Phase II study shows new cancer drug combination significantly delays breast cancer progression

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The first randomised trial to investigate the use of trastuzumab emtansine (T-DM1) - an antibody-guided drug - for the initial treatment of HER2- (human epidermal growth factor receptor-2) positive metastatic breast cancer has shown that it makes a significant difference to the time women live without their disease worsening.

Dr Sara Hurvitz, one of the trial investigators, will tell the 2011 European Multidisciplinary Cancer Congress in Stockholm today (Sunday 25 September): "Our results showed that patients with metastatic breast cancer who received T-DM1 had a 41% improvement in the time they lived without their breast cancer worsening compared to those who received standard docetaxel chemotherapy plus trastuzumab. These provocative Phase II data illustrate that first-line treatment with T-DM1 provides a longer time for patients to live without cancer progression and with fewer side effects than standard chemotherapy plus trastuzumab."

Trastuzumab emtansine (T-DM1) is a novel type of cancer therapy known as an antibody drug conjugate (ADC). It combines the monoclonal antibody, trastuzumab, with a potent cytotoxic agent DM1 through a stable linker and uses the HER2 targeting properties of trastuzumab to deliver the cell-killing agent DM1 into the cancer cells.

Dr Hurvitz, Director of the Breast Oncology Program for the Division of Hematology/ Oncology at The University of California, Los Angeles (UCLA), USA, will say that "T-DM1 is unique because it retains the cancer fighting properties of trastuzumab and delivers the DM1 agent directly to the tumour cell for destruction, while limiting exposure of the free DM1 drug to normal cells. This explains why patients who received T-DM1 had fewer side effects compared to those assigned to the chemotherapy-containing control arm in this study."

T-DM1 is specifically designed to attach trastuzumab to DM1 using a stable linker. The bound DM1 has little toxicity, but when it is delivered to the HER2-positive cancer cells, DM1 is released and its potent cytotoxic effect is enabled. The trastuzumab monoclonal antibody delivers its anti-cancer effects after targeting T-DM1 to the cancer cell.

About one in five breast cancer tumours are HER2-positive, meaning that the cancer cells overproduce the protein called HER2, which plays an important role in promoting cancer growth. This type of breast cancer is often more aggressive and difficult to treat than other types of breast cancer. HER2-positive tumours are usually treated with targeted therapy.

Dr Hurvitz will say: "The majority of patients with HER2-positive metastatic breast cancer will face resistance to the currently available HER2-directed therapies. Therefore, dealing with resistance to HER2-targeted therapy remains an unmet need and new, effective therapies for HER2-positive breast cancer are still necessary."

Dr Hurvitz and her colleagues enrolled 137 patients, who had never received chemotherapy or HER2-targeted therapy for locally advanced or metastatic HER2-positive breast cancer, in the open-label, randomised, Phase II clinical trial. Patients were randomly assigned to receive treatment with either T-DM1 or standard therapy (trastuzumab plus the chemotherapy drug docetaxel).

The median progression-free survival (time that elapses before the cancer worsens) was 14.2

months for women who received T-DM1 compared to 9.2 months for those who received trastuzumab plus docetaxel. Two deaths that were not due to disease progression occurred in the study, one in each treatment arm. The percentage of women who discontinued treatment due to side-effects was 7.2% in the T-DM1 arm and 28.8% in the standard therapy arm of the study.

Dr Hurvitz will say: "T-DM1 is unique in that it allows the targeted delivery of chemotherapy to cancer cells. Based on the results of this Phase II study, T-DM1 appears to be not only safer than the docetaxel/trastuzumab combination, but it may allow patients to live without disease progression for a significantly longer period of time. A safer, more effective treatment is likely to enhance patient quality of life and it may ultimately translate into fewer hospitalisations for complications more commonly reported with docetaxel/trastuzumab use."

"It is important to realise that while the current data are encouraging, results from the ongoing Phase III studies (EMILIA and MARIANNE) will be needed to more fully characterise the efficacy and safety profile of T-DM1 compared to the current therapy regimens used to treat HER2-positive metastatic breast cancer."

Professor Michael Baumann, president of ECCO said: "This is a very important trial which indicates that the more selective delivery of anticancer drugs, by conjugating them to antibodies which dock to cancer cells, bears considerable promise for personalised cancer treatment."

Commenting on the study, which he was not involved with, ESMO member Dr Angelo Di Leo from the Hospital of Prato, Istituto Toscano Tumori, Italy, said: "These promising data do not yet allow us to consider T-DM1 as a new standard of care for the first-line treatment of HER-2 positive breast cancer. The results from ongoing Phase III trials are eagerly awaited. Ongoing studies are also exploring the possibility of combining T-DM1 with other biological agents targeting receptors belonging to the HER family. It is expected that combining T-DM1 with these agents will further improve the level of care for women affected by HER-2 positive breast cancer."

Provided by ECCO-the European CanCer Organisation