Letter to the Editors

Some comments on the Million Women Study

A detailed analysis of the very important Million Women Study[1] may give some very relevant guidelines for clinical practice. Some sentences deserve to be quoted and commented on in view of their important content:

'The average period of follow-up was 2.6 years for analysis of the cancer incidence and 4.1 years for analysis of mortality.'

'The breast cancers were diagnosed on average 1.2 years after recruitment.' . . . 'For the women who died from breast cancer, the average time between diagnosis and death was 1.7 years.'

At recruitment, every woman had a normal mammography, for otherwise they would not have been selected for inclusion. A diagnosis of breast cancer made on average 1.2 years after recruitment is certainly a proof that the hormones did not cause the cancer, that it was already present at recruitment and that its growth was stimulated by the hormones. An average time of 1.7 years between diagnosis and death suggests a highly malignant tumor. There is no indication about the staging of these tumors (TMN) in order to better interpret the results.

'The magnitude of the relative risk of breast cancer varied significantly between these three HRT types ($p < 0.0001$) and was substantially greater in users of estrogen–progestogen combinations than other preparations.'

Thus, it seems that there is not much difference between estrogen-only preparations and tibolone.

As shown in Table 1, at less than 5 years and at more than 5 years total duration of treatment, women given tibolone had, respectively, 11% and 23% more breast cancers than those given estrogen alone (which is not significant in view of the above), but respectively 42% and 64% less breast cancers than women using estrogen–progestogen preparations. The latter result is significant!

Table 1 Risks of breast cancer in relation to total duration of use

	< 5 years	*> 5 years*
Estrogen	1.21	1.34
Estrogen–progestogen	1.70	2.21
Tibolone	1.32	1.57

'There seems to be little advantage to using estrogen–progestogen in preference to estrogen-only HRT for women who still have a uterus' . . . 'Use of either type of HRT is estimated to result in five to six extra cancers with 5 years' use and 15–19 extra cancers per 1000 women with 10 years' use of HRT' . . . 'The extra cancers are predominantly of the endometrium for users of estrogen-only preparations.'

Tibolone does not stimulate the endometrium as estrogens do. Therefore, it would be preferable to use estrogen-only preparations and estrogen–progestogen combinations in terms of the combined risk for endometrial and breast cancers, independently of the body mass index.

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Reference

1. Beral V and the Million Women Study collaborators. Breast cancer and hormone replacement therapy in the Million Women Study. *Lancet* 2003;362:419–27