Pergamon

European Journal of Cancer Vol. 32A, No. 10, pp. 1621–1626, 1996

Printed in Great Britain.
0959-8049/96 $15.00+0.00

International Cancer News

Compiled by Robert Short, News Editor, London

From The Globe

Breast Cancer Risk in Former Contraceptive Pill Users Lasts Only 10 years

There is no long-term increase in breast cancer for former contraceptive pill users. There is a small increase only while taking the pill and for a few years after. This was the conclusion of a major international report on the contraceptive pill and breast cancer published in the *Lancet* [1].

This report is the largest investigation into the cause of cancer ever undertaken, involving 200 scientists in 70 institutions in 25 countries. The report comprises virtually all the worldwide available evidence on the "Pill" and breast cancer. A team from the Imperial Cancer Research Fund's Cancer Epidemiology Unit brought together detailed information on 53 000 women with breast cancer and 100 000 women without breast cancer from 54 international studies.

The head of the charity's Oxford-based unit, Dr Valerie Beral, said: "We now know that more than 10 years after stopping the Pill, women are not at an increased risk. This result is very reliable, as it is based on information on about 10 000 women with breast cancer who stopped the Pill 10 or more years ago."

She added, "The absence of any increase 10 or more years after stopping is found consistently for all groups of women studied: young women, older women, women with a family history of breast cancer, women of different ethnic origin and women from developed or developing countries. It was also true, regardless of how old women were when they began taking the Pill, how long they took it and what type of Pill they took.

Researcher Dr Gillian Reeves said of the increases observed: "The small increase in the number of cancers diagnosed in Pill takers begins soon after starting use and is not affected by how long women take the Pill or by the specific type or dose of Pill used. After women come off the Pill this excess declines, disappearing completely after 10 years."

Although the researchers could not tell why there are these extra cancers among women who recently took the Pill, Dr Reeves said, "What we have found is that the cancers in women on the Pill are less likely to have spread beyond the breast than the cancers in women who have never taken the Pill and this raises the possibility that women on the Pill are picking up their cancers at an earlier stage. If this were so, it could explain why women on the Pill are more likely to be diagnosed with breast cancer."

Figure 1 shows that in 10 000 women who used the Pill from 25 to 29 years of

Topotecan Approved in U.S.A for Ovarian Cancer

The Food and Drug Administration (FDA) of the U.S.A. has approved topotecan, the first of a new class of drugs to treat patients with advanced ovarian cancers who have not responded favourably to standard treatments. The U.S.A. is the first major market for which the agent has been licensed although approval throughout Europe and the world is expected over the next year.

Topotecan (Hycamtin-R) is a SmithKline Beecham Pharmaceuticals drug derived from the active agent camptothecin, found in the bark of a Chinese tree. It works by interfering with topoisomerase I, an enzyme that uncoils DNA before cell division by creating and resealing nicks in the DNA. Altered function of the enzyme eventually leads to tumour cell death.

The EORTC Early Clinical Studies Group has conducted phase II studies with topotecan in patients with small cell lung cancer and colorectal cancer. In both studies, topotecan is given as a short infusion daily for 5 days at a dose of 1.5 mg/m^2/day. Patients with small cell lung cancer were grouped into those who were sensitive to earlier chemotherapy and those who were resistant. Chairman of the Early Clinical Studies Group, Dr Axel-R. Hanauske, said that activity of the agent was found to be significant: "An interim analysis has already shown significant activity of topotecan in small cell lung cancer, given preferably to patients who had responded to prior regimens. The Early Clinical Studies Group has thus pinpointed a tumour entity that warrants further clinical scrutiny of topotecan." The group found that topotecan's activity in colorectal cancer was minor. In the col-

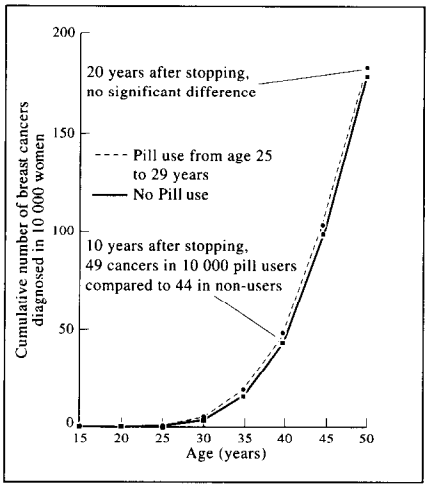

Figure 1. Cumulative number of breast cancers diagnosed in 10 000 women (reproduced with permission of *The Lancet* from The Lancet 1996, Vol. 347, pp. 1713–1727).

age, approximately 49 breast cancers would be diagnosed in the period from start of use up to 10 years after stopping, compared to 44 cancers diagnosed in women who had not taken the Pill. The estimated increase in the number of breast cancers diagnosed up to 10 years after stopping is smaller the younger the women were when they last used the Pill. For example, in 10 000 women who used the Pill from 16 to 19 years of age, the corresponding numbers would be 4.5 and 4.0 breast cancer.

Dr Beral said: "Overall, the results show that 20 years after stopping the Pill, there is little difference in the total number of breast cancers diagnosed between women who have and have not used the Pill. What is more, the cancers in women who have taken the Pill are less likely to have spread beyond the breast and are therefore potentially more curable."

Critique

A critique of the study recently appeared as an editorial in the *British Medical Journal* [2] by Professor Elina Hemminki, Research Professor at the National Research and Development Centre for Welfare and Health, Health Service Research Unit, Helsinki, Finland. She said that pooling data cannot overcome the limitations of individual case–control studies. "The report does not tell us how the controls were chosen, nor whether they were representative of the population from which the cases came."

She comments on a few possible selection biases. Possibly, women may decide not to use oral contraception because they believe themselves to be at high risk of breast cancer. Also, many women stop taking the Pill because of side-effects and possibly such sensitivity to external hormones could be related to risk of breast cancer.

At the time when the studies were done, prolonged use of the Pill before first pregnancy was rare. The median duration of use in the study was 3 years and the median age of starting the Pill was 26 years. Thus, Professor Hemminki says the review does not look at long-term use before first pregnancy. "In view of the current trend towards starting use before the age of 20, this would have been important. Neither does the review look at potential long-term consequences, when the early starters reach the age of high breast cancer risk or when users enter the new hormonal balance of menopause and possibly postmenopausal hormone therapy."

1. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with and 100,239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996, **347**, 1713–1727.
2. Hemminki E. Oral contraceptives and breast cancer. *Br Med J* 1996, **313**, 63–64.

orectal cancer study, 57 patients were evaluable for response and toxicity. Partial responses were observed in 4 patients with a median response duration of 11 months.

In phase III trials by other researchers examining topotecan as second-line therapy against ovarian cancers, response rates were 10–15% among patients who had not previously responded to standard treatment and 25–30% among patients who had responded to first-line therapy. In one study, comparing topotecan and taxol for the treatment of advanced, recurrent ovarian cancer, topotecan showed a 20% response rate, whereas taxol had a 12% response rate.

Response rates as high as 39% have also been seen in phase III trials using the drug as a first-line treatment for small cell lung cancer. Future studies will look at how topotecan performs when used in combination with other drugs, such as cisplatin in small cell lung cancer.

WHO Cancer Unit Moves to Lyon

The WHO Cancer Control Programme headquarters has moved from Geneva to the premises of the International Agency for Research on Cancer (IARC) in Lyon.

In May 1996, a memorandum of understanding was signed between Dr H. Nakajima (WHO Director-General), and Dr P. Kleihues (Director, IARC) transferring the unit as of 1 July 1996. This was after support by the IARC Governing Council during its Thirty-sixth session by Resolution GC/36/R5.

A memorandum of understanding regarding the transfer of the Cancer Programme to Lyon says that the unit of Cancer and Palliative Care (CPL) has been disestablished and that the staff transferred to Lyon will operate under the designation of "WHO Programme on Cancer Control" (PCC). The unit will retain its global public health mission.

The Director-General of WHO will delegate to the Director of IARC the authority to supervise the Programme on Cancer Control. The Director of IARC will report directly to the Director-General on all matters covered by this delegation. The programme's mission and activities will be developed within a policy framework to be determined by WHO, through the World Health Assembly, the Executive Board and the Global Policy Council.

The benefit of the move to Lyon is said to be that it enables interaction of PCC with IARC scientists. "The results of ongoing research at the Agency will be used without delay for the proposal and implementation of public health projects conducted by PCC," a memorandum states.