Website address:
https://www.gesundheitsindustrie-bw.de/en/article/news/testing-a-new-antibody-therapy-for-treating-blood-cancer

Testing a new antibody therapy for treating blood cancer

The fight against acute myeloid leukaemia is a long one. Cancer cells that cause the disease to recur may remain despite initially successful destruction of the tumour with chemotherapy drugs. Now researchers from Tübingen have identified an antibody that could potentially prevent cancer recurrence.

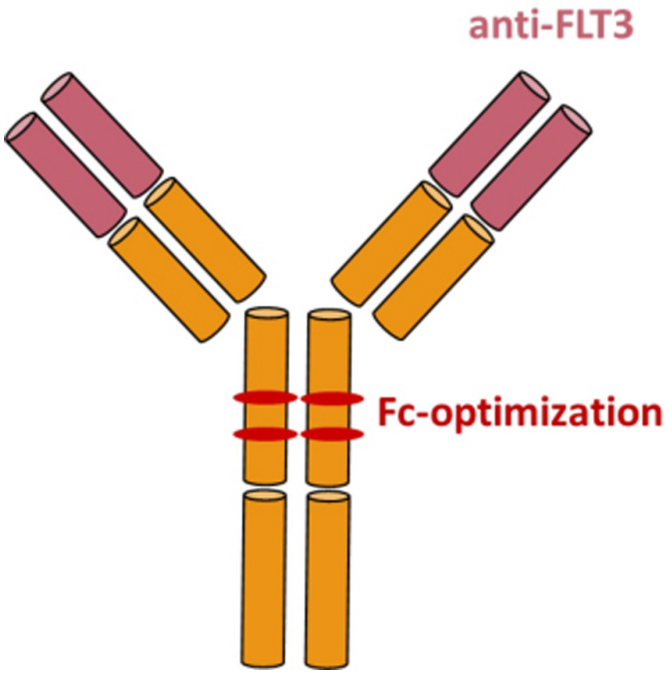
Prof. Dr. Helmut Salih is an internal medicine expert and specialised in haematology/internistic oncology. He has been professor for translational immunology at the DKFZ's partner institute in Tübingen, the German Consortium for Translational Cancer Research (DKTK), since 2014.
© Tobias Schwerdt / DKTK

In March 2017, doctors from Tübingen University Hospital joined forces with a company called SYNIMMUNE GmbH to carry out a phase I clinical trial that may usher in a new era for leukaemia treatment. The trial assesses the safety and efficacy of the new immunotherapy treatment in a cohort of patients with acute myeloid leukaemia (AML). The new therapy involves an antibody called FLYSYN that binds to a protein called FLT3 present on the surface of leukaemia cells. After binding to FLT3, the FLYSYN antibodies are able to stimulate immune system cells, in particular natural killer (NK) cells, with the antibody portion that points away from the cell. Stimulation enables NK cells to recognise and destroy cancer cells. The development of this therapeutic approach and the antibody are a hard-won research success that owes a great deal to the long-term commitment of the Tübingen researchers. The unusual cooperation between science and industry also played a crucial role in the development of the antibody therapy.

Prof. Dr. Helmut Salih from the Department of Internal Medicine II in Tübingen is coordinating the FLYSYN trial and was also involved in the development of the antibody therapy. Salih comments on initial difficulties: "The problem is that hardly any antigens are expressed solely on malignant cells. The binding of antibodies to healthy cells would lead to severe adverse drug effects. The objective is therefore to reduce off-target binding by selecting suitable and highly selective target

antigens. For me, FLT3 is one of the best antigens available for treating acute leukaemias. This is because high amounts of FLT3 are measured on leukaemic blast cells while only low amounts are expressed on healthy immune system and haematopoietic progenitor cells. We have not yet observed any destruction of haematopoietic cells by the antibody either in vitro or in patients treated in experimental treatment settings."

Salih went on to credit those who were instrumental in identifying FLT3 as an anti-cancer antigen: "Prof. Dr. Gundram Jung and Dr. Ludger Große-Hovest from the Department of Immunology at the University of Tübingen have made an outstanding contribution to the identification of FLT3. They have been working on the identification of antibodies for treating cancer for many years. The three of us selected FLT3 for treating AML."



FLYSYN is an antibody for treating AML patients at the minimum residual disease stage. The antibody binds highly specifically to FLT3 receptor proteins on the surface of leukaemia cells. The FC fragment of FLYSYN was optimised to bind and stimulate natural killer (NK) cells of the human immune system.
© SYNIMMUNE GmbH

Exemplary cooperation between industry and academia

Dr. Martin Steiner has been the CEO of the biotechnology company SYNIMMUNE GmbH from Tübingen since March 2016.
© SYNIMMUNE GmbH

Jung, along with Große-Hovest (CSO of SYNIMMUNE GmbH), has also been actively involved in the development of FLYSYN. The development of the AML antibody therapy was strongly supported with funds from the German government in the form of two successful GO-Bio proposals submitted between 2008 and 2015. These funds contributed to spinning out SYNIMMUNE GmbH from the Department of Immunology at the University of Tübingen. FLYSYN is now the young company's lead product. Dr. Martin Steiner, CEO of SYNIMMUNE GmbH, explains: "The development of FLYSYN was given priority in the second GO-Bio phase and used up most of our funding. Amongst other things, the money was used to develop the antibody production process under GMP conditions." Salih points out that this was something very special: "This was the first time that a therapeutic antibody had been developed in an academic setting. This was made possible because the University of Tübingen had established its own GMP building." In 2015, SYNIMMUNE produced the first FLYSYN batch in this GMP laboratory. This batch has been approved for use in the ongoing phase I clinical trial.

The trial is for AML patients who have undergone standard treatment and are in complete haematological remission. Steiner explains: “From a medical point of view, these patients are considered healthy as no leukaemia cells are detectable under the microscope. The trial treats patients in whom genetic markers for leukaemia-specific mutations can still be detected, and who therefore have a high probability of suffering a relapse. A few weeks after standard therapy when blood formation has recovered, these AML patients are given the FLYSYN antibody to eliminate potentially remaining leukaemia cells.” The researchers hope that this “relapse strategy” will prevent the disease from recurring.

Salih explains why the new drug is not used for primary treatment: “Immunotherapies generally work better the lower the tumour burden. Although the NK cells of the immune system are activated by FLYSYN, their efficiency nevertheless depends on the number of malignant cells – the fewer the better. This is why the optimum point to apply antibody treatment is thought to be after standard chemotherapy treatment, i.e. when treatment has reduced the tumour burden, leaving just a small number of tumour cells. In addition, there is a clearly recognised legal reason for this: the use of completely new drugs is not generally permitted before the patient has undergone established standard cancer therapy."

SYNIMMUNE expands antibody development with platform technology

Producing the FLYSYN antibody under GMP conditions requires specifically trained GMP personnel. The photo shows two SYNIMMUNE employees performing sterile filtration.

Volunteers are still needed for the phase I clinical trial. Suitable patients must not, amongst other things, already have received stem cell transplants. The trial is designed as a multicentre trial and is therefore being carried out in Tübingen, Heidelberg and Ulm. Steiner also mentioned that there is a plan to take further study centres on board. Meaningful interim results are expected for the

second half of 2018. SYNIMMUNE will be in charge of marketing the antibody in future, potentially in collaboration with a sales partner. In addition to the clinical trial, SYNIMMUNE and its clinical partners are also working on expanding the therapeutic principle. “The cancer cells of acute lymphatic leukaemia (ALL) patients also express FLT3. And FLT3 is also found on the surface of malignant cells in patients with MDS*, which is a pre-leukaemia stage. We want to use the antibody for treating these diseases as well,” says Salih.

SYNIMMUNE is not entirely reliant on FLYSYN. Steiner outlines the company’s long-term platform strategy: "We are also working on a platform technology for bispecific antibodies in which the antibodies are structurally modified to form no or very few aggregations. Aggregations can prevent antigen detection and cause side effects. If such aggregations can be excluded, higher dosages could be given, which in turn should improve treatment efficiency. "The company's overall goal is to develop even more potent, better antibodies that can also be used, for example, in combination therapies and for other types of cancer.

*MDS: myelodysplastic syndrome (ed. note)

Recruitment – information about the phase I trial with FLYSYN:

Recruitment of patients is not yet closed. Interested and suitable AML patients can still be included in the trial (as of October 2017). In addition to Tübingen, the trial will also be carried out in Heidelberg and Ulm. For further information, please visit:

http://www.uniklinikum-tuebingen-studien.de/aml-studie

Article

18-Oct-2017
Dr. Heike Lehmann

Further information

Universitätsklinikum Tübingen
Medizinische Klinik II
Prof. Dr. Helmut Salih
Otfried-Mueller-Str. 10
72076 Tübingen
Phone: +49 (0)7071 29-83275
E-mail: Helmut.Salih(at)med.uni-tuebingen.de

SYNIMMUNE GmbH
Dr. Martin Steiner (CEO)
Alte Landstraße 42
72072 Tübingen
Phone: +49 (0)7071 770-8382
E-mail: steiner(at)synimmune.de

- Universitätsklinikum Tübingen
- SYNIMMUNE GmbH

The article is part of the following dossiers

Cancer therapy and cancer diagnostics

cancer | antibody | therapy | cancer immunotherapy