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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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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Table 1. Effects of fenretinide on dark-adaptometry

	Standard dose	High dose + vitamin A supplementation
Cone threshold*	4.5 ± 0.1	4.3 ± 0.6
Time to cone–rod break (min)	12.3 ± 6.7	4.8 ± 1.5†
Rod threshold*	3.6 ± 0.7	2.6 ± 0.4†

*Expressed as log U picostilbs (psb).
Normal values are, respectively: <5 log U psb, <9 min, <3.5 log U psb.
†$P < 0.05$ compared with standard dose (t-test).

5 cases, mitomycin-C, 2 cases. The median interval between the last instillation and the beginning of the phase IIa study was 13 months (range 8–39).

Toxicity other than diminished dark adaptability was mild and consisted of skin dryness, 2 cases; eye dryness, 2 cases; ungeual distrophy, 1 case; increase in triglicerides, 1 case; increase in gamma glutamyl transpeptidase (γGT) 1 case; diarrhoea, 1 case. The effects on dark-adaptometry [4] of the combination regimen compared with the standard dose of 200 mg are reported in Table 1. Normalisation of time to cone–rod break and final rod threshold (the most sensitive indicator of rod retinal function) was observed with the new regimen.

Interestingly, there was a reduction in the rate of recurrences (number of recurrences/person-months of follow-up) when the total 4-HPR intervention period (200+400 mg) was compared with the preretinoid period: 0.025 (5/196) versus 0.094 (21/223), respectively ($\chi^2 = 9.81$, $P < 0.01$). Since 4-HPR enhances immunoresponse both *in vitro* [6] and *in vivo* [7], an interaction with BCG treatment cannot be excluded.

In conclusion, the results of this pilot study suggest that treatment with high dose 4-HPR plus vitamin A supplementation is feasible, relatively non-toxic even in a cohort of elderly patients and, more importantly, can prevent the occurrence of diminished dark adaptation. Since ophthalmologic alterations have so far prevented investigation of this compound at doses higher than 300 mg [8–10], our study provides evidence that vitamin A supplementation is the simplest, most logical way to overcome this secondary effect. Further studies are required to elucidate whether the addition of vitamin A may interfere at the molecular level with the mechanism of action of 4-HPR, which is presently still unknown.

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Correction

Influence of dexniguldipine-HCl on rhodamine-123 accumulation in a multidrug-resistant leukaemia cell line: comparison with other chemosensitisers—This paper by R. Boer, S. Haas and A. Schödl was published in *The European Journal of Cancer*, Vol. 30A, No. 8, pp. 1117–1123, 1994. Owing to an editorial error, a mistake was published in this paper. On p. 1119, third paragraph, lines 1–4, the reference to Figure 4 is incorrect, and should be Figure 6. Therefore, the paragraph should read "Figure 5 shows the respective concentration–response curves at pH 7.8 for quinidine, cyclosporin A and SDZ PSC 833 and in Figure 6 the data for amiodarone, dipyridamole and verapamil are presented". We apologise to the authors for this error.