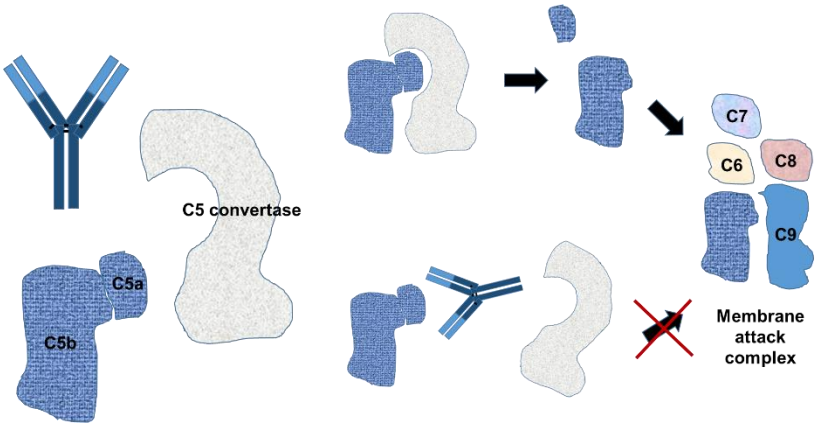
Eculizumab – Fact Sheet

Molecule

Eculizumab (Soliris®) is a humanized monoclonal antibody. This antibody is a immunoglobulin G-kappa type consisting of human constant regions and murine complementarity-determining regions. It has a molecular weight of approximately 148 kDa.

Mode of Action

Eculizumab binds to the complement component 5 (C5), which is a terminal molecule in the complement cascade. C5 normally activates cells by attracting pro-inflammatory immune cells, while also destroying cells by triggering the final pore formation. Eculizumab inhibits the cleavage of C5 by C5 convertase into C5a and C5b and subsequent generation of the terminal complement attack complex C5b-9. Paroxysmal Nocturnal Hemoglobinuria (PNH) patients are deficient in terminal complement inhibitors. Eculizumab thus inhibits terminal complement mediated intravascular hemolysis and therefore the destruction of erythrocytes.



Indication

Soliris® is indicated for treatment of patients with PNH to reduce hemolysis. It is also indicated for treatment of patients with atypical haemolytic uremic syndrome (aHUS) to inhibit complement mediated thrombotic micro-angiopathy.

Patent Situation

Dedicated patents on Soliris® will expire in USA in 2021 and in Europe in 2020. In 2017, in the US new patents directed to the composition of matter and pharmaceutical formulations of eculizumab, and methods of treating PNH were issued. These patents will expire in 2027.

Market and Competitive Field

The originator product, Actelion's Soliris®, was first approved by FDA and EMA in 2007 for the treatment of PNH and then in 2011 for the treatment of aHUS. Both indications are ultra-rare diseases, however, with an annual cost of around 400,000 Euro per patient (USA, in Canada even higher), Soliris® had 2.8 billion Euro in global sales in 2017. Soliris® is thus the highest priced monoclonal antibody.

VelaLabs GmbH
Brunner Straße 69 / Obj. 3, A-1230 Vienna / Austria
Phone: +43 1 890 5979 11, Fax: +43 1 890 5979 10
E-Mail: office@vela-labs.at

VelaLabs Portfolio

		Eculizumab
		Soliris®
	Clone selection/ comparability	
HPLC	Separation based on **size** (SE-HPLC)	
HPLC	Separation based on **hydrophobicity** (RP-HPLC)	
HPLC	Detection of **charge variants** (CEX-HPLC)	
Binding	Binding to **cell surface** expressed target (Flow cytometry)	
Binding	Binding to **soluble target** (ELISA)	
Binding	Binding to specific **antibody or antigen** (SPR-BIACORE, ELISA)	
Binding	**Affinity/ kinetic** to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, [1]**CDC surrogate** (ELISA)	
Effector function	**Affinity** to recombinant Fc-receptors (SPR-BIACORE)	
Effector function	Reporter gene assays, [2]**ADCC surrogate** (Luminescence)	
Effector function	[1]**CDC** (Flow cytometry)	
Effector function	[2]**ADCC** (DELFIA, Fluorescence)	
Effector function	Additional **bioassays** (Luminescence, fluorescence)	Potency assay
Gly	Glyco-pattern with **Lectin Microarray** (45 different lectins)	
	(Pre)clinical application	
Clinics	Pharmacokinetics – **PK** (ECL, ELISA)	
Clinics	Pharmacodynamics – **PD** (ECL, ELISA, flow cytometry, bioassay)	
Clinics	Immunogenicity - [3]**ADAs** (ECL, Biacore, ELISA, neutr. assay)	

[1]CDC = Complement Dependent Cytotoxicity
[2]ADCC = Antibody Dependent Cellular Cytotoxicity
[3]ADA = Anti-Drug-Antibody

	Vela portfolio
	Vela planned
	c.l.d. = cell line dependent
	n.a. = not applicable
	In development

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