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Alder grows with migraine success

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Alder Biopharmaceuticals obviously had more faith in its migraine antibody ALD403 than investors did. While the company was confident enough to start its phase III programme before reporting results from its phase IIb trial, its backers waited for the data before piling in, pushing Alder's share price up 50% yesterday.

The CLIN-005 study met its primary endpoint, with more patients in the higher-dose groups achieving a 75% reduction in migraine days over 12 weeks compared with the placebo group. Clearing this hurdle is good news for Alder, but the company will need to set its product apart from other migraine drugs in development, including three in the same anti-CGRP MAb class (see tables below).

Alder says ALD403 has shown a potentially best-in-class profile, but assessing this claim is far from easy given the usual problems with across-trial comparisons.

Top-line results from CLIN-005 phase IIb trial of ALD403

Migraine days per month	300mg	100mg	30mg	10mg	Placebo
50% reduction	57%**	54%*	55%*	44%	41%
75% reduction	33%*	31%*	28%	27%	21%
100% reduction	8%	5%	4%	8%	3%

*Notes: *p<0.05; **p<0.01 versus placebo.*

In migraine this is complicated further because some trials have assessed frequent episodic migraine, defined as up to 14 headache days per month, while others looked at chronic migraine, where patients have headaches on 15 or more days per month.

CLIN-005 evaluated the chronic form – Alder has previously released data with ALD403 in frequent episodic migraine, which seemed similar to results with other CGRP inhibitors (*IHS – Migraine rides to Alder's rescue, May 18, 2015*).

But even comparing the latest results with other chronic migraine trials can be problematic, noted Evercore ISI analyst Umer Raffat, who lined ALD403 up against Teva's TEV-48125 – the only other CGRP blocker with phase II results in chronic disease and the drug to beat if *EvaluatePharma* consensus forecasts are anything to go by.

CGRP inhibitors in phase III development

Project	Company	Approval expected	Chronic migraine phase II trial details	2020e sales ($m)
AMG 334	Amgen/Novartis	2017	NCT02066415; results due H2 2016	22
LY2951742	Lilly	2017	Not studied	153
ALD403	Alder	2018	NCT02275117; results reported	294
TEV-48125	Teva	2019	NCT02021773; results reported	500

Teva reported last year that nearly a third of patients receiving its candidate had had a 75% decrease in headache frequency, which seems to put it on a par with ALD403.

But Mr Raffat noted that while Alder evaluated migraine days Teva looked at moderate to severe headache days. So far, Alder has not given figures for average headache day or headache hour reduction.

Other factors that could have affected the CLIN-005 results include the background medications allowed, and

differing definitions of a migraine day.

Question of convenience

But it is not just clinical efficacy that will determine the uptake of CGRP inhibitors; convenience will also be an important consideration. Currently, Teva seems to have the edge as TEV-48125 is given subcutaneously, while ALD403 is administered intravenously.

Alder is already taking steps to address this, also reporting data from a phase I study evaluating intravenous, subcutaneous and intramuscular formulations of ALD403. According to the company, all three led to comparable levels of suppression of peripheral CGRP for three months.

This should allow a once-quarterly dosing schedule that could make even intravenous administration viable, noted Mr Raffat. More competition could come from small molecules targeting CGRP, although these are in earlier development (*Therapy focus – Another bet on the small-molecule approach to migraine, November 26, 2015*).

Perhaps phase III results will give a better idea of how the anti-CGRP MAbs stack up against each other. If efficacy remains similar, the companies might be forced to compete on price – which could be worthwhile if it means that they can grab a slice of a market forecast to reach $10bn.

Study	Details	Trial ID	Status
Promise 1	Phase III study of ALD403 in frequent episodic migraine	NCT02559895	Data expected H1 2017
Promise 2	Phase III study of ALD403 in chronic migraine	-	To begin mid-2016

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