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Recurrent Ovarian Carcinoma: Salvage Treatment with Platinum in Patients Responding to First-line Platinum-based Regimens

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DESPITE RESULTS obtained with cisplatin-based combination chemotherapy in advanced ovarian carcinoma, only 20–30% of patients will be disease-free at 5 years [1–3]. With few exceptions [4] salvage treatment of pretreated patients has yielded disappointing results [5, 6]. To evaluate whether ovarian cancer patients recurring after platinum-based initial therapy respond to retreatment with the same agents, 236 patients entered into two consecutive randomised trials [2, 7] were retrospectively reviewed.

38 patients receiving a median cumulative dose of initial platinum of 300 mg/m^2 (range 100–600 mg/m^2) with a treatment-free interval, that is, period of time between the completion of first-line treatment and salvage platinum-based therapy (TFI) > 3 months, had been retreated with a median number of four courses (range 2–12) of salvage therapy. Of 38 patients, 24 (63%) were treated with cisplatin, alone (CDDP, 100 mg/m^2 d. 1 q 28) or in combination (CDDP, 60 mg/m^2 d. 1 q 28); the remaining 14 patients (27%) received single-agent carboplatin (CBDCA, 400 mg/m^2 d. 1 q 28).

The overall response rate in 35 clinically/surgically evaluable patients was 49%: complete response (CR) 23% (8 patients), partial response (PR) 26% (9 patients), stable disease (SD) 37% (13 patients), progressive disease (PD) 14% (5 patients). Median duration of response was 5 months (range 2–18). Median survival was 11 months (range 2–43). Response was analysed according to TFI (Table 1). Objective response was observed in 27% of cases with TFI ≤ 12 months and 65% with TFI > 12 months, respectively (P 0.02). WHO Grade 2 neurotoxicity was observed in only 3 patients.

Ovarian cancer patients recurring after platinum-based initial therapy respond to salvage treatment with the same agents and response rate increases significantly in patients with longer TFI. However, the real impact on survival of salvage treatment has yet to be determined.

Table 1. Response rate according to TFI

TFI	≤12 months		>12 months	
CR	2	27%	6	65%
PR	2		7	
SD	7		6	
PD	4		1	

P = 0.02.

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P53 Immunostaining in Melanocytic Lesions

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IT HAS recently been suggested by Hall *et al.* that p53 immunostaining may be used as a marker of neoplastic disease in diagnostic cytopathology [1]. However, in a study of benign breast disease [2], Heyderman *et al.* concluded that immunopositivity for p53 protein is not a reliable indicator of malignancy.

The distinction between regular nevi and premalignant or malignant melanocytic lesions has been recognised as a difficult problem in diagnostic pathology, and various histopathological criteria for dysplastic nevi have been proposed [3]. Immuno-

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Table 1. Intensity of p53 immunostaining

Melanocytic lesions	Staining intensity 0/(+)	+	++/+++	Total
Regular nevi (n = 10)				
PAb-1801	0	7	3	10
PAb-240	0	8	1	9
Dysplastic nevi (n = 11)				
PAb-1801	2	7	2	11
PAb-240	4	6	1	11
Superficial spreading Melanoma (n = 12)				
PAb-1801	2	6	4	12
PAb-240	4	7	1	12
Nodular melanoma (n = 10)				
PAb-1801	1	6	3	10
PAb-240	0	6	3	9

histochemical detection of a reliable tumour marker would therefore be a great advantage.

Immunostaining of p53 protein was examined in 43 benign and malignant melanocytic lesions using two common antibodies (Oncogene Science, NY): PAb-1801 against human wild-type and mutant p53 and PAb-240 against mutant p53 protein. Formalin-fixed and paraffin-embedded routine specimens were used to examine the practical value of p53 immunostaining in diagnostic evaluation of these lesions.

Table 1 shows that there was no significant difference between benign, premalignant and malignant melanocytic lesions with respect to intensity of p53 immunostaining (χ^2 test), although some of the malignant melanomas showed a strong, dot-like staining in the cytoplasm of the tumour cells. As a rule, both nuclear and cytoplasmic positivity were present, corresponding to the results with fresh tissue [4]. These findings indicate that immunopositivity does not discriminate between benign and malignant melanocytic proliferations.

The positive staining in a large proportion of regular nevi was surprising. However, recent reports stress that deterioration of the p53 protein may be introduced by formalin fixation [5], and positivity may therefore be artificial and without biological significance in some cases. For these reasons, p53 immunostaining using the present antibodies on formalin-fixed, paraffin-embedded specimens should not be used in the routine evaluation of melanocytic lesions.

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Unexpected *Prad*-1 Amplification in Multiple Simultaneous Localisations of Squamous Cell Carcinoma of the Head and Neck

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PRAD-1 IS the most recent addition to the list of genes localised in 11q13 region. This gene may be equivalent to the cyclin D1 and it has been proposed that *Prad*-1 plays a key role in the regulation of cell growth [1]. Its clinical significance is not yet defined, but its amplification has been described in parathyroid adenomas, centrocytic lymphomas, breast adenocarcinomas, as well as in squamous cell carcinoma cell lines [2–5]. Analysed by polymerase chain reaction (PCR) techniques, *Prad*-1 is often coamplified with *hst*1 and *int*-2 genes, and in squamous cell carcinomas, these amplifications show a trend to be associated with poor prognosis [6]. In our previous multiparametric and prospective study, we found *Prad*-1 amplifications (with dopamine receptor gene as a control) in 27 out of 51 (53%) squamous cell carcinomas, and amplifications were related to small T volume and tumour vascularisation [7]. 7 other patients, presenting multiple simultaneous head and neck localisations, and biopsied at the principal tumour site, were analysed by PCR. Five tumours were amplified (three non-amplified normal

Table 1.

Patient number	Localisation	TNM (AJC-UICC 86)	Number of *Prad*-1 copies
5	Oral cavity and piriform sinus	T4N1	4
45	Hypopharynx and oesophagus	T1N0	2 (not amplified)
76	Oral cavity and oropharynx	T4N0	7
93	Oral cavity and oropharynx	T4N2c	4
114	Hypopharynx and oesophagus	T4N0	2 (not amplified)
120	Oral cavity and oropharynx	T3N0	12
141	Hypopharynx and oropharynx	T3N2c	7

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