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Trastuzumab Biosimilar HLX02 Met Primary Endpoint in Breast Cancer

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First China-manufactured Biosimilar HLX02 proven equally safe and effective as the reference trastuzumab in Global Phase III Trial trough rigorous evaluation by EMA regulatory authorities



The trastuzumab biosimilar HLX02 achieved similar overall response rate to reference trastuzumab in women with human epidermal growth factor receptor 2-positive (HER2+) recurrent or previously untreated metastatic breast cancer, according to a large, randomised phase III study to be reported at the ESMO Asia Congress 2019.

“Trastuzumab is not widely accessible around the world due to its high cost. The entry of more affordable versions of trastuzumab such as HLX02 could open up treatment access,” said study first author Binghe Xu, Department of Medical Oncology, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China.

The anti-HER2 antibody trastuzumab given in combination with chemotherapy has significantly improved overall survival in patients with HER2-positive breast cancer and become the standard of care over the past decade. However, the cost can limit patient access to this treatment in regions with limited financial resources for healthcare.

The development of biosimilars, which are medicinal products containing a similar version of the active substance of their biological originator or reference product and are derived from living organisms, offers a way of improving access to cancer treatments by increasing treatment options and reducing cost.

The new study randomised women with HER2-positive breast cancer to HLX02, a fully humanised anti-HER2 that was developed in China as a trastuzumab biosimilar, or to reference trastuzumab sourced from the European Union.

“Overall response rate at week 24 was similar for HLX02 and reference trastuzumab with no statistical difference observed between the two treatment groups,” reported Xu. The rates of adverse events and treatment-emergent adverse events were similar for HLX02 and reference trastuzumab and there were no differences in safety profiles or immunogenicity.

“HLX02 is equally safe and effective as the reference trastuzumab and has been rigorously evaluated by regulatory authorities such as the European Medicines Agency (EMA), based on sound scientific principles,” said Xu. He added, “HLX02 has a clear potential to drive down spending on HER2+ cancer treatment,” although he said the price has not yet been agreed.

Commenting on the relevance of the new data, Rosa Giuliani, Consultant Medical Oncologist, Clatterbridge Cancer Centre, Liverpool, UK, noted that other trastuzumab biosimilars have been approved in Europe so the potential approval of China-produced HLX02 would add a further option.

Giuliani warned: “Access to cancer medicines is a huge problem throughout the world, applying to relatively inexpensive medicines but even more to more expensive drugs such as monoclonal antibodies. A survey carried out by ESMO in 2016 and the subsequent follow-up study showed that many patients in different countries, including Europe, have difficulty in accessing cancer medicines. What is even more astonishing is that this includes medicines listed in the World Health Organization’s (WHO) Essential Medicines List, such as trastuzumab. It is not acceptable that medicines which have shown to have a major impact on patients survival are not given to patients in need. Biosimilars are safe and effective drugs which can finally allow those patients to receive an appropriate standard of care.”

Rebecca Dent, Head of Medical Oncology at the National Cancer Center Singapore, added: “The development of biosimilars means that more women will have access to potentially life-saving HER2-targeted therapies because of the cost-savings they provide. Development of biosimilars introduces competition and potentially lowers the price of drugs.”

Dent added, “As more biosimilar therapies are being developed there is also a need for vertical integration of the biomarkers that identify patients who will benefit.” For trastuzumab biosimilars, this means ensuring access to HER2 status testing.

Reviewing the quality of the study design, Dent considered it important that the clinical programme with HLX02 was developed in consultation with the EMA and the China National Medical Products Administration (NMPA). The interim results of the study have been submitted to the NMPA and EMA to support approval of HLX02 in China and Europe.

Study results

The phase III study randomised 649 women with HER2+ recurrent or previously untreated metastatic breast cancer to HLX02 or EU-sourced trastuzumab (EU-TZB) (dose of 8mg/kg for both drugs) with docetaxel on day 1. Cycle 1 was followed by a dose of 6mg/kg in three-weekly cycles for up to 12 months. The women were recruited from 89 centres in China, the Philippines, Poland and Ukraine.

Result showed similar overall response rate at 24 weeks with HLX02 (71.0%) as with EU-TZB (71.4%, p=0.952). All secondary endpoints, including overall response rates at weeks 6, 12 and 18, clinical benefit rate, disease control rate, duration of response, progression-free survival and overall survival at week 24 were similar for HLX02 and EU-TZB. The disease control rate was 83.0% in the HLX02 group and 84.3% in the reference trastuzumab group (p=0.646).

In each treatment group, 98.8% of the patients reported at least one adverse event or treatment-emergent adverse event and a similar number of adverse events were reported in the two treatment groups. There were no differences in safety profiles or immunogenicity between HLX02 and reference trastuzumab.