however, accounted for less than 2% of the total births over this period. The Hospital In-Patient Enquiry does not cover private patients in NHS hospitals, and the induction and caesarean section rates derived from it have been applied to all deliveries whether NHS or private in these hospitals. While this should technically result in an underestimate, the proportion of private patients is probably too small for the bias to be detectable. Thus the percentages quoted are probably slight underestimates, but the data that would be needed for better estimates are not collected.

References

¹ St Leger, A S, *Applied Statistics*, 1976, **25**, 280.

² Martins, J M, *Medical Journal of Australia*, 1972, **1**, 487.

³ Rindfuss, R R, and Ladinsky, J L, *Medical Care*, 1976, **14**, 685.

⁴ Chalmers, I, and Richards, M, in *Benefits and Hazards of the New Obstetrics*, ed T Chard and M Richards (Clinics in Developmental Medicine No 64). London, Spastics International Medical Publications, Heinemann, 1977.

⁵ Office of Population Censuses and Surveys, unpublished data.

⁶ Office of Population Censuses and Surveys, DHSS, and the Welsh Office, Hospital In-Patient Enquiry, 1966, 1974-5, Maternity Tables. To be published.

⁷ Cartwright, A, *British Medical Journal*, 1977, **2**, 745.

⁸ Stanley, F J, and Alberman, E D, *Developmental Medicine and Child Neurology*, 1978, **20**, 300.

⁹ Rush, R W, *et al*, *British Medical Journal*, 1976, **2**, 965.

¹⁰ Brimblecombe, F S W, Ashford, J R A, and Fryer, J G, *British Journal of Preventive and Social Medicine*, 1968, **22**, 27.

(Accepted 29 September 1978)

Treatment and survival in advanced breast cancer

T PRIESTMAN, M BAUM, VERA JONES, J FORBES

British Medical Journal, 1978, **2**, 1673-1674

Summary and conclusions

The final results of a clinical trial comparing endocrine with cytotoxic drug treatment for advanced breast cancer were analysed. Although cytotoxic treatment gave a significantly higher response rate with a remission duration comparable to that obtained with endocrine treatment, the sequence in which the two treatments were given did not appear to influence survival—except possibly in women with rapidly progressing disease, when cytotoxic treatment is preferred.

Introduction

In a previous paper we gave the initial results of a prospective, randomised study comparing endocrine with cytotoxic drug treatment in women with advanced breast carcinoma.¹ We now report the durations of remission, subsequent treatment, and survival of these women.

Patients and methods

One hundred women with locally recurrent or metastatic adenocarcinoma of the breast were allocated at random to receive either endocrine treatment or combination cytotoxic chemotherapy. Table I summarises the treatment regimens used; the rationale for their choice has been discussed.¹ The criteria used for objective response were those recommended by the UICC.² Entry to the study ended in December 1976. Most patients who failed to respond to or relapsed

on initial treatment were given further treatment. This treatment was not specified in the original protocol and so varied considerably. Several patients who received cytotoxic drugs initially were subsequently given endocrine treatment and vice versa.

Results

Of the 92 patients available for assessment, 47 were in the endocrine treatment group and 45 in the cytotoxic treatment group. Cytotoxic treatment produced significantly more responses than endocrine treatment ($P < 0.02$; χ^2 test with Yates's correction for small numbers). There were six complete and four partial responses in the endocrine treatment group, and 11 complete and 11 partial responses in the cytotoxic treatment group. The median duration of response was 49 weeks (range 24-114) in the endocrine-treated patients and 47 weeks (range 12-100) in patients given cytotoxic agents. In both groups the median durations of remission in complete responders (endocrine group 56 weeks, cytotoxic group 50 weeks) were longer than in partial responders (endocrine group 42 weeks, cytotoxic group 40 weeks), but the differences were not significant. In the cytotoxic group three patients were still in remission at 78, 92, and 98 weeks respectively,

FIG 1—Overall survival in cytotoxic- and endocrine-treated patients (life table analysis by Peto log rank test).

Cardiff Breast Clinic, Velindre Hospital, Cardiff CF4 7XL

T PRIESTMAN, MRCP, FRCR, consultant in radiotherapy and oncology (present address: Wellcome Research Laboratories, Beckenham, Kent)
VERA JONES, MB, BS, medical assistant

Surgical Unit, University Hospital of Wales, Cardiff

M BAUM, MCHIR, FRCS, reader in surgery (present address: King's College Hospital, London SE5 9RS)

J FORBES, MS, FRCS, Nuffield fellow in surgery (present address: Royal Melbourne Hospital, Melbourne, Australia)

TABLE I—Treatment regimens used in study

Subgroups of patients	Endocrine treatment	Cytotoxic agents
Premenopausal	Ovarian ablation	Doxorubicin 60 mg plus
Postmenopausal with soft-tissue disease	Tamoxifen 20 mg twice daily	cyclophosphamide 750 mg plus
Postmenopausal with secondary deposits in bone	Methyltestosterone 5 mg thrice daily plus nandrolone phenylpropionate 50 mg intramuscularly once weekly	fluorouracil 750 mg plus
Postmenopausal with secondary deposits in lung parenchyma	Stilboestrol 5 mg thrice daily	vincristine 2 mg by intravenous injection on one day every three weeks
Postmenopausal with spread to liver or lymphangitis carcinomatosa	Prednisone 10 mg thrice daily	

and in the endocrine series one patient was still in remission 91 weeks after starting treatment.

The median duration of survival was 32 weeks in the endocrine-treated patients and 67 weeks in patients given cytotoxic agents. This reflects the differing response rates, as the median duration of survival in responders (endocrine group 93 weeks, cytotoxic group 86 weeks) and non-responders (both groups 24 weeks) were closely similar. Analysis of life tables by the Peto log rank test disclosed no significant difference in overall survival between the two groups (fig 1). When individual subgroups were analysed the premenopausal women showed the greatest difference in survival (fig 2), although this did not reach statistical significance. The main feature in these patients was the rapid initial divergence in survival curves between the endocrine and cytotoxic groups.

FIG 2—Survival in premenopausal subgroup of women given endocrine or cytotoxic treatment (life table analysis by Peto log rank test).

Table II gives the results of subsequent treatment used. Out of 15 patients who failed to respond to cytotoxic agents and were then given endocrine treatment, six responded. Out of 14 patients who relapsed after a successful response to cytotoxic agents, five subsequently benefited from endocrine treatment. Of the 17 patients who failed to

TABLE II—Results of subsequent treatment

Subsequent treatment		Primary treatment							
		Response				Failure			
		T	O	E	C	T	O	E	C
Response	T	1			1	5	2	1	3
	O				2		1	2	1
	E				4				4
	C				2				2
Failure	T	2			3	4	2	2	5
	O				2				
	E				3				
	C				2				

T = Tamoxifen. O = Ovarian ablation. E = Other endocrine treatment. C = Cytotoxic treatment.

respond initially to endocrine measures, seven gained a remission from later chemotherapy. To date no patients who responded to primary endocrine treatment have needed cytotoxic agents.

Discussion

In contrast to the initial finding¹ there was no difference in overall survival between the two treatment groups. Nevertheless, there was a strong clinical impression throughout the study that several patients with rapidly progressive disease, particularly in the premenopausal subgroup, would have benefited from the immediate action of cytotoxic agents rather than the slower effect of endocrine manipulation. Furthermore, many patients received subsequent treatment with the alternative option and several responses were seen.

The choice of primary treatment did not appear to influence the likelihood of success with subsequent treatment. The response rate among patients receiving primary cytotoxic treatment was 49%, and among those receiving secondary cytotoxic treatment 41%. Similarly the response rate for primary endocrine treatment was 21%, and for endocrine treatment after cytotoxic treatment 38% (this figure being similar whether the patients had initially responded or failed with cytotoxic drugs).

As the success or failure of one form of primary treatment did not appear to jeopardise the chances of a subsequent response to the other, and as the overall survival curves for the two treatment modalities showed no significant difference, we suggest that the sequencing of treatment is relatively unimportant (except possibly for the clinical observation that in patients with rapidly progressing disease cytotoxic agents should be the first line of treatment).

When this trial was undertaken it was not possible to assess routinely the oestradiol receptor state of patients. In view of the evidence that oestrogen receptor state influences the response to treatment³ this trial merits repetition with the initial decision on treatment being made in the light of the receptor state of the patient.

References

- Priestman, T J, *et al*, *British Medical Journal*, 1977, **1**, 1248.
- Hayward, J L, *et al*, *European Journal of Cancer*, 1977, **13**, 89.
- Leclercq, G, and Heuson, J C, *European Journal of Cancer*, 1977, **13**, 1205.

(Accepted 19 October 1978)

ONE HUNDRED YEARS AGO The Medical Officer of Enniscorthy Union Workhouse having recently complained of the variable quality of the milk supplied to that institution, samples were forwarded lately to Dr Emerson Reynolds, Professor of Chemistry in the University of Dublin, for analysis. On examination, Dr Reynolds found that the milk, when subjected to the ordinary analysis, appeared to be merely skimmed milk and not adulterated, the solids being present in the usual quantities; but, on closer investigation, it was found to contain gelatine in the proportion of nearly .8 per cent. By this adulterant, the milk, when tested with the ordinary instrument, apparently had a higher specific gravity than it really possessed. Some years since, this method of adulteration was practised in some parts of France. (*British Medical Journal*, 1878.)