For Immediate Release

National Cancer Center of Japan
Japan Agency for Medical Research and Development
Daiichi Sankyo Company, Limited

Commencement of Phase 1 Trial for the Mutant IDH1 Inhibitor (DS-1001) Targeting Malignant Brain Tumors

Tokyo, Japan (March 1, 2017) – The National Cancer Center of Japan and Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) today announced a collaboration to develop an inhibitor for mutant isocitrate dehydrogenase IDH1 (DS-1001) as a new molecular targeting drug for malignant brain tumors (gliomas)[*1] and the commencement of a first-in-human phase 1 clinical trial[*2].

Mutations in the IDH1 and IDH2 genes are frequently observed in patients with malignant tumors, such as gliomas, acute myeloid leukemia (AML), cholangiocarcinoma, and chondrosarcoma. The National Cancer Center Research Institute, Division of Hematological Malignancy research group led by Issay Kitabayashi discovered that inhibitions of mutant IDH1/2 were able to eliminate AML cancer stem cells[*3]. In addition, preclinical studies using patient-derived xenograft (PDX) models[*4] showed that DS-1001, which has high blood-brain barrier permeability, was effective in suppressing the proliferation of malignant gliomas, AML, and chondrosarcoma.

Most molecular targeted drugs developed to date target molecules that are active or highly expressed in tumors. However, these drugs may have problematic side effects because the targeted molecules are to some extent also active in normal, healthy cells. DS-1001 selectively inhibits the mutant form of IDH1, which is expressed only in cancer cells, and has minimum effect against wild-type IDH1, which is expressed in normal cells.

Mutations in the IDH1 genes are observed in more than 70% of patients who are diagnosed as grade 2 or 3 gliomas (astrocytomas or oligodendrogliomas) [*5]. These types of glioma with IDH1 mutation are most frequently observed in 30 to 50 years old population, with multiple relapse and long term treatment course[*6]. DS-1001 may be effective in such a patient population.

This multicenter phase I clinical trial is planned to enroll patients with recurrent IDH1 mutant gliomas who have no standard treatment at the National Cancer Center Hospital (Chuo-ku, Tokyo) and other facilities in Japan.

Glossary

*1 Gliomas: Gliomas are tumors derived from glial cells of the brain and represents approximately 30% of all brain tumors. Since they spreads diffusely and infiltrates into normal brain tissue, total removal of glioma is difficult. Radiotherapy and chemotherapy are usually required for the prevention of recurrence. However, most gliomas relapse within several months to several years and there are few therapeutic options after recurrence. Therefore, there is still an unmet need for development of novel drugs for gliomas.

*2 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 anti-cancer drug, gradually increasing dosage to cancer patients is used to evaluate safety, and determine appropriate dose and dosage of the drug.

*3 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.

*4 Patient-derived xenograft (PDX) models: Experimental animal models where human cancer cells are transplanted into immunodeficient mice. The method allows human cancer to be replicated accurately, thus clarifying the molecular mechanisms and allowing testing of anticancer agent effectiveness.

Reference

*5 Yan H., *et. al.*, N Engl J Med; 360:765-773, 2009

*6 Narita Y., *et. al.,* Neurol Med Chir (Tokyo); 55:286-295, 2015

Media Inquiries

National Cancer Center of Japan
Office of Public Relations, Strategic Planning Bureau
5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
TEL:+81-3-3542-2511 (Switchboard) FAX:+81-3-3542-2545
E-mail: ncc-admin@ncc.go.jp

Japan Agency for Medical Research and Development
Division of Cancer Research, Department of Research Promotion
1-7-1 Otemachi, Chiyoda-ku, Tokyo 100-0004, Japan
TEL:+81-3- 6870-2221
E-mail：cancer@amed.go.jp

Daiichi Sankyo Co., Ltd.
Corporate Communications Department
3-5-1 Nihonbashi-honcho, Chuo-ku, Tokyo 103-8426, Japan
TEL: +81-3-6225-1126

Clinical trial inquiries

National Cancer Center Hospital
Clinical Trial Coordination (&Support) Office
5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
Telephone: +81-3-3542-2511