Evaluate Vantage

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Selecta feels the pain of gout

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Gout has always been a tricky indication, and the latest trial results from Selecta Biosciences will do little to encourage other companies thinking of tackling this disease. Yesterday the group saw its shares fall 54% after it failed to show a sustained treatment effect with SEL-212 in an ongoing phase II trial.

Nevertheless, Selecta management are insisting on ploughing on with a phase III trial due to start in the first half of 2018. With no changes to the treatment protocol planned, this stance could raise fears that this study will also disappoint.

In the latest trial of 79 patients, fewer than half on the highest dose regimen were able to maintain their serum uric acid (SUA) levels after completing the complex “3+2” treatment cycle of the study.

Breeding intolerance

One of the biggest issues with uricase enzyme therapy for treating gout is that patients eventually become intolerant of the enzymes, developing anti-drug antibodies (ADA) that reduce the effectiveness of the treatment.

Selecta had been hoping to overcome this by using its proprietary nanoparticle product SVP-rapamycin combined with pegsiticase, which together it calls SEL-212. The biodegradable nanoparticles in SVP-rapamycin contain immunomodular adjuvant components, which the group had expected would help induce tolerance of pegsiticase.

But rather than continuously dose SVP-rapamycin, Selecta had been hoping that its “3+2 teach and treat” dosing schedule would condition patients to maintain their tolerance of pegsiticase.

As part of the protocol patients were given three “teach and treat” doses of pegsiticase and SVP-rapamycin every 28 days, in the hope that adding SVP-rapamycin would teach the immune system to become tolerant to pegsiticase. This was followed by two “treat” doses of pegsiticase alone.

Fail

However, once treatment with SVP-rapamycin stopped, most patients rapidly became intolerant of pegsiticase and both their SUA and ADA levels rose, indicating immunogenicity.

Speaking on a conference call, Werner Cautreels, Selecta’s chief executive, said that while the dose of SVP-rapamycin and pegsiticase to be tested had yet to be decided, a phase III trial would start in the first half of 2018. Stifel analysts commented that the 70% response rate at three to four months was significantly better than anything seen before for the tolerance of uricase enzymes by gout patients, so perhaps the company sees a glimmer of hope for approval here.

Still, given the phase II results another logical step would have been revisiting the treatment protocol – potentially increasing the duration over which SVP-rapamycin was dosed. But Mr Cautreels insisted that there would be no change to the current “3+2” paradigm.

No alone

Gout has proved troublesome for many companies. Last year, Astrazeneca threw in the towel when it sold lesinurad to Ironwood Pharmaceuticals for an up-front fee of just $100m, despite having acquired it through the $1.3bn purchase of Ardea Biosciences. The project had been dogged by toxicity issues at higher doses and questions about efficacy at lower levels.

Horizon Pharma has also been the beneficiary of other companies’ difficulties in gout. In 2015 it spent $510m purchasing Crealta, owner of Krystexxa. Crealta had itself acquired Savient, Krystexxa’s originator, for just $120m following safety concerns.

With a better safety profile than its rivals, Selecta must hope that it has not squandered this advantage by not seeking to test a more effective pivotal treatment protocol.

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