Bispecific Immunoglobulin Therapeutic

Summary

Cancer remains the second leading cause of death in the U.S. Though treatments and survival rates have improved for some cancer types, there remains a need to develop more effective targeted therapies. A rapidly growing area of cancer research concerns bispecific antibody technologies because of their ability to effectively target and kill cancer cells. This technology concerns a bispecific immunoglobulin that is capable of binding cell surface molecules on a target cell, such as cancer cells, and cell surface molecules on immune effector cells. The bispecific acts as a platform technology allowing for multiple cancer targets. Furthermore, a new product, CD123xCD3 bispecific antibody, has been developed for the treatment of CD123-positive malignant diseases, including Acute Myeloid Leukemia and Blastic Plasmacytoid Dendritic Cell Neoplasm.

Key Investigator
Jung-Hee Woo, PhD

Field
Oncology

Technology
Bispecific scFv Immunofusion

Key Features
- Platform technology
- Targeted treatment
- Treatment therapy for CD123-positive malignant diseases

Stage of Development
Preclinical

Status
Available for licensing

Patent Status
Patents pending:
US 20150110789
EP 20130790217

Publication
Kuo, Shu-Ru et al "Engineering a CD123xCD3 bispecific scFv immunofusion for the treatment of leukemia and elimination of leukemia stem cells." *Protein Engineering Design and Selection* 25.10 (2012)

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Market

According to the National Cancer Institute, Americans have approximately a 40 percent risk of developing cancer during their lifetime. In 2016, there will be an estimated 1.6 million new cancer cases diagnosed and nearly 600,000 cancer-related deaths. Cancer is the second leading cause of death in the U.S., and costs hundreds of billions of dollars each year.

A portion of cancers overexpress CD123 (also known as interleukin-3 receptor). These CD123-positive malignant diseases include acute myeloid leukemia (AML), B-lymphoid leukemia, blastic plasmacytoid dendritic cell neoplasm (BPDCN), and hairy cell leukemia. The National Cancer Institute estimates 60,140 new cases of leukemia and 24,400 deaths attributed to the disease in 2016. Among leukemia patients, AML is the most common type of acute leukemia in adults. BPDCN is a rare, clinically aggressive malignancy with poor prognosis and a median survival rate under 16 months.

Though tremendous progress has been made in the treatment of cancers, additional research and more effective therapies are still needed. A rapidly growing area of cancer research concerns bispecific antibody technologies because of their ability to effectively target and kill cancer cells. Unlike monoclonal antibodies, bispecific antibodies can have improved structure and functionality to better combat diseases.

Technology

This technology concerns a bispecific antibody molecule that is capable of binding cell surface molecules on a target cell and cell surface molecules on immune effector cells resulting in killing of target cells, such as cancer cells.

Embodiments of the bispecific include CD33, expressed on myeloid cells, and prostate specific membrane antigen (PSMA) targeting antibodies that have been tested in in vitro tissue culture systems with promising results.

An advanced product of the bispecific is a CD123 targeting bispecific scFv immunofusion. This CD123xCD3 molecule consists of N-terminal anti-CD123 binding single-chain Fv (scFv) and an anti-CD3 binding scFv, which are fused to human IgG hinge-CH2-CH3 domains. This bispecific antibody forms a homo-dimeric quaternary structure, and it has been demonstrated to re-direct cytotoxic T lymphocytes to kill specific targeted cells, including CD123-transfected CHO-K1 cells and AML cell lines but not control CHO-K1 cells at an effector to target ratio as low as 2 and at the low pM range. In vivo efficacy is being evaluated in animal models, and work is being conducted to humanization and optimize CD123xCD3.

This bispecific immunoglobulin technology addresses problems associated with existing bispecific antibody drugs such as short serum half-life and drug heterogeneity.