

**Part (Item 20) of the Record of the
Pharmacology and Therapeutics Advisory Committee Meeting
held on 16 & 17 August 2006**

20 Herceptin new data

PTAC has twice considered trastuzumab for the treatment of early HER-2 positive breast cancer at its meetings of February and May 2006. These minutes should be read in conjunction with the February and May 2006 minutes found at <http://www.pharmac.govt.nz/pdf/ptacmins.pdf>

20.1 The Committee reviewed further information in support of a submission from Roche Pharmaceuticals for the listing of trastuzumab (Herceptin) on the Pharmaceutical Schedule for the treatment of early HER-2 positive breast cancer.

20.2 The Committee reviewed the following material:

- Roche Pharmaceuticals' response to previous PTAC and CaTSoP minutes regarding trastuzumab;
- A technology appraisal from the University of Sheffield School of Health and Related Research (SchHARR) commissioned by the National Institute of Clinical Excellence (NICE);
- Two year median follow-up of the one year treatment arm of the HERA trial in the format of a PowerPoint slide presentation from the American Society of Clinical Oncology (ASCO) 2006 conference;
- "Adjuvant Docetaxel or Vinorelbine with or without trastuzumab for Breast Cancer", *Heikki Joensuu et al.* (N Engl J Med 354;8, February 23 2006), the "FinHer study".

Correspondence from Roche Pharmaceuticals

20.3 The Committee noted Roche New Zealand's willingness to assist PHARMAC in the provision of evidence to support the use of trastuzumab.

20.4 The Committee expressed disappointment that additional trial data is unlikely to be available in a peer reviewed, published format in the near future.

SchHARR report

20.5 The Committee noted that the SchHARR report was very comprehensive and raised similar concerns regarding the costs and benefits of trastuzumab that had been highlighted in PHARMAC's own cost utility analysis and previous PTAC minutes.

20.6 Members noted that the final recommendation of the SchHARR report did not appear to correlate to specific findings of the report.

ASCO 2006 slide presentation for the HERA study

20.7 The Committee noted the limitations of clinical data presented as a PowerPoint slide presentation, which have not been subjected to external peer review for a reputable scientific journal. The Committee reiterated its view that it does not consider slide

presentations alone to be adequate for the purpose of making important clinical recommendations.

- 20.8 The Committee noted that after a median follow-up of one year, as presented in Piccart-Gebhart et al (N Engl J Med. 2005 Oct 20; 353(16): 1659-72.), there was a reported absolute increase in two-year disease-free survival of 8.4% in the trastuzumab arm compared with control. The Committee noted that the slides indicated that after a median follow-up of two years the absolute increase in disease-free survival at three years in the trastuzumab arm compared with control had been reduced to 6.3%.
- 20.9 The Committee noted that the slides indicated that after two years follow-up the absolute overall survival difference at three years from randomisation, as displayed, was 2.7% in the trastuzumab arm against control, and appeared to be statistically significant. Members noted that this translated into a number needed to treat (NNT) of 37 patients.
- 20.10 The Committee considered that in an adjuvant setting an ongoing treatment effect would be expected with efficacy differences becoming greater over time. The Committee considered, however, that the difference in the HERA treatment groups would have been anticipated to continue to diverge, rather than converge, which appears to be the case from the slide data presented. The Committee noted that 861 patients in the non-trastuzumab arm switched to trastuzumab after 12 months. Members noted that some of the convergence seen may have been due to the loss of patients from the observation arm, although there was insufficient data presented in the slides to clarify this.
- 20.11 Members noted that switching of patients from the observation arm to trastuzumab treatment meant that the validity of the long-term efficacy and safety profile of trastuzumab from the HERA trial may be significantly compromised. Members noted that although half of the patients in the observation arm who had not switched over by two years would be able to be measured in subsequent years, they would no longer necessarily be representative of all patients randomised to the observation arm. Members noted that this inconsistency would only be rectified by maintaining intention-to-treat analysis of the efficacy of trastuzumab beyond the one year.
- 20.12 The Committee noted that in data presented as 'censored', (data that excluded patients who had switched from control to trastuzumab), the denominators were not small enough to account for removal of all switched patients. The Committee concluded that this apparent inconsistency would likely be addressed in a formal peer-reviewed publication of this data and highlighted the difficulties of evaluating clinical data from a slide presentation.

The FinHer study

- 20.13 The Committee considered that the FinHer study cast doubt over the optimal duration and timing of trastuzumab treatment. The Committee noted that the cost utility of trastuzumab use as per the FinHer protocol (9 weeks treatment) was likely to be appreciably better than 12 months treatment.
- 20.14 The Committee considered that the number of patients treated in the FinHer study (232) was substantial compared to many other cancer treatment trials.
- 20.15 The Committee noted that although HERA was a far larger trial, the number of patients treated in FinHer was not insignificant, and therefore the data from FinHer was valuable.
- 20.16 The Committee considered that the trastuzumab regimen used in the FinHer study resulted in comparable health gains to the regimen used in the HERA trial (11.7%

absolute reduction in disease recurrence at three years against no trastuzumab), but produced less cardiotoxicity and other side effects, and was associated with a significantly reduced pharmaceutical and service cost.

20.17 The Committee considered that funding of trastuzumab as per the FinHer protocol (9 weeks treatment) could be considered.

Recommendations

20.18 The Committee recommended that the application for the funding of trastuzumab as per the HERA protocol (12 months 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.

20.19 The decision criteria relevant to PTAC's recommendation were: (i) The clinical benefits and risks of pharmaceuticals; (v) the cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services; (vi) The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget).

20.20 The Committee **recommended** that the application be referred back to the Cancer Treatment Subcommittee of PTAC to consider the clinical appropriateness of any funding regimen consistent with the FinHer protocol (9 weeks treatment).