

Appendix Six. Comparisons between 12-month and 9-week trastuzumab regimens for HER2-positive early breast cancer

Comparisons of eligible patient pools and treatment regimens

	12 months sequential treatment	9 weeks concurrent treatment
Eligible patient population	<p>Eligible patients were those presenting with HER-2 positive early breast cancer, with acceptable heart function (assumes some patients excluded from treatment for inadequate heart function).</p> <p>The weight of patients (and correspondingly, the dose per patient) was calculated using the appropriate distributions as per the age and weight distributions for HER 2 positive early breast cancer patients in New Zealand.</p>	
Patient Numbers	<p>Year 1: 280¹ Year 5: 339</p>	<p>Year1: 340² Year 5: 413</p>
Regimen	<p>1 loading dose (8mg/kg) trastuzumab, then 6mg/kg every 3 weeks for one year</p> <p>Total of 17 infusions (each requiring an extra visit to the hospital).</p>	<p>9 trastuzumab infusions at 1 week intervals. Loading dose 4mg/kg, remaining doses 2mg/kg</p> <p>Total of 9 infusions (6 more visits than standard chemotherapy)</p> <p>Alternative is 3 trastuzumab infusions at 3 week intervals. Loading dose 8mg/kg, remaining doses 6mg/kg</p> <p>Total of 3 infusions (no extra visits compared with standard chemotherapy)</p>

¹ 15-20% of patients with early stage HER2-positive breast cancer eligible for trastuzumab treatment will need to be excluded following anthracycline chemotherapy for the 12 month sequential regimen because of anthracycline-induced cardiotoxicity.

² Note that more patients are eligible for treatment under the 9 week regimen because this allows treatment with trastuzumab before patients receive their cardiotoxic anthracycline chemotherapy.

Comparison of annual Drug Cost and impact on DHB services

	12 months sequential treatment	9 weeks concurrent treatment
Total dose	104mg/kg	20mg/kg
Drug cost per patient (\$NZ) trastuzumab Docetaxel	\$71,000 n/a	\$13,000 ~\$7,000
Total drug cost	~\$20 million	\$5 million
Approximate DHB services costs	\$5 million	\$700,000
Total Cost	~\$25 million per annum	~\$6 million per annum
Description of costs	<p>DHB services costs include the costs of compounding, administration (infusion and monitoring costs) and cardiac monitoring.</p> <p>Patients who experienced an adverse event that lead to treatment discontinuation were assumed to accrue the costs of drug up until the time of drug discontinuation (drop out rates were as per the drop outs reported in the HERA trial).</p> <p>This does not include costs incurred for treating patients who experience cardiac adverse events (however, this is included in the cost-utility analysis).</p>	

Cost- effectiveness comparison

The cost-utility analysis³ for 12 months of trastuzumab given after chemotherapy indicates a base-case result of about \$70,000-\$80,000 per QALY (12-15 QALYs per million dollars spent)⁴. However, this analysis showed a large range of plausible outcomes, largely due to the uncertainty surrounding duration of benefit and untreated disease progression. None of the plausible outcomes gave sufficient confidence that 12 months of trastuzumab treatment would be a cost-effective use of health funds compared with other investments.

PHARMAC has estimated the revised cost-utility analysis of a nine-week concurrent regimen to be, under fairly conservative assumptions, \$14,500-\$16,500 per QALY (60-70 QALYs per \$1 million spent). Trastuzumab in this setting should therefore be as, or more, cost-effective than many other medicines PHARMAC has funded.

The nine week concurrent regimen is likely to be four times more cost-effective than the 12 month sequential regimen (60-70 QALYs per \$1 million for 9 weeks, vs. around 12-15 QALYs per \$1 million spent for 12 months).

³ PHARMAC. TAR 75 Trastuzumab (Herceptin) in HER-2 positive early breast cancer with 9 week regimen CUA. Released May 2007. <http://www.pharmac.govt.nz/pdf/030307c.pdf>

⁴ A QALY stands for a 'Quality-adjusted life year'. A QALY is a standard economic measure that considers how treatment affects patient quality of life and quantity of life'; QALYs combine the effects of changes in the length and quality of life that result from treatment. The difference in net costs and QALYs between treatments informs the relative cost-effectiveness of an intervention, with a lower cost per QALY being more cost-effective.