

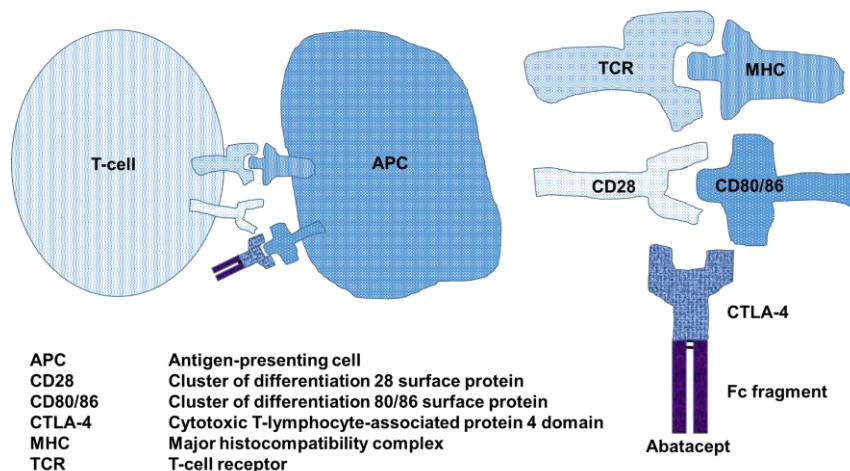
Abatacept – Fact Sheet

Molecule

Abatacept (Orencia®) is a fusion protein composed of the Fc region of the immunoglobulin IgG1 linked to the extracellular domain of cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). The molecular weight of abatacept is about 92 kDa.

Mode of Action

To activate a T-cell and subsequently produce an immune response, an antigen-presenting cell must show two signals to the T-cell. One of those signals is the major histocompatibility complex (MHC), combined with the T-cell receptor (TCR), and the other signal is the CD80/CD86 molecule. Abatacept binds to the CD80/CD86 molecule, and prevents the second signal. Without the second signal, the T-cell cannot be activated. Abatacept is thus down-regulating the activation of T-cells by binding to CD80/CD86 ligand proteins and modifies inflammation and immune activity, which causes major symptoms of rheumatoid arthritis.



Indication

Orencia® is indicated for reducing signs and symptoms in adult patients with moderately to severely active rheumatoid arthritis. It is also indicated for juvenile idiopathic arthritis and adult psoriatic arthritis.

Patent Situation

Patents on Orencia® will expire in US in October 2019 and expired in Europe in December 2017. When challenged by Momenta, the validity of a formulation patent for Orencia® was upheld in 2016.

Market and Competitive Field

The originator product, Bristol-Myers Squibb's Orencia®, was approved by FDA in 2005 and by EMA 2007. In 2018, Orencia® had sales of 2.71 billion Euro. Potential biosimilar products are at a very early stage.

		Abatacpt
		Orencia®
	Clone selection/ comparability	
HPLC	Separation based on size (SE-HPLC)	
	Separation based on hydrophobicity (RP-HPLC)	
	Detection of charge variants (CEX-HPLC)	
Binding	Binding to cell surface expressed target (Flow cytometry)	c.l.d.
	Binding to soluble target (ELISA)	
	Binding to specific antibody or antigen (SPR-BIACORE, ELISA)	n.a.
	Affinity/ kinetic to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, ¹ CDC surrogate (ELISA)	n.a.
	Affinity to recombinant Fc-receptors (SPR-BIACORE)	
	Reporter gene assays, ² ADCC surrogate (Luminescence)	n.a.
	¹ CDC (Flow cytometry)	n.a.
	² ADCC (DELFI, Fluorescence)	n.a.
	Additional bioassays (Luminescence, fluorescence)	IL2 bioassay
GLY	Glyco-pattern with Lectin Microarray (45 different lectins)	
	(Pre)clinical application	
Clinics	Pharmacokinetics – PK (ECL, ELISA)	
	Pharmacodynamics – PD (ECL, ELISA, flow cytometry, bioassay)	
	Immunogenicity - ³ ADAs (ECL, Biacore, ELISA, neutr. assay)	

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

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