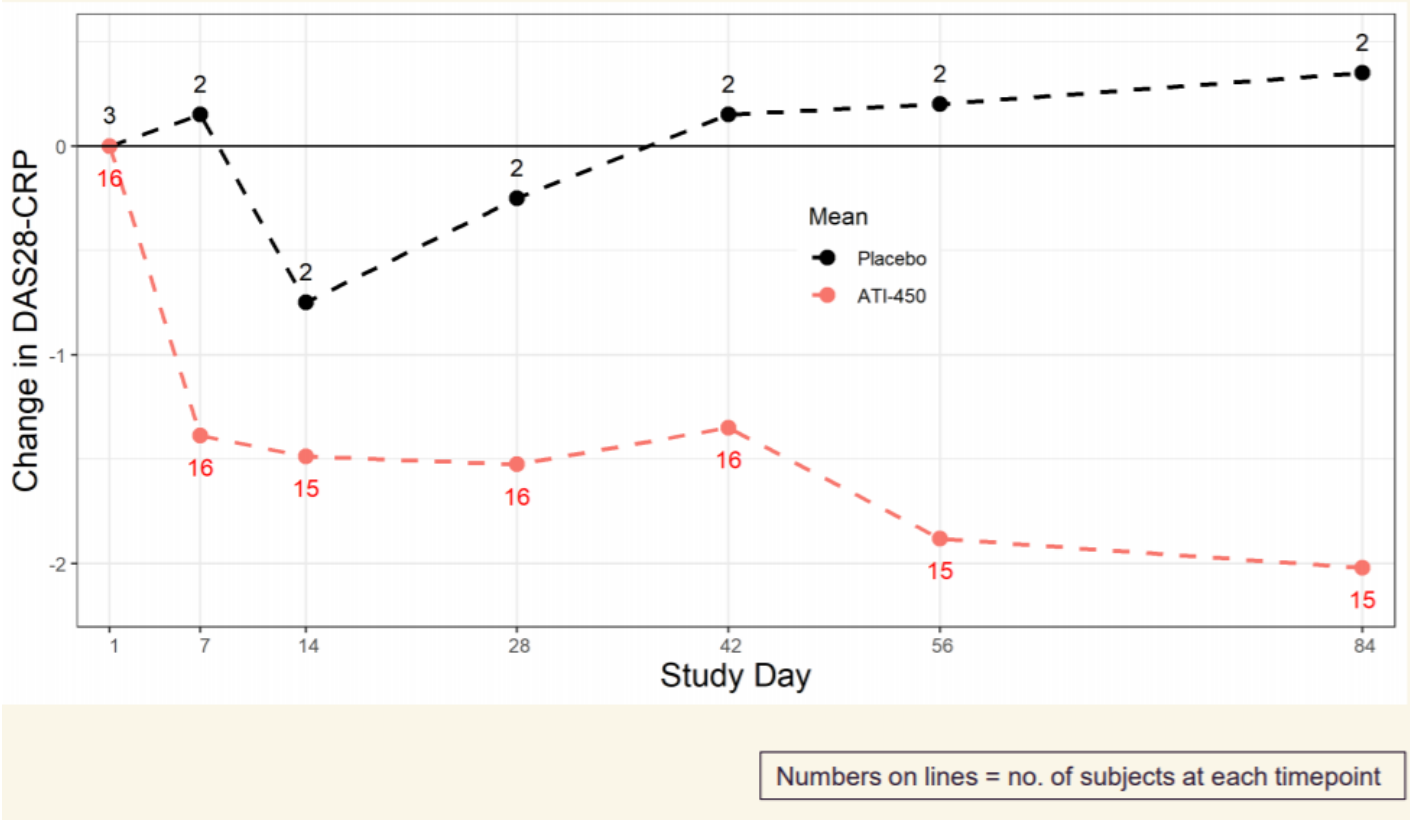
Aclaris's refocus following the failure of its Jak inhibitors in alopecia is starting to pay off. The company opened up 140% this morning on promising phase II data with its oral rheumatoid arthritis project ATI-450, albeit in just 17 subjects.

The results have generated excitement because ATI-450's target, mitogen-activated protein kinase-activated protein kinase 2 (MK2), has proven tough to hit in the past. Still, Aclaris has a long way to go to make ATI-450 a real contender in the fiercely competitive RA space.

The phase II study compared ATI-450, dosed at 50mg twice daily, plus methotrexate versus methotrexate alone over 12 weeks in patients with moderate to severe RA.

The primary endpoint was safety; secondary endpoints included the disease activity score DAS28-CRP and ACR20/50/70 responses. On the latter measures, 60%, 33% and 20% of patients in the treatment group achieved ACR20, 50 and 70 respectively, versus none in the control cohort.

DAS28-CRP
Mean Change From Baseline



Source: Company presentation

But there are reasons to be cautious: as well as the small study size overall, the control arm only included three patients initially, and the trial was poorly balanced in terms of baseline characteristics.

In addition, the final analysis excluded two patients who dropped out, one in the placebo and one in the treatment group. The ATI-450 dropout came after the patient was evaluated for heart palpitations and high levels of creatine phosphokinase, a marker of muscle or heart injury.

Aclaris's chief medical officer, David Gordon, said during a conference call today that after an investigation by a cardiologist this was not deemed a cardiac event or associated with ATI-450.

Patient baseline characteristics in ph2 trial of ATI-450

Parameter	Placebo (n=3) Median (Min – Max)	ATI-450 (n=16) Median (Min – Max)
Age (years)	53 (50 – 63)	59.5 (32 – 65)
Gender	(F) 3/3 (100%) (M) 0/0 (0%)	(F) 11/16 (68.75%) (M) 5/16 (31.25%)
Weight (kg)	105.4 (82.2 - 109.2)	88.15 (52.7 - 141.5)
Duration of Disease	1.6 (0.3 - 20.6)	6.45 (0.3 - 33.4)
hsCRP (mg/L)	21.3 (12.6 - 31.2)	11.7 (2.6 - 29.5)
DAS-28	5.3 (5.3 - 6.7) Mean (SD): 5.77 (0.808)	5.65 (3.9 - 7.4) Mean (SD): 5.71 (0.937)

Source: Company presentation

Aclaris now plans to take ATI-450 into phase IIb, and reckons it can dose the project higher given pharmacokinetic data seen in phase I with 80mg and 120mg twice daily.

Three for one

The group also believes that it could have a “pipeline in a product” with ATI-450, with numerous potential indications on the cards given that hitting MK2 blocks three cytokines: TNFα, IL-1 and IL-6.

Bristol Myers Squibb also has an unnamed MK2 inhibitor in phase I, according to its website, but no others are in active clinical development, according to *EvaluatePharma*.

Hitting this target has previously been a bust, as have efforts to inhibit p38α, which is upstream in the same pathway. Aclaris now needs to prove that it has fully cracked this mechanism.