

PHARMAC

Pharmaceutical Management Agency

Media Statement – Friday 16 February 2007

All comments can be attributed to Matthew Brougham, Acting Chief Executive

HERCEPTIN: SIGNIFICANT DOUBTS REMAIN OVER 12-MONTH TREATMENT

Not all evidence related to Herceptin has been published and New Zealanders need to be aware of that.

There are two large studies on the efficacy of 12 months sequential treatment – one of these studies shows benefit (HERA), the other one does not (N9831).

Both trials were published, but the sequential arm of the N9831 trial was missing – this arm showed Herceptin to have no significant benefits over chemotherapy alone. PHARMAC has seen the conference presentation related to this arm, but Roche has told PHARMAC it is unable to supply the full data. For the amount of money involved, and Roche's interest in the company holding the data, PHARMAC finds this unacceptable.

N9831 also shows that "sequential treatment" (taken after chemotherapy, as promoted by Roche) is significantly less effective than "concurrent treatment" (taken with chemotherapy, as is done for other cancer-related treatments). Concurrent versus sequential treatment is a fundamental issue most public commentators are ignoring.

Another study (E2198) – comparing a short-term treatment with a long-term treatment – casts doubt over whether the longer term treatment is any better.

Longer term treatment regimens treat fewer women, and may expose those treated to prolonged treatment effects, including risks of toxicity – all this when there may be no additional treatment benefit.

Overall, it is far from clear that long-term treatment is any better than short-term treatment. Given the level of public interest, it is critical the full evidence picture is better understood.

Drug companies have commercial interests and these are not always aligned with what is genuinely best for patients. Whether Roche or any other drug supplier, PHARMAC needs to ask the hard questions to ensure the best possible decision is made – not doing so risks making decisions that compromise peoples' health, for example:

- data for use of paroxetine by children was not initially publicised despite widespread use; once investigated, the data showed no benefit for use by children and significant risks, including links to suicide risk and self-harm; and

- other countries (except New Zealand on PHARMAC's judgment) ran to embrace Cox-2 inhibitors, only to find that evidence had been selectively reported and so the risks probably outweighed the benefits for most people (leading to product withdrawal). In this instance, PHARMAC's rigorous approach (and that of its clinical advisory committee) avoided these risks in New Zealand.

PHARMAC is not suggesting these sorts of risks necessarily apply with Herceptin (although like other drugs there are risks, such as the increased toxicity risk of longer term treatment); the general point is that *all* data needs to be rigorously considered (not just data cherry-picking).

As much as commercial interests behind Herceptin may like it used for an extended period (like hormonal therapy for example), PHARMAC – on behalf of New Zealanders – needs to be sure long-term treatment is justified and current evidence suggests it is not.

Reasons for international momentum around 12 months include:

- there has been widespread hype around Herceptin as a “wonder drug” with associated raising of public expectations and pressures on funding bodies worldwide;
- some countries, given Roche's registered indication, were not able to consider shorter term or concurrent therapy options (i.e. Roche decided to only seek regulatory approval and funding for extended sequential treatment in many countries); and
- other countries may not have considered the 9-week evidence as carefully as PHARMAC (or were not able to), particularly with respect to concurrent versus sequential treatment.

Debate in other countries is now further exploring the wisdom of 12-months funding, including the significant foregone opportunities to use resources in other health areas – areas where health gains may be greater and more certain.

New Zealand must make up its own mind, as we have done for other difficult and contentious decisions, including being different from international peers. A rigorous approach needs to be taken (including advice from PHARMAC's clinical advisory committees), not simply deference to overseas decisions or Roche's commercial interest.

The uncertainty around the best treatment length of Herceptin led PHARMAC to support an international trial announced today. Support for the trial is a separate issue to whether funding will be made available for Herceptin in New Zealand and, separate again, to whether New Zealand women choose to participate in the trial.

PHARMAC has not made a decision on a funding option and wants to ensure all options are carefully considered, particularly 9 weeks given what the full evidence shows. PHARMAC is open minded on whether 12 months is ultimately shown to be the best option – the point is, current evidence does not support this.

Contact Simon England, Communications Manager, 021 863 342

ENDS (Background follows)

Background

General

- PHARMAC was not invited to the Thursday meeting of oncologists (appropriately in our view to allow for scientific debate, but it was incorrectly made out PHARMAC was there and trying to influence oncologists)
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Evidence slides

Attached are slides that show:

- Slide 1 – short duration concurrent treatment is effective at preventing recurrence of disease
 - Slide 2 (N9831) – sequential treatment with Herceptin (like HERA) did not show any significant benefit over no treatment with Herceptin
 - Slide 3 (N9831) – concurrent treatment showed significantly better efficacy than sequential treatment – this casts doubt on the superiority of the sequential treatment regimen promoted by Roche
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Evidence around commercial versus public interest

Publication bias is where studies with significant results are more likely to get published than studies without significant results. Failing to publish information can lead to harmful health effects, or the wrong decisions being made. Examples include:

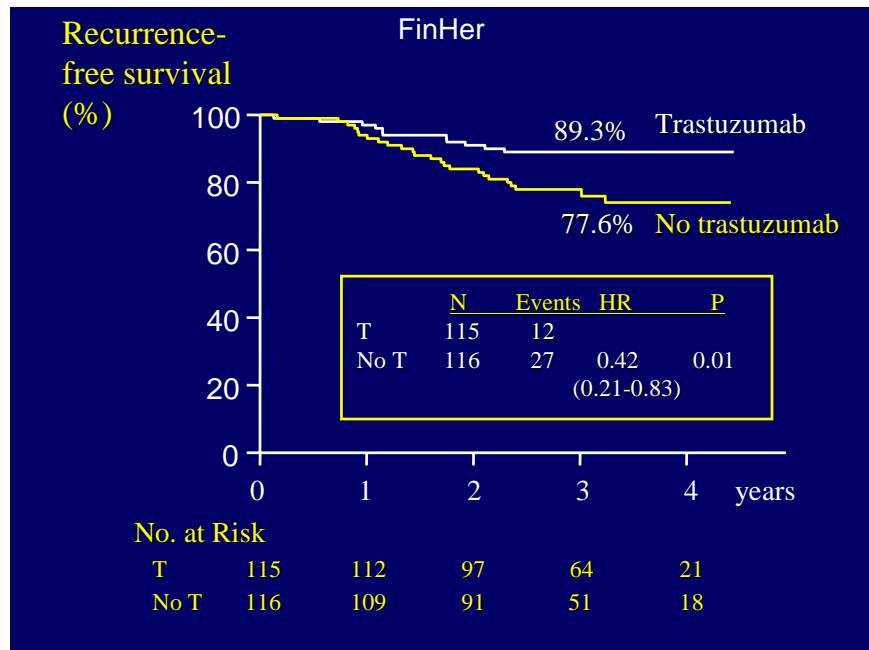
- with respect to paroxetine – EBMH 2004 <http://ebmh.bmj.com/cgi/content/full/7/4/98>; and
 - with respect to COX-2 inhibitors – (BMJ 2005 <http://www.bmj.com/cgi/content/full/330/7504/1342>).
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Full references supporting evidence in the media release

- Slide 1 – 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 Feb 23;354(8):809-20. <http://content.nejm.org/cgi/content/full/354/8/809>.
- Slide 2– 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.
- Slide 3 – 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.
- E2198 – Sledge, G.W., O’Niell, A., Thor, A.D., Kahanic, S.P., Zander, S.P., Davidson, N.E. Adjuvant trastuzuman: long term results of E2198. Poster presentation 2075, SABCS 2006 http://www.abstracts2view.com/sabcs06/view.php?nu=SABCS06L_561.

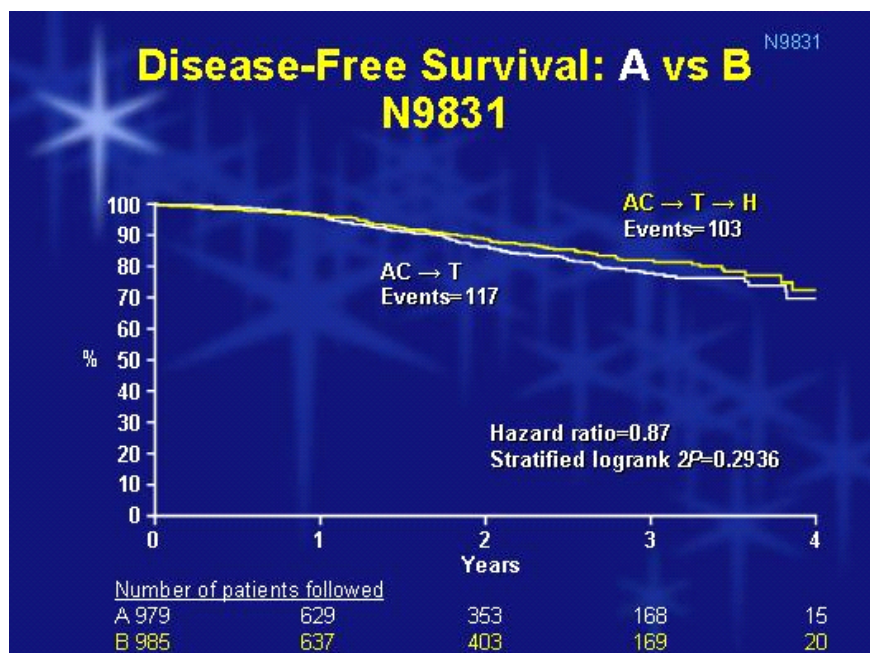
EVIDENCE SLIDES

Slide 1 – shows short duration concurrent treatment is effective at preventing recurrence of disease



Slide 2 (N9831) – sequential treatment with Herceptin (like HERA) did not show any significant benefit over no treatment with Herceptin

A = Observation; B = Sequential and C = Concurrent
(nb. Disease free survival = recurrence free survival (used above))



Slide 3 (N9831) – concurrent treatment showed significantly better efficacy than sequential treatment – this casts doubt on the superiority of the sequential treatment regimen promoted by Roche

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