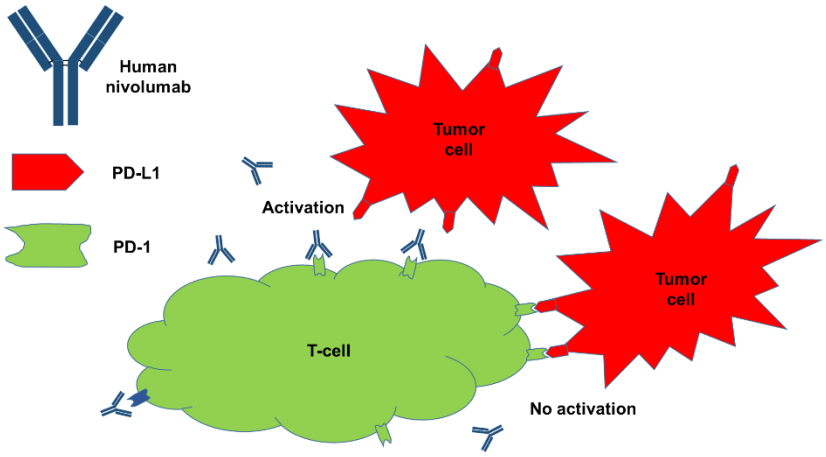
Nivolumab – Fact Sheet

Molecule

Nivolumab, (Opdivo®), is a fully human monoclonal IgG4 antibody. It has a molecular weight of 143.6 kD 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. Nivolumab 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

Opdivo® is indicated, among other cancer types, as a first or second line treatment for inoperable or metastatic melanoma. This includes advanced Non-Small Cell Lung Cancer, Metastatic Melanoma, advanced Renal Cell Carcinoma, Squamous Cell Carcinoma of the Head and Neck.

Patent Situation

Owner of the originator product Opdivo®, Bristol-Myers Squibb (BMS) and collaborator Ono Pharmaceuticals filed several patent families around this drug, with expiration dates of up to 2027 in US and 2026 in EU. This includes patents directed to the inhibition to PD-1. BMS is filing lawsuits against competitors marketing antibodies with this target (e.g. Merck USA).

Market and Competitive Field

Opdivo® was approved as first PD-1 immune checkpoint inhibitor in the world for its first indication by FDA in 2014 and in EU in 2015. In 2017, BMS had sales for Opdivo® of 4.17 billion €, up from 3.18 billion € in 2016 (791 million € in 2015).

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		Nivolumab Opdivo®
	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)	
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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