

Cancer Risk Reflections

HRT AND RECENT STUDY RESULTS

The Women's Health Initiative (WHI) study results on Prempro use have been reported as conclusively showing that hormone replacement therapy increases breast cancer risk and does not reduce cardiovascular risk. This interpretation is out of proportion to the study's findings and does not hold up under careful scrutiny. Unfortunately, important aspects about actual risks of breast cancer and cardiovascular disease to women who use Prempro and other types of hormone replacement therapy are being strangely overlooked.

First, the WHI study found *no* statistically significant increase in breast cancer risk to women who took Prempro. This reassuring news has been neglected. It should be emphasized that the actual annual difference in risk between women who did and did not take Prempro was exceedingly small – 8 in 10,000 women, which is 0.08% or *eight hundredths of one per cent*.

Even this very small difference in breast cancer risk may *not* be due to Prempro use. Breast cancers take an average of eight years to reach a little less than half an inch in size, and in older women grow more slowly. In the WHI study, the average follow-up was only 5.2 years. Therefore, most or all of the breast cancers detected during the study were present in an undetectable state *before* the study began.

Furthermore, the annual differences in cardiovascular risk between women who did and did not use Prempro were very small – 7 cases of heart disease and 8 of stroke per 10,000 women. These differences also may not be due to Prempro use, since about 75% of the women had never used hormone replacement until they entered the study, when their average age was 63. This means that for ten or more years after menopause women were without the cardiovascular benefits of replacement hormones that have been found in observational and laboratory studies. In these ten years some of the women may have developed cardiovascular disease which three to five years of Prempro use could not correct. In any event, the results apply to women whose hormone use starts some years after menopause, *not to those who start using hormones at menopause*.

Also, in the WHI study the risks were based on the group to which a woman was assigned, not on her actual Prempro use. A whopping 42% discontinued Prempro use during the study. Nevertheless, in calculating risks, a woman was counted as taking Prempro even if she had stopped using it. Risks may differ when women who were actually using Prempro are taken into account.

Most importantly, Prempro users did NOT have a higher overall mortality than non-users. In fact, by the end of the study, Prempro users began to have a lower mortality rate than non-users.

Finally, the Prempro regimen is one in which both a synthetic estrogen and progestin are taken every day. The results of this study do not apply to other, newer approaches where more natural hormones are used and where progestin is taken only part of the time.

The results of this and previous studies suggest that *if* hormone replacement therapy does at all increase breast cancer risk, it does so to a very tiny extent. To determine the effects of hormone replacement therapy on cardiovascular disease rates, more studies are needed of women who start replacement hormones at menopause and who use regimens other than Prempro.