

Emerging Company Profile

InflaRx: Safety in sepsis

By Stephen Hansen
Staff Writer

Xigris drotrecogin alfa is the only drug approved to treat sepsis, but a narrow label and bleeding risks have limited its use to severely septic patients at high risk of death. **InflaRx GmbH** believes its antibodies against undisclosed activation products of the complement system will be safer and more broadly applicable.

"We know that these activation products are heavily involved in the initial strong response, so they are directly involved in the organ damage, but also in the long run in the development of paralysis of the immune system," co-founder and CEO Niels Riedemann told BioCentury.

Sepsis occurs when an infection leads to overstimulation of the immune system. During the early stages, the complement system is activated and produces large amounts of products including complement 5a (C5a), C3a, C4a and membrane-attack complex (MAC). This in turn leads to the release of pro-inflammatory cytokines, systemic inflammatory response syndrome (SIRS) and activation of the coagulation cascade, followed by disseminated intravascular coagulation, neutrophil dysfunction and immune paralysis.

Standard treatment involves controlling the source of infection through surgical intervention, broad-spectrum antibiotic therapy and supportive therapy to preserve organ function.

Xigris, a recombinant version of human activated protein C from **Eli Lilly and Co.**, works by decreasing inflammation and coagulation while increasing fibrinolysis, the breakdown of fibrin clots. It is approved only for severely septic patients who are at high risk of death as determined by the APACHE II (Acute Physiology and Chronic Health Evaluation) scoring system.

In addition, Xigris' label contains a warning for an increased risk of serious bleeding events attributable to the drug's antithrombotic mechanism of action.

According to Riedemann, one theory for the reason Xigris only showed clinical benefit in severe sepsis in Phase III testing is that patients with more severe sepsis may have worse coagulation events.

By contrast, Riedemann said InflaRx's

InflaRx GmbH

Jena, Germany

Technology: Antibodies against complement activation products

Disease focus: Infectious, inflammation

Clinical status: Preclinical

Founded: 2007 by Niels Riedemann and Renfeng Guo

University collaborators: Friedrich Schiller University and University of Michigan

Corporate partners: Beijing Mabworks Biotech Co. Ltd.

Number of employees: Undisclosed

Funds raised: Undisclosed

Investors: Affentranger Associates and bm-t beteiligungsmanagement thüringen GmbH

Patents: 4 issued covering therapeutic strategies for sepsis within the complement system

antibody targets an activation product that is believed to be central to the pathology of sepsis, so its therapeutic use should be broadly applicable for sepsis patients.

"We have identified our target as being one of the key factors in driving some of the most detrimental effects which are ongoing in the early stage of sepsis. That is why we believe if we can take this molecule out or slow it down, that the treatment can be very beneficial in general to sepsis patients," he said.

InflaRx is not disclosing the target. However, the company's IP is exclusively licensed from the **University of Michigan**. Last year, researchers at the University of Michigan Medical School published mouse studies in *Nature Medicine* suggesting inhibition of two complement proteins — C5a receptor and/or complement 5a-like receptor (C5L2) — could help treat some forms of sepsis (see *SciBX: Science-Business eXchange*, May 22, 2008).

Riedemann did say that the IP licensed from the University of Michigan is focused on targeting the complement system in the sepsis indication.

As for safety, Riedemann said InflaRx's lead antibody has not produced any signals so far.

"We have no indication from *in vitro* and toxicology studies that our antibody has any safety risk. I don't see any reason why we should have bleeding complications," he said, because the antibody doesn't directly interfere with the coagulation system and, unlike Xigris, has no direct antithrombotic effect.

Riedemann noted that targeting the downstream activation products of the complement system does not interfere with the system's ability to defend against secondary infections.

"When we are blocking the activation products, we are not interfering with the rest of the cascade or the complement system in general," he said. "I don't believe you could just knock out one of the complement pathways and be successful, because you need the complement system to defend the body against foreign microorganisms."

Riedemann said antibodies targeting complement activation products could be suitable for treating other inflammatory diseases such as rheumatoid arthritis (RA), Crohn's disease or inflammatory bowel disease (IBD). InflaRx chose sepsis as its lead indication, despite its difficulty, because management's background, research and clinical experience is in the pathology and treatment of sepsis. The company also has strong links to the **German Sepsis Society** and a network of clinics that focus on sepsis.

InflaRx has identified a lead candidate and expects to start a Phase I trial within the next year. Riedemann believes InflaRx could take the lead candidate through Phase II testing but would need a partner beyond proof of concept, because of the size and expense of sepsis trials.

He did not disclose the amount of funding InflaRx has raised, but said the company has enough cash for two years.

COMPANIES AND INSTITUTIONS MENTIONED

Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.

German Sepsis Society, Jena, Germany

InflaRx GmbH, Jena, Germany

University of Michigan Medical School, Ann Arbor, Mich.