Evaluate Vantage

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Event – Do or die for Clavis in leukaemia trial

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Events do not get more binary than results from Clavis Pharma's phase III study of elacytarabine in leukaemia. The choice is stark: either the drug extends survival over existing therapies, or the Norwegian group calls it quits.

After Clavis's previous lead project, CP-4126, showed no survival benefit in pancreatic cancer patients, the company needs success from elacytarabine to demonstrate the value of its technology. Success could trigger talks to sign up an ex-Europe marketing partner; failure would result in the company scrapping the technology, laying off its workforce and distributing its remaining cash to shareholders – a refreshing and candid stance compared with most biotech firms' attempts to limp on when all seems lost.

Wait, what?

This was the unambiguous message coming from Clavis executives in presenting fourth-quarter results earlier this month. When the Clavela trial in relapsed or refractory acute myeloid leukaemia reports by the end of March, the group will be looking for an odds ratio of 0.7 or better. This would represent a median survival of 4.5 months compared with three months on other therapies such as cytarabine.

Data from a phase II trial published in September 2012 showed a 5.3-month median survival for patients taking elacytarabine, known also as Elacyt, compared with a median survival of 1.5 months achieved by matched historical controls.

Elacytarabine was created using a lipid vector technology, attaching a lipid tail to cytarabine. The hope is that by putting a lipid tail on a cytotoxic nucleoside, the company can extend the half-life and overcome resistance related to low levels of cellular transporter proteins like human equilibrative nucleoside transporter 1 (hENT1).

The hENT1 hypothesis was recently tested by another Clavis product created with its lipid vector technology, CP-4126, which was based on the pancreatic cancer treatment gemcitabine. But the study, called Leap, detected no difference between patients with low and high levels of hENT1, or indeed with historical gemcitabine studies, leading to a discontinuation of all work by Clavis and partner Clovis Oncology (*Leap failure sends Clavis and Clovis crashing back to earth, November 12, 2012*).

Best-case scenario

Clavela tests Elacyt against the investigator's choice of treatment, such as cytarabine, Vidaza or Dacogen; no product is approved in the relapsed or refractory setting, so there was no gold standard with which Elacyt could be compared. Some 380 relapsed or refractory patients were enrolled, with half randomised into the elacytarabine arm.

Analyses other than overall survival include remission rates and duration; however, no separate high vs low hENT1 subgroup exploration is pre-specified in information listed at clinicaltrials.gov or on the company's website.

With failure, the company reckons the NKr223m ($39m) it had at the end of 2012 will be sufficient to close down the trials, pay termination costs for employees and possibly return some cash to shareholders.

With success, it has cash to last into the fourth quarter of 2013, so achieving a commercial partnership this year, and an accompanying licensing fee, will be a key goal. An uplift in the share price can also be expected should there be positive results. Clavis shares stood at NKr7.78 in afternoon trading today, compared to NKr65 before the Leap failure. The company could well use any Clavela-driven rise in market value to raise more funds, however the depressed share price suggests few are betting on positive results.

By the end of March the sector should know whether Clavis can be a successful drug developer or will be carried feet-first into the biotech graveyard. Its leadership should be congratulated for being clear about the future and not destroying shareholder value for months or years to come.

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