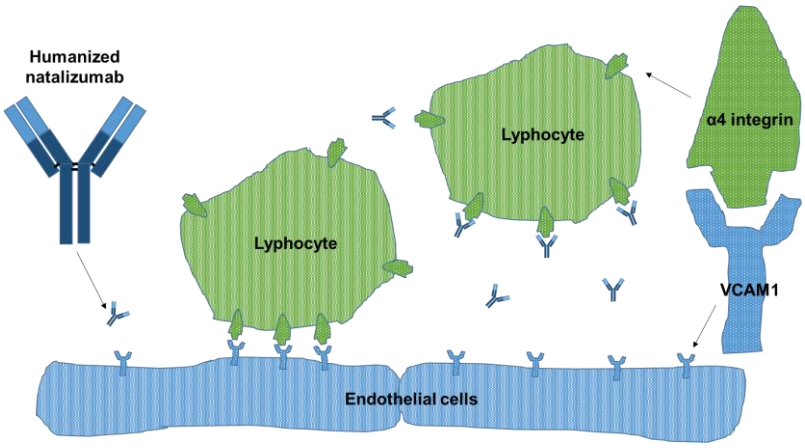
Natalizumab – Fact Sheet

Molecule

Natalizumab (Tysabri®) is a humanized monoclonal IgG_4 antibody directed against α4 integrin, a cellular adhesion molecule. It is the first antibody in the class of selective adhesion molecule inhibitors. Natalizumab contains human framework regions and the complementarity-determining regions of a murine antibody. It has a molecular size of 149 kDa.

Mode of Action

Integrins are transmembrane receptors that facilitate cell-extracellular matrix adhesion. Upon ligand binding, integrins activate signal transduction pathways that mediate cellular signals such as regulation of the cell cycle and movement of receptors to the cell membrane. α4-integrin is required for lymphocytes to move into organs, which is mediated by vascular cell adhesion molecule 1 (VCAM1). Natalizumab functions by reducing the ability of inflammatory immune cells to attach to and pass through cell layers lining intestines and blood–brain barrier.



Indication

Tysabri® is indicated as monotherapy for treatment of relapsing forms of multiple sclerosis (MS) and in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation, which have had an inadequate response or intolerance to conventional CD therapies.

Patent Situation

Patents on Tysabri® expired in March 2015 in US and in August 2015 in Europe.

Market and Competitive Field

Tysabri® was developed by Elan / Biogen and got its first approval by FDA in 2004 for MS and subsequently for CD. In EU it was approved for MS in 2006. In 2021, Biogen had sales of 1.93 billion € for Tysabri®. Only one biosimilar is currently at clinical stage, which might be due to potential risks of the severe side effect progressive multifocal leukoencephalopathy. Furthermore, there is severe competition from other MS drugs.

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VelaLabs Portfolio

		Natalizumab
		Tysabri®
	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)	n.a.
Binding	Binding to specific **antibody or antigen** (SPR-BIACORE, ELISA)	
Binding	**Affinity/ kinetic** to recombinant target (SPR-BIACORE)	n.a.
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)	
Effector function	[1]**CDC** (Flow cytometry)	
Effector function	[2]**ADCC** (DELFIA, Fluorescence)	
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

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

If you are interested in the full version including patent and originator data please contact us: velabd@vela-labs.at

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