

Facilitating International Clinical Trials Initiated by Japanese Academic Institutions

Japan-led Global Investigator-Initiated Registration-Directed Trial of Advanced or Metastatic Breast Cancer (PATHWAY trial) Has Started

November 12, 2018
National Cancer Center Japan

National Cancer Center Hospital (President: Hitoshi Nakagama, Director: Toshiro Nishida, Tokyo, Japan) is proud to announce the launch of an investigator-initiated registration-directed clinical trial (IIRDT) of the cyclin-dependent kinase (CDK) 4/6 inhibitor palbociclib in advanced or metastatic breast cancer patients (Study ID: NCCH1607, UMIN ID: UMIN000030816, ClinicalTrials.gov registration number: NCT03423199). This NCCH-led IIRDT is conducted in the Asian region with participation of 12 sites in Japan, 6 in South Korea, 3 in Taiwan and 2 in Singapore, and patient enrollment has now been started in all 4 countries.

This trial is a randomized, double-blind, placebo-controlled, phase 3 trial of palbociclib in female patients with hormone receptor (HR) positive/HER2 negative advanced or metastatic breast cancer, targeting 180 patients enrolled in 2 years. The primary objective of this study is to assess the progression free survival of the combination of palbociclib plus tamoxifen, a frequently used endocrine therapy in this setting, versus tamoxifen plus placebo. Current approved indication is based on the studies of palbociclib in combination with letrozole or fulvestrant. A successful study would provide evidence to support an additional endocrine therapy partner in combination with palbociclib, and could be the basis for potential future discussions with regulators. A major objective for NCCH of conducting this study is to establish a new standard treatment.

[Facilitating international collaborative research initiated by academic institutions in Japan]

In recent years, the number of pharmaceutical company-sponsored global clinical trials is dramatically increasing, anticipating its advantage of recruitment speed and the pace of treatment development. It is quite important also for academia to perform global clinical research in terms of providing new standard cancer treatment for patients at an earlier stage. Many global clinical trials initiated by academic research groups have been conducted in the US and Europe, and it has become increasingly common for Japanese institutions, including our hospital, to participate in the overseas-initiated global clinical trials. However, a Japanese

investigator/academia-led global clinical trial has rarely been conducted due to the language (English) barrier, personnel shortage, or limited research budget.

National Cancer Center Hospital have actively been conducting many domestic IIRDTs for diseases of which pharmaceutical manufacturers are having difficulty in development of new therapies, while there has been a strong need of its establishment. In 2016, among all the Clinical Research Core Hospitals in Japan, NCCCH has been selected by AMED (Japan Agency for Medical Research and Development) as one of the Global Clinical Trials Core Center, focused on the reinforcement of facilitating international clinical trials in Japan between 2016 and 2018. We therefore initiated this first global IIRDT, taking advantage of our experience and support structure for clinical trials. International, comprehensive research and development of treatments in this type of form is an extremely advanced approach in the whole world.

PATHWAY trial is a research collaboration with Pfizer Inc., a research funder and a study drug provider. As a research collaboration with a pharmaceutical manufacturer, it is conducted as an IIRDT in Japan, and as a global clinical trial with NCCCH as a sponsor playing the same role of pharmaceutical manufacturers in other countries. A successful study within the clinical trial framework would provide evidence to support an additional endocrine therapy partner in combination with palbociclib, and could be the basis for potential future discussions with regulators. We are also planning several translational researches in our trial, collaborating with National Cancer Center Research Institute, where researchers make a contribution to development of cancer diagnosis and advanced treatment.

Currently, National Cancer Center Hospital is making the particular effort for networking in the Asian region. By conducting more number of international collaborative trials to expand this initiative, we strongly continue pursuing an advancement of new therapy/drug development to provide a strong impetus to the development of treatments and new drugs, in the Asian region.

[About palbociclib]

Palbociclib, the drug used in this trial, is a novel oral molecular target drug that inhibits CDK 4/6. CDK 4/6 has the primary role of adjusting of the cell cycle, and causes cell proliferation. It is believed that palbociclib selectively inhibits CDK 4 and 6, halting progression of the cell cycle and thus suppressing tumor proliferation.

Palbociclib has been approved in more than 85 countries including the US, and was approved in Japan in September 2017. However, it is approved based on results for combination with letrozole or fulvestrant, and its efficacy and safety when in combination with tamoxifen has not been established.

[Sites participating in this trial]

Japan: National Cancer Center Hospital / Hokkaido Cancer Center / Chiba Cancer Center/ National Cancer Center Hospital East / Toranomon Hospital / Kanagawa Cancer Center / Aichi Cancer Center Hospital / Osaka National Hospital / Kindai University Hospital / Hyogo Cancer Center / Shikoku Cancer Center / Kyushu Cancer Center

South Korea: Severance Hospital, Yonsei University Health System / Seoul National University Hospital / Seoul National University Bundang Hospital / Asan Medical Center / National Cancer Center (Korea) / Ajou University Hospital

Taiwan: National Taiwan University Hospital / Sun Yat-Sen Cancer Center / and 1 other site

Singapore: National Cancer Centre Singapore / National University Hospital

[Details of this trial]

• Trial title: Asian, International, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial of Tamoxifen With or Without Palbociclib +- Goserelin in Women with Hormone Receptor-Positive, HER2-Negative Advanced or Metastatic Breast Cancer (NCCH1607, PATHWAY trial)

- Study Chair: Kenji Tamura, MD. PhD,
- UMIN trial ID: UMIN000030816
- ClinicalTrials.gov registration number: NCT03423199

Please refer the following for details of this trial.

https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000034267

<https://clinicaltrials.gov/ct2/show/NCT03423199>

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