

LETTERS TO THE EDITOR

LHRH analogues and breast cancer

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Sir – A very welcome recent editorial in the Journal (Smith, 1991) addressed the important question of the use of LHRH analogues in breast cancer, but we do not consider all of the viewpoints expressed to be either definitive or necessarily correct: Firstly, the word analogues is used throughout as being synonymous with LHRH agonists. This is now a historical viewpoint as pure LHRH antagonists are now available for clinical study and, although still experimental, the problems of the early antagonist compounds (viz short half-life and histamine release) seem to be overcome with newer agents (Bajuez *et al.*, 1988). The ability to produce an immediate 'medical castration' without any transient initial stimulation phase, may be considered an advance for both breast and prostate cancer therapy.

Results of suppression of DNA synthesis and inhibition of cell growth of 'oestrogen-independent' MDA-MB-231 cell line by LHRH antagonists (Sharoni *et al.*, 1989) and excellent inhibition of mouse MXT mammary tumour (Szende *et al.*, 1990) suggest another possible role for LHRH antagonists in the treatment of human breast cancer.

The statement that 'oophorectomy is already a redundant treatment', as an editorial comment in the Journal on breast cancer management, cannot be allowed to pass unchallenged. The two randomised trials cited (Buchanan *et al.*, 1986; Ingle *et al.*, 1986) to support the notion that tamoxifen is as effective as oophorectomy do not ' ... show ... that tamoxifen is as effective as oophorectomy in every respect and with minimal toxicity', they only found no significant difference in response rates in favour of one or other of the two treatments in studies of low statistical power. Further, all the tamoxifen treated patients later relapsed and, at this time, the physicians were left with potentially endocrine sensitive cancer patients with premenopausal levels of oestrogens circulating, proven by crossover oophorectomy responses.

We would draw further attention to other studies (e.g., Mathe *et al.*, 1987), including those analysing effects of tamoxifen on endometrium and the rare but increased incidence of uterine cancer in patients treated with tamoxifen (Fornander *et al.*, 1989), tamoxifen flare (Hartley *et al.*, 1987) and relative merits of different endocrine therapies (Rose & Mouridsen, 1988).

In the treatment of human breast cancer there is an optimal sequence of hormone manipulations and it would be agreed by all that tamoxifen therapy is, for all individuals, near the top. However, with their immediate action, effectiveness in inducing 'medical castration' with no side effects and possible direct action on tumour cells, newer LHRH antagonists deserve more basic and clinical research in the treatment of breast cancer.

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