Tisagenlecleucel

Targets (1)

IDENTIFICATION

Name

Tisagenlecleucel

Accession Number

DB13881

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Cell transplant therapies
Autologous cell transplant

Description

Tisagenlecleucel is a CD19-directed genetically modified autologous T cell immunotherapy, or a CAR-T cell therapy for B-cell acute lymphoblastic leukemia. It was granted approval by FDA in August 2017 under the market name Kymriah. Tisagenlecleucel is an immunocellular therapy that involves autologous T cells that are collected from each individual patient and genetically engineered to express a specific protein called a chimeric antigen receptor (CAR) that specifically target CD19 antigens. Modified T cells are infused back into the patient's body. These CD19-directed chimeric antigen receptors (CD19 CAR-T cells) direct the T cells to targt and kill leukiemia cells that express a specific antigen (CD19) on the cell surface.

83 percent [L+].

Synonyms

Adoptive immunotherapy agent CTL019

CAR.CD19-Redirected T cells

Tisagenlecleucel-T

External IDs

CART-19 / CART19 / CTL-019 / CTL019

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Kymriah	Injection, suspension	2000000 1/1	Intravenous	Novartis	2017-08-30	Not applicable		
Kymriah	Injection, suspension	60000000 1/1	Intravenous	Novartis	2018-05-01	Not applicable		

Showing 1 to 2 of 2 entries

‹ ›

Categories

Not Available

UNII

Q6C9WHR03O

CAS number

1823078-37-0

PHARMACOLOGY

Indication

Indicated for the treatment of patients up to 25 years of age with B-cell precursor acute

Structured Indications

Refractory B-cell precursor acute lymphoblastic leukemia

Second or later relapsed B-cell precursor acute lymphoblastic leukemia

Pharmacodynamics

Tisagenlecleucel demonstrates efficacy in re-inducing remission in patients with refractory B-cell precursor acute lymphoblastic leukemia. The sole purpose of the therapy is to eliminate CD19-expressing malignant and normal cells with specificity and increased chance of remission.

Mechanism of action

Tisagenlecleucel is a CD19-directed genetically modified autologous T cell immunotherapy that involves genetically modified autologous T cells isolated from each individual patient. The reprogramming of the patient's T cells uses a lentiviral vector to encode an anti-CD19 chimeric antigen receptor (CAR). The CAR is comprised of a murine single-chain antibody fragment (scFv) specific for CD19, followed by a CD8 hinge and transmembrane region that is fused to the intracellular signaling domains from 4-1BB (CD137) and CD3 zeta [FDA Label]. These intracellular costimulatory signaling domains increase the expansion, longer-term persistence and potency of CAR T cells [1, 3]: the CD3 zeta component is critical for initiating T-cell activation and antitumor activity, while 4-1BB enhances the expansion and persistence of tisagenlecleucel {FDA Label, A20379]. Upon binding to CD19-expressing cells, the CAR transmits a signal to promote T-cell expansion, activation, target cell elimination, and persistence of the tisagenlecleucel cells [FDA Label].

(A) B-lymphocyte antigen CD19

antibody

Human

Absorption

In pediatric and young adult relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) patients receiving tisagenlecleucel infusion, the mean peak plasma concentration was approximately 34,700 copies/mcg with a median time of 9.91 days to reach this value (Tmax) [FDA Label].

Volume of distribution

The drug is found to be distributed in the blood as well as the bone marrow. Blood to bone marrow partitioning suggested that tisagenlecleucel distribution in bone marrow was 44% of that present in blood at Day 28 while at Months 3 and 6 tisagenlecleucel distributed at 67% and 69%,

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

The mean half life was 16.8 days in pediatric and young adult relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) patients [FDA Label].

Clearance

Not Available

Toxicity

Genotoxicity assay, carcinogenicitiy assay, and studies assesssing the effect of drug on fertility have not been conducted for tisagenlecleucel. According to *in vitro* T cell expansion studies involving transduced T cells from healthy donors and patients, there is no evidence of transformation and immortality [FDA Label].

Affected organisms

Not Available

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Not Available

REFERENCES

General References

1. Tasian SK, Gardner RA: CD19-redirected chimeric antigen receptor-modified T cells: a promising immunotherapy for children and adults with B-cell acute lymphoblastic leukemia (ALL). Ther Adv Hematol. 2015 Oct;6(5):228-41. doi: 10.1177/2040620715588916. [PubMed:26425336]
2. Wei G, Ding L, Wang J, Hu Y, Huang H: Advances of CD19-directed chimeric antigen receptor-modified T cells in refractory/relapsed acute lymphoblastic leukemia. Exp Hematol Oncol. 2017 Apr 14;6:10. doi: 10.1186/s40164-017-0070-9. eCollection 2017. [PubMed:28413717]
3. Davila ML, Brentjens RJ: CD19-Targeted CAR T cells as novel cancer immunotherapy for relapsed or refractory B-cell acute lymphoblastic leukemia. Clin Adv Hematol Oncol. 2016 Oct;14(10):802-808. [PubMed:27930631]
4. FDA Press Announcements: FDA approval brings first gene therapy to the United States [Link]

External Links

PubChem Substance

347911451

Wikipedia

Tisagenlecleucel

FDA label

Download (222 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Active Not Recruiting	Treatment	B Cell Leukemias / Lymphoma, B Cell	1
1	Completed	Treatment	Acute Lymphocytic Leukemia (ALL)	1

			Adult Acute Lymphoblastic Leukemia / B Cell Chronic Lymphocytic Leukemia / Hematopoietic/Lymphoid Cancer / Leukemia, Prolymphocytic / Recurrent Adult Diffuse Large Cell Lymphoma / Recurrent Grade 1 Follicular Lymphoma / Recurrent Grade 2 Follicular Lymphoma / Recurrent Grade 3 Follicular Lymphoma / Recurrent Mantle Cell Lymphoma / Refractory Chronic Lymphocytic Leukemia / Stage III Adult Diffuse Large Cell Lymphoma / Stage III Chronic Lymphocytic Leukemia / Stage III Grade 1 Follicular Lymphoma / Stage III Grade 2 Follicular Lymphoma / Stage III Grade 3 Follicular Lymphoma / Stage III Mantle Cell Lymphoma / Stage IV Adult Diffuse Large Cell Lymphoma / Stage IV Chronic Lymphocytic Leukemia / Stage IV Grade 1 Follicular Lymphoma / Stage IV Grade 2 Follicular Lymphoma / Stage IV Grade 3 Follicular Lymphoma / Stage IV Mantle Cell Lymphoma	
1	Recruiting	Treatment	Acute Lymphoblastic Leukaemias (ALL)	1
1	Recruiting	Treatment	Lymphoma, B Cell	1
1, 2	Recruiting	Treatment	Safety and Efficacy	1
2	Active Not Recruiting	Treatment	Adult Patients Who Have Relapsed or Refractory CLL (3rd Line) or SLL	1
2	Active Not Recruiting	Treatment	B-cell Acute Lymphoblastic Leukemia / Refractory B-cell Acute Lymphoblastic Leukemia / Relapsed B-Cell Acute Lymphoblastic Leukemia	1
2	Active Not Recruiting	Treatment	Curative Treatment Options (Such as Autologous or Allogeneic Stem Cell / Patients With B Cell ALL, Relapsed or Refractory, With no Available / Patients With B Cell ALL, Relapsed or Refractory, With no Available Curative Treatment Options / Transplantation) Who Have Limited Prognosis (> 12 Weeks Survival Expectancy) / With Currently Available Therapies	1
2	Active Not Recruiting	Treatment	Curative Treatment Options Who Have a Limited Prognosis With Currently Available Therapies / Non-Hodgkins Lymphoma (NHL) Patients, With CD19+B Cell Lymphomas / Non-Hodgkins Lymphoma (NHL) Patients, With CD19+B Cell Lymphomas With no Available Potentially	1

Showing 1 to 10 of 14 entries

‹ ›

PHARMACOECONOMICS

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection, suspension	Intravenous	2000000 1/1
Injection, suspension	Intravenous	60000000 1/1

Showing 1 to 2 of 2 entries

‹ ›

Prices

Not Available

Patents

Not Available

PROPERTIES

State

Not Available

Experimental Properties

Not Available

TAXONOMY

Classification

Not classified

TARGETS

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Antibody

General Function

Receptor signaling protein activity

Specific Function

Assembles with the antigen receptor of B-lymphocytes in order to decrease the threshold for antigen receptor-dependent stimulation.

Gene Name

CD19

Uniprot ID

P15391

Uniprot Name

B-lymphocyte antigen CD19

Molecular Weight

61127.985 Da

Drug created on September 01, 2017 12:43 / Updated on May 02, 2018 00:40

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