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.

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European Journal of Cancer Vol. 30A, No. 12, pp. 1908–1909, 1994.

0959–8049/94 $7.00 + 0.00

0959-8049(94)00254-1

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

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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

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Revised 10 June 1994; accepted 24 June 1994.

Table 1. Patients' characteristics

No. of patients entered	14
Mean age years (range)	59 (45–70)
Male/female	13/1
Mean Karnofsky index (range)	80 (50–90)
Squamous cell carcinoma (SCC) histology	14
Well differentiated	9 (64%)
Moderately differentiated	4 (29%)
Poorly differentiated	1 (7%)
Tumour localisations	
Upper third	3 (21%)
Middle third (MT)	8 (57%)
Lower third (LT)	2 (14%)
MT + LT	1 (7%)
Tumour staging (AJC 1986)	
T1	1 (7%)
T2	8 (57%)
T3	5 (36%)
Evolutive pattern	
Locoregional (LR) only	8 (57%)
LR + metastases (MTS)	6 (43%)
Metastatic deposits	
Lung + bone + liver	1
Lung + bone	1
Lung + liver	2
Lung alone	1
Liver alone	1

7 months duration [response rate = 7%, (range 0.18 – 33.8%)], and 2 other patients achieved short-lived minor responses (2 months). 5 patients had stable disease. No patient responded on their primary tumours. The median survival calculated by the Kaplan–Meier method is 6 months (range 2–36).

The fact that 13 patients had bulky primary tumours (T2/T3) may explain the local chemotherapy results. The lack of a more objective response made us stop the accrual at 15 patients. The only patient with PR had a particular clinical presentation: she was the only female and the only patient with a poorly differentiated tumour.

In conclusion, we obtained similar results with epirubicin as those obtained with doxorubicin as single agent in this indication [3]. This schedule has minimal activity. If anti-tumoral activity may still be expected for this drug in advanced oesophageal cancer, a different set of eligibility criteria is essential, in terms of lower tumour burden and taking into account the initial performance status.

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European Journal of Cancer Vol. 30A, No. 12, pp. 1909–1910, 1994.

0959–8049/94 $7.00 + 0.00

0959-8049(94)00336-X

Pilot Study of High Dose Fenretinide and Vitamin A Supplementation in Bladder Cancer

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THE PRESENCE of moderate to severe dysplasia in the bladder mucosa surrounding a papillary tumour has been recognised as the major determinant of progression to muscle-invasive cancer [1]. Since retinoids can inhibit bladder carcinogenesis in rodents [2], the systemic use of these molecules after tumour resection appears rational in an attempt to arrest or slow the process of field cancerisation. Inasmuch as preclinical data suggest a dose-dependent activity of retinoids [3], we performed a pilot study of dose intensification of the synthetic retinoid fenretinide (N-4-hydroxyphenylretinamide or 4-HPR) in patients with recurrent superficial bladder cancer. However, since administration of 4-HPR induces a dose-dependent decrease of plasma retinol, which may account for diminished dark-adaptation [4], a low dose vitamin A supplementation was initiated in conjunction with the retinoid dose escalation.

7 patients, part of a phase IIa trial previously described [5], were included in the pilot study. They had been treated with 4-HPR (R.W. Johnson Pharmaceutical Institute, Spring House, Pennsylvania, U.S.A.) at the conventional dose of 200 mg/day (with a monthly 3-day drug interruption) for a median of 19 months (range 18–33). The dose was escalated to 400 mg/day plus oral retinyl acetate (Arovit, Roche, Milan, Italy) at the dose of 100 000 I.U. (2 tablets) every other day. The median treatment time with this regimen was 14 months (range 12–16) and the main patient characteristics were: median age, 67 years (range 29–79); male/female, 6/1: highest stage (UICC criteria), pT1 G1, 1, pT1 G2, 4, pT1 G3, 2; previous intravesical treatment, BCG,

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Revised 12 Aug. 1994; accepted 16 Aug. 1994.