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Editorial

Chemotherapy for ovarian cancer – a consensus statement on standard practice

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BACKGROUND

The management of patients with ovarian cancer is a complex and evolving field. Optimal results from therapy are obtained when patients with ovarian cancer are treated by specialist multidisciplinary teams (Junor et al, 1994).

The earliest stages of ovarian cancer can be treated by surgery alone with excellent results.

The majority of women with ovarian cancer have advanced disease at presentation and require chemotherapy as well as surgery to improve their quality of life and increase survival.

DATA FROM RANDOMIZED TRIALS

A large meta-analysis and previous consensus statements have established that standard chemotherapy should include a platinum compound (Advanced Ovarian Cancer Trialists Group, 1991; Allen et al, 1993; National Institute of Health, 1994).

Randomized trials performed before the introduction of paclitaxel show that carboplatin and cisplatin are equally effective in terms of long-term survival (Advanced Ovarian Cancer Trialists Group, 1991).

Before the introduction of paclitaxel, there had been controversy surrounding the use of platinum-based combination chemotherapy as opposed to single-agent platinum treatment. A meta-analysis of randomized trials suggested a small advantage for platinum combined with other drugs. However, early data from a recent very large randomized trial suggest no benefit for a three-drug (non-paclitaxel-containing) platinum-based regimen over single-agent carboplatin (Advanced Ovarian Cancer Trialists Group, 1991; Torri, 1996).

Increasing the amount of treatment by more frequent dosing, more cycles of treatment, intraperitoneal delivery of chemotherapy or high-dose consolidation therapy are all areas of current research. As yet, no conclusive data exist to suggest that such approaches confer a survival benefit.

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Two large independent studies (totalling over 1000 patients) have demonstrated that the combination of cisplatin and paclitaxel confers a highly statistically significant survival advantage compared with a standard platinum-based combination (cisplatin–cyclophosphamide). The survival benefit is approximately 1 year (Table 1). This represents the largest step forward in the drug treatment of ovarian cancer since the introduction of platinum itself (McGuire et al, 1996; Stuart et al, 1998).

In a third randomized study, the paclitaxel–cisplatin combination was compared with either drug given alone (Muggia et al, 1997). This showed no significant survival advantage for patients randomized to the combination arm. However, cross-over between treatment arms occurred at an early stage in many patients and, as the trial progressed, the majority of patients received both drugs. It is therefore difficult to interpret this trial, and the results do not negate the data of McGuire et al (1996) and Stuart et al (1998).

All the current data showing that patients with ovarian cancer obtain a survival advantage from being treated with platinum–paclitaxel are based on regimens that use cisplatin. There are extensive data from the pre-taxane era that indicate that cisplatin and carboplatin are equally effective (Advanced Ovarian Cancer Trialists Group, 1991). Carboplatin–paclitaxel combinations have been compared with cisplatin–paclitaxel combinations in three separate trials (Neijt et al, 1997; du Bois et al, 1998; Gynecologic Oncology Group, 1998), and early data from two of these trials suggest that carboplatin combinations are better tolerated in terms of neurotoxicity and are equally effective in terms of response rates and progression-free survival (Neijt et al, 1997; du Bois et al, 1998).

There are no overall survival data as yet comparing the two platinum analogues when given in combination with paclitaxel. However, data on overall survival from these recently completed trials aimed at establishing the role of carboplatin in combination with paclitaxel will become available over the next 1–2 years (Neijt et al, 1997; du Bois et al, 1998; Gynecologic Oncology Group, 1998).

Patients who relapse after first-line treatment with platinum-based chemotherapy may respond to a number of drugs. The response rate to second-line treatment depends on the length of the initial remission (Blackledge et al, 1989; Gore et al, 1990; Markman et al, 1991).

Table 1 Survival data from the two randomized studies of cisplatin–cyclophosphamide (CC) versus cisplatin–paclitaxel (CP)

	n	Median survival (months)		Relative risk	*P*-value
		CC	CP	Cis-paclit	
McGuire et al (1996)	386	24	38	0.6 (0.5–0.8)	<0.001
Stuart et al (1998)	668	25	35	0.71 (0.57–0.87)	0.003
Cumulative data	1054	–	–	0.66 (0.56–0.77)	<0.000001

Trials have shown that one in four or five patients will respond to paclitaxel at relapse but the duration of response is short (median 6–9 months from the start of treatment for relapse) and none of these patients are cured (Trimble et al, 1993; Aravintinos et al, 1994; Athanassiou et al, 1994; Eisenhauer et al, 1994; Markman et al, 1994; Seewaldt et al, 1994; Thigpen et al, 1994; Uziely et al, 1994; Gore et al, 1995).

RECOMMENDATIONS

Patients with ovarian cancer should be managed in joint clinics by specialist multidisciplinary teams.

Standard chemotherapy for patients with ovarian cancer should include a platinum compound, and in general the preferred analogue is carboplatin.

Six cycles of treatment should usually be given; other options, such as prolonged treatment, high-dose regimens, or intraperitoneal chemotherapy, should only be administered within the context of clinical trials.

Treatment with single-agent carboplatin represents a reasonable option in certain situations, e.g. the frail and elderly or those for whom alopecia is unacceptable.

For the majority of women with ovarian cancer, the recommended chemotherapy should comprise a combination of paclitaxel with a platinum compound. On current evidence, the platinum compound used may be either cisplatin or carboplatin.

There are no data that justify delaying the use of paclitaxel until relapse, including those results obtained in the randomized study of Muggia et al (1997).

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APPENDIX

Meeting held on 6 February 1998 at the Royal Marsden Hospital, London, UK.

Attendees

Dr ME Gore (Chairman)	Royal Marsden Hospital, London
Prof AH Calvert (Speaker)	Newcastle General Hospital, Newcastle
Prof SB Kaye (Speaker)	Beatson Oncology Centre, Glasgow
Dr MJ Piccart (Speaker)	Jules Bordet Institute, Brussels
Dr H Thomas (Speaker)	Hammersmith Hospital, London
Dr M Adams	Velindre Hospital, Cardiff
Dr RE Coleman	Weston Park Hospital, Sheffield
Dr HM Earl	Addenbrooke's Hospital, Cambridge
Dr RJ Osborne	Poole General Hospital, Dorset
Dr TJ Perren	St James' University Hospital, Leeds
Dr CJ Poole	Queen Elizabeth Hospital, Birmingham
Dr JA Radford	Christie Hospital, Manchester
Dr GJS Rustin	Mount Vernon Hospital, Middlesex
Prof JF Smyth	Western General Hospital, Edinburgh

Non-attending co-signatories

Prof J Carmichael	City Hospital, Nottingham
Dr PI Clark	Clatterbridge Centre for Oncology, Wirral
Dr CJ Gallagher	St Bartholomew's Hospital, London
Dr TS Ganesan	Radcliffe Hospital, Oxford
Dr JD Graham	Bristol Royal Infirmary, Bristol
Dr PG Harper	Guy's Hospital, London
Dr GC Jayson	Christie Hospital, Manchester
Dr JA Ledermann	University College Hospital, London
Dr ML Slevin	St Bartholomew's Hospital, London
Dr PM Wilkinson	Christie Hospital, Manchester