

Herceptin

Keeping Faith With Clinical Trial Participants


WORDS BY RICHARD ISAACS AND FRAN BOYLE

THE RECENT DECISION BY PHARMAC NOT TO FUND

12 months of adjuvant Herceptin for women with Her2 positive breast cancer calls into question our carefully crafted approach to ethical clinical trials research into cancer. Since that decision there has also been much discussion in the media about the rationale for 12 months of therapy and challenging this duration as the standard of care internationally. Large clinical trials and combined analyses have become the usual standard for new treatments to enter a clinical trial for common cancers. These trials receive extensive scrutiny from ethical and scientific perspectives before they begin and during their course, and the best studies are run by academic research groups that provide a further objective distance from the pharmaceutical industry. Well designed trials are expensive to run, and add significantly to the cost of bringing new medicines to market. But they give us the greatest confidence that the results are sound. It is the opinion of the research community that the large adjuvant Herceptin trials, including 12 months of therapy, fulfil these criteria of excellence.

The much smaller FINHER study, which used nine weeks of Herceptin, is also of interest, but due to its small size should be regarded as a reason to proceed to a definitive study, and not as immediate proof of equal effectiveness with the 12 month studies. Confidence in trial results: The 12 month trials included >11,000 patients, while the nine week FinHer trial, on which PHARMAC base their funding, had only 232 patients. This gives much greater certainty with results from the 12 month trials. Clear evidence of lives saved by therapy: The 12 month trials now all show an overall survival benefit - less women will die from this form of breast cancer when treated in this way. The risk of dying following 12 months therapy is reduced by about 1/3. In New Zealand the current data indicates we would save

the lives of 12 women after only three years and the cumulative number of lives saved will continue to increase with time. It takes time and study size to show these benefits, which the nine week trial is too small to confidently show.

Cardiac safety has been highlighted as a concern. Indeed, up to four out of 100 women developed reversible heart failure related to Herceptin in the 12 month trials compared to none in the nine week study. However, this is likely to be another result of trial size - since nine week funding was introduced heart failure has also occurred with that regimen, indicating we can not have faith in its absolute safety. Treatment cost has been another major area of discussion, although PHARMAC stated their decision was based on the science not the cost. All countries will need to make decisions on health care costs based on setting thresholds for both cost effectiveness (the extra cost of saving each life) and total cost (the total number of people who might need treatment) and competing health priorities. Transparency of the decision-making process will allow resources to be allocated in ways that increase public trust. What is vital is to keep separate the debates about the quality of the science and its ethical constraints from decisions about how much a nation wants to spend. Confusing the two is of no benefit to the public, to women with breast cancer and to the volunteers, both patients and clinicians, who have laboured to bring this knowledge to light. 

Richard Isaacs is Chair, Breast Cancer Special Interest Group of the NZ Association of Cancer Specialists; and is a Medical Oncologist member of the ANZ Breast Cancer Trials Group.

Fran Boyle is an Associate Professor of Medical Oncology at the University of Sydney and Chair of the Scientific Advisory Committee of the ANZ Breast Cancer Trials Group.