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Clarivate™

June 13, 2025
Volume 36, No. 113
Special Reprint

Enterome raises $19M to advance non-Hodgkin lymphoma therapy

By Nuala Moran, Europe Editor

As it prepares to present the latest data from the phase I/II clinical trial of EO-2463, Enterome SA has secured $19 million to expand and complete the study, and to scope phase III development of the microbiome-derived off-the-shelf immunotherapy in the treatment of non-Hodgkin lymphoma (NHL).

The financing follows on from positive recent meetings with both the FDA and the EMA, which sketched a clear path to registration for marketing authorizations in watch-and-wait indolent NHL.

This is currently the most attractive option for phase III development of EO-2463, based on the clinical data accrued in the ongoing phase I/II study, and the regulatory advice from the FDA and the EMA, said Pierre Bélichard, CEO of Paris-based Enterome.

EO-2463 monotherapy in the watch-and-wait setting would be a first in this indication, thus minimizing competition. In addition, "from a timeline perspective it is assumed that a pivotal study in [iNHL] could start fastest, that is, directly after [the phase I/II] has long enough follow up regarding time to progression, for the currently planned sample size," Bélichard told BioWorld.

Such a trial would test EO-2463 against no active anti-lymphoma treatment, since there currently is no defined standard-of-care treatment for indolent NHL on either side of the Atlantic.

Enterome most recently presented data from the phase I/II at the December 2024 American Society of Hematology (ASH) meeting in San Diego, showing a 46% objective response rate, with 15% complete responses and 31% partial responses, in patients with early-stage follicular lymphoma.

The therapy was well-tolerated, with no severe adverse events, suggesting EO-2463 may offer a safe treatment option for patients with early-stage disease.

Selective targeting

EO-2463 is a combination of four synthetic peptides, originally discovered in the gut microbiome, that mimic the B lymphocyte-specific lineage markers CD20, CD22, CD37 and CD268. By selectively targeting multiple B-cell markers, these Oncomimics are intended to prime the immune system to destroy malignant B lymphocytes.

In the second cohort of the phase I/II trial, patients with newly diagnosed, asymptomatic follicular lymphoma, received EO-2463 monotherapy as an alternative to the standard watch-and-wait approach.

Most patients were still on study treatment at the point the data were presented at ASH. An objective response rate of 46% was seen in the first 13 patients, including 15% complete responses and 31% partial responses.

The latest data from the phase II study in 48 indolent NHL patients, will be presented at the International Conference on Malignant Lymphoma in Lugano, Switzerland, on June 21.

Predictor of clinical benefit

Enterome also has reported on a biomarker analysis conducted in the first cohort of the phase I/II, involving patients with relapsed/refractory disease who received EO-2463 in monotherapy and in combination with lenalidomide/rituximab. This looked to see if early CD8+ T-cell expansion in response to EO-2463 administration could serve as a predictor of later clinical benefit.

The assessment indicated that measuring fast expansion of EO-2463 specific CD8 T cells is predictive of clinical response, both for EO-2463 monotherapy, and for EO-2463 in combination with lenalidomide + rituximab.

"[This] indicates …. that measuring fast expansion of EO-2463 specific CD8 T cells can predict for clinical response," said Bélichard. "In the current limited size dataset, the biomarker can at week five predict complete remission at week 42, with a sensitivity of 100% and specificity of 100%," he said. "Obviously, these data need to be validated in a larger dataset."

Escaping immune detection

Enterome's Oncomimics are intended to overcome the problem that tumor-associated antigens escape immune detection because of thymic deletion, the process by which the immune system learns not to attack "self" proteins.

Oncomimics can do this because they are distinct enough from tumor-associated antigens to elicit an immune response, but also similar enough to trigger a response against the specific tumor antigens.

Bélichard said that in the phase I/II trial – and consistent with the preclinical hypothesis – "expansion of CD8 memory T cells

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specific for the microbiome mimic peptides and the B cell targeted antigens …. are seen in the majority of patients."

With the new financing, it is now planned to expand cohort 4 of the phase I/II to include treatment of patients with relapsed refractory disease with EO-2463 + lenalidomide + rituximab. The expansion would include a further 25 patients.

The Oncomimics concept has now been evaluated in phase I/II studies in patients with first recurrent glioblastoma; in previously treated and untreated patients with adrenocortical carcinoma, an immune desert tumor type; in slow-developing neuroendocrine tumors; and in previously treated patients with microsatellite stable/mismatch repair proficient metastatic colorectal cancer.

"It is our opinion that the combined knowledge from the different settings in solid tumors … which have currently been assessed in phase I/II studies convey a coherent picture of very efficient expansion of specific CD8+ memory T cells," said Bélichard.

There were clear efficacy signals in each setting, all of which warrant further evaluation, he said, adding, "the seemingly broad applicability also poses the interesting problem of a need to focus."

For now, Enterome will devote its resources to the development of EO-2463 in B-cell malignancies, having attracted a new U.S. investor, the Institute for Follicular Lymphoma Innovation (IFLI), a nonprofit foundation dedicated to advancing research and treatment for follicular lymphoma, which invested $9 million in the financing round.

Existing investors committing an additional $10 million were Symbiosis Capital Management, Seventure Partners, Lundbeckfonden Biocapital, Italian venture capital and private equity firm Primo Capital; and the U.S. Leukemia & Lymphoma Society Therapy Acceleration Program.

"Attracting highly specialized blood cancer investor IFLI to this financing demonstrates the conviction of our new and existing investors in the potential of Oncomimics for blood and solid tumor cancers," said Bélichard.

"Most importantly, EO-2463 has shown robust clinical efficacy and exceptional safety and tolerability – which is especially impressive for such a potent immunotherapy."