For Immediate Release

National Cancer Center
The University of Tokyo
Daiichi Sankyo Company, Limited

Commencement of First-in-Human Clinical Trial for New Molecular Targeting Drug, Co-Developed with The University of Tokyo and National Cancer Center, to Treat Malignant Lymphoma (Including Adult T-cell Leukemia-Lymphoma)

TOKYO, Japan (March 22, 2016) –The National Cancer Center, The University of Tokyo, and Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced a collaboration to develop a histone methylation enzyme EZH1/2 dual inhibitor (DS-3201), as a new molecular targeting agent for hematologic malignancy, and the commencement of Phase 1*[1] clinical trial in patients with malignant lymphoma and adult T-cell leukemia-lymphoma (ATL).

One contributing factor to the poor prognosis for malignant lymphoma is the existence of Cancer Stem Cells*[2] capable of regenerating cancer cells and thought to persist after treatment, making the eradication of Cancer Stem Cells essential to the cure of hematologic malignancy. National Cancer Center Research Institute, Division of Hematological Malignancy research group led by Issay Kitabayashi discovered that EZH1/2 are essential enzymes in the maintenance of Cancer Stem Cells, and produced research results suggesting that inhibiting both enzymes may eradicate Cancer Stem Cells to overcome drug-resistance and suppress recurrence. To date, several preclinical studies suggest that this may be an effective treatment for acute myeloid leukemia (AML) and malignant lymphoma.

Searching for an effective ATL treatment, a research group chiefly led by Professor Toshiki Watanabe and Project Research Assistant, Makoto Yamagishi, of The University of Tokyo, Graduate School of Frontier Sciences, discovered an abnormal accumulation of epigenetic changes*[3] due to inappropriate activation of EZH1/2 in ATL cells. Also, as ATL cells are more strongly dependent on epigenetic changes caused by EZH1/2 compared to normal cells, the research developed a new compound that simultaneously inhibits the function of both EZH1 and EZH2. This dual inhibitor reversed inappropriate methylation of histones in ATL cells and also selectively eliminated ATL cells and HTLV-1-infected immortalized cells in the peripheral blood.

Malignant lymphoma

Malignant lymphoma is the most prevalent hematologic malignancy. Malignant lymphoma is classified into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). Recent advances in the management have led to the improvement in therapeutic outcomes of patients with malignant lymphoma, especially Hodgkin lymphoma and B-cell non-Hodgkin lymphoma. However, relapsed or refractory patients with both diseases and T-cell lymphoma patients are still of unfavorable prognosis. Among various subtypes of T-cell lymphoma, ATL is the disease caused by human T-cell leukemia virus type I (HTLV-1) with the poorest prognosis. About 1,000 patients suffer from ATL every year in Japan, where approximately 1.2 million individuals are infected by HTLV-1. The number of HTLV-1-infected individuals (carriers) is estimated to be about 10 to 20 million in the world. About 5 percent of carriers develop ATL during their lifetimes. However, no onset prevention methods or effective treatments of ATL have been established. The prognosis of ATL is very poor mainly because of the high frequency of drug resistance. As the only HTLV-1 endemic country among developed nations, the world expects Japan to lead global efforts to develop new treatments towards onset prevention and effective treatments of ATL.

Clinical trial

This Phase I is the multicenter, study conducted by the National Cancer Center Hospital (Chuo-ku, Tokyo), and other facilities in Japan.

Glossary

*1 Phase 1 trial: Testing a new drug for the first time in humans, normally in a small group of people (healthy volunteers or patients). In phase 1 trial for cancer patients ,gradually increasing dosage is used to evaluate safety, determine safe dosage, and examine methods of administration.

*2 Stem cells: undifferentiated cells capable of renewing themselves for long periods and maintaining the potential to develop into other types of cells. Cancer stem cells are cells capable of regenerating cancer.

*3 Epigenetic changes: heritable changes in gene expression that do not involve change to the underlying DNA sequence. The epigenome refers to the chemical modification of the histone and DNA.

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