Cost considerations in determining the affordability of adjuvant trastuzumab in breast cancer (2)

To the Editor: Cost considerations in determining affordability are extremely important for the sustainable health policy of all countries. It is of utmost importance that applied cancer treatment would result in a significantly improved cure rate being the primary objective, or at least a meaningfully reduced recurrence rate.

The proposition presented by Abratt,[1] that state institution and lower-level medical schemes should consider <6 months of trastuzumab adjuvant therapy, is not supported by any solid clinical evidence and, if implemented, would result in fruitless depletion of resources.

Two small trials included in the Cochrane analysis, to which his article refers, merely suggested possible efficacy of shortened time of treatment.[2] Both studies were conducted with different primary objectives, other than duration of treatment and its effectiveness. In addition: (*i*) the first one included only 42 patients and the effect on overall survival (OS) was not reported;[3] and (*ii*) the 5-year update of the second trial (FinHer) demonstrated no statistical difference in metastatic recurrence and mortality between control and trastuzumab arms.[4]

The lack of effectiveness of 6 months' therapy has been confirmed by the robust PHARE trial.[5]

The National Institute for Health and Care Excellence (NICE) UK, known for its rigorous approach to cost-effectiveness, approved 1 year of trastuzumab treatment as being appropriate for the cash-strapped National Health Service (NHS).[6]

Emerging 10-year follow-up BCIRG-006 data show that the addition of 12 months of trastuzumab therapy resulted in a 24 - 36% improvement in OS and a 24 - 36% reduction in recurrence rates, depending on the chemotherapy regimen used. Cardiac toxicity risk could be halved by the choice of a non-anthracycline chemotherapy regimen.[7]

When calculating any cost-effectiveness, the state should also look at the cost of education of persons affected by the disease, as well as their role in the much-required stabilisation of the South African community.

Cost-effectiveness calculations should include savings resulting from cure and avoidance of further lines of treatment. It should also include costs incurred by state, funders, community and family for continuous care of affected patients, should their breast cancer relapse. Any other calculations are usually biased to the financial needs of relevant interest groups.

Should we rather advocate the use of scarce resources to effectively treat patients with defined intermediate and high risk for mortality and recurrence, instead of wasting them on futile, 6-month and less trastuzumab treatment regimens, as suggested by the author of this clinical alert?

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Prof. Raymond Abratt responds: The original article[1] focused on cost considerations in determining the affordability of adjuvant trastuzumab. In the final section of the article, the clinical ethical principle was noted that 'clinicians should provide the best treatment possible with available resources, provided there is evidence of benefit and the clinician is prepared to undertake the treatment.'

In a well-resourced environment, 12 months of trastuzumab should be offered to patients. However, for the vast majority of patients in South Africa (SA) this is not available and they receive no adjuvant trastuzumab treatment at all. An option which oncologists in SA may consider, is <12 months of adjuvant trastuzumab.

In the PHARE trial,[2] 6 months of adjuvant trastuzumab was shown to be marginally less effective than the 12-months regimen in terms of disease-free survival (DFS). The 2-year DFS was 93.8% (95% confidence interval (CI) 92.6 - 94.9) in the 12-month group and 91.1% (89.7 - 92.4) in the 6-month group. However, significantly more patients in the 12-month group experienced a cardiac event than did those in the 6-month group, 5.7% v. 1.9%, $p<0.0001$.

So, the number needed to treat (NNT) to prevent 1 recurrence at 2 years, by giving an extra 6 months of trastuzumab, is 100/(93.8 – 91.1) = 37. The NNT to prevent 1 recurrence at 23 months is 16 when 12 months of trastuzumab is compared with no treatment.[3] This suggests a diminishing return in benefit and decreasing value, that is outcome/cost,[4] with the additional 6 months of therapy.

But toxicity increases with the additional 6 months of treatment. The number needed to harm (NNH) for an extra cardiac event is 100/(5.7 – 1.9) = 26. It is therefore more likely that a patient will suffer a cardiac event than have a breast cancer event prevented with an extra 6 months of trastuzumab.

The drug cost for an additional 6 months of trastuzumab is ZAR205 000 per patient. The drug cost to prevent one recurrence in the treated population, as described in the PHARE study, for an NNT of 37 = ZAR7 585 000. This is not affordable for SA's healthcare systems. Downstream differences in costs between 6 and 12 months of adjuvant trastuzumab are irrelevant to patients who do not receive the drug at all.

The study findings and drug costs indicate that the 6-month regimen is a sound option and will increase the number of patients who will have access to adjuvant trastuzumab within the budgetary constraints of SA's healthcare systems. The 12-month regimen should not be regarded as the only acceptable option in SA. The view that it is preferable that patients receive no adjuvant trastuzumab treatment rather than 6 months of adjuvant trastuzumab does not serve the purpose of benefiting patients.

Scientific questions and costs influence patient care globally.[5] We need to work with Pharma and others to reduce the price of treatment and also to clarify all the associated cost-to-benefit patients in different prognostic groups.[1] Our aim is to provide high-quality care to all patients within the necessary constraints of cost.

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