Anti-cancer drug T-DM1 benefits women with advanced breast cancer who've failed previous treatments

27 September 2013

Amsterdam, The Netherlands: First results from a phase III clinical trial of the combination drug, T-DM1, show that it significantly improves the length of time before the disease worsens in women with advanced HER2 positive breast cancer whose cancer has recurred or progressed despite previous treatments, including trastuzumab and lapatinib.

In a late-breaking presentation to the 2013 European Cancer Congress (ECC2013) [1] on Saturday, Professor Hans Wildiers will say: "This study shows that even in heavily pre-treated women, 75% of whom had cancer that has spread to the internal organs, T-DM1 nearly doubles progression-free survival – the length of time before disease progression or death, whichever occurs first – compared to standard therapy, and with a more favourable safety profile. Few drugs have been able to achieve both improved progression-free survival and a better toxicity profile. These results indicate this drug has important clinical benefit for patients."

T-DM1 is a conjugated monoclonal antibody in which trastuzumab [2] is combined with a cell-killing drug emtansine (DM1) to target and kill breast cancer cells that have large amounts of the protein HER2 on their cell surfaces – known as HER2 positive breast cancer. T-DM1 has already been shown to benefit patients with HER2 positive breast cancer that has spread to other parts of the body (metastasised), and who have already been treated with trastuzumab and a taxane-based chemotherapy.

"Despite the availability of improved treatments, virtually all patients with HER2 positive metastatic breast cancer develop progressive disease and require additional therapies for palliation. Currently there is no clear standard of care for patients who progressed after two or more treatments for their disease, including the use of the anti-HER2 drugs trastuzumab and lapatinib, and new treatment options are needed for these patients," says Prof Wildiers, who is adjunct head of clinic at the department of medical oncology, and coordinator of the chemotherapy and related clinical trial programme in the multidisciplinary breast centre at the University Hospitals Leuven, Belgium.

The international phase III clinical trial, called TH3RESA, enrolled patients whose cancer was inoperable, or had recurred or metastasised after several treatments including trastuzumab and lapatinib. By February 2013, 602 patients had been randomised to receive 3.6 mg/kg intravenous infusion of T-DM1 every three weeks or a treatment of their physician's choice (TPC). The majority (75%) had visceral disease (cancer that had spread to internal organs) and they had received a median [3] of four previous treatment regimens (excluding single agent hormonal therapy).

Results showed that median progression-free survival increased by nearly three months from 3.3 months for the TPC patients to 6.2 months for patients receiving T-DM1. Among the T-DM1 patients, 31.3% showed a response to the drug, compared with 8.6% of the TPC patients. An interim analysis of overall patient survival showed a similar trend, but it did not reach the level at which a statistically significant benefit for T-DM1 treatment could be confirmed. Patients in the TPC group, whose disease progressed, were given the option of crossing over into the T-DM1 arm and 44 patients have done this so far. Generally, there were fewer serious adverse side-effects in the T-DM1 patients than in the TPC group.

"These data reaffirm the potential of T-DM1 as a treatment for HER2-positive metastatic breast

cancer. They demonstrate that T-DM1 has the potential to be a new treatment paradigm for this group of patients who currently have few options," Prof Wildiers will say.

"In the earlier, EMILIA trial, T-DM1 was shown to be superior to capecitabine and lapatinib in patients who had previously received trastuzumab and a taxane. TH3RESA demonstrates that T-DM1 offers statistically significant and clinically meaningful improvement in delaying disease progression compared to a treatment of physician's choice, which was predominantly trastuzumab and chemotherapy combinations, in patients who have previously received trastuzumab and lapatinib.

"This trial will continue until the final overall survival analysis takes place or until the survival benefit for treatment with T-DM1 reaches statistical significance at an interim analysis. T-DM1 is also being tested both alone and in combination with pertuzumab in patients with previously untreated HER2 positive metastatic breast cancer in the MARIANNE trial," he will conclude.

ECCO President, Professor Cornelis van de Velde, commented: "These results from the TH3RESA trial are important because they confirm and extend the usefulness of T-DM1 for the treatment of women with advanced HER2 positive breast cancer. Once HER2 positive breast cancer has recurred and metastasised, there are few treatment options available that show any clear benefit for women who have probably undergone several previous treatments for the disease. The fact that T-DM1 extends progression-free survival is good news for these women."

More information: [1] The 2013 European Cancer Congress is the 17th congress of the European CanCer Organisation (ECCO), the 38th congress of the European Society for Medical Oncology (ESMO) and the 32nd congress of European Society for Therapeutic Radiology and Oncology (ESTRO).

[2] Trastuzumab, also known by its brand name Herceptin, is a drug that targets cancer cells that produce too much of a protein called HER2 (human epidermal growth factor receptor 2). Trastuzumab attaches to HER2 and kills the cancer cells by preventing them from dividing and growing.

[3] The median average is the number separating the higher half of a set of figures from the lower half i.e. the middle number.

[4] The trial was sponsored by Roche.

Abstract no: LBA15, "T-DM1 for HER2-positive metastatic breast cancer (MBC): Primary results from TH3RESA, a phase 3 study of T-DM1 vs treatment of physician's choice". Breast cancer –advanced disease proffered papers session, 11.15 hrs CEST, Saturday 28 September, Hall 7.1.

Provided by ECCO-the European CanCer Organisation