国立研究開発法人
国立がん研究センター
National Cancer Center Japan

Result of a Japan-led International Investigator-Initiated Registration-Directed Trial Offers a New Treatment Option of Palbociclib in Combination with Tamoxifen

Revision of Japanese Package Insert Contributes to Patients with Hormone Receptor-Positive/HER2-Negative Advanced Breast Cancer

15 Jan. 2024

National Cancer Center Japan

The point of this Press Release

- The combination of palbociclib and tamoxifen has become a new treatment option in palbociclib plus endocrine therapies based on results of National Cancer Center Hospital (NCCH)-led International Investigator-Initiated Registration-Directed Trial (IIRDT) conducted in Asia. This has expanded treatment options for premenopausal breast cancer patients who have few treatment options as well as for postmenopausal breast cancer patients.
- PATHWAY trial is a successful example of meeting unmet medical needs based on an international clinical trial which was conducted in Asia beyond the border and led by Japanese academia.
- NCCH will move forward in providing more new therapeutic drugs and treatments to the medical community both in Japan and overseas with the know-how developed through this experience.

Overview

The NCCH (President: Hitoshi Nakagama, Director: Kazuaki Shimada, Tokyo, Japan) announced that Japanese package inserts for palbociclib was revised based on results of a Japan-led International IIRDT [NCCH1607/PATHWAY trial] which investigated palbociclib in combination with tamoxifen in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer. The combination of palbociclib and tamoxifen has become a new treatment option in palbociclib plus endocrine therapies. This has expanded treatment options for patients with HR+/HER2 advanced breast cancer

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 100 countries including the US, and was approved in Japan in September 2017. However, this approval was based on the data in combination with letrozole or fulvestrant which are used for postmenopausal patients, and the efficacy and safety in combination with tamoxifen had not been established. Therefore, NCCH planned PATHWAY trial. Premenopausal breast cancer patients, for which a larger proportion of patients exist in Asian region

than western countries and with fewer treatment options. To meet this unmet medical need, NCCH conducted a Japan-led International IIRDT in collaboration with Pfizer Inc. to confirm efficacy and safety of this combination therapy. Based on the study results, Pfizer held a Pharmaceutical Consultation on Package Insert Revision in the Pharmaceutical and Medical Devices Agency (PMDA), and the Japanese package insert was revised based on PMDA's conclusion. The combination of palbociclib and tamoxifen has become a new treatment option in palbociclib plus endocrine therapies.

NCCH1607/PATHWAY trial is a successful example of meeting unmet medical needs based on an international clinical trial which was conducted in Asia beyond the border and led by Japanese academia. This achievement shows that NCCH can take initiative to conduct International IIRDTs. NCCH will move forward in providing more new therapeutic drugs and treatments to the medical community both in Japan and overseas with the know-how developed through this experience.

Background

About breast cancer:

Breast cancer is the most common cancer in women worldwide. The treatment options for breast cancer include surgery, radiation therapy, and drug treatment. HR+ breast cancer may use hormones to accelerate their growth. Endocrine therapy blocks the production of hormones or interferes effects of hormones on breast cancer cells. Endocrine therapy is recommended for patients with HR+/ HER2- advanced or metastatic breast cancer. Depending on several factors such as menopausal status, history of treatment, age, and extent of the cancer, the appropriate endocrine therapy is selected for each patient. Treatment options for premenopausal women have been limited.

About the PATHWAY trial (NCCH1607):

NCCH1607/PATHWAY trial is an IIRDT of the CDK 4/6 inhibitor palbociclib in HR+/HER2- advanced or metastatic breast cancer patients, including premenopausal, perimenopausal and postmenopausal patients. This NCCH-led IIRDT has been conducted in the Asian region with participation of 12 sites in Japan, 6 in South Korea, 3 in Taiwan and 2 in Singapore and 184 patients were participated. PATHWAY trial is a clinical research collaboration with Pfizer Inc., a research funder and a study drug provider. It has been conducted as an IIRDT in Japan, and as an international clinical trial with the NCCH as the regulatory sponsor in other Asian countries. The efficacy and safety with the combination of palbociclib plus tamoxifen was confirmed in women with HR+/HER2- advanced or metastatic breast cancer in PATHWAY trial. The topline results were announced in Febrary 2023.

https://www.ncc.go.jp/en/ncch/news/20230220/index.html

Please refer the following for details of this trial.

• UMIN trial ID: UMIN000030816

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

• ClinicalTrials.gov registration number: NCT03423199

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

Result

Based on the PATHWAY trial results, Pfizer held a Pharmaceutical Consultation on Package Insert Revision in the PMDA, and the Japanese package insert was revised based on PMDA's conclusion. The combination of palbociclib and tamoxifen has become a new treatment option in palbociclib plus endocrine therapies.

Future prospects:

PATHWAY trial is a successful example of meeting unmet medical needs based on an international clinical trial which was conducted in Asia beyond the border and led by NCCH (academia). This achievement shows that NCCH can take initiative to conduct Japan-led International IIRDT. NCCH will move forward as a top runner in providing more new therapeutic drugs and treatments to the medical community both in Japan and overseas with the know-how developed through this experience.

Reference information

Facilitating international collaborative research initiated by academic institutions in Japan and ATLAS project:

In recent years, the number of industry-sponsored global clinical trials is increasing, anticipating its advantage of recruitment speed and accelerating treatment development in broader area. Global clinical trials are also important for academia for establishing new standard cancer treatment earlier. While many academic global clinical trials have been conducted by some research groups in the US and Europe, some Japanese institutions come to participate in overseas-led global clinical trials. However, a Japanese investigator-led global clinical trial has rarely been conducted due to the language (English) barrier, personnel shortage, or limited research budget.

NCCH has 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, NCCH and Osaka University Hospital have been selected by the AMED (Japan Agency for Medical Research and Development) as the Global Clinical Trials Core Center[1)], focused on the reinforcement of facilitating international clinical trials in Japan. NCCH therefore initiated this first global IIRDT, taking advantage of its experience and support function for clinical trials.

Currently, NCCH is making the particular effort to facilitate the ATLAS (Asian clinical TriaLs network for cAncerS) project[2)], which will establish a clinical research network across Asia, including not only the participating regions of PATHWAY trial but also some ASEAN countries. Based on the experience and network gained from the PATHWAY trial, NCCH continues to expand the research network through the ATLAS project pursuing an advancement of new treatment development in Asia.

WEB site https://atlas.ncc.go.jp/

1) This project has been transferred to one of the programs of the AMED Project for Comprehensive

Program for Improving Infrastructure to Promote Clinical Application of Innovative Medical Seeds since FY2017.

2) This project is funded by AMED as the Project Promoting Clinical Trials for Development of New Drugs （Project to Create a Clinical Research and Trial Network in the Asian Region）

Contact information

About the clinical trial

Tomomi Hata

International Trial Management Section, Clinical Trial Management Division, Clinical Research Support Office, National Cancer Center Hospital

5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan

Phone: +81-3-3547-5201 (ex 6137)

E-mail: NCCH1607_office@ml.res.ncc.go.jp

Press and media enquiries

Publicity Planning Office, Strategic Planning Bureau, National Cancer Center

5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan

Phone: +81-3-3547-5201 (ex 2632)

E-mail：ncc-admin@ncc.go.jp