in the tissue and blood of patients with primary breast cancer. *Cancer* 1989, **63**, 490–495.
24. Lee YN. Bone scanning in patients with early breast carcinoma should it be a routine staging procedure? *Cancer* 1981, **47**, 486–495.

Acknowledgements—We thank Pia Powell, Daniela Bionda and Christine Schlumpf-Zürcher for technical assistance. This work was supported by the Wissenschaftlicher Kredit, Kantonsspital Basel.

Eur J Cancer, Vol. 27, No. 2, pp. 131–135, 1991.
Printed in Great Britain

0277–5379/91 $3.00 + 0.00

Breast Size, Handedness and Breast Cancer Risk

C.-c. Hsieh and D. Trichopoulos

Bra cup size and handedness were studied as possible risk factors for breast cancer. Data for 3918 cases and 11 712 controls from 7 centres were used to examine the association of handedness with laterality of breast cancer; data for 2325 cases and 7008 controls from 4 centres were used to assess the relation of bra cup size to breast cancer risk. There was a suggestive (*P* about 0.10) association of handedness with breast cancer laterality: odds ratio of a left-handed (or ambidextrous) woman having a left-sided cancer 1.22 (95% CI 0.96–1.56). Handedness may affect the lateral occurrence of breast cancer, although this tumour is in general more common in the left breast, possibly because this breast is usually slightly larger. Premenopausal women who do not wear bras had half the risk of breast cancer compared with bra users (*P* about 0.09), possibly because they are thinner and likely to have smaller breasts. Among bra users, larger cup size was associated with an increased risk of breast cancer (*P* about 0.026), although the association was found only among postmenopausal women and was accounted for, in part, by obesity. These data suggest that bra cup size (and conceivably mammary gland size) may be a risk factor for breast cancer.
Eur J Cancer, Vol. 27, No. 2, pp. 131–135, 1991.

INTRODUCTION

MOST HYPOTHESES to explain the aetiology of human breast cancer have focused on mammotropic hormones, particularly oestrogens [1–4]. Several investigations have suggested that cell number and mammary gland size (or mass) may be important risk factors for breast cancer [5, 6]. This view is compatible with data from experimental carcinogenesis [6, 7] as well as with epidemiological observations linking breast cancer to diet [8] and to adult height [9, 10]. However, studies that examined the relation of bra cup size (possibly correlated with mammary gland size) to breast cancer risk have given equivocal results. Wynder *et al.* [11], Soini [12] and Hirohata *et al.* [13] found no evidence for an association in their case–control studies, but these studies were not sufficiently large to overcome the sustantial misclassification in the measurement of bra cup size (itself a poor measure correlate of mammary gland size). Katariya *et al.* [14] assessed breast size from mammograms and found no difference between breast cancer cases and controls in a small number of women. In contrast, Deapen *et al.* [15] noted a 43% lower frequency of breast cancer among small-breasted women who had undergone augmentation mammoplasty, and Dupont and Page [16] found that breast size was a risk factor for breast cancer among women with proliferative breast disease.

We have examined the association between bra cup size and breast cancer in a large set of data, collected by MacMahon *et al.* [17, 18] during the late 1960s, in the context of an international multicentre case-control study of breast cancer. The relation between breast cancer laterality and handedness was also assessed.

Correspondence to C.-c. Hsieh.
The authors are at the Department of Epidemiology, Harvard School of Public Health, 677 Huntington Avenue, Boston, Massachusetts 02115, U.S.A.
Revised and accepted 5 Nov. 1990.

SUBJECTS AND METHODS

The international multicentre case-control study was done with an agreed common protocol in seven areas of the world in populations with a low, intermediate and high incidence of breast cancer (Athens, Greece; Boston, USA; Glamorgan, Wales; São Paulo, Brazil; Slovenia, Yugoslavia; Taipei, Taiwan; and Tokyo, Japan). Except in Tokyo, the breast cancer cases included most of the female residents of the study area who were admitted for a first diagnosis of breast cancer during the study period. For each breast cancer patient interviewed, 3 eligible patients in beds closest to the index case were interviewed as controls. A control had to be a resident of the study area, to have never had cancer of the breast, and to be over 35 years of age (except when the index case was under 35, in which case controls were age-matched within 2 years). Details about the original study and collective results have been reported for lactation [17], age at first and at any birth [18, 19] and age at menarche, age at menopause and anthropometric variables [10].

Subjects were excluded from the subsequent analyses when their interviews were judged unreliable or when information was not available for the variables included in the analyses. Among 4395 interviewed women with breast cancer in all seven centres, 443 (10.1%) were excluded from the analysis of laterality of breast cancer and handedness; among the corresponding 12 888 controls, 1176 (9.1%) were excluded. The association between breast size and breast cancer was studied only among women in Athens, Boston, Glamorgan and São Paulo; in the remaining three centres information on bra cup size was not collected (Slovenia, Taipei) or most women were not customarily wearing a bra (Tokyo). Among 2561 interviewed women with

breast cancer in the four included centres, 236 (9.2%) with missing information were excluded from the analysis on bra usage and bra cup size; among the corresponding 7682 controls in the four included centres, 674 (8.8%) were excluded. Table 1 shows the laterality of breast cancer among the affected women and the handedness of breast cancer cases and controls, by study centre. Table 2 shows the distribution of breast cancer cases and control women in the four included centres, by centre, usage of bra and (among users) cup size of bra.

Statistical analysis of the association between handedness and laterality of breast cancer was done with the Mantel–Haenszel procedure [20], controlling for study centre. Left-handed women and ambidextrous women were analysed separately but they were also combined, since ambidextrous people, by definition, use their left hand as much as their right. Women with right-sided breast cancer were compared with women with left-sided breast cancer, and each of the above groups was also individually compared with control women. Cases with cancer in both breasts were very few (34) and were not analysed. Right-handed women were considered as the baseline (unexposed) category of the risk determinant.

The importance of bra usage and cup size of bra were assessed through multiple logistic regression [21, 22]. Separate analyses were done for premenopausal and postmenopausal women, as well as for all women, controlling for menopausal status. Women were considered as postmenopausal when they had their last menstrual period more than 6 months before the interview; otherwise they were considered premenopausal. No attempt was made to distinguish between women with artificial and those with natural menopause. In all analyses a core model was used to control possible confounding by study centre (categorical variable), parity (parous = 1, nulliparous = 0), age at first birth (continuous variable) and age at interview (continuous variable). Height was not controlled for, since its association with breast cancer could be accounted for by a possible "intermediate" association with mammary gland mass. Models were fitted with and without terms for obesity index (in kg/m^2 as a continuous variable). Obesity index, rather than weight, was considered because weight is a composite measure of height and obesity and each component may have independent risk associations with breast cancer [5].

Table 1. Distribution of breast cancer cases and controls by laterality of breast cancer, handedness and study centre

	Laterality of breast cancer				Handedness			
	Right	Left	Both	Total	Right	Left	Both	Total
Athens								
Cases	329	381	8	718	679	6	33	718
Controls	–	–	–	–	2125	18	105	2248
Boston								
Cases	256	281	2	539	491	18	30	539
Controls	–	–	–	–	1513	54	83	1650
Glamorgan								
Cases	244	269	2	515	489	12	14	515
Controls	–	–	–	–	1462	47	35	1544
Sao Paulo								
Cases	275	252	3	530	507	9	14	530
Controls	–	–	–	–	1437	33	58	1528
Slovenia								
Cases	338	368	6	712	623	31	58	712
Controls	–	–	–	–	1904	99	152	2155
Taipei								
Cases	114	93	0	207	198	2	7	207
Controls	–	–	–	–	600	4	26	630
Tokyo								
Cases	359	359	13	731	674	24	33	731
Controls	–	–	–	–	1796	64	97	1957
Total								
Cases	1915	2003	34	3952	3661	102	189	3952
Controls	–	–	–	–	10837	319	556	11712

Table 2. Distribution of breast cancer cases and controls by study centre, bra usage and (among users) bra size

	Non-users of bra	Bra users by cup size*						
		1	2	3	4	Unknown (wore bra)	All bra users	All women
Athens								
Cases	10	127	252	205	126	10	720	730
Controls	35	376	824	631	353	41	2243	2278
Boston								
Cases	30	90	235	125	33	30	513	543
Controls	88	261	757	371	80	98	1567	1655
Glamorgan								
Cases	74	85	223	114	13	9	444	518
Controls	173	326	626	355	41	25	1373	1546
Sao Paulo								
Cases	7	67	190	180	5	85	527	534
Controls	47	252	544	453	30	203	1482	1539
Total								
Cases	121	369	900	624	177	134	2204	2325
Controls	343	1215	2769	1810	504	367	6665	7008

*In Athens, 1 corresponds to smaller and 4 to larger cup size of bra; in Boston and Glamorgan 1 = AA or A, 2 = B, 3 = C and 4 = D; and in Sao Paulo 1 = A (−42), 2 = B (43–46), 3 = C (47–50) and 4 = D (51–54).

RESULTS

The association between handedness and laterality of breast cancer is examined in Table 3. Crude odds ratio estimates, based on the total data in the table, were almost identical to those derived after adjustment for study centre by the Mantel–Haenszel procedure. Left-handed and ambidextrous women were 13% less likely than right-handed to develop cancer in the right breast, but were 7% more likely to develop cancer in the left breast. None of these differences was, in itself, statistically significant but they appeared internally consistent; indeed, the odds ratio that contrasted the laterality of breast cancer between left-handed (and ambidextrous) women and right-handed women was 1.22 (two-tailed $P = 0.10$). Furthermore, when left-handed and ambidextrous women were separately considered, breast cancer laterality followed an exposure-dependent pattern; the odds ratio (and 95% CI) for a left-sided cancer was 1.31 (0.87–1.97) for left-handed women, 1.17 (0.87–1.57) for ambidextrous women and 1.00 (baseline) for right-handed women.

Table 3. Cross-classification of right-side and left-side breast cancer cases and of controls by handedness (seven centres)

Subjects	Left-handed	Ambidextrous	Right-handed	Total
Breast cancer, right	42 (2.19%)	84 (4.39%)	1789 (93.42%)	1915
Breast cancer, left	57 (2.85%)	103 (5.14%)	1843 (92.01%)	2003
Controls	319 (2.72%)	556 (4.75%)	10837 (92.53%)	11712

Left-handed and ambidextrous women were combined and considered as exposed.
Centre-adjusted odds ratios for left-handed and ambidextrous women (95% CI): right breast cancer vs. controls, 0.87 (0.72–1.06); left breast cancer vs. controls, 1.07 (0.90–1.28); and left breast cancer vs. right breast cancer, 1.22 (0.96–1.56).

Table 4. Adjusted odds ratios for breast cancer of bra users vs. non-users, by menopausal status (four centres)

Menopausal status	Odds ratio (95% CI)*	Odds ratio (95% CI)†
Premenopausal	2.26 (0.87–5.84)	2.25 (0.87–5.84)
Postmenopausal	1.03 (0.82–1.31)	1.00 (0.79–1.26)
All women	1.11 (0.89–1.39)	1.08 (0.86–1.35)

*Adjusted by multiple logistic regression for study centre, age, age at first birth, parity and (in all women) for menopausal status.
†Adjusted for all same variables *and for obesity.

Table 4 shows adjusted odds ratios for breast cancer, contrasting bra users with non-users. There was a suggestion (odds ratio 0.44, 0.17–1.15; P about 0.09) that, among premenopausal women, those who did not wear a bra had a lower risk of breast cancer. The association, if real, could point to obesity or breast size as the relevant risk factor. It can be seen in Table 5 that in all four study centres bra-wearing controls were substantially heavier than those who did not wear a bra and cup size was strongly correlated with body weight and obesity.

The association between bra cup size and breast cancer risk is examined in Table 6; the table is restricted to women wearing a bra of known cup size. Cup size was a risk factor for breast cancer, although part of the association was accounted for by obesity. The relation was stronger among postmenopausal women, but the interaction with menopausal status was not significant.

Table 5. Relation between anthropometric measures and usage of bra and, among users, cup size of bra, adjusted for age (four centres, controls only)

	Mean difference users minus non-users			Average change per unit cup size increase among users		
Centre	Height (cm)	Weight (kg)	Obesity (kg/m²)	Height (cm)	Weight (kg)	Obesity (kg/m²)
Athens	0.96	4.93*	1.68*	0.17	5.62*	2.19*
Boston	−1.94*	4.24*	2.35*	−0.27	5.62*	2.27*
Glamorgan	0.90	4.54*	1.53*	0.56*	7.79*	2.93*
Sao Paulo	2.19*	4.20*	1.07*	1.68*	7.21*	2.46*

*$P < 0.05$

DISCUSSION

There are several lines of indirect evidence linking breast size and/or mammary gland size to breast cancer risk. Oestrogens, which are likely to be involved in the aetiology and natural history of breast cancer, are important factors for the growth and development of the mammary gland, and it is possible that pre-initiation events and conditions affecting mammary gland size influence breast carcinogenesis [23]. Breast cancer is overwhelmingly more common in women than in men, and breast and mammary gland sizes are also much larger in women. Breast cancer incidence is substantially higher in caucasian than in oriental women, and breast size is also substantially larger among caucasians than among oriental women. Adult height is a risk factor for breast cancer [9, 10] and it is conceivable that there is a positive relation between height and mammary gland mass (both reflecting, to various degrees, overall growth). Dense mammographic parenchymal patterns are established predictors of breast cancer [24, 25] and, since mass is a function of density, dense patterns may also reflect larger mammary gland mass. Male breast cancer appears to be substantially more common in people with Klinefelter's syndrome [26]. Finally, it is well-known that unilateral breast cancer is more frequently left-sided (the ratio of left-sided to right-sided tumours has been reported [2] to vary from 1.05 to 1.26) and that the left breast is usually slightly larger than the right [27, 28].

Studies that have directly examined the association, if any, between bra cup size or mammary gland size and breast cancer risk are equivocal [11–16]. This should not be unexpected even if there was a positive association of moderate strength. The correlation of bra cup size with mammary gland size has not been formally assessed but it is likely to be weak, since adipose tissue is a dominant component of the breast, particularly among postmenopausal women.

Our results suggest that breast size is a risk factor for breast cancer. It is, of course, possible that the association was accounted for by obesity, since overweight is an established risk factor for postmenopausal breast cancer [24]. However, about one-half of the excess risk among women with larger breasts was unrelated to obesity and it is also conceivable that overweight women have larger mammary gland mass (if the effect of obesity on breast cancer risk is mediated through a possible association with mammary gland size, adjustment for obesity would not be appropriate). Finally, it is possible that the adipose tissue in the breast itself affects breast cancer risk, by acting as a slow-release depot for lipid-soluble carcinogens [29], in which case adjustment for adiposity would again be inappropriate.

The results on the association between handedness and laterality of breast cancer were neither striking nor nominally significant but they were intriguing and they are reported to stimulate additional research (the relevant studies will not have to be sophisticated or even controlled, but they should be at least as large as the present study). A possible interpretation of the association, if it is real, is that handedness may have an influence on the relative size of the two breasts. However, even with such a large data set, the association was only marginal. Given the generally larger size of the left breast and the weakness of the association between handedness and breast cancer lat-

Table 6. Adjusted odds ratios (95% CI) for breast cancer among bra users of progressively larger cup size, by menopausal status (four centres)*

Adjustment for obesity	Cup size of bra 1	2	3	4	*P* (linear trend)
Premenopausal					
No	1.00 (baseline)	0.99 (0.79–1.24)	0.94 (0.73–1.20)	1.12 (0.77–1.61)	0.977
Yes	1.00 (baseline)	0.99 (0.79–1.25)	0.95 (0.72–1.25)	1.14 (0.77–1.68)	0.878
Postmenopausal					
No	1.00 (baseline)	1.13 (0.94–1.35)	1.28 (1.06–1.55)	1.27 (0.97–1.65)	0.009
Yes	1.00 (baseline)	1.08 (0.90–1.30)	1.18 (0.96–1.45)	1.12 (0.84–1.49)	0.194
All women					
No	1.00 (baseline)	1.06 (0.92–1.22)	1.15 (0.99–1.33)	1.22 (0.98–1.50)	0.026
Yes	1.00 (baseline)	1.03 (0.90–1.19)	1.08 (0.92–1.28)	1.12 (0.89–1.42)	0.237

*Adjusted by multiple logistic regression for study centre, age, age at first birth, parity, obesity (where indicated) and (in all women) for menopausal status.

erality, the high proportion of right-handed women in the general population could only reduce the left-to-right breast cancer ratio but not inverse the lateral pattern of breast cancer occurrence.

If mammary gland size (or mass) is a risk factor for breast cancer, the relation could be linear or more complicated, and could depend on the number of cells at risk and/or other factors. If established, the association would indicate that factors in early life, possibly energy intake, are contributing factors in the aetiology of breast cancer. This has also been suggested by several others on the basis of similar or different arguments [5, 6, 30–32].

1. MacMahon B, Cole P, Brown J. Etiology of human breast cancer: a review. *J Natl Cancer Inst* 1973, **50**, 21–42.
2. Kelsey JL, Hildreth NG. *Breast and Gynecologic Cancer Epidemiology*. Boca Raton, CRC Press, 1983, 5–70.
3. Boyle P. Epidemiology of breast cancer. In: Veronesi U, ed. *Bailliere's Clinical Oncology*. Eastborne, Bailliere Tindall 1988, Vol. 2. pp. 1–57.
4. Adami H-O, Adams G, Boyle P, *et al.* Breast cancer etiology. *Int J Cancer* (in press).
5. De Waard F, Trichopoulos D. A unifying concept of the aetiology of breast cancer. *Int J Cancer* 1988, **41**, 666–669.
6. Albanes D, Winick M. Are cell number and cell proliferation risk factors for cancer? *J Natl Cancer Inst* 1988, **80**, 772–775.
7. Ames BN, Gold LS. Too many rodent carcinogens: mitogenesis increases mutagenesis. *Science* 1990, **249**, 970–971.
8. Rogers AE, Longnecker MP. Dietary and nutritional influences on cancer: A review of epidemiologic and experimental data. *Lab Invest* 1988, **59**, 729–759.
9. Tretli S. Height and weight in relation to breast cancer morbidity and mortality. A prospective study of 570,000 women in Norway. *Int J Cancer* 1989, **44**, 23–30.
10. Hsieh C-c, Trichopoulos D, Katsouyanni K, Yuasa S. Age at menarche, age at menopause, height and obesity as risk factors for breast cancer: associations and interactions in an international case-control study. *Int J Cancer* 1990, **46**, 796–800.
11. Wynder EL, Bross IJ, Hirayama T. A study of the epidemiology of cancer of the breast. *Cancer* 1960, **13**, 559–601.
12. Soini I. Risk factors of breast cancer in Finland. *Int J Epidemiol* 1977, **6**, 365–73.
13. Hirohata T, Nomura AMY, Kolonel LN. Breast size and cancer. *Br Med J* 1977, **2**, 641.
14. Katariya RN, Forrest APM, Gravelle IH. Breast volumes in cancer of the breast. *Br J Cancer* 1974, **29**, 270–273.
15. Deapen DM, Pike MC, Casagrande JT, *et al.* The relationship between breast cancer and augmentation mammoplasty: an epidemiologic study. *Plast Reconstr Surg* 1986, **77**, 361–7.
16. Dupont W, Page D. Breast cancer risk associated with proliferative disease, age at first birth and a family history of breast cancer. *Am J Epidemiol* 1987, **125**, 769–779.
17. MacMahon B, Lin TM, Lower CR, *et al.* Lactation and cancer of the breast. *Bull WHO* 1970, **42**, 185–194.
18. MacMahon B, Cole P, Lin TM, *et al.* Age at first birth and breast cancer risk. *Bull WHO* 1970, **43**, 209–221.
19. Trichopoulos D, Hsieh C-c, MacMahon B, *et al.* Age at any birth and breast cancer risk. *Int J Cancer* 1983, **31**, 701–704.
20. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959, **22**, 719–748.
21. Breslow NE, Day NE. *Statistical Methods in Cancer Research. Volume 1: The Analysis of Case-control Studies* (IARC Scientific Publications No. 32). Lyon, International Agency for Research on Cancer, 1980.
22. Schlesselman JJ. *Case-control Studies*. New York, Oxford University Press, 1982.
23. Ponten, J, Holmberg L, Trichopoulos D, *et al.* Biology and natural history of breast cancer. *Int J Cancer* (in press).
24. Kelsey JL, Berkowitz GS. Breast cancer epidemiology. *Cancer Res* 1988, **48**, 5615–5623.
25. Brisson J, Verreault R, Morrison AS, Tennina S, Meyer F. Diet, mammographic features of breast tissue, and breast cancer risk. *Am J Epidemiol* 1989, **130**, 14–24.
26. Harnden DG, MacLean N, Langlands AO. Carcinoma of the breast and Klinefelter's syndrome. *J Med Genet* 1971, **8**, 460–461.
27. Schaeffer JP, ed. *Morris' Human Anatomy* 11th ed. New York, McGraw-Hill 1953, 82.
28. Gray H. Anatomy, descriptive and surgical. Pick TP, Howden R eds. Philadelphia, Running Press, 1974, 1038.

29. Beer AE, Billingham. Adipose tissue, a neglected factor in aetiology of breast cancer? *Lancet* 1978, **ii**, 296.
30. Cole P, MacMahon B. Oestrogen fractions during early reproductive life in the aetiology of breast cancer. *Lancet* 1969, **i**, 604–606.
31. Micozzi MS. Nutrition, body size, and breast cancer. *Yearbook of Phys Anthropol*, 1985, **128**, 175–206.
32. Willett W. The search for the causes of breast and colon cancer. *Nature* 1989, **338**, 389–394.

Acknowledgements—We thank Dr B. MacMahon, Dr T-m. Lin, Dr C.R. Lowe, Dr A.P. Mirra, Dr B. Ravnihar, Dr E.J. Salber, Dr V.G. Valaoras and Dr S. Yuasa for providing the data. The analysis of these data was made possible by a grant to our department from Captain Nikolas S. Lemos.

Eur J Cancer, Vol. 27, No. 2, pp. 135–138, 1991.
Printed in Great Britain

0277–5379/91 $3.00 + 0.00

Second-line Treatment of Advanced Measurable Ovarian Cancer with Iproplatin: a Southwest Oncology Group Study

Geoffrey Weiss, Stephanie Green, David S. Alberts, James Tate Thigpen, Harry E. Hines, Karl Hanson, H. Irving Pierce, Laurence H. Baker and John Wendall Goodwin

105 patients with advanced ovarian cancer previously treated with cisplatin or carboplatin were entered into a study of iproplatin as second-line therapy. Patients were either clinically resistant to cisplatin or carboplatin, or had relapsed after complete response to these agents. Patients were treated intravenously at an initial dosage of 270 mg/m^2 with dosage adjustments to 340, 200 or 135 based on observed toxicity. Of 101 eligible patients, 7 responses (3 complete, 4 partial; 12%) were observed in 60 patients resistant to cisplatin. 2 partial responses (11%) occurred in 18 patients resistant to carboplatin. 2 complete and 3 partial responses were observed in 19 patients (26%) previously treated with but not resistant to cisplatin. Response durations were 2–20 months. Toxicities of iproplatin included thrombocytopenia in 93% of patients, leukopenia in 76% of patients, anaemia in 68% of patients, and diarrhoea in 40% of patients. Thus iproplatin shares cross-resistance with cisplatin and carboplatin in the treatment of ovarian cancer and is not recommended as an effective second-line agent for platinum-resistant ovarian cancer.
Eur J Cancer, Vol. 27, No. 2, pp. 135–138, 1991.

INTRODUCTION

OF APPROXIMATELY 18 000 new patients with ovarian cancer diagnosed annually in the United States, two thirds will ultimately die of their malignancy [1]. This high proportion failing to achieve satisfactory control of disease reflects both the tendency for patients with this disease to present in an advanced state and the capacity of advanced disease to acquire resistance to most conventional systemic therapies. Clinical research in the management of advanced ovarian cancer, including cytoreductive surgery, intraperitoneal therapies and multidisciplinary approaches to treatment, seeks to overcome the therapeutic limitations imposed by refractory disease, dose-limiting toxicities of treatment and the marginal activity of existing drugs.

Alkylating agents and cisplatin have long been recognised as representatives of the more active agents in modern combination regimens for advanced ovarian cancer. Cisplatin's well-known gastrointestinal, renal and neurological toxicities have stimulated the search for analogues that are at least equivalently active yet less toxic. Carboplatin was approved for marketing in the USA on the strength of therapeutic equivalence with cisplatin as second-line therapy against advanced ovarian cancer, yet producing substantially less gastrointestinal and renal toxicity [2]. Iproplatin, another second generation analogue, has been undergoing similar evaluation as an alternative to cisplatin.

Iproplatin is more water soluble than cisplatin and has preclinical antitumour activity similar to cisplatin [3]. In phase I and II trials, the dose-limiting toxicity of iproplatin was thrombocytopenia [4, 5]. In previously untreated advanced ovarian cancer, iproplatin produced an overall response rate of 74–78% [6, 7]. In patients with ovarian cancer previously treated with cisplatin, the response rate was 22%, suggesting cross-resistance with cisplatin. In 1985, the Southwest Oncology Group launched a trial of iproplatin in advanced ovarian cancer previously treated with cisplatin or carboplatin. This trial sought

Correspondence to Southwest Oncology Group Operations Office 5430 Fredericksburg Road, Suite #618 San Antonio, Texas TB229-6197, U.S.A.
G. Weiss is at the University of Texas Health Science Center at San Antonio, San Antonio, Texas; S. Green is at the Southwest Oncology Group Statistical Center, Seattle, Washington; D.S. Alberts is at the University of Arizona Cancer Center, Tucson, Arizona; J.T. Thigpen is at the University of Mississippi Medical Center, Jackson, Mississippi; H.E. Hines is at the Wichita CCOP, Wichita, Kansas; K. Hanson is at the Midwest CCOP; H.I. Pierce is at the Northwest CCOP, Tacoma, Washington; L.H. Baker is at the Wayne State University Medical Center, Detroit, Michigan; and J.W. Goodwin is at the Ozarks CCOP, Springfield, Missouri, U.S.A.
Revised 19 Nov. 1990; accepted 23 Nov. 1990.