

Biogen struggles to get the Lingo right



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The highly ambiguous nature of yesterday's phase II data for BIIB033, Biogen Idec's early-stage anti-Lingo-1 antibody for multiple sclerosis, explains why the company was so eager to rein back sellside exuberance last year.

Despite this earlier caution Biogen yesterday tried to play up the Renew trial's "positive" topline results. Given that the study failed to meet its primary endpoint in all comers – even the analysis of those who complied with the protocol is questionable – and missed all secondary measures, it hardly suggest an overwhelming success.

The study, in acute optic neuritis, was seen as important because this condition is thought to serve as a model for MS, another demyelinating disease. Enthusiasm behind BIIB033 had been driven by its mechanism of action – remyelination – which represents the holy grail of the next stage of MS drug development ([Biogen bulls learn to speak a new Lingo, July 25, 2014](#)).

Of course, this being a phase II trial in just 82 patients, such minutiae as the strict lack of statistical significance in the intent-to-treat population might seem like nitpicking. And, true enough, the cited 34% improvement in the primary endpoint of optic nerve conduction velocity can be seen as supportive.

But it is the totality of the data that disappointed investors, who initially sent Biogen Idec stock down 3% yesterday before the shares recovered slightly. Secondary measures included anatomical and functional endpoints such as improving nerve fibre thickness or visual acuity, and none was met.

Fails to hit

Renew recruited 82 patients, and counting all of these the data failed to hit statistical significance on the primary efficacy measure. Only when looking at those who completed the full protocol – and Biogen Idec did not reveal how many dropped out – is the 34% primary endpoint improvement seen, with $p=0.0504$, which on a strict reading also misses statistical significance.

Lingo-1 is a protein expressed in the CNS and known to prevent myelination, and the hope is that blocking it might actually repair neuronal axons and myelin. All eyes thus turn to the 2016 readout of Synergy, BIIB033's larger phase II study in MS, though handicapping this on the basis of Renew is now pure guesswork.

Biogen said Renew was the first clinical study to provide evidence of biological repair in the CNS by facilitating remyelination, and said it looked forward to the Synergy data.

Analysts were split, Leerink opining that the results were in line with expectations, while UBS stated that the data "did not look very good... No effect in secondary endpoints is a concern since ultimately the drug is going to have to show a differentiated functional benefit to be relevant."

Consensus 2020 sales forecasts, as compiled by *EvaluatePharma*, stand at \$111m, but last year Credit Suisse speculated that the project could be worth \$10bn or more. Against such enthusiasm it is little wonder that the market was not thrilled by Renew, even though many banks assume zero contribution from BIIB033 in their models.

As to two other remyelinating approaches, no news has been revealed as to a phase II study of GlaxoSmithKline's histamine H3 receptor antagonist GSK239512, even though according to [clinicaltrials.gov](#) the trial ended last September. Acorda Therapeutics hopes to report phase I data for rHlgM22, described as a remyelination antibody, early this year.

In the absence of strong data from Acorda, the underwhelming optic neuritis readout with BIIB033 basically forces Lingo bulls to sit back until Synergy generates results. In the current market two years is a long time to wait.

Selected studies of remyelinating approaches to MS

Company	Project	Study	Enrolment	Trial ID	Completion
GlaxoSmithKline	GSK239512	Ph II, vs placebo	131 relapsing-remitting MS patients	NCT01772199	Sep 2014
Biogen Idec	BIIB033	Ph II, vs placebo (Renew)	82 acute optic neuritis patients	NCT01721161	Oct 2014
Acorda	rHlgM22	Ph I, vs placebo	71 MS pts, ascending-dose trial	NCT01803867	Jan 2015
Biogen Idec	BIIB033	Ph II, on top of Avonex (Synergy)	396 relapsing-remitting MS patients	NCT01864148	Jun 2016

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