Lapatinib and trastuzumab shrinks HER2+ breast cancer in 11 days after diagnosis

March 10 2016

Amsterdam, The Netherlands: Approximately a quarter of women with HER2 positive breast cancer, who were treated with a combination of the targeted drugs lapatinib and trastuzumab before surgery and chemotherapy, saw their tumours shrink significantly or even disappear, according to results from a clinical trial.

Professor Nigel Bundred told the 10th European Breast Cancer Conference (EBCC-10) today (Thursday): "This has ground-breaking potential because it allows us to identify a group of patients who, within 11 days, have had their tumours disappear with anti-HER2 therapy alone and who potentially may not require subsequent chemotherapy. This offers the opportunity to tailor treatment for each individual woman."

Prof Bundred, who is Professor of Surgical Oncology at The University of Manchester and the University Hospital of South Manchester NHS Foundation Trust (UK), was presenting results from the UK EPHOS-B multi-centre, clinical trial, in which 257 women with newly-diagnosed, operable, HER2 positive disease were recruited between November 2010 and September 2015.

The trial had two parts; in part one, 130 women were randomised to receive no pre-operative treatment (the control group), or trastuzumab (Herceptin) only, or lapatinib (Tyverb) only, for 11 days after diagnosis and before surgery. However, as evidence emerged from other trials of the efficacy of the combination of lapatinib and trastuzumab to treat HER2 positive breast cancer in other settings, the second part of the trial

was amended so that, from August 2013, the next 127 women were randomised to the control group, or to receive trastuzumab only, or the combination treatment. For both parts of the trial, the women continued to receive standard of care treatment after surgery.

Samples of tumour tissue were taken from the first biopsy, which had been used to confirm the cancer diagnosis, and then again during surgery. The samples were analysed to see if there had been a drop in levels of the Ki67 protein, an indicator of cell proliferation, or a rise in apoptosis (programmed cell death) of 30% or more from the time of the first biopsy. In addition, investigators reviewed the pathology reports on the tissue taken during surgery, and the women were then categorised as either having pathological complete response (pCR) if no active cancer cells had been found, minimal residual disease (MRD) if the tumour was less than 5mm in diameter, or other.

Results from the second part of the trial, analysed in February 2016, showed that, in addition to observing a drop in Ki67, for women who received the combination treatment 11% had pCR and 17% had MRD. For those women randomised to receive only trastuzumab, 0% had pCR and 3% had MRD and no patients had either pCR or MRD in the control group.

The group of women who responded to the combination treatment included women who had presented with Stage 2 breast cancer (where it had spread to their lymph nodes).

Speaking at the EBCC-10 press conference, Professor Judith Bliss, lead researcher from The Institute of Cancer Research, London, which co-led the trial, said: "These results show that we can get an early indication of pathological response within 11 days, in the absence of chemotherapy, in these patients on combination treatment. Most previous trials have only looked at the pathological response after several months of treatment.

"Clearly these results need further confirmation, but I suspect the excitement from seeing the speed of disappearance of the tumours will mean that several trials will attempt to confirm these results."

So far, EPHOS-B is the only trial that has investigated giving combination treatment alone, without chemotherapy, in the two weeks between diagnosis and routine surgery. "Other trials have looked at anti-HER2 therapy, with and without chemotherapy, including an assessment of the combination of trastuzumab and lapatinib, and have reported impressive response rates but these trials have only reported results after several months of therapy. Potentially, giving treatment while waiting for surgery can identify a group of patients whose disease is particularly sensitive to anti-HER2 therapy, which would allow individualisation of therapy in women with HER2 positive cancers," said Prof Bundred.

Chair of EBCC-10, Professor Fatima Cardoso, who is Director of the Breast Unit at the Champalimaud Clinical Centre, Lisbon, Portugal, said: "The results of this important trial confirm previous initial suggestions that most probably there are patients who can be treated with dual-blockade (two anti-HER2 agents simultaneously) alone, without chemotherapy. This study proposes a simple way to identify those patients very early on, which could help spare them unnecessary chemotherapy. What is now indispensable is to confirm if these early responses translate into better or equal long-term survival."

HER2 positive breast cancer is breast cancer that has a high number of receptors for the human epidermal growth factor (HER2) on the surfaces of the cancer cells. These receptors stimulate the cancer cells to divide and grow. HER2 positive breast cancers tend to grow more quickly than HER2 negative cancers but can be treated with targeted therapies such as trastuzumab and lapatinib.

More information: Abstract no: 6 LBA. "Effects of perioperative

lapatinib and trastuzumab, alone and in combination, in early HER2+ breast cancer - the UK EPHOS-B trial (CRUK/08/002)", Thursday, Clinical science symposium: HER2 positive breast cancer, 16.00-17.30 hrs, Elicium.

Provided by ECCO-the European CanCer Organisation