

## Appendix Five

### Clinical information for trastuzumab – summary, interpretation and policy implications

District health boards (DHBs) and PHARMAC decided in July not to fund trastuzumab, as adjuvant treatment of early HER2-positive breast cancer as a 12-month regimen, at that time, but committed to ongoing active review of the evidence.

PHARMAC was asked by the supplier to make a decision on funding 12 months trastuzumab predominantly on the basis of the results of the HERA trial's interim report of the effects of 1-year's sequential treatment after 12 months median follow-up (Piccart-Gebhart et al NEJM 2005). The Pharmacology and Therapeutics Advisory Committee (PTAC, PHARMAC's independent clinical advisory body <http://www.pharmac.govt.nz/ptac.asp>) raised a concern over the durability of response and the long-term balance of safety and efficacy. PHARMAC had concerns over the uncertainty from a cost-effectiveness point of view for such a relatively large investment in a pharmaceutical (around \$25m per annum out of a total cancer spend of about \$50m per annum), in relation to PHARMAC's legal responsibility to secure the best health outcomes within available resources across all new medicines across the whole population. According to PHARMAC's analysis (TAR 75), in order for 12 months trastuzumab to be considered cost-effective in comparison with other pharmaceuticals being considered for funding, the response would have to be durable and become progressively better over time. This finding was consistent with the result of other international analyses.<sup>1 2</sup>

Fundamentally, funding for the 12-month sequential regimen was not approved largely because of uncertainty of the long-term treatment benefits in relation to the very high cost and impact on hospital services. This uncertainty had implications for future treatments measured against (or added to) standard-of-care regimens that include 12-months of sequential trastuzumab in the clinical trial setting.

As of April 2007, PHARMAC has been consulting on a proposal to fund an alternative 9 week concurrent treatment course for trastuzumab.

#### Treatment regimens and available trial data

To date, adjuvant treatment of HER2+ breast cancer with trastuzumab has been investigated in three broad treatment regimens:

1. trastuzumab for 12 months following completion of chemotherapy (anthracycline +/- taxane) ('sequential treatment')
2. trastuzumab for 12 months started in combination with chemotherapy (taxane) following completion of anthracycline ('concurrent treatment post-anthracycline')
3. trastuzumab for 9-10 weeks started in combination with chemotherapy (taxane) and completed prior to anthracycline treatment ('concurrent treatment pre-anthracycline').

There have been five open-label randomised trials reporting to date outcomes for adjuvant trastuzumab against standard treatment in early stage breast cancer<sup>2</sup>—HERA<sup>3 4</sup>, NSABP B31<sup>5 6</sup>,

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<sup>1</sup> Ward S, Pilgrim H, Hind D. Trastuzumab for the Treatment of Primary Breast Cancer in HER2 Positive Women: A Single Technology Appraisal. University of Sheffield School of Health and Related Research (ScHARR), May 2006. <http://www.nice.org.uk/page.aspx?o=328487>. Update with revised cost per QALY at <http://www.nice.org.uk/page.aspx?o=328530>

<sup>2</sup> Belgian Health Care Knowledge Centre (KCE). Trastuzumab in early stage breast cancer. KCE reports vol. 34C, 2006. [http://kce.fgov.be/index\\_en.aspx?ID=0&SGREF=5211&CREF=7198](http://kce.fgov.be/index_en.aspx?ID=0&SGREF=5211&CREF=7198)

<sup>3</sup> Piccart-Gebhart M.J, Procter M, Leyland-Jones B. et al., Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer. N Engl J Med 2005;353(16):1659-1672. <http://content.nejm.org/cgi/content/full/353/16/1659>

<sup>4</sup> Smith I, Procter M, Gelber RD, Guillaume S, Feyereislova A. et al. 2 year follow up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. Lancet 2007;369:29-36. <http://www.thelancet.com/journals/lancet/article/PIIS0140673607600282/fulltext>

NCCTG N9831<sup>5 6 7</sup>, BCIRG006<sup>8</sup>, and FinHer.<sup>9</sup> The information from these trials is summarised on the bpac<sup>nz</sup> website at <http://www.bpac.org.nz/magazine/2007/april/herceptin.asp> and in Appendix Three of this TAR; the following table and figure summarises the primary efficacy results in terms of disease-free survival (DFS):

Table/Figure 1. Hazard ratios for disease recurrence by trial and regimen type and across studies

<b>Trial</b>	<b>Sequential (trastuzumab post taxane)</b> n tmt/N tmt vs. n obs/N obs, hazard ratio (95% CI)	<b>Concurrent (trastuzumab with taxane)</b> n tmt/N tmt vs. n obs/N obs, hazard ratio (95% CI)
(HERA 1 year f/up–interim result)	127/1694 vs. 220/1693, <b>HR 0.54 (0.43-0.67)</b>	
HERA 2 year median follow-up	218/1703 vs. 321/1698, <b>HR 0.64 (0.54-0.76)</b>	
<i>NSABP B31</i>		<i>83/864 vs. 171/872, <b>HR 0.45 (CI not reported; 2P=10<sup>-9</sup>)</b></i>
NCCTG N9831	103/985 vs. 117/979, <b>HR 0.87 (0.67-1.13)</b>	<i>50/808 vs. 90/807, <b>HR 0.55 (CI not reported; 2P=0.0004)</b></i>
joint analysis of N9831/B31		134/1217 vs. 261/1162, <b>HR 0.48 (0.39-0.59)</b>
BCIRG006 arm AC-TH (3 year median follow-up)		128/1074 vs. 192/1073, <b>HR 0.61 (0.48-0.76)</b>
<b>Overall post-anthracycline treatment</b>	321/2688 vs. 438/2677, <b>HR 0.70 (0.61-0.81)</b>	262/2291 vs. 453/2235, <b>HR 0.53 (0.46-0.62)</b>
FinHer (pre-anthracycline treatment)		12/115 vs. 27/116, <b>HR 0.42 (0.21-0.83)</b>
<b>Overall, all regimens</b>	595/5094 vs. 918/5028, <b>HR 0.61 (0.55-0.68)</b>	

Note: The hazard ratio for sequential treatment comprises the N9831 sequential (B) and HERA trastuzumab arms compared with respective control groups (HERA 2-year median follow-up results). The hazard ratio for concurrent treatment comprises N9831 concurrent (C), NSABP B31 trastuzumab and BCIRG006 AC-TH arms compared with respective control groups. The HR for concurrent trastuzumab is for post-anthracyclines, and hence does not include concurrent treatment given in FinHer (pre-anthracyclines).

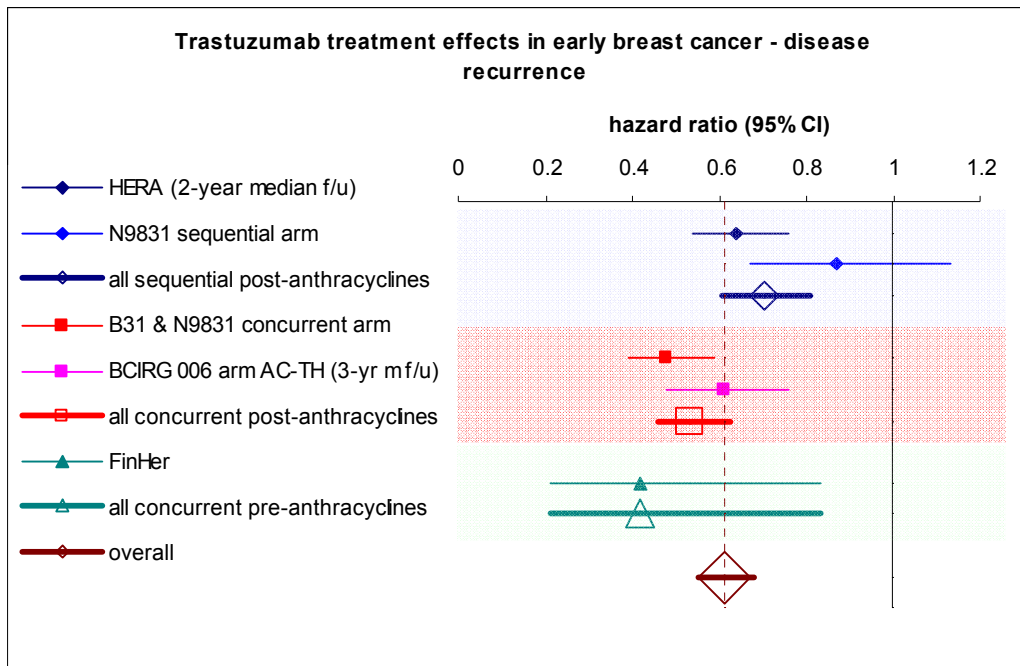
<sup>5</sup> Romond, EH, Perez EA, Bryant J. et al., Trastuzumab plus Adjuvant Chemotherapy for Operable HER-2 positive breast cancer. N Engl J Med 2005;353(16):1659-1672. <http://content.nejm.org/cgi/content/full/353/16/1673>

<sup>6</sup> Supplemental Figure 1 in the on-line Supplementary Appendix to Romond et al NEJM 2005, available at <http://content.nejm.org/cgi/content/full/353/16/1673/DC1>.

<sup>7</sup> Perez EA. Further Analysis of NCCTG-N9831. Slide presentation ASCO annual meeting 2005, available online at [http://www.asco.org/ac/1.1003\\_12-002511-00\\_18-0034-00\\_19-005815-00\\_21-001.00.asp](http://www.asco.org/ac/1.1003_12-002511-00_18-0034-00_19-005815-00_21-001.00.asp)

<sup>8</sup> Slamon D, Eiermann W, Robert N, Pienkowski T, Martin M, et al, on behalf of the BCIRG 006 Investigators. Phase III Trial Comparing AC-T with AC-TH and with TCH in the Adjuvant Treatment of HER2 positive Early Breast Cancer Patients: Second Interim Efficacy Analysis. Slide presentation ASCO annual meeting 2006, available online at <http://www.bcirg.org/NR/rdonlyres/eqkdodg2dy7t557o7s6uvj7ytpe6gcf5gmh2elv6hnhh5pjlaz3nd6jddlnao7qoikej3edohsijvii sfvp367uuc/BCIRG006+2nd+Interim+Analysis.pdf>

<sup>9</sup> Joensuu H, Kellokumpu-Lehtinen PL, Bono P, Alanko T, Kataja V, et al; FinHer Study Investigators. Adjuvant docetaxel or vinorelbine with or without trastuzumab for breast cancer. N Engl J Med. 2006;354(8):809-20. <http://content.nejm.org/cgi/content/full/354/8/809>



Altogether, these results indicate that trastuzumab does confer improved disease free survival compared with standard chemotherapy. However, the results for the N9831 sequential arm raise questions about the place of 12-months sequential therapy as the standard of care, because the trials with concurrent therapy (trastuzumab in combination with a taxane) consistently report better results in terms of DFS. Interestingly, the results of the FinHer trial appear to be comparable those of the longer treatment regimens (see Appendix Six of this TAR).

In conclusion, the information available to date from the clinical trials considering the use of trastuzumab for early breast cancer indicates that the optimal treatment schedule and duration of treatment for trastuzumab has not yet been determined.

### 12-month sequential treatment is no longer a funding option

The 12 month sequential regimen was not approved by both the PHARMAC and DHB Boards in July 2006 for reasons relating to the uncertainty surrounding long term clinical benefits and risks, the high budgetary impact, and the associated high cost-effectiveness ratio (i.e. the proposal is relatively poor value for money). PHARMAC's indicative cost-utility analysis for 12 months trastuzumab suggested relatively poor quality adjusted survival benefits and nominal savings to DHBs, at \$70-80,000/QALY base case. This analysis showed a large range of plausible outcomes, largely due to the uncertainty surrounding duration of benefit and untreated disease progression. However, none of the plausible outcomes gave sufficient confidence that 12 months of Herceptin treatment would be a cost-effective use of health funds compared with other investments.

Since the time of the decision not to fund, no new information has become available to suggest the 12 month sequential regimen is a viable option. The 12 month sequential regimen does not provide the level of health benefits that PHARMAC would expect to get from spending the \$25 million per annum compared with other investment options.<sup>2 10</sup>

The already significant questions over the extent that sequential treatment prevents recurrence have increased since that time. In particular the disease free survival gain in the HERA trial at 2 years' median follow-up was less than that reported at the 12 month interim follow-up (the HERA DFS 12-month median follow-up hazard ratio was 0.54 (95% CI 0.43-0.67)<sup>3</sup>; 2-year median f/u HR 0.64 (0.54-0.76)<sup>4</sup>)—leading to doubt around the durability of efficacy<sup>11</sup> (see Appendix Six). As well, there are

<sup>10</sup> Ward S, Pilgrim H, Hind D. Trastuzumab for the Treatment of Primary Breast Cancer in HER2 Positive Women: A Single Technology Appraisal. University of Sheffield School of Health and Related Research (ScHARR), May 2006.

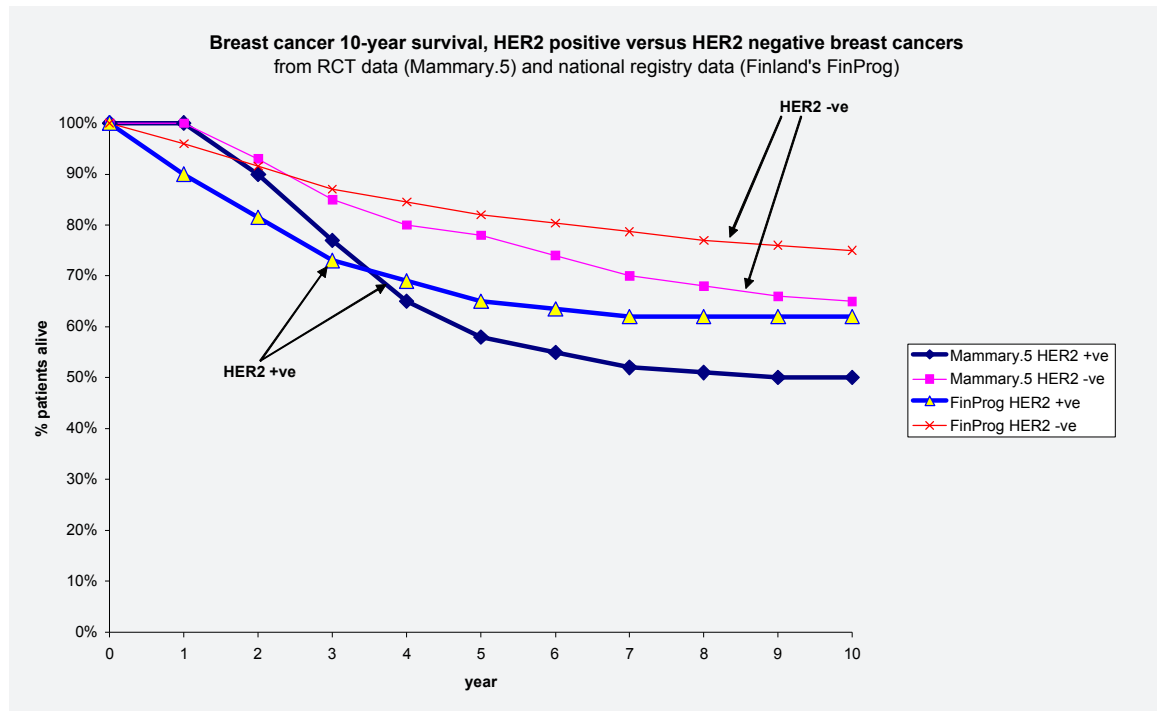
<http://www.nice.org.uk/page.aspx?o=328487>

<sup>11</sup> Hind D, Pilgrim H, Ward S. Questions about adjuvant trastuzumab still remain. *Lancet* 2007; 369:3-5.

<http://www.thelancet.com/journals/lancet/article/PIIS014067360760004X/fulltext>

concerns raised by the unpublished results of the unplanned interim analysis of the sequential treatment arm of the N9831 trial<sup>7</sup>, which indicated no statistically significant benefit for sequential trastuzumab over standard chemotherapy <sup>7</sup> (also Appendix Six).

In addition, other questions over the long-term impact of demonstrable cardiac toxicity still remain (also Appendix Six). The impact of long-term cardiac effects should not be disregarded when it is likely that 70% or more of women with HER2-positive breast cancer will still be alive the end of 10 years with standard chemotherapy regimens without trastuzumab. (According to historical registry data from Finland (FinProg [1]), and a large RCT comparing two regimens of conventional chemotherapy (Mammary.5, NEJM 2006 [2]), around 50-60% of patients with HER2 positive breast cancer still alive by 10 years (see graph).

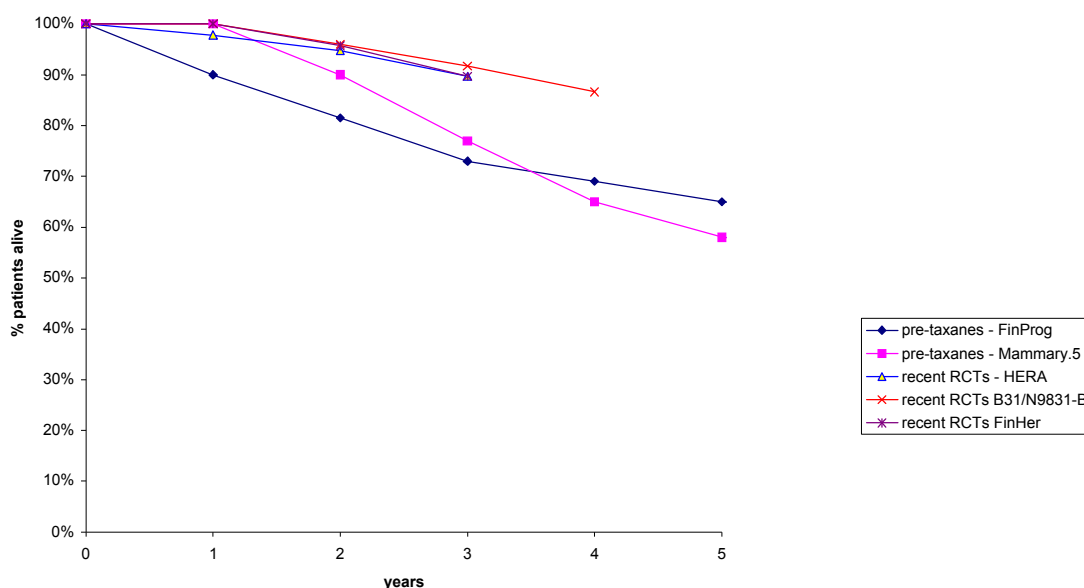


[1] FinProg data (<http://www.finprog.org/>)—HER2-positive vs. HER-2 negative

[2] Pritchard KI, Shepherd LE, O'Malley FP, Andrulis IL, Tu D, Bramwell VH, Levine MN; National Cancer Institute of Canada Clinical Trials Group. HER2 and responsiveness of breast cancer to adjuvant chemotherapy. N Engl J Med. 2006 May 18;354(20):2103-11. <http://content.nejm.org/cgi/content/full/354/20/2103> from Figure 1. Relapse-free Survival (Panel A) and Overall Survival (Panel B) among Women with Breast Cancer, According to HER2 Amplification Status on FISH.

Both sets of data pre-date the use of taxanes, and survival rates nowadays are likely to be appreciably better, as evidenced by survival in the standard treatment arms of more recent RCTs (e.g. HERA, B31/N9831-C, FinHer—see graph).

HER2 +ve breast cancer survival, pre-taxane vs recent RCTs



Combining these HER2-specific patterns [3] with New Zealand overall breast cancer survival figures for women aged 45-54 [4] suggests HER2-positive breast cancer has a 71% 5-year survival.)

[3] HER2 status-specific 1,3,5,8,10-year survival rates from Finland registry data (FinProg)

[4] calculated NZ cancer data 1994-2004 82% 5-year survival for all breast cancers in women 45-54 years (personal communication Martin Tobias, Public Health Intelligence, Ministry of Health)

### Proposed 9-week concurrent regimen

PHARMAC is currently consulting on a proposal to subsidise trastuzumab for HER 2+ early breast cancer when administered for 9 weeks concurrent with taxane chemotherapy. Because in the FinHer regimen docetaxel was the taxane of choice, PHARMAC also proposes to subsidise docetaxel for early breast cancer when given concurrently with trastuzumab; paclitaxel is already funded for node positive early breast cancer. Further details can be found in PHARMAC's consultation document at <http://www.pharmac.govt.nz/herceptin.asp>.

A comparison of the eligible patient population and the dosing schedules for 12 months sequential and 9 weeks concurrent regimens is included as Appendix Four.

The 9 week concurrent regimen is considered to be clinically and cost effective in terms of improving DFS, and affordable for DHBs in terms of drug and resource costs. Both the PTAC and the PTAC's Cancer Treatments subcommittee (CaTSOP) have indicated that 9 weeks is a viable option and have recommended it be funded with a high priority. (It should be noted that CaTSOP's high priority recommendation for 9 weeks treatment was made in the absence of availability of funding for 12 months treatment, and the subcommittee wished to emphasise that its recommendation was strongly based on financial considerations<sup>12</sup>).

Advantages with the 9 week concurrent regimen are:

1. the 9 week concurrent regimen as examined by the FinHer trial appears to give disease-free results comparable to longer duration treatments [The efficacy results of the FinHer trial suggest that concomitant administration of trastuzumab with docetaxel is effective in the treatment of HER2-positive early breast cancer. In the FinHer study trastuzumab was administered weekly

<sup>12</sup> CaTSOP recommended that, in the absence of availability of funding for 12 months treatment, 9 weeks treatment would be reasonable and gave this recommendation a high priority. The subcommittee did however wish to emphasise that this recommendation was strongly based on financial considerations, since the subcommittee had more confidence in the 12 month treatment results.

concomitantly either with 3-weekly docetaxel or weekly vinorelbine, followed by 3 cycles of FEC in each arm. Docetaxel improved recurrence-free survival as compared to vinorelbine (hazard ratio 0.58, 95% CI 0.40 to 0.85), and trastuzumab improved recurrence-free survival as compared to the same chemotherapy administered without trastuzumab (hazard ratio 0.42, 95% CI 0.21 to 0.83).];

2. the shorter timeframe and fewer infusions would be more convenient for patients and for DHBs to deliver, without severely impact on existing services for other patients;
3. one fifth more patients would be able to be treated by the 9 week concurrent regimen—because patients are not exposed to anthracycline chemotherapy beforehand (anthracyclines being severely cardiotoxic, and hence sequential trastuzumab will be contraindicated for perhaps 18% of patients<sup>13</sup>);
4. the 9 week concurrent regimen may be less cardiotoxic than long duration regimens, although this requires further data<sup>14</sup>; and
5. PHARMAC's cost-effectiveness analysis indicates that the result for the 9 week regimen is, under conservative assumptions, less than \$20,000/QALY. At this level the 9-week regimen would be as, or more, cost-effective than other proposals for funding. Further, the 9 week treatment regimen is likely to be four times more cost-effective than the 12 months sequential regimen (50 QALYs per million spent for 9 weeks, 12.5 QALYs per million spent for 12 months).

### **The PTAC's view**

The PTAC had recommended 12 month treatment be declined, due to the uncertainty surrounding long term clinical benefits and risks, the uncertainty over optimal duration of treatment, and the high budgetary impact associated with treatment.

The PTAC subsequently considered the information on short term trastuzumab treatment from the FinHer and E2198<sup>15</sup> trials suggested that comparable health gains, and possibly less cardiac toxicity, could be achieved with a shorter trastuzumab treatment regimen. The Committee considered that the FinHer results cast doubt over the optimal duration/timing; numbers of patients treated were not insignificant and the data were valuable; and there were comparable health gains to the HERA results but less cardiotoxicity.

The PTAC has since reiterated that there is still uncertainty about the best way to administer trastuzumab in terms of optimal treatment duration, dose and schedule (sequential to, or concurrent with, chemotherapy, before or after anthracyclines), minimising cardiovascular toxicity; and long-term clinical outcomes. The Committee's November 2006 recommendation still stands, that 9 weeks treatment with trastuzumab (concurrent with chemotherapy and before anthracycline) should be funded with a high priority.

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<sup>13</sup> More patients would be eligible for trastuzumab under the FinHer regimen than the 12 month HERA sequential regimen or Romond (B31, N9831 arm C) concurrent regimen, because patients receive their cardiotoxic chemotherapy (anthracycline) after trastuzumab in the 9 week regimen, therefore, more patients would be expected to meet the cardiac inclusion criteria required for trastuzumab treatment. Using the methods and base assumptions used in the KCE 2006 report (pages 51, 72), applying excess rates of LVEF decline (sourced from Romond 2005, etc.—see KCE 2006) to age-specific New Zealand HER2+ve breast cancer registration data (Cancer Register breast cancer registrations August 2001-December 2005, obtained from NZHIS) means potentially 18% more patients would be able to receive trastuzumab treatment with the 9 week concurrent regimen as per FinHer compared with 12 month sequential or concurrent treatment regimens.

<sup>14</sup> The low cardiotoxicity observed in FinHer could also be explained by the relatively low cumulative total dose of 180 mg/m<sup>2</sup> epirubicin while the maximum tolerated cumulative dose of epirubicin is around 720mg/m<sup>2</sup>. In the B31/N9831 studies doxorubicin was administered at a cumulative dose of 240 mg/m<sup>2</sup> while its maximum tolerated cumulative dose is only 500 mg/m<sup>2</sup>. Epirubicin is generally presented as a less cardiotoxic agent compared with doxorubicin. The KCE report states that in terms of cardiotoxicity that no conclusions however can be drawn on the relative importance of the trastuzumab anthracycline treatment order, on the duration of trastuzumab administration, nor on the type of anthracycline and its dose. Multiple variables differ between the pre- and post-anthracycline regimens studied.

<sup>15</sup> Sledge GW, O'Niell A, Thor AD, Kahanic SP, Zander SP, Davidson NE. Adjuvant trastuzuman: long term results of E2198. Poster presentation 2075, SABCs 2006 [http://www.abstracts2view.com/sabcs06/view.php?nu=SABCs06L\\_561](http://www.abstracts2view.com/sabcs06/view.php?nu=SABCs06L_561)

The PTAC has also considered that more clinical research is needed to determine if long duration concurrent treatment (12 months) is any better than short duration concurrent treatment (9 weeks), and has recommended that a comparative study should be performed.

Full minutes of relevant discussion at the PTAC February, May, August and November 2006 and February 2007 meetings are attached (Appendix One).

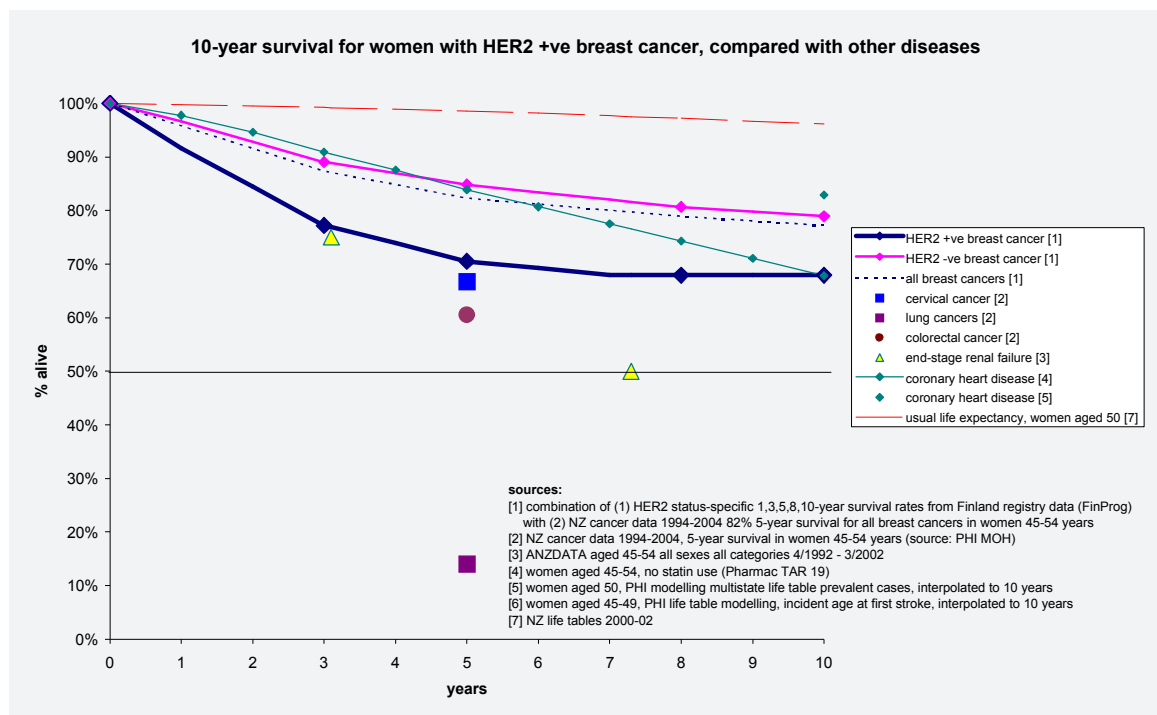
### DHBs' views and PHARMAC's role

DHBs support the funding of the 9 week option, and have stated the \$5m-\$6m per annum overall cost (which includes drug cost and administration costs) of providing this regimen to be viable. A comparison of the 12 months sequential and the 9 weeks concurrent trastuzumab regimens, in terms of both opportunity cost (costs of trastuzumab and impacts on DHB services related to administration) and cost-effectiveness, is included in Appendix Four.

PHARMAC's role is to allocate taxpayer funds efficiently and ensure pharmaceuticals are assessed comparably to result in fair decisions. Cost-effectiveness and budgetary impact (determining the relative value for money of a proposal in order to maximise health gains from the budget available) are two of PHARMAC's nine decision criteria (see <http://www.pharmac.govt.nz/pdf/opps.pdf>).

Hence, the way that PHARMAC is considering the 9-week option for trastuzumab is no different to any other targeting means that PHARMAC uses to get the best health gains for a given medicine and ensure that other patient groups are not denied other treatments.

Health need, the availability of other treatments and the Government's priorities for health funding (which includes cancer) are also included in PHARMAC's decision criteria. With regards to these criteria, HER2 positive breast cancer is an area of high need, but there are other areas of high need that also need to be considered when assessing investment choices. (Combining historical HER2-specific survival patterns with New Zealand overall breast cancer survival figures for women aged 45-54 suggests HER2-positive breast cancer has a 71% 5-year survival [1]. This compares with, for example, a 14% 5-year survival rate for lung cancer, 61% for colorectal cancer and 67% for cervical cancer for women aged 50 [2], and 65% for end-stage renal failure (both sexes) [3] (see graph).



[1] combination of (1) HER2 status-specific 1,3,5,8,10-year survival rates from Finland registry data (FinProg) with (2) calculated NZ cancer data 1994-2004 82% 5-year survival for all breast cancers in women 45-54 years (personal communication Martin Tobias, Public Health Intelligence, Ministry of Health)

[2] NZ cancer data 1994-2004, 5-year survival in women 45-54 years (personal communication Martin Tobias, Public Health Intelligence, Ministry of Health)

[3] ANZDATA aged 45-54 all sexes all categories 4/1992-3/2002. ANZDATA 25th Annual Report Chapter 14 Integrated survival. <http://www.anzdata.org.au/anzdata/AnzdataReport/25thReport/files/Ch.14%20%20Integrated%20survival>

Numerically, non-disseminated HER2-positive breast cancer affects some 385 new patients each year (all ages), being women with a median age of 50 years [4]. This compares with around 700 new women patients with lung cancer (median age ~66 years), 1240 with colorectal cancer (median age ~70) and 180 with cervical cancer (median age 42) [5]. 436 new patients were accepted for renal replacement therapy in New Zealand during 2005 (both sexes) [6].

[4] HER2-positive breast cancer registration data for the calendar year 2005, derived from PHARMAC analysis of NZ Cancer Register breast cancer registrations August 2001-December 2005, data supplied to PHARMAC by NZHIS.

<http://www.nzhis.govt.nz/stats/tables/cancer2002.xls>

[5] cancer registrations for the calendar year 2002 in women all ages for C34 bronchus and lung (n = 687), C18-20 colorectal (1241) and C53 cervix (70). Table 5a of statistical tables at <http://www.nzhis.govt.nz/stats/tables/cancer2002.xls> which accompany NZHIS. Cancer: New Registrations and Deaths 2002 at <http://www.nzhis.govt.nz/publications/cancer.html>. Median ages calculated using 5-year age-band numbers of registrations

[6] ANZDATA 29th Annual Report 2006 Report - Data to 2005. Chapter 2 New patients

<http://www.anzdata.org.au/anzdata/AnzdataReport/29thReport/Ch02NewPatients.pdf>

In summary, DHBS and PHARMAC are seeking a practical and workable solution to enable cost-effective access to an effective trastuzumab treatment.

### Trastuzumab around the world

A number of other countries have approved funding for trastuzumab, using a 12-month treatment regimen. It should be noted that in some of these countries, assessment of the medicine is limited to how a supplier wishes for it to be used. Trastuzumab treatment regimens vary throughout the world. In the United States, trastuzumab is approved for use in combination with taxane chemotherapy.<sup>16</sup> In Europe, however, it can only be used as sequential treatment. In Australia, clinicians have a number of options for using trastuzumab including long and short duration, and using it concurrently with, or sequentially to, taxane chemotherapy.<sup>17</sup>

Funding for cancer treatments in New Zealand takes place within a budget (in this case the budget of DHBS), so choices have to be made about how to allocate spending most efficiently.<sup>18</sup> Most other countries, including the United Kingdom (UK) and Australia, do not have such direct budgetary constraints.

In the UK, the National Institute for Health and Clinical Excellence (NICE) makes its recommendations independent of budgetary considerations. However, debate in the UK is now suggesting that approving funding for trastuzumab will force the National Health Service to cut the funding from other health services, underlining the need to make careful choices.<sup>19</sup>

The PTAC's and PHARMAC's view on trastuzumab for early breast cancer has differed from those of clinical committees in other countries. There has been a strong emphasis by The PTAC and PHARMAC on the uncertainty in current clinical evidence and potential future outcomes given the cost. The PTAC also took into account both 12 month trastuzumab's poor cost effectiveness compared to other funded drugs or drugs awaiting funding, and the practical implications for health services of administering this medicine under a 12 month regimen.

This is not the first time NZ has chosen a different path to other countries, for instance PHARMAC declined to fund COX-2 inhibitors in 2004 because of concerns over both safety and cost—a stance vindicated with time.<sup>20</sup>

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<sup>16</sup> US datasheet: Initial US Approval: September 1998, Revision Date: November 2006.

<http://www.gene.com/gene/products/information/oncology/herceptin/insert.jsp>

<sup>17</sup> Australian datasheet: HERCEPTIN® PRODUCT INFORMATION, dated 21 April 2006.

<http://www.pbs.gov.au/html/healthpro/search/results?term=herceptin&publication=&form-type=simple>

<sup>18</sup> Brougham M, Metcalfe S, McNeen W. Our Advice? Get a budget! HealthCare Papers 2002;3:83-6.

<http://www.longwoods.com/hp/3-1DrugPolicy/HP31DrugPolicy.pdf>

<sup>19</sup> Barrett A, Roques T, Small M, Smith RD. How much will Herceptin really cost? BMJ. 2006 Nov 25;333(7578):1118-20.

<http://www.bmj.com/cgi/content/full/333/7578/1118>

<sup>20</sup> Grocott R, Metcalfe S. Going against the flow: the impact of PHARMAC not funding COX-2 inhibitors for chronic arthritis. N Z Med J. 2005 Oct 7;118(1223):U1690. <http://www.nzma.org.nz/journal/118-1223/1690/>