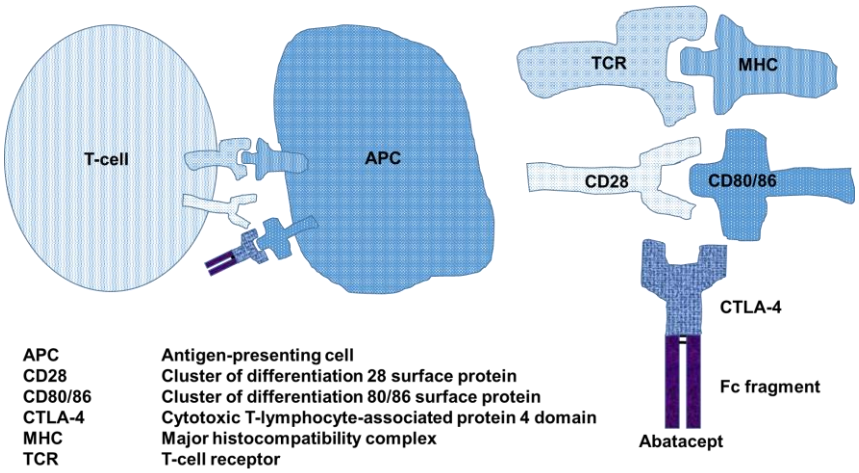
Abatacept – Fact Sheet

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.



APC	Antigen-presenting cell
CD28	Cluster of differentiation 28 surface protein
CD80/86	Cluster of differentiation 80/86 surface protein
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4 domain
MHC	Major histocompatibility complex
TCR	T-cell receptor

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 2017, Orencia® had sales of 2.01 billion Euro. Potential biosimilar products are at a very early stage.

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		Abatacpt Orencia®
	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)	c.l.d.
Binding	Binding to **soluble target** (ELISA)	
Binding	Binding to specific **antibody or antigen** (SPR-BIACORE, ELISA)	n.a.
Binding	**Affinity/ kinetic** to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, [1]**CDC surrogate** (ELISA)	n.a.
Effector function	**Affinity** to recombinant Fc-receptors (SPR-BIACORE)	
Effector function	Reporter gene assays, [2]**ADCC surrogate** (Luminescence)	n.a.
Effector function	[1]**CDC** (Flow cytometry)	n.a.
Effector function	[2]**ADCC** (DELFIA, Fluorescence)	n.a.
Effector function	Additional **bioassays** (Luminescence, fluorescence)	IL2 bioassay
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

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

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