

In Brief

Drug for the treatment of the blood borne infection known as sepsis and stroke. Mutants of APC retain anti-inflammatory and protective effects, while having low bleeding risk.

Description

Numerous in vivo studies documented the beneficial effects of APC. Recombinant activated protein C (rAPC), sold as Xigris® (Eli Lilly), was approved for treating severe sepsis. However, clinical studies show APC treatment to be associated with risk of serious bleeding. This increased risk of bleeding presents a major limitation of current APC therapy.

Mutants of APC retaining the beneficial anti-inflammatory and cytoprotective effects, but with low anticoagulant activity hold promise as an improved form of APC therapy. Moreover, there is evidence that the full anticoagulant activity of APC might impair mechanisms involving the beneficial fibrin-dependent clearance of bacteria. Additionally, the use of bolus dosing for treatment of sepsis or ischemic injury provides protective effects without bleeding.

Inventors

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Benefits

- Mutant APC molecules that lack anticoagulant activity and the associated bleeding complications are expected to improve patient survival
- Bolus dosing of the drug offers more simplified use and lowers bleeding risk
- Exclusively licensed in 2010

Patent protection

[WO2008073603A2](#) "Dosing regimen of activated protein c and variants having reduced anticoagulant activity"

Publications

Kerschen, E.J., Fernandez, J.A., Cooley, B.C., Yang, X.V., Sood, R., Mosnier, L.O., Castellino, F.J., Mackman, N., Griffin, J.H. and Weiler, H. Endotoxemia and sepsis mortality reduction by non-anticoagulant-activated protein C. *Journal of Experimental Medicine*. 2007; 204(10), pp.2439-48. PMID: 17893198.

Mosnier, L.O., Yang, X.V. and Griffin, J.H. Activated protein C mutant with minimal anticoagulant activity, normal cytoprotective activity, and preservation of thrombin activable fibrinolysis inhibitor-dependent cytoprotective functions. *Journal of Biological Chemistry*. 2007; 282(45), pp.33022-33. PMID: 17872949.

Weiler, H. and Ruf, W. Activated protein C in sepsis: the promise of non-anticoagulant activated protein C. *Current opinion in hematology*. 2008; 15(5), p.487. PMID: 18695372.