Launched an Asian international collaborative prospective study on 6 advanced cancers common in Asia

Establishment of a database of genomic analysis and clinical information by liquid biopsy, for developing personalized treatment

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National Cancer Center Japan

- An international collaborative prospective study on 6 advanced cancers, which occur frequently in Asia, will be launched to build and analyze a database of blood-based genomic profiles and clinical information.
- The project involves five companies and eight Asian countries including Japan. We are to build a database for research and development in Asia, using cancer gene panel tests appropriate for each cancer, while ensuring compliance with all applicable privacy laws.
- Through analysis of the database, we aim to identify genomic abnormalities that can be used as therapeutic targets, and to develop personalized treatments for advanced cancers common in Asia.

Summary

The National Cancer Center Hospital Japan will launch an international joint research project (Asian multicenter prospective study of circulating Tumör DNA Sequencing; A-TRAIN) in eight Asian countries (Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand and Vietnam) to develop novel treatments based on genomic abnormalities for cancers common in Asia. For patients with cervical cancer, ovarian cancer, nasopharyngeal carcinoma, endometrial cancer and breast cancer, the database will be constructed and analyzed by examining genomic abnormalities comprehensively by liquid biopsy, together with clinical information such as treatment details and prognosis.

As these cancers occur more frequently in Asia and are more difficult to treat, there is a strong need to develop new treatments. It is difficult to anticipate that the pharmaceutical developers of Europe and the United States would take the lead in research and development addressing these cancers, therefore, it is necessary to drive research and development through collaboration in the Asian region. In this study, we aim to solve these problems by using blood for genetic analysis. Genomic analysis of blood samples is expected to be used more widely in clinical practice as it is a less invasive procedure,
enables testing and analysis according to the course of treatment, and facilitates quality control of samples. This study will be conducted as an international collaborative study under the "Asian clinical Trials network for Cancer (ATLAS) project" which aims to accelerate the implementation of clinical research and trials and early drug development in the Asian region.

**A-TRAIN; Asian multicenter prospective study of circulating Tumor DNA Sequencing**

A-TRAIN is an Asian multicenter prospective study that comprehensively analyzes genomic abnormalities in the blood of cancer patients with metastatic and/or recurrent diseases. In this study, cancer-related genes will be analyzed using a genomic panel test for blood, and information on genomic abnormalities in each cancer will be analyzed with patient information. This study will be done in collaboration with companies and the National Cancer Center Research Institute Japan.

We will comprehensively analyze circulating tumor DNA (ctDNA) in the blood of approximately 500 patients with six cancer types who have metastatic and/or recurrent disease, and at the same time collect clinical information to build and analyze a database, with the aim of identifying genetic abnormalities that may be therapeutic targets, and conducting clinical trials.

**Figure 1. Overview of A-TRAIN**

**PARTICIPATING COUNTRIES**

- Japan
- Korea
- Malaysia
- Philippines
- Singapore
- Taiwan
- Thailand
- Vietnam

**Cancers Analyzed**

- Cervical Cancer N = 100
- Ovarian clear cell carcinoma N = 60
- Nasopharyngeal Carcinoma N = 96
- Ovarian Cancer N = 192
- Endometrial Cancer N = 60
- Triple Negative Breast Cancer N = 100

**Institutes**

- Guardant
- Thermo Fisher Scientific
- Illumina
- Roche
- National Cancer Center Japan
**Cervical Cancer cohort:**
- Start date: December 2021
- Participating countries: Japan, Malaysia, Thailand, Singapore, Vietnam
- Number of registrants: 100
- Genetic analysis: Guardant Health Asia, Middle East & Africa (AMEA)

**Ovarian Clear Cell Carcinoma cohort:**
- Start date: December 2021
- Participating countries: Japan, Philippines, Malaysia, Thailand, Singapore, Vietnam
- Number of registrants: 50
- Genetic analysis: Thermo Fisher Scientific Japan Group (hereafter referred to as “Thermo Fisher”)

**Nasopharyngeal Carcinoma cohort:**
- Start date: December 2021
- Participating countries: Japan, Philippines, Malaysia, Thailand, Singapore, Taiwan, Vietnam
- Number of registrants: 96
- Genetic analysis: Illumina, Inc.

**Ovarian Cancer cohort:**
- Start date: December 2021
- Participating countries: Japan, Taiwan, Vietnam
- Number of registrants: 100
- Genetic analysis: Chugai Pharmaceutical Co Ltd and Roche Ltd

**Endometrial Cancer cohort:**
- Start date: February 2022
- Participating countries: Japan, Philippines, Malaysia, Thailand, Taiwan, Vietnam
- Number of registrants: 60
- Genetic analysis: Thermo Fisher and National Cancer Center Research Institute, Japan

**Triple-negative Breast Cancer cohort:**
- Start date: January 2022
- Participating countries: Japan, Korea, Philippines, Thailand, Singapore, Vietnam
- Number of registrants: 100
- Genetic analysis: National Cancer Center Research Institute, Japan
Participating institutions (as of 23 December 2021)
- National Cancer Center Hospital
- St. Luke’s Medical Center, Philippines
- Hospital Umum Sarawak, Malaysia
- University Malaya Medicine Center, Malaysia
- Hospital Kuala Lumpur, Malaysia
- National Cancer Institute, Malaysia
- National University Cancer Institute, Singapore
- National Taiwan University Hospital, Taiwan
- National Cancer Hospital of Vietnam, Vietnam
- Ho Chi Minh City Oncology Hospital Vietnam
- Others from the above countries, Thailand and Korea will also participate.

Participating companies
- Guardant Health Asia, Middle East & Africa (AMEA)
- Thermo Fisher
- Illumina Corporation
- Chugai Pharmaceutical Co.
- Roche Corporation
- Intellim Corporation
- SRL Corporation
- Eurofins

Message from the Principal Investigator

The National Cancer Center Hospital has started the Asian multicenter prospective study of circulating TumoR DNA Sequencing (A-TRAIN) after discussions with doctors and researchers in Asia to promote the development of Asian therapies for Asian cancer patients.

A-TRAIN, a train going through Asia.
What do you think of when you hear the word “TRAIN”?
Possibly a steam locomotive moving powerfully forward, a train taking you on an exciting adventure in life, stopping by stations where you meet people and say goodbye.

This project started its journey as A-TRAIN with the support of the National Cancer Center Hospital, Japan Agency for Medical Research and Development, various companies, and the enthusiasm, passion and energy of those involved as the driving force. We will continue to advance with each of us playing own roles, as we welcome in others. Let's hold hands and drive our aspirations into the dream train of ideas that will take us to an exciting future in Asia.

**Background**

According to statistics in 2020, the number of newly diagnosed cancers worldwide is estimated at 19.3 million, and of deaths resulting from cancer at 9.96 million. Of these new cancer cases, Asia accounts for about half (Fig. 2).

In developing countries, including Asian nations, cancer types unique in Asia, such as cervical cancer, pharyngeal cancer, and liver cancer, in addition to the extension in life expectancy, the high smoking rate, and the lack of cancer screening schemes are believed to be behind this phenomenon.

**Figure 2. Estimated number of newly diagnosed cancer cases worldwide (2020)**

In recent years, genomic testing for cancer has been advanced by the development of cancer gene panel tests\(^3\) that determine treatments based on the genomic profiles of cancers. The OncoGuide™ NCC OncoPanel System, developed by the National Cancer Center Japan, was approved in Japan as a medical device on December 25, 2018. However, this test cannot be performed on patients with cervical cancer, pharyngeal cancer, etc., from whom sufficient tumor tissue cannot be collected. Therefore, developing a gene panel test using blood samples called liquid biopsy is necessary. Genomic analysis
using blood samples is attracting attention for its low invasiveness, its ability to provide real-time information on genetic abnormalities, and its use for monitoring after treatment completion.

**ATLAS Project**

The "ATLAS project: Asian clinical Trials network for cAnceS project" is a Japan-led initiative to establish a platform for international collaborative trials with Malaysia, Thailand, the Philippines, Indonesia and Vietnam, which are actively promoting cancer treatment development in the Asian region. We aim to develop early-stage drug development for cancer in the Asian region through the introduction of cancer genomic medicine and the implementation of investigator-initiated clinical trials and corporate trials for regulatory approval. It also aims to improve drug access in Asia and to promote the full-scale introduction of cancer genomic medicine in the region, thereby enhancing development capabilities in Asia as a whole and solving Asia's specific problems on its own.

Conducting clinical trials in collaboration with other Asian countries is expected to speed up completion of the trials and lead to accelerated approval of new drugs for us all. Finally, we aim to build a well-established clinical trial network in the Asian region, to lead the world in therapeutic development.

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**Terminology**

*1 Prospective study*

Prospective studies start in the present and continue collecting new data and samples forward in time, with the cooperation of patients. Retrospective studies, on the other hand, is a study that investigates various subjects using medical records, clinical specimens, and other information recorded in medical records, test result data, and tissue samples.
*2 Circulating tumor DNA

Circulating tumor DNA (ctDNA) are produced when tumors shed small pieces of their genetic material into the bloodstream. These traces of this tumor DNA can be detected in the blood using digital sequencing technology. In the future, the technology is expected to be widely used for various purposes in cancer treatment such as companion diagnostics to determine therapeutic agents, screening, monitoring of treatment efficacy, and evaluation of residual disease after curative treatments such as surgery or radiotherapy.

*3 Cancer gene panel tests:

A cancer gene panel test examines a large number of genes simultaneously in a single test using an analyzer called a "next-generation sequencer," which reads a large amount of genomic information at high speed using cancer tissues taken from biopsies or surgeries. If a gene mutation is found with a drug expected to be effective against it, we will consider using that drug, including clinical trials. The National Cancer Center has developed a genetic testing system (OncoGuide™ NCC OncoPanel System) using multiplex gene panel test reagents that can detect mutations, amplifications, and fusions of cancer-related genes in a single assay, in collaboration with Sysmex Corporation, for rapid and accurate identification of genetic variants. The product has been approved for manufacturing and marketing as an in vitro diagnostic drug and medical device (December 25, 2018) and for insurance coverage (June 2019) for "patients with solid tumors for which no standard treatment is available or for which standard treatment has been terminated due to local progression or metastasis".


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