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Latest results from PHOEBE trial show patients with advanced HER2-positive breast cancer live longer on pyrotinib

Lisbon, Portugal: Patients with HER2-positive breast cancer that has started to spread to other parts of the body survive for longer if they are treated with a new drug called pyrotinib, according to results from the longest follow-up of the PHOEBE randomised clinical trial in China.

Presenting the latest results at the Advanced Breast Cancer Seventh International Consensus Conference (ABC 7), Professor Xichun Hu, of Fudan University Cancer Hospital, Shanghai, China, said the researchers had been able to analyse data on overall survival from the trial up to March 15, 2023.

"We now have data with a median follow-up period of 52 months for 134 patients receiving pyrotinib plus capecitabine and 49.4 months for 132 patients receiving lapatinib plus capecitabine," he said. "Patients in the pyrotinib group lived, on average, longer than those in the lapatinib group; the median overall survival was 39.4 months compared to 28.6 months – a reduction in the risk of dying of 22%."

HER2-positive breast cancer is a cancer that has high quantities of a protein called human epidermal growth factor receptor 2 (HER2). It is more likely to grow and spread faster than cancers that are HER2-negative, but it responds very well to monoclonal antibody treatments such as trastuzumab and pertuzumab, plus chemotherapy. However, it eventually becomes resistant to these treatments and so other treatments that target HER2 are needed.

International guidelines recommend T-DM1, a combination of trastuzumab and emtansine, as a second-line therapy but in some countries, such as those in South America, Eastern Europe and Asia, it is not yet approved or accessible for cancer that has started to spread (metastasise). Instead, lapatinib with capecitabine or lapatinib with trastuzumab are recommended.

Pyrotinib targets several proteins involved in HER2-positive breast cancer: HER2, HER4 and EGFR (epidermal growth factor receptor). It has been commercially available in China since 2018 and its performance is being tested in the multi-centre PHOEBE trial by Prof. Hu and researchers led by Professor Binghe Xu, of the National Cancer Center / Cancer Hospital and the Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. A total of 267 patients with HER2-positive, metastatic cancer were enrolled in the trial between June 2017 and October 2018.

Earlier results from March 2021 indicated that patients randomised to receive pyrotinib plus capecitabine lived significantly longer without their disease progressing than patients randomised to receive lapatinib plus capecitabine. However, the median (average) overall survival time was not reached for the pyrotinib group, while it was 26.9 months for the lapatinib group.

By March 2023, 72 (53.7%) patients in the pyrotinib group and 80 (60.6%) patients in the lapatinib group had died. The overall survival rate after 48 months of follow-up was 44% in the pyrotinib group and 38% in the lapatinib group [1].

When the researchers analysed specific groups of patients within the trial, they found overall survival was better with pyrotinib than lapatinib for patients without prior trastuzumab resistance (24% reduction in risk of death compared to patients on lapatinib), with prior trastuzumab resistance (14% reduction), patients with metastatic disease who had not received prior chemotherapy (12% reduction), and those with two previous lines of chemotherapy (35% reduction).

Prof. Hu said: “These results confirm that, compared to lapatinib plus capecitabine, pyrotinib plus capecitabine consistently shows a benefit to patients with HER2-positive metastatic disease in terms of progression-free and overall survival, irrespective of prior treatments. It brings hope of longer life to hundreds of thousands of patients. We will continue to follow up the patients in this trial to see if the survival benefits persist and for how long.”

Prof. Xu, who was unable to attend ABC 7, spoke before the conference. He said: “Pyrotinib has changed the treatment landscape for HER2-positive breast cancer patients in China, based on these outstanding efficacy results and a manageable safety profile.”

The most common serious adverse effects from pyrotinib plus capecitabine included diarrhoea, and hand and foot syndrome (pain, redness or swelling of the palms or soles of the feet). There were no treatment-related deaths among patients receiving pyrotinib, and one in the group receiving lapatinib.

Currently, pyrotinib is only available in China, and is being tested further by Prof. Xu and colleagues as a first line treatment for untreated HER2 positive breast cancer [2]. A second study is investigating pyrotinib as a neoadjuvant treatment with trastuzumab and docetaxel [3] and is led by Professor Jiong Wu, of Fudan University Cancer Hospital, Shanghai, China. Professor Zhimin Shao, of Fudan University Cancer Hospital, Shanghai, China is also investigating pyrotinib versus a placebo for extended treatment after surgery (adjuvant treatment) in a phase III clinical trial for patients with HER2-positive breast cancer [4].

Prof. Xu said: “Hengrui Medicine, the manufacturer of pyrotinib, is exploring opportunities to bring the drug to other countries where unmet needs still exist.”

Chair of the ABC 7 conference, Dr Fatima Cardoso, Director of the Breast Unit of the Champalimaud Clinical Centre, Lisbon, Portugal, and President of the ABC Global Alliance, said: “These latest results from the PHOEBE trial, presented at ABC 7 for the first time, show that pyrotinib improves survival of HER2-positive advanced breast cancer. This is good news for patients living with this disease in countries where availability of other anti-HER2 agents is limited. This subtype of ABC has one of the longest survival times, but only if patients have access to several different lines of anti-HER2

therapies. It is crucial to have access to different types of these therapies, to be able to control the disease for several years."

(ends)

[1] These data have been updated from those in the abstract and are the most recent figures available.
[2] The first line trial of pyrotinib is led by Professor Binghe Xu, of the National Cancer Center / Cancer Hospital and the Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. Ma F, Yan M, Li W, et al. Pyrotinib versus placebo in combination with trastuzumab and docetaxel as first-line treatment in patients with HER2-positive metastatic breast cancer (PHILA): a randomized, double-blind, multicenter, phase 3 trial. *British Medical Journal* 2023 (In Press).
[3] The neoadjuvant trial of pyrotinib is led by Professor Jiong Wu, of Fudan University Cancer Hospital, Shanghai, China. Wu J, Jiang Z, Liu Z, et al. Neoadjuvant pyrotinib, trastuzumab, and docetaxel for HER2-positive breast cancer (PHEDRA): a double-blind, randomized phase 3 trial. *BMC Med*. 2022;20(1):498. doi: 10.1186/s12916-022-02708-3.
[4] The adjuvant trial of pyrotinib is led by Professor Zhimin Shao, of Fudan University Cancer Hospital, Shanghai, China. The study is ongoing and results pending.

This release relates to the following presentation made on Thursday 9 November in the "**Best Abstract**" session, 15.10-15.50 hrs GMT: "Updated overall survival (OS) outcomes from the phase 3 PHOEBE trial of pyrotinib plus capecitabine versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast cancer", by Xichun Hu.

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