Durvalumab

Targets (2) Biointeractions (2)

IDENTIFICATION

Name

Durvalumab

Accession Number

DB11714

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Durvalumab is a a human monoclonal antibody that blocks programmed death ligand 1 (PD-L1), or CD 274. In May, 2017 it received FDA approval for previously treated patients with locally advanced or metastatic cancer in the urinary system (as Imfinzi). It is shown to be effective in patients with continued disease progression after the platinum-based chemotherapy. This drug has a relatively tolerable safety profile and its structural modification advantageously prevents the induction of antibody-dependent cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) [5].

Protein chemical formula

$C_{6502}H_{10018}N_{1742}O_{2024}S_{42}$

Protein average weight

Sequences

```
>Durvalumab heavy chain
EVQLVESGGGLVQPGGSLRLSCAASGFTFSRYWMSWVRQAPGKGLEWVANIKQDGSEKYY
VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGGWFGELAFDYWGQGTLVTVS
SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS
SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEFEG
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
```

```
>Durvalumab light chain
EIVLTQSPGTLSLSPGERATLSCRASQRVSSSYLAWYQQKPGQAPRLLIYDASSRATGIP
DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSLPWTFGQGTKVEIKRTVAAPSVFIFP
PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL
TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

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Synonyms

Not Available

External IDs

MEDI 4736 / MEDI-4736 / MEDI4736

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Imfinzi	Injection, solution	120 mg/2.4mL	Intravenous	Astra Zeneca Lp	2017-05-01	Not applicable		
Imfinzi	Solution	50 mg	Intravenous	Astra Zeneca	2017-11-20	Not applicable		
Imfinzi	Injection, solution	500 mg/10mL	Intravenous	Astra Zeneca Lp	2017-05-01	Not applicable		

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Categories

Antibodies

Antineoplastic Agents

Blood Proteins

Globulins

Immunoglobulins

Immunoproteins

Programmed Death Ligand-1 Blocker

Proteins

Serum Globulins

UNII

28X28X9OKV

CAS number

1428935-60-7

PHARMACOLOGY

Indication

Durvalumab is indicated for patients with urothelial carcinoma, such as urinary bladder, urethra or ureter cancer. Patients with prolonged disease progression due to failed platinum-based chemotherapy such as cisplatin and carboplatin are most likely to benefit from durvalumab treatment. Its clinical effectiveness is especially enhanced in PD-L1-positive patient groups [1].

Structured Indications

Urothelial carcinoma ureter metastatic

Locally advanced Urothelial Carcinoma

Pharmacodynamics

PD-L1 (programmed cell death ligand 1) is a ligand of PD-1 receptor on activated T cells. Tumor cells and tumor-associated immune cells express this inhibitory immune checkpoint molecule

that interrupts normal signalling of T cell and subsequent immune responses in the tumor microenvironment by binding to PD-1 receptors. As a novel anticancer immunotherapy, durvalumab enhances T cell responses at tumor sites. Durvalumab acts as a selective antibody

inhibitor.

Mechanism of action

Durvalumab is a human immunoglobulin G1 kappa (IgGIk) monoclonal antibody that blocks PD-L1 binding to PD-1 and CD80. PD1 signalling pathway serves to physiologically limit the activity of T cells and autoimmune or inflammatory responses in the body however can be a mechanism of immunity resistance by tumor cells. Blockage of ligand-mediated PD1 pathway enhances further T cell activation, effector T cell proliferation, NK cell activity and cytokine production to minimize the growth of locally advancing or metastasizing solid tumors.

(A) Programmed cell death 1 ligand 1	
binder	
Human	
(A) T-lymphocyte activation antigen CD80	
binder	
Human	

Absorption

Not Available

Volume of distribution

Mean Vd approximately 5.6 L with 17% coefficient of variation.

Protein binding

Not Available

Metabolism

Most likely to be degraded into peptides and amino acids by circulating phagocytic cellsor by target antigen-containing cells [4].

Route of elimination

Not Available

Half life

Clearance

Mean steady state clearance is approximately 8.24 mL/h (37.3% coefficient of variation).

Toxicity

Many toxic effects of durvalumab therapy are immune-mediated inflammation in various tissues including pneumonitis, hepatitis and colitis. Disturbances in endocrine system are possible adverse effects such as hypo/hyperthyroidism, type I diabetes mellitus and adrenal insufficiency. Cessation of therapy is recommended in case of any immune-mediated or infusion-related adverse reactions. Animal studies suggest a possibility of embryo-fetal toxicity.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Acetyldigitoxin	Acetyldigitoxin may decrease the cardiotoxic activities of Durvalumab.	Approved
Acetyldigoxin	Acetyldigoxin may decrease the cardiotoxic activities of Durvalumab.	Experimental
Ancestim	The risk or severity of cytotoxicity can be increased when Ancestim is combined with Durvalumab.	Approved, Investigational, Withdrawn
Anthrax immune globulin human	The therapeutic efficacy of Anthrax immune globulin human can be decreased when used in combination with Durvalumab.	Approved

substrain connaught live antigen	substrain connaught live antigen can be decreased when used in combination with Durvalumab.	Investigational
Bacillus calmette-guerin substrain tice live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain tice live antigen can be decreased when used in combination with Durvalumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Durvalumab.	Investigational
Bevacizumab	Bevacizumab may increase the cardiotoxic activities of Durvalumab.	Approved, Investigational
Cabazitaxel	The risk or severity of adverse effects can be increased when Cabazitaxel is combined with Durvalumab.	Approved
Clostridium tetani toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Clostridium tetani toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Durvalumab.	Approved

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Food Interactions

Not Available

REFERENCES

General References

1. Massard C, Gordon MS, Sharma S, Rafii S, Wainberg ZA, Luke J, Curiel TJ, Colon-Otero G, Hamid O, Sanborn RE, O'Donnell PH, Drakaki A, Tan W, Kurland JF, Rebelatto MC, Jin X, Blake-Haskins JA, Gupta A, Segal NH: Safety and Efficacy of Durvalumab (MEDI4736), an Anti-Programmed Cell Death Ligand-1 Immune Checkpoint Inhibitor, in Patients With Advanced Urothelial Bladder Cancer. J Clin Oncol. 2016 Sep 10;34(26):3119-25. doi: 10.1200/JCO.2016.67.9761. Epub 2016 Jun 6. [PubMed:27269937]
2. Pardoll DM: The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012 Mar 22;12(4):252-64. doi: 10.1038/nrc3239. [PubMed:22437870]
3. Medina PJ, Adams VR: PD-1 Pathway Inhibitors: Immuno-Oncology Agents for Restoring Antitumor Immune Responses. Pharmacotherapy. 2016 Mar;36(3):317-34. doi: 10.1002/phar.1714. [PubMed:26822752]
4. Keizer RJ, Huitema AD, Schellens JH, Beijnen JH: Clinical pharmacokinetics of therapeutic monoclonal antibodies. Clin Pharmacokinet. 2010 Aug;49(8):493-507. doi: 10.2165/11531280-000000000-00000. [PubMed:20608753]
5. Durvalumab IMGT/mAb-DB card [Link]

External Links

KEGG Drug

PubChem Substance

347911229

Drugs.com

Drugs.com Drug Page

Wikipedia

Durvalumab

AHFS Codes

10:00.00 — Antineoplastic Agents

FDA label

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Recruiting	Basic Science	Bevacizumab-alone Maintenance Treatment Progression / Metastatic Breast Cancer (MBC)	1
0	Recruiting	Treatment	Cancer, Breast / Hormone Receptor Positive, HER2 Negative Breast Cancer	1
0	Recruiting	Treatment	Malignant Neoplasms of Oropharynx	1
0	Recruiting	Treatment	Malignant Neoplasms of Urinary Tract	1
0	Recruiting	Treatment	Thyroid Cancers	1
0	Withdrawn	Treatment	Cutaneous T Cell Lymphomas (CTCL)	1
1	Active Not Recruiting	Other	Metastatic Breast Cancer (MBC)	1
1	Active Not Recruiting	Other	Solid Malignancies	1
1	Active Not Recruiting	Prevention	Smoldering Multiple Myeloma (SMM)	1

	Recruiting		Cancer, Breast / Colorectal Cancers / Gastrooesophageal Cancer / Head and Neck Carcinoma / Lung Cancers / Melanoma	

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection, solution	Intravenous	120 mg/2.4mL
Injection, solution	Intravenous	500 mg/10mL
Solution	Intravenous	50 mg

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Prices

Not Available

Patents

Not Available

PROPERTIES

State

Liquid

Not Available

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Programmed cell death 1 ligand 1

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Binder

General Function

Not Available

Specific Function

Involved in the costimulatory signal, essential for T-cell proliferation and production of IL10 and IFNG, in an IL2-dependent and a PDCD1-independent manner. Interaction with PDCD1 inhibits T-cell ...

Gene Name

CD274

Uniprot ID

Q9NZQ7

Uniprot Name

Programmed cell death 1 ligand 1

Molecular Weight

33275.095 Da

References

1. Bellmunt J, Powles T, Vogelzang NJ: A review on the evolution of PD-1/PD-L1 immunotherapy for bladder cancer: The future is now. Cancer Treat Rev. 2017 Mar;54:58-67. doi: 10.1016/j.ctrv.2017.01.007. Epub 2017 Feb 2. [PubMed:28214651]

2. T-lymphocyte activation antigen CD80

Protein

Organism

Human

Pharmacological action

Yes

Actions

Binder

General Function

Virus receptor activity

Specific Function

Involved in the costimulatory signal essential for T-lymphocyte activation. T-cell proliferation and cytokine production is induced by the binding of CD28, binding to CTLA-4 has opposite effects an...

Gene Name

CD80

Uniprot ID

P33681

Uniprot Name

T-lymphocyte activation antigen CD80

Molecular Weight

33047.625 Da

References

1. Reichert JM: Antibodies to watch in 2017. MAbs. 2017 Feb/Mar;9(2):167-181. doi: 10.1080/19420862.2016.1269580. Epub 2016 Dec 14. [PubMed:27960628]

Drug created on October 20, 2016 14:41 / Updated on May 15, 2018 11:55

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