VAXIMM: Vaccines that impede cancer growth

VAXIMM GmbH, a young biotechnology company from Mannheim, Germany, specialises in the development of vaccines for cancer treatment. The company's first product candidate, VXM01, is a live oral vaccine that targets the VEGFR-2 receptor and hence the blood supply of tumours. VXM01 is currently undergoing clinical testing in pancreatic cancer patients.

In addition to traditional cancer therapies such as surgery, chemotherapy, radiotherapy and hormone therapy, approaches involving immunological treatment are increasingly gaining in importance. Researchers are particularly focused on immunotherapies that target a tumour's vasculature.

Tumours need an adequate supply of oxygen and nutrients in order to be able to grow and metastasise. Solid, multicellular tumours produce angiogenic growth factors that induce the development of new blood vessels, i.e. the formation and growth of blood vessels from pre-existing vasculature in order to cover their nutrient and oxygen supply needs. The vascular endothelial growth factor (VEGF) is regarded as the most important angiogenic factor produced by human tumours.

VAXIMM, a privately owned Swiss-German biotechnology company, is developing a vaccine that targets VEGFR-2 (VEGF receptor 2). The vaccine destroys the blood vessel cells that make up the tumour vasculature. This leads to the breakdown of the vessels that supply the tumour with oxygen and nutrients. As a result, the tumour shrinks and growth is inhibited.

VAXIMM – the company

VAXIMM GmbH is based in Mannheim, Germany, and is a wholly-owned subsidiary of Swiss VAXIMM AG that was jointly established in 2008 by the pharmaceutical giant Merck KGaA in Darmstadt and the venture capital firm BB Biotech Ventures. In 2010, further investors joined the venture, including Merck Serono Ventures, Sunstone Capital and BioMedPartners. The company focuses on the development of active immunotherapies for the treatment of cancer. Company establishment was motivated by research carried out by PD Dr. Andreas Niethammer during his post-doctoral study period at the Scripps Research Institute in La Jolla (San Diego, California).

He showed in mice that a vaccine that targets VEGFR-2 significantly reduces the size of a number of different tumours as well as slowing the spread of metastases. The treated animals survived for much longer than untreated animals. Niethammer observed no vaccination-related adverse effects

The team at Mannheim-based VAXIMM GmbH
© VAXIMM

and the protection provided by the vaccine lasted for a relatively long period of time.

The project was out-licensed to Merck KGaA and formed the basis for the foundation of VAXIMM. The company was founded by Dr. Heinz Lubenau, CEO and head of development at VAXIMM GmbH, and Dr. Klaus Breiner, managing director at BB Biotech Ventures and chairman of the VAXIMM AG board of directors. PD Dr. Hubertus Schmitz-Winnenthal, senior physician in the Section of Endocrine Surgery at the University Hospital of Heidelberg's Department of Surgery, was also instrumental in Merck's spin-off project as well as acting as principal investigator in the first clinical trial that assessed the efficacy of VAXIMM's VXM01 vaccine targeting VEGFR-2 as a cancer treatment. Prior to relocating to the MAFINEX Technology Centre in Mannheim, the initial experiments were carried out at the University Hospital in Heidelberg.

A professional development team led by Dr. Lubenau manages the project and also oversees the VXM01 clinical trials. Most of the laboratory work, production, quality testing and control as well some of the work packages for the clinical trials were outsourced to specialised service providers. An R&D laboratory was acquired in the city of Regensburg in 2013 and is used for the preclinical development of other product candidates in VAXIMM's pipeline. The team is supported by VAXIMM's experienced board of directors and a network of advisors.

Dr. Heinz Lubenau.
© VAXIMM

The advantages of active immunotherapy of tumour endothelial cells

In contrast to Avastin (bevacizumab), an angiogenesis inhibitor and therapeutic antibody that slows the growth of new blood vessels by binding to the soluble growth factor VEGF, and other therapeutic antibodies, VXM01 is a vaccine that targets the VEGF receptor on the endothelial cells of the tumour. VXM01 and similar vaccines are active immunotherapies that stimulate the patient's own immune system to kill cancerous cells. There is a strong rationale for pursuing a cancer treatment approach that targets tumour cells as well as endothelial cells.

First, tumour endothelial cells exposed to the blood are more accessible to the so-called killer cells of the immune system than tumour cells are. Second, endothelial cells are genetically more stable than tumour cells, and thus less prone to resistance mechanisms (e.g. changes to or the loss of antigen-presenting structures). Third, a vaccine that targets the tumour endothelium is more effective than a vaccine that targets tumour cells, because the blockage of a single endothelial cell leads to the inhibition of up to one hundred cancer cells. Since many different tumours induce a neovasculature, the tumour endothelium presents a ubiquitous target for many different tumour indications. The Scripps Research Institute found that mice vaccinated against VEGFR-2 showed an impressive resistance to various types of tumours, including pancreatic cancer, lung and colon cancers as well as malignant melanomas. VAXIMM's VXM01 vaccine is a human version of the Scripps Research Institute's mouse vaccine.

Mechanism of action of VXM01

MAFINEX Technology Centre in Mannheim where VAXIMM GmbH has its headquarters.
© Stadt Mannheim

The vaccine VXM01 is based on VAXIMM's oral vaccination platform which involves using a live attenuated bacterial strain as an information carrier for tumour- and tumour stroma-specific antigens. In order to yield VXM01, the bacterial strain was modified to carry the genetic information of VEGFR-2 which is present in large quantitites on the tumour vasculature. The carrier bacterium is a well-characterised target for anti-angiogenic intervention. It has been applied in millions of individuals and has been shown to be well tolerated. VAXIMM is currently developing a pipeline of complementary cancer vaccines on the same platform.

Following oral vaccination with VXM01, the patients' cells mount a strong cellular immune response to VEGFR-2. The so-called killer cells of the immune system then go on to target and destroy the neovascular endothelial cells that make up the tumour vasculature. This leads to the breakdown of the vessels that nurture the tumour. As a result, the tumour shrinks and its growth is prohibited. In addition, VXM01 causes an inflammatory reaction close to the tumour. This is believed to not only self-sustain the immune response to the tumour's vasculature, but also promote an immune response to the tumour itself.

In December 2011, VAXIMM commenced the first clinical trial at the University Hospital in Heidelberg. The VXM01 vaccine is being tested in a randomised, placebo-controlled double blind (phase I) trial with pancreatic cancer patients. 72 patients are enrolled in the clinical trial. In addition to undergoing standard therapy, they are also being given several doses of VXM01. In 2013, VAXIMM was able to present initial promising results at the 2013 ASCO (American Society of Clinical Oncology) Annual Meeting. The vaccine has been proven safe and effective and is well tolerated by patients. The results also show that the vaccine prompts or enhances a VEGFR-2-specific T cell immune response as well as significantly impeding the blood flow through the tumour.

"The data are very encouraging," says Dr. Lubenau. "They give us a strong boost for the further development of VXM01 into into vaccines for other cancers." Based on the ongoing phase I trial, phase II clinical trials will be carried out for different cancer indications.

Dr. Heinz Lubenau, co-founder and general manager of VAXIMM GmbH, is a pharmacist by training and gained his PhD from the University of Mainz. Prior to joining VAXIMM, Dr. Lubenau held increasingly senior positions at BioGeneriX, a pharmaceutical company that develops and markets biosimilars, and then at Servier, a leading research-based pharmaceutical company based in Paris, France. Dr. Lubenau has over 20 years of hands-on experience in preclinical and clinical drug development and regulatory affairs. At BioGeneriX, he was the project leader

responsible for the development of the first G-CSF (granulocyte-colony stimulating factor) biosimilar (Ratiograstim™) up to EMA approval and market launch. He also oversaw preclinical development and managed the phase II clinical development of Lonquex™, a long-acting second-generation form of G-CSF. Both products have since received marketing authorisation in the EU and the USA. At Servier, Dr. Lubenau was involved in the clinical development of several drugs for various indications, including cardiology, cardiovascular diseases and diabetes.

Further information:

Dr. Heinz Lubenau
General Manager and Head of Development
VAXIMM GmbH
MAFINEX-Technologiezentrum
Julius-Hatry-Straße 1
68163 Mannheim
Tel.: +49 (0)621/8359 687-10
E-mail: info(at)vaximm.com

Article

18-Aug-2014
EJ
BioRN

The article is part of the following dossiers

Boosting the immune system can improve cancer prevention and treatment

VAXIMM