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By Kevin Grogan

THE DUTCH BIOTECH'S CEO TELLS SCRIP that one-week treatment with T-Guard could change the paradigm for tackling steroid-refractory graft-versus-host disease.

Xenikos BV of the Netherlands has been given the green light by the US Food and Drug Administration to start a Phase III trial of T-Guard, a potential practice-changing therapy for acute graft-versus-host disease.

Earlier today (11 June), the Nijmegen-headquartered biotech announced that the FDA has approved its investigational new drug application to initiate a US-based Phase III trial designed to evaluate T-Guard in 47 patients who receive an allogeneic stem cell transplantation and subsequently develop steroid-refractory acute graft-versus-host disease (SR-aGVHD). T-Guard combines two toxin-conjugated monoclonal antibodies that target the CD3 and CD7 molecules on T-cells and NK cells and tests thus far show that it can safely and swiftly reset the immune system in patients, Xenikos stated.

The primary endpoint of the study will be complete response rate at day 28, and key secondary goals will include the duration of complete response and overall survival rate at six months. Although GVHD can often be treated successfully with steroids, there are limited options once the disease progresses or becomes resistant to the latter, and the long-term survival of patients with SR-aGVHD is only 20%.

The Phase I/II trial enrolled 20 adults who all had received an allogeneic stem cell transplant for myeloid or lymphoid malignancies and had grade 2-4 SR-aGVHD. Twelve of the patients achieved an overall clinical response on day 28, which was the primary endpoint of the trial, while ten of them achieved a complete response, which Xenikos said was especially noteworthy considering the severity of the patient population.

Receiving FDA approval to start the Phase III trial "is a major milestone for us and follows a very positive end of Phase II meeting with the agency," CEO Ypke van Oosterhout told *Scrip*. He noted that Xenikos would benefit hugely from the fact that the study will be conducted in the US by the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), which is funded by the National Heart, Lung and Blood Institute and the National Cancer Institute at the National Institutes of Health; to date, the BMT CTN has completed accrual to 40 Phase II and III trials and enrolled over 10,700 participants.

The BMT CTN, which is providing about $1.4m in funding for the T-Guard trial, can count on a vast network of over 100 leading transplant centers throughout the US and will be able to quickly recruit patients for the trial, he noted. "They were very enthusiastic to get involved and for a smaller company that is excellent. They have all kinds of procedures in place to efficiently run the study," van Oosterhout (***pictured above***) added, pointing out that Xenikos has to compete with lots of other companies in recruiting GVHD patients, "an indication that is getting crowded."

T-Guard is administered as four infusions in a treatment course of just one week and due to its short half-life – about nine hours – T-Guard is rapidly washed out after the last infusion, allowing the swift restoration of the T-cell compartment with newly formed (non-disease causing) cells.

The company claims that this compares favorably to alternative therapies consisting of monoclonal antibodies that cause depletion of T-cells and/or other immune cells, or biologics and small-molecule inhibitors that induce a functional suppression of the immune system. "The often prolonged and rather broad immunosuppression induced by many of these agents frequently results in infectious complications and a potential loss of the beneficial graft-versus-leukemia effect, thereby nullifying the benefits achieved by controlling the GVHD reaction," Xenikos stated.

Van Oosterhout said that T-Guard was quite a complicated product to make given that it combines two antibodies, but Xenikos has an agreement with Spanish contract development and manufacturing organization 3P Biopharmaceuticals which passed an FDA inspection earlier this year. "We have the material for the Phase III study in the fridge and are ready to go," he added.

On the cash front, Xenikos raised $30m from a series B financing in May last year, with two new backers – Medicxi and RA Capital Management – participating in the round. Van Oosterhout, who had just returned from BIO 2019 in Philadelphia when he spoke to ***Scrip***, said it was "great to bring two very reputable investors onboard, one from Europe and one from the US."

He described BIO as "pretty intense but very useful, lots of good meetings, as always," and acknowledged that having a drug going into Phase III puts Xenikos in the spotlight. Van Oosterhout said that the firm would "continue some of those discussions with potential partners which could be interesting and we will also consider the possibility of going it alone and staying independent, they're the two scenarios and we are actively exploring both options."

Ypke van Oosterhout

If all goes well, Xenikos will be playing catch-up with Incyte Corp.'s JAK1/JAK2 inhibitor Jakavi (ruxolitinib) which became the first therapy for SR-aGVHD to be approved by the FDA at the end of last month. It represented the third US approval for Jakavi, which is already marketed for polycythemia vera and myelofibrosis. *(Also see "Incyte Will File Jakafi For Acute GVHD In US Based On Phase II Success" - Scrip, 22 Jun, 2018.)*

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