

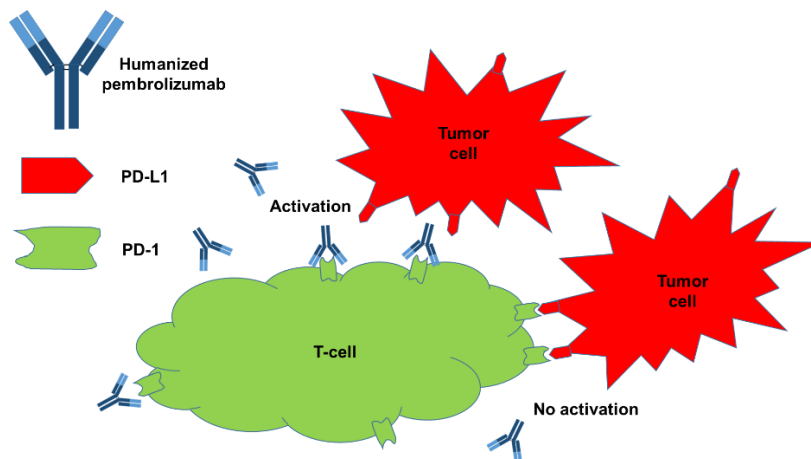
Pembrolizumab – Fact Sheet

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 2020, MSD had sales for Keytruda® of 12.1 billion €, up from 10.2 billion € in 2019. 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.

		Pembrolizumab
		Keytruda®
		Clone selection/ comparability
HPLC	Separation based on size (SE-HPLC)	
	Separation based on hydrophobicity (RP-HPLC)	
	Detection of charge variants (CEX-HPLC)	
Binding	Binding to cell surface expressed target (Flow cytometry)	
	Binding to soluble target (ELISA)	
	Binding to specific antibody or antigen (SPR-BIACORE, ELISA)	If applicable
	Affinity/ kinetic to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, ¹CDC surrogate (ELISA)	
	Affinity to recombinant Fc-receptors (SPR-BIACORE)	
	Reporter gene assays, ²ADCC surrogate (Luminescence)	
	¹CDC (Flow cytometry)	n.a.
	²ADCC (DELFI, Fluorescence)	n.a.
	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.
	Pharmacodynamics – PD (ECL, ELISA, flow cytometry, bioassay)	n.a.
	Immunogenicity - ³ADAs (ECL, Biacore, ELISA, neutr. assay)	n.a.

¹CDC = Complement Dependent Cytotoxicity
²ADCC = Antibody Dependent Cellular Cytotoxicity
³ADA = Anti-Drug Antibody

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