Ramucirumab

Targets (1) Biointeractions (1)

IDENTIFICATION

Name

Ramucirumab

Accession Number

DB05578

Type

Biotech

Groups

Approved, Investigational

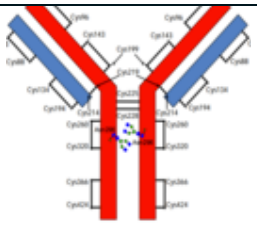
Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Ramucirumab is a human monoclonal antibody (IgG1) against vascular endothelial growth factor receptor 2 (VEGFR2), a type II trans-membrane tyrosine kinase receptor expressed on endothelial cells. By binding to VEGFR2, ramucirumab prevents binding of its ligands (VEGF-A, VEGF-C, and VEGF-D), thereby preventing VEGF-stimulated receptor phosphorylation and downstream ligand-induced proliferation, permeability, and migration of human endothelial cells. VEGFR stimulation also mediates downstream signalling required for angiogenesis and is postulated to be heavily involved in cancer progression, making it a highly likely drug target. In contrast to other agents directed against VEGFR-2, ramucirumab binds a specific epitope on the extracellular domain of

VEGFR-2, thereby blocking all VEGF ligands from binding to it. Ramucirumab is indicated for us in advanced gastric or gastro-esophageal junction adenocarcinoma as a single agent or in



Protein chemical formula

$C_{6374}H_{9864}N_{1692}O_{1996}S_{46}$

Protein average weight

143600.0 Da

Sequences

```
>9098_H|ramucirumab|Homo sapiens||H-GAMMA-1 (VH(1-116)+CH1(117-214)+HINGE-REGION(215-
229)+CH2(230-339)+CH3(340-446))|||||||446|||MW 48696.0|MW 48696.0|
EVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYY
ADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARVTDAFDIWGQGTMVTVSSASTK
GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSPGK
```

```
>9098_L|ramucirumab|Homo sapiens||L-KAPPA (V-KAPPA(1-107)+C-KAPPA(109-214))|||||||214||||MW
23124.7|MW 23124.7|
DIQMTQSPSSVSASIGDRVTITCRASQGIDNWLGWYQQKPGKAPKLLIYDASNLDTGVPS
RFSGSGSGTYFTLTISSLQAEDFAVYFCQQAKAFPPTFGGGTKVDIKGTVAAPSVFIFPP
SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT
LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

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Synonyms

Not Available

External IDs

1121B / IMC-1121B / LY3009806

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END	
Cyramza	Solution	10 mg	Intravenous	Eli Lilly & Co. Ltd.	2015-09-10	Not applicable	
Cyramza	Solution	10 mg/mL	Intravenous	Eli Lilly & Co. Ltd.	2014-04-21	Not applicable	
Cyramza	Solution	10 mg/mL	Intravenous	Eli Lilly & Co. Ltd.	2014-04-21	Not applicable	

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Categories

Amino Acids, Peptides, and Proteins

Antibodies

Antibodies, Monoclonal

Antineoplastic Agents

Antineoplastic and Immunomodulating Agents

Blood Proteins

Globulins

Immunoglobulins

Immunoproteins

Proteins

Serum Globulins

Vascular Endothelial Growth Factor Receptor 2 Antagonist

UNII

D99YVK4L0X

CAS number

947687-13-0

For use in advanced gastric or gastro-esophageal junction adenocarcinoma as a single agent or in combination with paclitaxel after prior fluoropyrimidine- or platinum-containing chemotherapy.

Associated Conditions

Advanced Gastric Cancer

Advanced gastro-esophageal junction adenocarcinoma

Refractory, metastatic Colorectal cancer

Refractory, metastatic Non small cell lung cancer

Pharmacodynamics

Not Available

Mechanism of action

Ramucirumab is a human monoclonal antibody (IgG1) against vascular endothelial growth factor receptor 2 (VEGFR2), a type II trans-membrane tyrosine kinase receptor expressed on endothelial cells. By binding to VEGFR2, ramucirumab prevents binding of its ligands (VEGF-A, VEGF-C, and VEGF-D), thereby preventing VEGF-stimulated receptor phosphorylation and downstream ligand-induced proliferation, permeability, and migration of human endothelial cells.

A	Vascular endothelial growth factor receptor 2	
	antagonist	
	Human	

Absorption

Not Available

Volume of distribution

5.5 L

Protein binding

Not Available

Metabolism

Not Available

Half life

15 days

Clearance

0.014 L/hour

Toxicity

Ramucirumab packaging includes warnings for arterial thromboembolic events, hypertension, infusion-related reactions, gastrointestinal perforation, clinical deterioration in patients with cirrhosis, and reversible posterior leukoencephalopathy syndrome. The most common reactions observed in single-agent-treated patients at a rate of >10% and >2% higher than placebo were hypertension and diarrhea. The most common adverse reactions observed in patients treated with ramucirumab plus paclitaxel at a rate of of >30% and >2% higher than placebo plus paclitaxel were fatigue, neutropenia, diarrhea, and epistaxis.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Abciximab	The risk or severity of adverse effects can be increased when Abciximab is combined with Ramucirumab.	Approved

	Ramucirumab.	
Adalimumab	The risk or severity of adverse effects can be increased when Adalimumab is combined with Ramucirumab.	Approved
Ancestim	The risk or severity of cytotoxicity can be increased when Ancestim is combined with Ramucirumab.	Approved, Investigational, Withdrawn
Anthrax immune globulin human	The therapeutic efficacy of Anthrax immune globulin human can be decreased when used in combination with Ramucirumab.	Approved
Bacillus calmette-guerin substrain connaught live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain connaught live antigen can be decreased when used in combination with Ramucirumab.	Approved, 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 Ramucirumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Ramucirumab.	Investigational
Belimumab	The risk or severity of adverse effects can be increased when Ramucirumab is combined with Belimumab.	Approved

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Food Interactions

Not Available

REFERENCES

Synthesis Reference

http://www.ema.europa.eu/docs/en*GB/document*library/EPAR-Public*assessment*report/human/002829/WC500180726.pdf

General References

1. Casak SJ, Fashoyin-Aje I, Lemery SJ, Zhang L, Jin R, Li H, Zhao L, Zhao H, Zhang H, Chen H, He K, Dougherty M, Novak R, Kennett S, Khasar S, Helms W, Keegan P, Pazdur R: FDA Approval Summary: Ramucirumab for

3. Javle M, Smyth EC, Chau I: Ramucirumab: successfully targeting angiogenesis in gastric cancer. Clin Cancer Res. 2014 Dec 1;20(23):5875-81. doi: 10.1158/1078-0432.CCR-14-1071. Epub 2014 Oct 3. [PubMed:25281695]
4. Aprile G, Bonotto M, Ongaro E, Pozzo C, Giuliani F: Critical appraisal of ramucirumab (IMC-1121B) for cancer treatment: from benchside to clinical use. Drugs. 2013 Dec;73(18):2003-15. doi: 10.1007/s40265-013-0154-8. [PubMed:24277700]
5. Goodkin R, Zaias B, Michelsen WJ: Arteriovenous malformation and glioma: coexistent or sequential? Case report. J Neurosurg. 1990 May;72(5):798-805. [PubMed:2182794]
6. Grothey A, Galanis E: Targeting angiogenesis: progress with anti-VEGF treatment with large molecules. Nat Rev Clin Oncol. 2009 Sep;6(9):507-18. doi: 10.1038/nrclinonc.2009.110. Epub 2009 Jul 28. [PubMed:19636328]
7. Spratlin JL, Cohen RB, Eadens M, Gore L, Camidge DR, Diab S, Leong S, O'Bryant C, Chow LQ, Serkova NJ, Meropol NJ, Lewis NL, Chiorean EG, Fox F, Youssoufian H, Rowinsky EK, Eckhardt SG: Phase I pharmacologic and biologic study of ramucirumab (IMC-1121B), a fully human immunoglobulin G1 monoclonal antibody targeting the vascular endothelial growth factor receptor-2. J Clin Oncol. 2010 Feb 10;28(5):780-7. doi: 10.1200/JCO.2009.23.7537. Epub 2010 Jan 4. [PubMed:20048182]
8. Lu D, Jimenez X, Zhang H, Bohlen P, Witte L, Zhu Z: Selection of high affinity human neutralizing antibodies to VEGFR2 from a large antibody phage display library for antiangiogenesis therapy. Int J Cancer. 2002 Jan 20;97(3):393-9. [PubMed:11774295]

External Links

KEGG Drug

D09371

PubChem Substance

347910183

ChEMBL

CHEMBL1743062

RxList

RxList Drug Page

Drugs.com

Drugs.com Drug Page

Wikipedia

Ramucirumab

ATC Codes

L01XC21 — Ramucirumab

- L01XC — Monoclonal antibodies
- L01X — OTHER ANTINEOPLASTIC AGENTS

10:00.00 — Antineoplastic Agents

FDA label

Download (493 KB)

MSDS

Download (206 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Active Not Recruiting	Treatment	Adenocarcinomas of the Gastroesophageal Junction / Biliary Tract Cancer / Gastric Adenocarcinoma / Lung Cancer Non-Small Cell Cancer (NSCLC) / Transitional Cell Carcinoma	1
1	Active Not Recruiting	Treatment	Adenocarcinomas of the Gastroesophageal Junction / Hepatocellular,Carcinoma / Lung Cancer Non-Small Cell Cancer (NSCLC) / Malignant Neoplasm of Stomach	1
1	Active Not Recruiting	Treatment	Cancer, Advanced / Colorectal Cancers / Mantle Cell Lymphoma (MCL)	1
1	Active Not Recruiting	Treatment	Lung Cancer Non-Small Cell Cancer (NSCLC)	1
1	Active Not Recruiting	Treatment	Non-Small Cell Lung Carcinoma (NSCLC)	1
1	Completed	Not Available	Advanced Solid Tumors	1
1	Completed	Treatment	Adenocarcinomas	1
1	Completed	Treatment	Advanced Solid Tumors	1
1	Completed	Treatment	Cancer, Breast / Metastatic Breast Cancer (MBC)	1
1	Completed	Treatment	Cancers	2

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Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Solution	Intravenous	10 mg
Solution	Intravenous	10 mg/mL

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Prices

Not Available

Patents

Search

PATENT NUMBER	PEDIATRIC EXTENSION	APPROVED	EXPIRES (ESTIMATED)	
US2013067098	No	2011-11-02	2031-11-02	

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PROPERTIES

State

Solid

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

Protein

Organism

Human

Pharmacological action

Yes

Actions

Antagonist

General Function

Vascular endothelial growth factor-activated receptor activity

Specific Function

Tyrosine-protein kinase that acts as a cell-surface receptor for VEGFA, VEGFC and VEGFD. Plays an essential role in the regulation of angiogenesis, vascular development, vascular permeability, and ...

Gene Name

KDR

Uniprot ID

P35968

Uniprot Name

Vascular endothelial growth factor receptor 2

Molecular Weight

151525.555 Da

References

1. Goodkin R, Zaias B, Michelsen WJ: Arteriovenous malformation and glioma: coexistent or sequential? Case report. J Neurosurg. 1990 May;72(5):798-805. [PubMed:2182794]

Drug created on November 18, 2007 11:26 / Updated on August 15, 2018 09:53

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