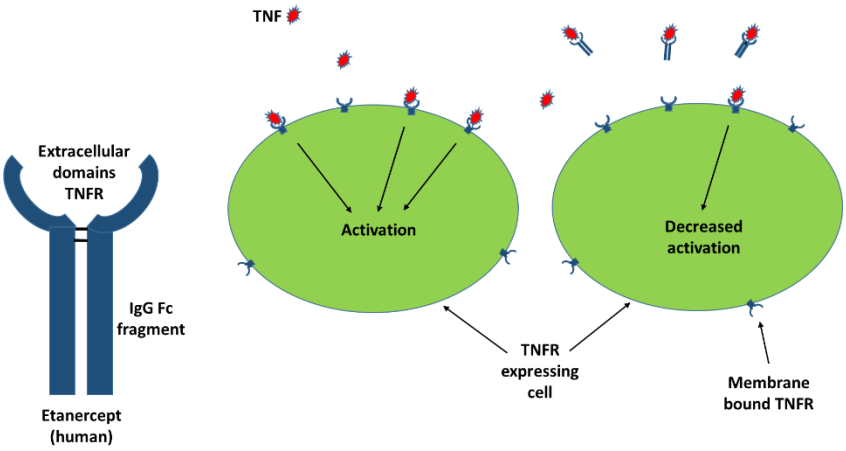
Etanercept – Fact Sheet

Molecule

Etanercept (Enbrel®) is a dimeric human receptor fusion protein consisting of the extracellular ligand-binding domain of human 75kD (p75) tumor necrosis factor receptor (TNFR) linked to the Fc-part of human IgG1. The Fc-part of etanercept contains CH2 domain, CH3 domain and the hinge region. The molecular weight is approximately 150kD.

Mode of Action

TNF is a cytokine primarily produced by activated macrophages and T cells. One of the naturally occurring receptors is a 75kD (p75) TNFR. Monomers of the extracellular portion of TNFR are physiologically cleaved from cell surface (soluble TNFR, sTNFR) and bind with high affinity to circulating TNF-α. As such, they act as competitive inhibitors to TNF-α preventing it from binding to cell-bound TNFRs. Thus, the fusion protein etanercept competitively inhibits binding of TNF-α to TNFRs, rendering TNF-α biologically inactive. Etanercept also modulates indirectly different biological functions such as expression of adhesion molecule E-selectin, production of interleukin-6 (IL-6) and matrix metalloproteinase 3 (MMP-3), as well as IL-1.



Indication

Etanercept is applied for treatment of Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis and Plaque Psoriasis.

Patent Situation

Enbrel® patents expired in 2012 in US and in 2015 in Europe. However, Amgen, the owner of originator Enbrel® fights to hold off biosimilars from the market until 2029 with new preparation patents.

Market and Competitive Field

Amgen's Enbrel® (co-marketed by Pfizer) has received its first approval by FDA in 1998 and by EMA in 2000. In 2018, Enbrel® had sales of 4.45 billion € (Amgen) and 461 million € (Pfizer). In respect of these blockbuster sales many companies are developing or marketing biosimilars of the drug, e.g. Sandoz and Merck. Benepali® is already approved by EMA and Erelzi™ by EMA and FDA.

		Etanercept Enbrel® Altebrel™, Benepali®, Brenzys™, Davictrel™, Etacept, Erelzi™, Etanar®, Infinitam, Qiangke®
	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)	
Effector function	**Affinity** to recombinant Fc-receptors (SPR-BIACORE)	
Effector function	Reporter gene assays, [2]**ADCC surrogate** (Luminescence)	c.l.d.
Effector function	[1]**CDC** (Flow cytometry)	c.l.d.
Effector function	[2]**ADCC** (DELFIA, Fluorescence)	c.l.d.
Effector function	Additional **bioassays** (Luminescence, fluorescence)	
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

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