1. Siegel JP, Puri RK. Interleukin-2 toxicity. *J Clin Oncol* 1991, **9**, 694–704.
2. Gore ME, Galligioni E, Keen CW, *et al.* The treatment of metastatic renal cell carcinoma by continuous intravenous infusion of recombinant interleukin- 2. *Eur J Cancer* 1994, **30A**, 329–333.
3. Webb DE, Austin HA III, Belldegrum A, *et al.* Metabolic and renal effects of interleukin-2 immunotherapy for metastatic cancer. *Clin Nephrol* 1988, **30**, 141–145.
4. Osborne RJ, Joel SP, Slevin ML. Morphine intoxication in renal failure: the role of morphine-6 glucuronide. *Br Med* 1986, **292**, 1548–1549.
5. Stiefel F, Morant R. Morphine intoxication during acute reversible renal insufficiency. *J Palliative Care* 1991, **7**, 45–47.
6. Fainsinger R, Schoeller T, Boiskin M, Bruera T. Palliative care round: cognitive failure and coma after renal failure in a patient receiving captopril and hydromophone. *J Palliative Care* 1993, **9**, 53–55.
7. Caraceni A, Martini C, Belli F, *et al.* Neuropsychological and neurophysiological assessment of the central effects of interleukin-2 administration. *Eur J Cancer* 1993, **29A**, 1266–1269.
8. Ellison MD, Povlishock JT, Merchant RE. Blood–brain barrier dysfunction in cats following recombinant interleukin-2 infusion. *Cancer Res* 1987, **47**, 5765–5770.
9. Denikoff KD, Rubinow DR, Papa MZ, *et al.* The neuropsychiatric effects of treatment with interleukin-2 and lymphokine-activated killer cells. *Ann Inter Med* 1987, **107**, 293–300.
10. Saris SC, Patronas NJ, Rosemberg SA, *et al.* The effect of intravenous interleukin-2 on brain water content. *J Neurosurg* 1989, **71**, 169–174.

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Prognostic Impact of DNA Content and a Classification System for Ploidy (AUER Classification) in Primary Fallopian Tube Carcinoma (FTC)

A.C. Rosen, A.H. Graf, G.W. Hacker and M. Klein

Nuclear DNA content (ploidy) has been correlated with biological behaviour in ovarian cancer and other solid tumours including breast, colon, lung and prostate cancer but there appears to be no data available on ploidy status in Fallopian tube carcinoma (FTC) [1, 2]. Recently, numerous reports have described methods of ploidy determination employing image cytometry (ICM) [3–6].

The present study describes, for the first time, ploidy analysis carried out in 61 cases of primary FTC using ICM. Since the so-called AUER classification has proved to be of prognostic impact in female breast cancer we evaluated the correlation between prognostic parameters of FTC as well as the prognostic influence of this classification system for this disease [7]. Patient characteristics are shown in Table 1.

Histological evaluation and grading for FTC was according to the criteria of Hu and colleagues [8]. For the staging of FTC, the latest FIGO classification was used [9].

For DNA ploidy analysis, three to four 30-μm-thick paraffin sections were cut from a representative area of each tumour and transferred into Eppendorf microvials. The disintegration procedure used is described in Mack and Hacker [6]. A standard Feulgen procedure was used for stoichiometric DNA staining [20]. In addition, the histogram types according to the AUER classification were assessed for prognostic value [6].

The mean age of the 61 patients included into this study was 61.8 years (range 37.3–80.2). Correlation analysis of ploidy and FIGO stage did not reveal any statistically significant relationship between these two parameters (Kendall's Tau—b 0.088, *P* value 0.457).

There was no statistically significant relationship between histologic grading and ploidy (Kendall's Tau—b 0.166, *P* value 0.171) or between AUER classification and FIGO stage (Kendall's Tau b: b 0.271, *P* value 0.814). Furthermore, there was no correlation between AUER classification and histologic garding (Kendall's Tau b: b = 0.120, *P* value 0.309).

The median survival time for all stages was 29.7 months (range 0.3–126). The median survival time for all euploid cases was 33.8 months (range 1.8–126.3) compared with 24.5 months (range 0.3–103.5) for the aneuploid cases; statistically significant (log rank, $P = 0.83$). Although patients with euploid tumours

Table 1. Patients' classification of 61 primary Fallopian tube cancers

	Total		Euploid		Aneuploid	
	No.	(%)	No.	(%)	No.	(%)
Stage						
I*	22	(36)	5	(23)	17	(77)
II*	13	(21)	4	(31)	9	(69)
III	17	(28)	3	(18)	14	(82)
IV	9	(15)	1	(11)	8	(89)
Grade						
G1	16	(26)	5	(31)	11	(69)
G2	22	(36)	5	(23)	17	(77)
G3	23	(38)	3	(13)	20	(87)
Ascites						
Positive	15	(25)	3	(20)	12	(80)
Negative	46	(75)	10	(22)	36	(78)
Adjuvant therapy						
Radiation	19	(31)	5	(26)	14	(74)
Chemotherapy	32	(53)	5	(25)	24	(75)
None	10	(16)	—	—	10	(100)
Surgical procedure						
BSO + TAH + omentectomy + lymph nodes	37	(61)	10 (27)	27 (73)		
BSO + TAH + omentectomy	24	(39)	3	(14)	21	(86)
Total	61	(100)	13	(100)	48	(100)

* 15 patients showed cancer confined to the adnexa and/or the uterus but did not undergo retroperitoneal lymphadenectomy.

Correspondence to A.C. Rosen.
A.C. Rosen and M. Klein are at the Department of Obstetrics & Gynecology, SMZ-Ost/Danubehospital, Langobardenstraße 122, Vienna; and A.H. Graf and G.W. Hacker are at the Department of Obstetrics and Gynecology and Pathology, Salzburg General Hospital, Austria.
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in stage I and II showed a relatively better median survival time of 41.5 months compared with patients with aneuploid tumours, this was not statistically significant (log rank, $P = 0.59$). For stage III and IV patients with euploid DNA median survival was 27.4 months compared with 20.8 months for patients with aneuploid tumours (log rank, $P = 0.40$). The 75th quantile (median survival was not reached) for tumours according to AUER type I and II was 41.4 months (mean survival time 81.2 months), whereas patients in AUER type III and IV showed a 75th quantile of 19.4 months (median = 29.2; mean = 43.1; $P = 0.07$).

We observed aneuploid DNA in 79% of cases. This high incidence of aneuploid tumours was consistently found among all FIGO subgroups as well as among the different groups of histological grading. However, we did not observe any correlation between the presence of aneuploid tumours and more advanced FIGO stages or more dedifferentiated tumours.

These findings are similar to those made by Longin and colleagues in breast cancer [10]. The high incidence of aneuploid DNA content in FTC patients is in agreement with our observations of a high rate of anaplastic tumours (Rosen *et al.*, personal communications). Although these examinations by light microscopy provided evidence for the high rate of proliferation found in FTC tumours, the determination of DNA content by flow cytometry has confirmed these findings more objectively.

Caspersson and colleagues [7] used the AUER classification in breast cancer as a prognostic factor and we wanted to evaluate this classification system for FTC. Although a strong trend was observed in the survival analysis ($P = 0.07$), there was no statistically significant difference and so we cannot recommend routine determination of ploidy in FTC in the clinical setting.

1. Seckinger D, Sugarbaker E, Frankfurt O. DNA content in human cancer. *Arch Pathol Lab Med* 1989, **113**, 619–626.
2. Erhardt K, Auer G, Björkholm E, *et al.* Prognostic significance of the nuclear DNA content in serous ovarian tumors. *Cancer Res* 1984, **44**, 2198–2202.
3. Falkmer U. *Methodological Aspects on DNA Catometry*. Thesis, Karolinska Hospital, Stockholm, 1989, 171.
4. Gurley AM, Hidvegi DF, Bacus JW, Bacus S. Comparison of the Papanicolaou and feulgen staining methods for DNA quantification by image analysis. *Cytometry* 1990, **11**, 468–474.
5. Berchuk A, Boente MP, Kerns BJ, *et al.* Ploidy analysis of epithelial ovarian cancers using image cytometry. *Gynecol Oncol* 1992, **44**, 61–65.
6. Mack D, Hacker GW. Image cytometry of DNA ploidy. In Gu J, Hacker GW, eds., *Modern Analytical Methods in Histology*. New York, Plenum Press, 1994.
7. Caspersson TO, Auer G, Fallenius A, Kudynowski J. Cytochemical changes in the nucleus during tumour development. *Histochem J* 1983, **15**, 337.
8. Hu CY, Taymor ML, Hertig AT. Primary carcinoma of the Fallopian tube. *Am J Obstet Gynecol* 1950, **59**, 58–67.
9. Creasman WT. Revision in classification by the International Federation of Gynecology and Obstetrics. *Am J Obstet Gynecol* 1991, **167**, 857–858.
10. Longin A, Fontaniere B, Pinzani V, *et al.* An image cytometric DNA-analysis in breast neoplasms. Parameters of DNA-aneuploidy and their relationship with conventional prognostic factors. *Pathol Res Pract* 1992, **188**, 466–472.

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Phase II Study of 4'Epirubicin in Advanced Squamous Cell Oesophageal Cancer

M. Spielmann, D. Gandia, K. Fizazi, T. Guillot, E. Cvitkovic, L. Kayitalire, T. Girinsky, D. Elias, P. Rougier and J. Kac

Squamous cell carcinoma of the oesophagus is associated with poor prognosis. Over the past decade, clinical research has focused on finding useful chemotherapy and integrating it with local approaches [1, 2]. Response rates are in the 15–25% range with single-agent chemotherapy, and between 14 and 64% with combination chemotherapy [3]. Despite these higher response rates, survival remains unchanged.

Anthracyclines, particularly 4'epirubicin, have not been fully explored in this disease [4]. However, Kolaric and associates showed interesting results using this class of agents in combination with radiation therapy [5, 6]. With the interesting results of these trials in mind, we performed a phase II trial of 4'epirubicin followed by hyperfractionated radiotherapy for non-metastatic inoperable patients.

14 previously untreated patients bearing histologically-proven and measurable disease were entered in this study. Patients' characteristics are shown in Table 1.

Treatment consisted of two cycles of 4'epirubicin administered at a dose of 90 mg/m^2 by intravenous bolus injection, every 3 weeks. The dose was reduced by 17% (15 mg/m^2) if grade 4 myelosuppression occurred and by 28% (25 mg/m^2) in case of fever. A third cycle was given in the absence of progressive disease or a clinical deterioration status. Three weeks after this third chemotherapy cycle, the non-metastatic patients began the hyperfractionated and accelerated radiotherapy delivered by a linear accelerator with 18 MeV photons. The total dose delivered was 60 Grays, or 65 Grays if progression occurred during chemotherapy. Evaluation was performed 8 weeks after the end of radiotherapy.

Neutropenia > grade 2, according to WHO criteria [7], was found in 11 patients, 4 of them presenting fever that required hospitalisation. Other toxicities included one anaemia grade 3, one emesis grade 3 and alopecia in 57% of the patients. Radiotherapy was well tolerated: one oral mucositis grade 3, using RTOG-EORTC scoring for tolerance to radiotherapy [8].

3 metastatic patients presented clinical response to chemotherapy. One female presented a partial response (PR) ≥ 50% of

Correspondence to M. Spielmann.
M. Spielmann, D. Gandia, K. Fizazi, T. Guillot, E. Cvitkovic, L. Kayitalire, P. Rougier and J. Kac are at the Department of Clinical Oncology; T. Girinsky is at the Department of Radiotherapy; and D. Elias is at the Department of Surgical Oncology, Institut Gustave-Roussy, 39 rue Camille Desmoulins, 94805 Villejuif Cedex, France.
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