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Plan B saves Celyad after heart failure therapy flops

Amy Brown

As Celyad proves today, it is always wise to have a plan B. The failure of a pivotal trial of its heart failure cell therapy C-Cure, erased 38% from the Belgian company's valuation this afternoon, an outcome that will make its search for a partner considerably harder.

Indeed, without a partner the project is effectively dead, as Celyad confirmed today that it would not conduct further clinical work alone. All of which would have been disastrous if not for the presence of its fledgling immuno-oncology pipeline, which no doubt prevented an even bigger share price collapse.

Celyad – then Cardio-3 Biosciences – bought an NKR-T cell platform from Celdara Medical, a private US biotech, for $6m plus $4m in equity in January 2015 and this is already its main focus. This generates autologous adoptive T-cell therapies similar to CAR-T, but using receptors normaly found on human natural killer cells.

Last month the third dosage level was completed in a study of an asset called NKR-2, which uses engineered T cells with an NKG2D receptor, in acute myeloid leukaemia and multiple myeloma patients.

Further data updates are expected in the coming months, and indeed this afternoon Celyad's chief executive, Christian Homsy, ended a conference call discussing the C-Cure results by flagging approaching good news in oncology. Given the relatively small amount paid to access this technology and the huge hopes for the adoptive T-cell space, investors could indeed soon forget the C-Cure failure.

Casting the net

C-Cure is a therapy based on cells harvested from a patient's bone marrow, which are reprogrammed so they become heart precursor cells and then injected back into a patient's heart. The hope is that these will heal the failing heart and improve its function.

The Chart-1 phase III study failed to show this: it recruited 271 patients with chronic advanced symptomatic heart failure, and compared C-Cure against sham treatment. The primary endpoint was a composite of mortality, morbidity, quality of life, six-minute-walk test and left ventricular structure and function at 39 weeks, and on this measure C-Cure patients failed to show any difference versus placebo.

Celyad identified a subset representing 60% of the enrolees, based on baseline end diastolic volume (EDV) segmentation, that showed a p value of 0.015 on the primary endpoint measure. This was not a prespecified subgroup, executives admitted, although they insisted that EDV was widely recognised as a measure to find patients more or less likely to respond to heart failure therapies.

This approach clearly lacks statistical rigour, however, and the company will need to make a very convincing argument with the full dataset to convince partners to take on the project on this basis. This will become available at the ESC conference in Italy, at the end of August.

Mr Homsy also pledged to take the data to European regulators in an attempt to win conditional approval. "We are not overly confident we will obtain approval, but we are hopeful," he said.

Talks will also be held with the US FDA on breakthrough therapy designation and on changing the design of a planned US-based phase III trial to incorporate the findings from the subset analysis.

"We are not claiming victory, but seeing if there is a signal that can be used in further development and benefit patients, and give enough evidence to the FDA to pursue the development further, granted by someone with more muscle that us," he said.

Drag and drain

That someone will no doubt wait to hear regulators' opinions first. Should they ultimately fail to materialise, C-Cure is surely finished. Celyad ended 2015 with €108m ($119m) in cash, and clearly intends to spend that on its oncology pipeline.

While C-Cure is set to remain a drag on the company’s attention as executives search for a partner with a big appetite for risk, investors can perhaps take comfort that it will not represent a drain on the company’s cash.

To contact the writer of this story email Amy Brown in London at AmyB@epvantage.com or follow @AmyEPVantage on Twitter