Therapeutic Antibody against Herpes Simplex Viruses type 1 and 2 (P-1048)

Key Facts
- High therapeutic potential for the treatment of herpes virus infections
- Proof of concept established in animal models and in resistant clinical virus isolates
- Novel mechanism of action
- Favorable competitor situation

Background
Herpes simplex viruses type 1 and 2 (HSV-1 and HSV-2) infection-related diseases are considered a global health problem. After primary infection the virus persists in sensory and autonomic neural ganglia for the lifetime of its host. However, infections may become chronic and result in physical disabilities, social exclusion, and psychological distress over time. Moreover, severe and even life-threatening infections can particularly occur in newborns and in immunocompromised individuals like cancer patients.

The Technology
A humanized monoclonal antibody (mAb hu2c) was developed that completely abrogates viral cell-to-cell spread, a key mechanism by which HSV-1/2 escapes humoral immune surveillance. Moreover, mAb hu2c neutralized HSV fully independent of complement and/or immune effector cell recruitment in a highly efficient manner.

Development Stage
Prophylactic and therapeutic administration of mAb hu2c completely prevented infection-related mortality of severely immunodeficient mice being challenged with a lethal dose of HSV-1. The high neutralization capacity of mAb hu2c was fully maintained toward clinical HSV isolates, being multiresistant to standard antiviral drugs, and infection was fully resolved in 7/8 nonobese diabetic/SCID mice infected with a multidrug-resistant HSV-1 patient isolate. Immunohistochemical studies revealed no significant cross-reactivity of the antibody toward human tissues.

Applications and Commercial Opportunity
These features warrant further clinical development of mAb hu2c as an immunotherapeutic compound for the management of severe and particularly drug-resistant HSV infections in newborns and cancer patients.

Inventors
The invention was jointly conceived by researchers at the University of Essen and the Deutsches Krebsforschungszentrum (German Cancer Research Center, DKFZ) by Arndt MA, Krawczyk A, Krauss J, Eis-Hübinger AM, Exner E, Däumer MP, Schneweis KE, Röggendorf M.

Scientific References

Intellectual Property
DKFZ holds patent applications in Brasilia (BR112012009432-7), China (CN102791733A), Canada (2,776,271), Japan (2013-506403) and India (2833/DELNP/2012). University Essen holds patent applications in US (US2013058952) and Europe (EP2308895).
Figure: Protection of immunodeficient mice against dissemination of established HSV-1 infection by systemic treatment with mAb hu2c. NOD/SCID mice intravaginally infected with either (A) a laboratory HSV-1 strain (F), or (B) a multidrug-resistant clinical HSV-1 isolate (ACVR/CDVR/PFVR) were treated with antibodies i.v. 24 h, 40 h, and 56 h after infection at 15 mg/kg (n = 8). Control groups received either (A and B) PBS (n = 7) or (B) ACV at 50 mg/kg every 12 h i.p. (n = 9). In contrast to the control groups, antibody-treated mice with established HSV-1 infections exhibited complete virus clearance from vaginal mucosa by day 8 independent of the viral drug resistance pattern (A and B, Upper) and were significantly protected from death (**P < 0.0001, log–rank test) (A and B, Lower). In mice infected with the multiresistant HSV-1 isolate ACV treatment had only a minor effect on the virus load in the vaginal mucosa and could only delay the lethal outcome of the infection (**P = 0.0008, log–rank test) (B). Error bars represent SEM.