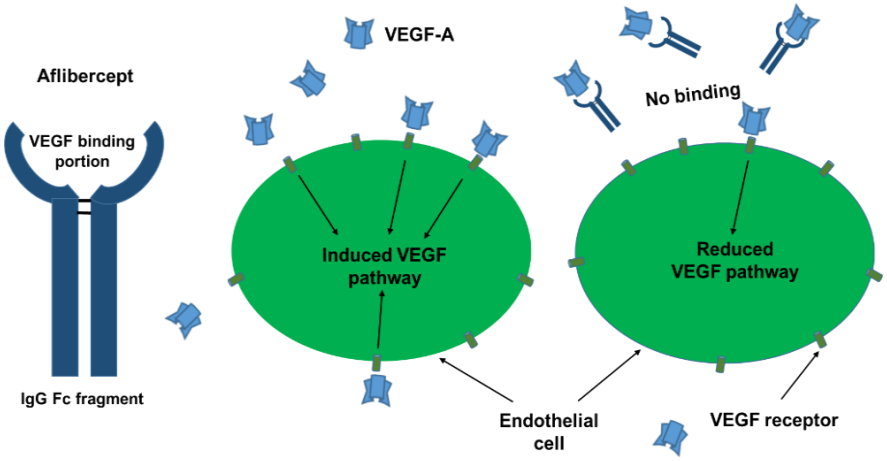
Aflibercept – Fact Sheet

Molecule

Aflibercept (Eylea®, Zaltrap®) is a recombinant fusion protein consisting of vascular endothelial growth factor (VEGF) - binding portion from the extracellular domains of human VEGF receptors 1 and 2 fused to the Fc portion of a human IgG1 immunoglobulin. Together with the glycosylation pattern of the FC-part, its molecular weight is 115 kDa.

Mode of Action

Like ranibizumab, aflibercept is an inhibitor of VEGF. It binds to the receptor binding site of active forms of VEGF-A, including the biologically active, cleaved form of this molecule, VEGF-110. The binding of aflibercept to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.



Indication

Eylea® (aflibercept) is indicated for the treatment of neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy. Zaltrap® (ziv-aflibercept) is indicated in combination with 5-fluorouracil, leucovorin, irinotecan (cytostatic medication) for metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing therapy.

Patent Situation

A basic US patent for aflibercept will expire in 2020 (with extension 2023), European patents will expire in 2021. Other patents in combination with their extensions may be valid until 2027 and it remains to be seen whether these patents can prevent the market entry of biosimilars.

Market and Competitive Field

The originator product from Regeneron was co-developed with Bayer and approved by FDA (2011) and EMA (2012) for the treatment of eye diseases under the trade name Eylea®. The second originator was co-developed with Sanofi and approved by FDA (2012) and EMA (2013) for the treatment of cancer under the trade name Zaltrap®. In 2020, global sales of Eylea® were 6.90 billion €.

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

		Aflibercept Eylea®, Zaltrap®
	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)	
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 assay, [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)	
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, neutralization 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
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