Mogamulizumab

Targets (1)

IDENTIFICATION

Name

Mogamulizumab

Accession Number

DB12498

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Mogamulizumab is a humanized monoclonal antibody (mAb) directed against CC chemokine receptor 4 (CCR4) for the treatment of Mycosis Fungoides (MF) and Sézary Syndrome (SS), the most common subtypes of cutaneous T-cell lymphoma. Cutaneous T-cell lymphomas occur when certain white blood cells, called T cells, become cancerous; these cancers typically affect the skin, causing various types of skin lesions [8].

On August 8 2018, the U.S. Food and Drug Administration (FDA) approved mogamulizumab injection (also known as *Poteligeo*) for intravenous use for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy [7].

leukemia-lymphoma [2].

Protein chemical formula

Not Available

Protein average weight

Not Available

Sequences

Not Available

Synonyms

mogamulizumab-kpkc

External IDs

AMG-761 / KM-8761 / KM8761 / KW 0761 / KW-0761

Categories

Amino Acids, Peptides, and Proteins

Antibodies

Antibodies, Monoclonal

Blood Proteins

Globulins

Immunoglobulins

Immunoproteins

Proteins

Serum Globulins

UNII

YI437801BE

Indication

For the intravenous use for the treatment of adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy. This approval provides a new treatment option for patients with MF and is the first FDA approval of a drug specifically for Sézary Syndrome [Label].

Pharmacodynamics

This drug is a CC chemokine receptor 4 (CCR4) antagonist. It is a monoclonal antibody which blocks T cell proliferation, which leads to malignancy [1], [6]. CCR4 is a chemokine receptor that is preferentially expressed by Th2 and regulatory T (Treg) cells. In response to its ligands, CCL17 (TARC) and CCL22 (MDC), CCR4 promotes T-cell migration to extranodal sites, including the skin [6].

Mechanism of action

Mogamulizumab selectively binds to and inhibits the activity of CCR4, which may block CCR4-mediated signal transduction pathways and, so, chemokine-mediated cellular migration and proliferation of T cells, as well as chemokine-mediated angiogenesis. Additionally, this agent may induce antibody-dependent cell-mediated cytotoxicity (ADCC) against CCR4-positive T cells. CCR4, a G-coupled-protein receptor for C-C chemokines such MIP-1, RANTES, TARC and MCP-1, is expressed on the surfaces of some types of T cells, endothelial cells, and certain types of neurons. CCR4, also known as CD194, may be overexpressed on adult T-cell lymphoma (ATL) and peripheral T-cell lymphoma (PTCL) cells [10]. In addition to directly targeting malignant T cells expressing CCR4, mogamulizumab depletes Treg cells, an important therapeutic target in many human cancers because of their role in suppressing host antitumor immunity [6].

A	C-X-C chemokine receptor type 4
	antagonist
	Human

Absorption

Following repeated dosing of the approved recommended dosage, steady-state concentrations were reached after 8 doses (12 weeks), and the systemic accumulation was 1.6-fold. At steady state, the peak concentration (Cmax,ss) is 32 (68%) µg/mL, the trough concentration (Cmin,ss) is 11 (239%) µg/mL, and AUCss is 5577 (125%) µg•hr/mL [Label].

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

The terminal half-life is 17 days [Label].

Clearance

Clearance is 12 mL/h [Label].

Toxicity

The most common adverse reactions (reported in ≥20% of patients randomized to mogamulizumab) were rash (including drug eruption), infusion-related reactions, fatigue, diarrhea, upper respiratory tract infection and musculoskeletal pain [Label]. Due to various adverse effects related to this drug, the adverse reactions have been categorized by organ system. Because of the risk of serious/fatal ADRs, patients administered mogamulizumab should be carefully monitored [3].

Upper respiratory tract infection: This may occur due to decreased immunity following the administration of this drug. Monitor for signs of respiratory infection including fever, cough and shortness of breath [9].

Dermatological: Patients must contact their healthcare provider immediately if they experience a new or worsening skin rash. Treatment should be temporarily interrupted for moderate or severe skin rashes and permanently discontinued for a life-threatening rash. Fatal and life-threatening skin adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have occurred in recipients of mogamulizumab. Rash (drug eruption) is one of the most common adverse reactions associated with mogamulizumab [9], [Label].

Infusion Reactions: Patients must contact their healthcare provider immediately for signs or symptoms of infusion reactions. Treatment should be suspended for any infusion reaction and permanently discontinued for any life-threatening infusion reaction [9].

have included myositis, myocarditis, polymyositis, hepatitis, pneumonitis, and a variant of Guillain- Barré syndrome [Label]. Patients must notify their healthcare provider of any history of autoimmune disease. Treatment should be suspended or permanently discontinued as appropriate [9]. Fatal and life-threatening immune-mediated complications have been reported in recipients of this drug [Label].

Musculoskeletal pain: This drug may cause musculoskeletal pain [Label]

A note on complications of allogeneic hematopoietic stem cell transplantation: Patients must be aware of the possible risk of post-transplant complications when taking this agent. Patients should be monitored for severe acute graft-versus-host disease (GVHD) and steroid-refractory GVHD.

Females of Reproductive Potential: Females who are able to become pregnant should use an effective method of birth control during treatment with Poteligeo and for at least three months after the last dose [9].

Affected organisms

Not Available

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Anthrax immune globulin human	The therapeutic efficacy of Anthrax immune globulin human can be decreased when used in combination with Mogamulizumab.	Approved

antigen	when used in combination with Mogamulizumab.	
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 Mogamulizumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Mogamulizumab.	Investigational
Belimumab	The risk or severity of adverse effects can be increased when Mogamulizumab is combined with Belimumab.	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 Mogamulizumab.	Approved
Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Mogamulizumab.	Approved
G17DT	The therapeutic efficacy of G17DT can be decreased when used in combination with Mogamulizumab.	Investigational
GI-5005	The therapeutic efficacy of GI-5005 can be decreased when used in combination with Mogamulizumab.	Investigational
Hepatitis A Vaccine	The therapeutic efficacy of Hepatitis A Vaccine can be decreased when used in combination with Mogamulizumab.	Approved

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Food Interactions

Not Available

REFERENCES

General References

1. Makita S, Tobinai K: Mogamulizumab for the treatment of T-cell lymphoma. Expert Opin Biol Ther. 2017 Sep;17(9):1145-1153. doi: 10.1080/14712598.2017.1347634. Epub 2017 Jul 3.

results of postmarketing all-case surveillance. Int J Hematol. 2017 Oct;106(4):522-532. doi: 10.1007/s12185-017-2270-9. Epub 2017 Jun 9. [PubMed:28597329]
4. Sato T, Coler-Reilly ALG, Yagishita N, Araya N, Inoue E, Furuta R, Watanabe T, Uchimaru K, Matsuoka M, Matsumoto N, Hasegawa Y, Yamano Y: Mogamulizumab (Anti-CCR4) in HTLV-1-Associated Myelopathy. N Engl J Med. 2018 Feb 8;378(6):529-538. doi: 10.1056/NEJMoa1704827. [PubMed:29414279]
5. Ni X, Jorgensen JL, Goswami M, Challagundla P, Decker WK, Kim YH, Duvic MA: Reduction of regulatory T cells by Mogamulizumab, a defucosylated anti-CC chemokine receptor 4 antibody, in patients with aggressive/refractory mycosis fungoides and Sezary syndrome. Clin Cancer Res. 2015 Jan 15;21(2):274-85. doi: 10.1158/1078-0432.CCR-14-0830. Epub 2014 Nov 5. [PubMed:25376389]
6. Wilcox RA: Mogamulizumab: 2 birds, 1 stone. Blood. 2015 Mar 19;125(12):1847-8. doi: 10.1182/blood-2015-02-625251. [PubMed:25792728]
7. FDA approves treatment for two rare types of non-Hodgkin lymphoma [Link]
8. Sezary Syndrome [Link]
9. POTELIGEO [Link]
10. Mogamulizumab NCI [Link]

External Links

PubChem Substance

347911339

Wikipedia

Mogamulizumab

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Active Not Recruiting	Treatment	Tumors, Solid	2
1	Completed	Treatment	Advanced Solid Tumors	1
1	Completed	Treatment	Lung Cancer Non-Small Cell Cancer (NSCLC)	1
1	Recruiting	Treatment	Cancers / Carcinoma NOS / Tumors, Solid	1

1, 2	Not Yet Recruiting	Treatment	Lymphoma, Large B-Cell, Diffuse (DLBCL) / Recurrent Hodgkin Lymphoma / Recurrent Non-Hodgkin Lymphoma / Refractory Hodgkin Lymphoma / Refractory Non-Hodgkin's lymphoma	1
1, 2	Recruiting	Treatment	Advanced Solid Tumors / Metastatic Solid Tumors	1
1, 2	Recruiting	Treatment	Cancers / Carcinoma NOS / HCC / Hepatocellular,Carcinoma / Tumors, Solid	1
2	Completed	Treatment	Adult T-cell lymphomas/leukaemias	2
2	Completed	Treatment	Peripheral T-Cell Lymphoma (PTCL)	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Not Available

Prices

Not Available

Patents

Not Available

PROPERTIES

State

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

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Antagonist

General Function

Virus receptor activity

Specific Function

Receptor for the C-X-C chemokine CXCL12/SDF-1 that transduces a signal by increasing intracellular calcium ion levels and enhancing MAPK1/MAPK3 activation. Acts as a receptor for extracellular ubiq...

Gene Name

CXCR4

Uniprot ID

P61073

Uniprot Name

C-X-C chemokine receptor type 4

Molecular Weight

39745.055 Da

References

1. Makita S, Tobinai K: Mogamulizumab for the treatment of T-cell lymphoma. Expert Opin Biol Ther. 2017 Sep;17(9):1145-1153. doi: 10.1080/14712598.2017.1347634. Epub 2017 Jul 3. [PubMed:28649848]
2. Beck A, Reichert JM: Marketing approval of mogamulizumab: a triumph for glyco-engineering. MAbs. 2012 Jul-Aug;4(4):419-25. doi: 10.4161/mabs.20996. Epub 2012 Jul 1. [PubMed:22699226]
3. Ishitsuka K, Yurimoto S, Kawamura K, Tsuji Y, Iwabuchi M, Takahashi T, Tobinai K: Safety and efficacy of mogamulizumab in patients with adult T-cell leukemia-lymphoma in

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