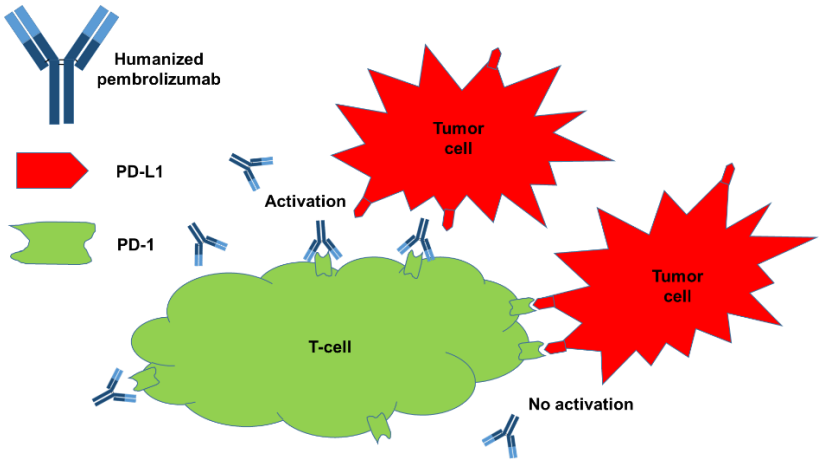
Pembrolizumab – Fact Sheet

Molecule

Pembrolizumab (Keytruda®) is a humanized monoclonal IgG4 antibody that contains an engineered hinge region mutation (S228P). It has a molecular weight of 146.3 kDa and is targeted to the cellular programmed cell death protein -1 (PD-1).

Mode of Action

Programmed cell death ligand 1 or ligand 2 (PD-L1 or PD-L2) is upregulated on 40–50 % of melanomas and has limited expression otherwise. Both ligands bind to PD-1, a protein on the surface of activated T-cells. If PD-L1 binds to PD-1, a T-cell becomes inactive and inhibited from attacking a tumor. The inhibitory effect results from promotion of apoptosis in antigen specific T-cells while simultaneously blocking apoptosis in suppressor T-cells. Pembrolizumab binds to PD-1, thus blocks PD-L1 or PD-L2 from binding to PD-1, and T-cells can again attack tumor cells.



Indication

Keytruda® is indicated for, among other cancer types (more than 30 indications), melanoma, non-small cell lung cancer, head and neck squamous cell cancer, classical Hodgkin lymphoma, gastric cancer, cervical cancer, hepatocellular carcinoma, and primary mediastinal large B-cell lymphoma.

Patent Situation

Patents for Keytruda® have expiry dates of up to 2036 in US and 2028 in EU. BMS owns patents directed to the inhibition to PD-1 and is filing lawsuits against competitors marketing antibodies with this target. This also included Keytruda® resulting into royalty payments of MSD.

Market and Competitive Field

Keytruda® from MSD was approved for its first indication by FDA in 2014 and by EMA in 2015. In 2019, MSD had sales for Keytruda® of 10.2 billion €, up from 6.60 billion € in 2018. Due to late patent expiry dates and to the development of novel antibodies also targeting PD-1, there are currently no biosimilars in a late stage of clinical development.

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		Pembrolizumab Keytruda®
	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)	
Binding	Binding to **soluble target** (ELISA)	
Binding	Binding to specific **antibody or antigen** (SPR-BIACORE, ELISA)	If applicable
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)	
Effector function	[1]**CDC** (Flow cytometry)	n.a.
Effector function	[2]**ADCC** (DELFIA, Fluorescence)	n.a.
Effector function	Additional **bioassays** (Luminescence, fluorescence)	PD-1/PD-L1 blockage bioassay
Gly	Glyco-pattern with **Lectin Microarray** (45 different lectins)	
	(Pre)clinical application	
Clinics	Pharmacokinetics – **PK** (ECL, ELISA)	n.a.
Clinics	Pharmacodynamics – **PD** (ECL, ELISA, flow cytometry, bioassay)	n.a.
Clinics	Immunogenicity - [3]**ADAs** (ECL, Biacore, ELISA, neutr. assay)	n.a.

[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

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