Anti-CD40 Agonistic Monoclonal Antibody for Cancer Immunotherapy

Overview

Drug Name	Anti-CD40-7409
Description	Anti-CD40-7409 is a humanized agonistic monoclonal antibody targeting CD40 with an engineered Fc capable of selectively binding to FcγRIIB. Anti-CD40-7409 activates CD40 in Fc-FcγRIIB cross-link dependent manner and therefore operates optimally in a CD40 and FcγRIIB-enriched tumor microenvironment. Anti-CD40-7409 is in early clinical development for the treatment of advanced or metastatic solid tumors, both as monotherapy and in combination with other therapies.
Target	CD40
Drug Modality	Monoclonal antibody
Indication	Advanced or metastatic solid tumors
Product Category	Cancer immunotherapy
Mechanism of Action	FcγRIIB mediated CD40 activation
Status	Phase 1
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for Anti-CD40-7409. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

Target

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CD40

Introduction	CD40 is a 48 kDa type 1 transmembrane protein that expressed on antigen-presenting cells (APCs) including dendritic cells (DCs), B cells, macrophages, and classical and non-classical monocytes, and on a variety of non-immune cells including platelets and endothelial cells. The binding of CD40 and CD40 ligand (CD40L) plays a crucial role in both adaptive and innate immunity and engages signaling pathways that are involved in maturation, proliferation, and survival of DCs, production of inflammatory cytokines, and expression of costimulatory molecules.
Approved Name	CD40 molecule
Official Symbol	CD40
Gene Type	Protein coding
Synonyms	p50; Bp50; CDW40; TNFRSF5
Ensembl	ENSG00000101017
Gene ID	958
mRNA Refseq	NM_001250
Protein Refseq	NP_001241
OMIM	109535
UniProt ID	P25942
Chromosome Location	20q13.12

Clinical Resources

Gene Function	This gene is a member of the TNF-receptor superfamily. The encoded protein is a receptor on antigen-presenting cells of the immune system and is essential for mediating a broad variety of immune and inflammatory responses including T cell-dependent immunoglobulin class switching, memory B cell development, and germinal center formation.
Major Conditions	Cancers; Autoimmune disease; Transplant rejection

Drug Modality

Monoclonal Antibody with Engineered Fc Region

Based on a proprietary monoclonal antibody functional platform, Anti-CD40-7409 is developed with tumor-localized immunostimulatory activities by balancing multiple functions of antibodies. Anti-CD40-7409 is an agonistic IgG antibody that activates CD40 optimally in the presence of FcγRIIB to increase selectivity for tumors. FcγRIIB is expressed on immune cells enriched in the tumor microenvironment, including B cells, macrophages, dendritic cells, monocytes, and NK cells. The higher expression profile and level of FcγRIIB in tumor tissues relative to normal tissues supports robust antitumor efficacy and superior safety profile of Anti-CD40-7409 driven by Fc-FcγRIIB cross-linking.

- Natural IgG structure
- High-affinity/specificity binding to CD40
- Avidity-driven selective binding to FcγRIIB
- No Fc effector activity
- FcγRIIB-dependent CD40 agonism
- Optimal target agonism in tumor microenvironment

Indication

Advanced or Metastatic Solid Tumors

Solid tumors are abnormal mass of tissue that usually does not contain cysts or liquid areas. Solid tumors may be benign or malignant. Different types of solid tumors are named for the type of cells that form them, such as lung cancer and breast cancer. According to the WHO Global Cancer Observatory (GLOBOCAN), lung cancer (1.80 million deaths), colon and rectum cancer (916,000 deaths), and liver cancer (830,000 deaths) were the three most deadly cancers in 2020. 18.09 million new cases of cancer had been diagnosed in 2020 in which breast (2.26 million cases), lung (2.21 million cases), and colon and rectum (1.93 million cases) being the three most frequent.
Anti-CD40-7409 monotherapy and in combination with anti-PD-1 antibody therapy are in early clinical development for the treatment of advanced or metastatic solid tumors.

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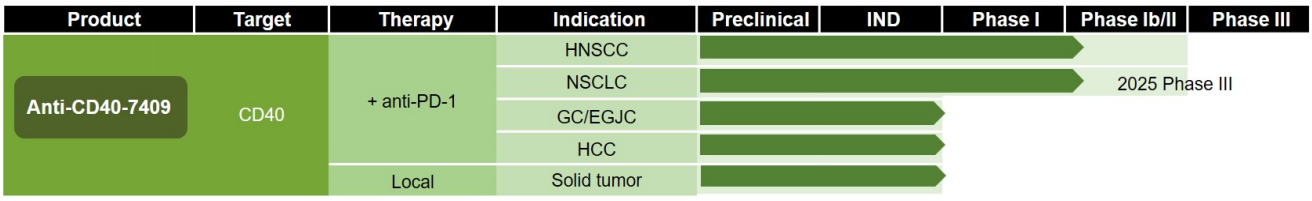

Mechanism of Action

FcγRIIB Mediated CD40 Activation

CD40 is a costimulatory protein expressed on antigen-presenting cells (APCs) and its interaction with the CD40L plays an important role in the amplification of the immune response and the production of antibodies. Similar to the endogenous CD40L, agonistic antibody Anti-CD40-7409 binds to CD40 to activate APCs and induce a variety of downstream effects, such as the cellular proliferation, activation, and antigen presentation of B cells, and activation of antigen-specific T cells. This results in an enhanced immune response against tumor cells.

The modified Fc fragment of Anti-CD40-7409 retains residual binding to FcγRIIB. Anti-CD40-7409 activates CD40 signaling in an Fc-FcγRIIB cross-link dependent manner and therefore operates optimally in a CD40 and FcγRIIB-enriched tumor microenvironment.

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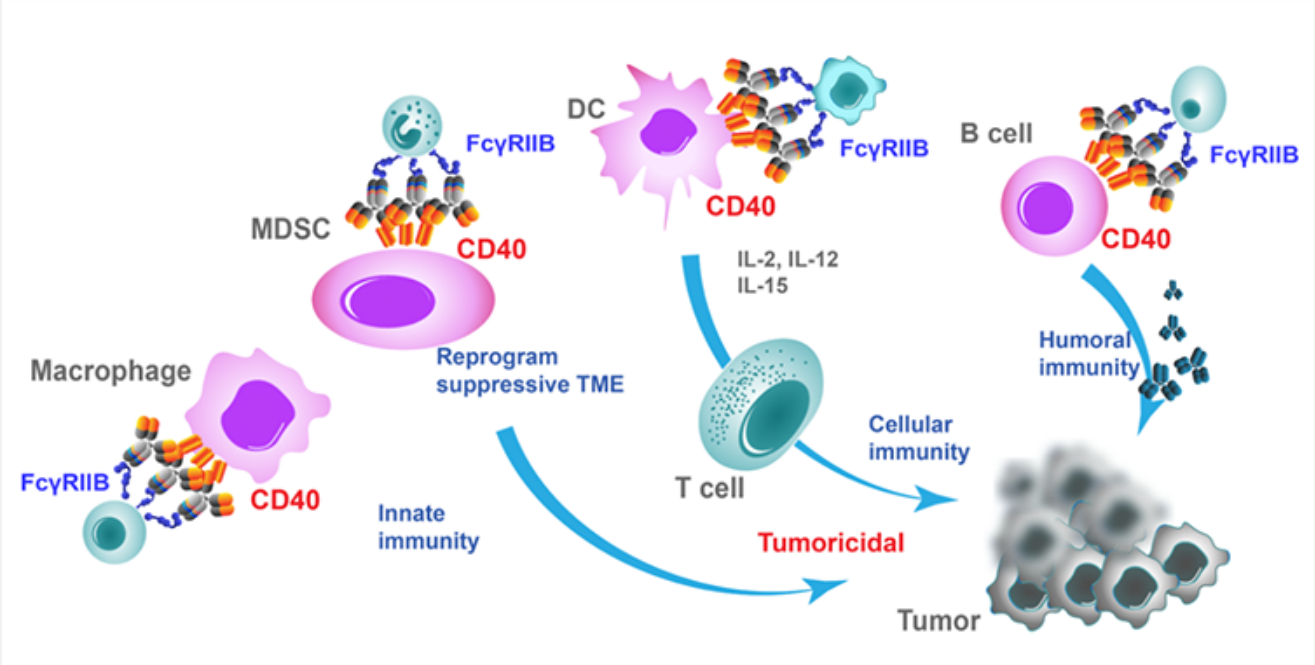
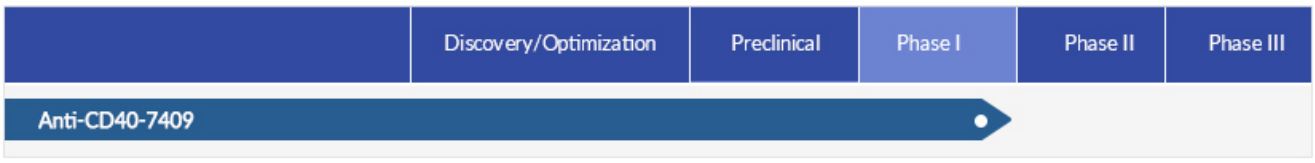


Status

The Status of Anti-CD40-7409

Phase I trials of Anti-CD40-7409 monotherapy and combination therapy with anti-PD-1 antibody are nearing completion.



Data

Comparison of Anti-tumor Effects in the Mouse MC38 Colon Cancer Model

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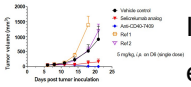

In the tumor model of human CD40 knock-in mice, Anti-CD40-7409 showed higher anti-tumor efficacy than the Selicrelumab analogue.

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