Trastuzumab biosimilar in early breast cancer setting: will there be direct patient benefits?

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The inclusion of trastuzumab in the management of both early and metastatic HER2-positive breast cancer has significantly improved survival of these patients and is regarded as a standard of care. However, the cost of 12 months of adjuvant trastuzumab which is currently regarded as the standard duration of administration and an indefinite use of trastuzumab in the metastatic setting, limits the global use of this monoclonal antibody for all patients. The latter was shown in our Lancet Oncology Commission of cancer control in China, India and Russia; where these three nations account for 40% of the world's population. At the time of our report in April 2014, approximately one third of breast cancer patients in China with HER2-positive disease were able to access trastuzumab (1). The results of the study reported by Stebbing *et al.* (2) is the first reported multicentre study in the early breast cancer setting—which included approximately one quarter of patients from non-Caucasian ethnicity. The study demonstrated equivalence of the biosimilar, CT-P6 with trastuzumab in the primary outcome measure of pathological complete response (pCR). Although local HER2 evaluation was conducted for study entry and local assessment of pCR was undertaken, it is commendable that masked central review was performed for the purpose of reporting the results. In line with the US Food and Drug Administration (FDA) guideline paper on using pCR as an endpoint in high-risk early-stage breast cancer following neoadjuvant therapy to support accelerated drug approval, the use of pCR is an appropriate clinical endpoint to demonstrate equivalence of the two monoclonal antibodies (3). As recommended in the guidance for industry regarding scientific considerations in demonstrating biosimilarity to a reference product (4), the investigators were able to show equivalent efficacy—using both the 95% confidence interval being contained within a greater or lesser than 15% margin, as well the risk ratio for pCR being within a range of 0.74–1.35; for the ITT and per protocol population. The investigators also evaluated pharmacokinetic measures and immunogenicity profile of the biosimilar and demonstrated comparable results between CT-P6 and the reference agent.

The lower rates of pCR in patients with hormone receptor positive disease is aligned with other neoadjuvant studies where trastuzumab with or without pertuzumab were evaluated and the proportion of patients did not appear to differ in the current study between the two arms. However, though patients with hormone receptor negative disease had higher rates of pCR as to be expected, there was a numerically greater difference of 6% in favour of trastuzumab when compared to CT-P6. Patient numbers in this subset are small but it may be worthwhile to ensure this difference was not a real difference in efficacy between the two agents, but perhaps may be a result of an imbalance in tumour size at baseline or was a chance finding.

In regard to the safety profile, the treatment emergent adverse events appeared balanced between the two agents. Importantly, the administration of concurrent anti-HER2

agent with the anthracycline component of neoadjuvant treatment did not give rise to differences in rates of symptomatic cardiac dysfunction, albeit with cardiac function follow-up only being reported up until the end of the neoadjuvant phase of treatment. A similar rate of infusion reactions was reported in both treatment arms which is reassuring to know for this class of drug. Finally, the plan for further follow-up for disease events up until a minimum of 3 years from enrolment of the last patient will be important to ensure that the equivalent efficacy is maintained.

Having demonstrated efficacy and safety equivalence, the true benefits of the results of this study will be whether the presumed lower drug costs of the biosimilar translates into greater utilisation of this targeted therapy for patients with HER2-positive breast cancer, in those who currently do not receive this treatment. Clearly the greatest impact will be its use in the adjuvant setting and if this can be achieved, will undoubtedly lead to lives saved and may alter the incidence of metastatic HER2-positive breast cancer worldwide. This global incremental survival benefit with a lower cost drug may then further impact on drug expenditure for newer targeted therapies such as pertuzumab, T-DM1, neratinib, other HER2 cytotoxic conjugates and tyrosine-kinase inhibitors; not to mention HER2-directed immunotherapies. As concluded in the editorial by Bauchner *et al.* (5), it will remain to be seen if the increasing availability of trastuzumab biosimilar agents will change clinical practice as financial barriers are lowered. To this end, as greater numbers of biosimilars enter the clinical setting for breast cancer and other HER2-positive solid tumours, it will be important to measure certain outcomes. These include institutional and national data collection to show a greater proportion of patients receiving this standard of care therapy, actual cost savings that ensues for national health care funders which may then lead to judicious distribution of cost savings to other health care needs and long-term reporting of adverse events attributable to this class of agents.

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Footnote

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References

1. Goss PE, Strasser-Weippl K, Lee-Bychkovsky BL, et al. Challenges to effective cancer control in China, India, and Russia. Lancet Oncol 2014;15:489-538.
2. Stebbing J, Baranau Y, Baryash V, et al. CT-P6 compared with reference trastuzumab for HER2-positive breast cancer: a randomised, double-blind, active-controlled, phase 3 equivalence trial. Lancet Oncol 2017;18:917-28.
3. Guidance for Industry Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval. Available online: https://www.fda.gov/downloads/drugs/guidances/ucm305501.pdf
4. Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Guidance for Industry. Available online: https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf
5. Bauchner H, Fontanarosa PB, Golub RM. Scientific Evidence and Financial Obligations to Ensure Access to Biosimilars for Cancer Treatment. JAMA 2017;317:33-4.

