



CLINICAL ALERT

Cost considerations in determining the affordability of adjuvant trastuzumab in breast cancer

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The drug cost of adjuvant trastuzumab to benefit one patient with localised human epidermal growth factor receptor 2 (HER2)-positive breast cancer depends on the baseline survival rate (BLSR) of the prognostic group of the patient. This varies from ZAR13 752 900 (BLSR 90%) to ZAR4 006 100 (BLSR 60%). All treated patients are exposed to potential toxicity. The value and affordability of treatments need to be considered, as there are finite resources available in our healthcare system. All patients must have access to cost-effective treatments. However, patient selection for expensive treatments is important, as expenditure on patients where the gains are relatively small will result in resources not being available for other patients. The state, healthcare institutions and the pharmaceutical industry need to work together to optimise the benefits of treatment to patients.

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The rapid increase in costs in medicine has highlighted the affordability and value of medical treatments.^[1] Affordability is the cost relative to the amount that the purchaser is able to pay. Value is the ratio of patient benefit to cost.

A topical issue is the affordability and value of adjuvant trastuzumab for 1 year after surgery for localised human epidermal growth factor receptor 2 (HER2)-positive breast cancer, particularly in low- and middle-income countries. Affordability and value differ in patient groups with different baseline prognoses. This is illustrated below using the hazard ratio (HR) of survival rates obtained from a Cochrane review^[2] and personal communication with Roche.

The HR is the ratio of the relative survival of two patient groups, with and without the test therapy. This ratio will not vary much over time. Patients can be divided into prognostic groups with different outcomes, depending on tumour stage and nodal status. For an assessment of affordability, a specific time point needs to be determined for the calculation of baseline survival. Expected baseline survival rates (BLSRs) for periods up to 15 years can be determined with breast cancer outcome calculators, which are available on the internet (e.g. <https://www.adjuvantonline.com/> and <http://www.lifemath.net/cancer/breastcancer/therapy>).

Number needed to treat (NNT) to benefit one patient at any selected endpoint

For clinical purposes, this may be approximated from the BLSR and the HR. The HR for overall survival in the calculation below was 0.69 (95% confidence interval (CI) 0.58 - 0.81).

- The number of patients who will benefit when 100 patients are treated = $(100 - \text{BLSR}) \times (1 - \text{HR})$.
- Therefore, for a BLSR survival rate of 90%, the number who will benefit = $10 \times 0.31 = 3$. The survival rate therefore increases from 90% to 93%.
- The NNT to benefit one patient = $100/3 = 33$.

More accurate numbers can be determined using more sophisticated formulae.^[3]

Toxicity

The relative risk (RR) for increased toxicity for congestive heart failure = 5.11 (90% CI 3.00 - 8.72), and for decrease in left ventricular ejection fraction = 1.83 (90% CI 1.36 - 2.47).

Toxicity risk occurs in all treated patients, which means that the higher the BLSR, the higher is the proportion of patients who are free of disease who are exposed to potential toxicity. The toxicity also has cost implications, as all patients need to have their left ventricular function evaluated objectively with an echocardiogram or multigated acquisition (MUGA) scan every 3 months while on treatment.

The drug costs for 1 year on adjuvant trastuzumab

This analysis will restrict itself to a review of immediate drug costs alone, which are the largest cost factor. It excludes costs related to the facility fee, professional fees or associated investigations. A full economic analysis will include these costs as well as downstream costs for possible toxicity and savings from benefit.

The drug cost of 17 cycles of trastuzumab, allowing for vial sharing, for 1 year is ZAR413 000.

There are proponents for the use of adjuvant trastuzumab in all scenarios. The NNT to benefit one patient at a selected endpoint and the related drug cost to benefit one patient are shown in Table 1. The table indicates that the drug cost to benefit one patient ranges from ZAR13 752 900 (BLSR 90%) to ZAR4 006 100 (BLSR 60%).

Clinical ethics

It is a principle of clinical ethics that the clinician 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 the Cochrane analysis,^[2] the comment is made that the data indicate that the same efficacy is achieved with <6 months of treatment compared with 12 months of treatment and that there is less cardiac toxicity, but that this is not statistically significant with the numbers in the relevant studies. These studies are underpowered and there is relatively little incentive to undertake them. Although this is

Table 1. NNT to benefit one patient and the related drug costs with adjuvant trastuzumab in patients with breast cancer^[3]

Patient baseline survival rate, %	Survival rate with trastuzumab, %	NNT to benefit one patient	Drug cost (ZAR) to benefit one patient
90	93	33.4	13 794 200
80	86	17.5	7 227 500
70	78	12.2	5 038 600
60	70	9.7	4 006 100

a lower level of evidence compared with that found with higher numbers, it is not an absence of evidence. Where funders are not able to provide 12 months of trastuzumab, as

happens at present in state institutions and the lower-level medical schemes, <6 months of trastuzumab should be considered as a treatment option to benefit patients.

Clinicians rightly wish to extend the benefits from advances in cancer treatment to all suitable patients. This requires an appreciation of the costs involved and an ongoing engagement of state and healthcare institutions and the pharmaceutical industry.

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