prostate, NPY immunoreactivity has been reported in autonomic nerves, but the functions of NPY in the prostate are currently unknown. It has been suggested that NPY in the prostate could act either to modulate sympathetic stimulation of prostate contraction or to modulate the effects of VIP and/or other neuropeptides/transmitters on prostate epithelial cells [10]. In our study, NPY immunoreactive cells were found in epithelial cells, numerous nerve fibres, and carcinoma and hyperplastic epithelial cells. The role of NPY contained in prostate glandular cells is unknown, but may include a control function in hormone secretion, contractility and/or blood flow.

VIP is another peptide usually found in central and peripheral nervous systems, including the male genitalia, and acts as a potent vasodilator [11]. In our study, VIP was found abundantly in autonomic nerves close to the prostate acini and may act on prostate epithelial cells shown to contain VIP receptors. cAMP is produced in response to VIP in the rat prostate gland. The effects of VIP on normal human prostate epithelial cells have not been studied [10]. In addition to nerve fibres, we found VIP immunoreactive carcinoma cells in normal and hyperplastic glandular cells. It cannot be concluded whether the VIP-like peptide demonstrated in the epithelial cells is identical to the VIP found in nerves, or if it is an immunologically related substance.

The production of regulatory peptides by the prostate is a phenomenon which might have diagnostic, prognostic and therapeutic implications for disease of this gland. The findings of VIP and NPY immunoreactive substances in NE differentiated prostate carcinoma cells may be of significance in understanding the possible roles these cells play in hyperplastic and malignant prostate tissue.

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Carboplatin and 5-Fluorouracil in Squamous Cell Carcinoma of the Head and Neck Previously Responding to Cisplatin and 5-Fluorouracil

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SECOND-LINE CHEMOTHERAPY regimens give only sporadic responses in head and neck cancer, while toxicity is generally high due to the poor conditions of these patients. Therefore, outside clinical trials, only supportive care may be a reasonable choice in this advanced setting.

We treated 13 male patients with a second-line chemotherapy regimen consisting of carboplatin, 100 mg/m^2/day in a 30 min i.v. infusion on days 1, 3, 5 and 5-fluorouracil (5-FU), 200 mg/m^2/day i.v. bolus for 5 consecutive days, every 21 days. Patients' characteristics are reported in Table 1. All patients had previously responded to a cisplatin/5-FU combination (minimum cumulative dose of cisplatin for each patient: 400 mg/m^2) given for relapsed disease (4 patients) or in a front-line chemoradiotherapy programme for unresectable disease (9 patients). The median interval from the end of the first-line chemotherapy was 9 months.

Thirty-nine courses were administered (median 3; range 1–4). The tolerance to the carboplatin/5-FU regimen was good, with thrombocytopenia being the most frequent side-effect (5 out of 13 patients). It was severe (grade III–IV) in 4 patients (31%) but no episode of bleeding was recorded and platelet transfusion was not necessary. 3 patients (23%) had grade I–II leucopenia and 2 (15%) grade II anaemia. Non-haematological toxicity was mild and consisted of grade I–II nausea and vomiting in 2 patients (15%) and grade I transitory renal toxicity in 1 patient (serum creatinine 2.2 mg/dl after the second course). Because of haematological toxicity, 13% (5/39) of the chemotherapy courses were delayed by 1 week, 18% (7/39) by 2 weeks.

A partial response was observed in 3/13 patients (23%). Stable disease was obtained in 8/13 patients (62%), while 2/13 (15%) progressed during the treatment. Median overall time to progression was 9 weeks (range 4–43). The duration of response was 21, 34 and 43 weeks, respectively. The

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Table 1. Patient's characteristics

Median age (years) (range)	63 (41–71)
Median ECOG PS (range)	1 (0–3)
Hystological type	
Squamous cell	13
Site of primary	
Nasopharynx	2/13
Oral cavity	1/13
Oropharynx	5/13 (1)
Larynx	3/13 (1)
Hypopharynx	2/13 (1)
Previous treatments	
CT + RT	8/13 (1)
S → CT + RT	2/13
CT + RT → S	1/13
S → RT → CT	2/13 (2)
Site of relapse	
T	6/13 (2)
N	3/13
TN	1/13
M	3/13 (1)

S, surgery; CT, chemotherapy; RT, radiotherapy.
The number of patients who responded to carboplatin and 5-FU are in parentheses.

characteristics of the patients who responded to carboplatin and 5-fluorouracil are shown in the table.

The overall antitumour activity (23% response rate) observed with carboplatin and 5-fluorouracil at the doses employed in the present study can be considered satisfactory considering that in these chemotherapy-pretreated patients, the possibility of reaching a response with a second-line regimen is generally extremely low [1] and that this combination, in pretreated but chemotherapy-naive patients, gives an average response rate of 26% [2]. Moreover, in our experience, the efficacy of a second-line chemotherapy is particularly low when given to patients already treated with cisplatin. In a previous trial, with a methotrexate-based regimen, all 10 patients who had previously responded to cisplatin and 5-FU progressed [3], while in the present study only 2/13 patients progressed under treatment.

In conclusion, our experience suggests that, in clinical practice, when previous responsiveness to cisplatin and the long chemotherapy-free interval lead the physician to offer a second-line chemotherapy to heavily pretreated patients, a further platinum-based chemotherapy can be considered. In this line, a carboplatin/5-FU combination may be a reasonable choice in terms of toxicity/activity ratio.

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Oral Glutamine in the Prevention of Chemotherapy-induced Gastrointestinal Toxicity

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GLUTAMINE (GLN) is the most abundant amino acid in the body [1] and the main energy fuel for enterocytes [2, 3]. Catabolic stress markedly increases the needs for GLN [2, 4] which becomes an essential substrate for damaged intestinal mucosa. The observation that the mucosal brush border doubles GLN uptake in neoplastic diseases, while GLN extraction from blood is significantly reduced [5], prompted us to test oral administration of GLN in adult acute myelogenous leukaemia patients in an attempt to reduce intestinal toxicity induced by combined intensive chemotherapy. The morbidity (nausea, vomiting, abdominal pain, severe diarrhoea, ileus, ileotyphlitis) and mortality secondary to chemotherapy-induced gastro-intestinal toxicity are relatively high [6] and warrant new, cost-effective supportive care measures.

Based on previous clinical studies, in which the administration of 16–30 g/day of GLN was proven safe [7–9], a dose of 18 g of GLN (6 g three time daily, orally in water during meals) was started on day 3 prior to chemotherapy initiation and discontinued if neutrophils recovered (polymorphonuclear leucocytes >500 ml) or parenteral nutrition was initiated. 14 patients (9 M, 5 F), admitted to the Hematology, Department of Human Biopathology of the University of Rome 'La Sapienza', from September 1994 to January 1995 for first intensive remission induction, receiving the EORTC-GIMEMA AML10 protocol (containing either idarubicin or mithoxantrone or daunorubicin in combination with etoposide and cytarabine) were studied. Three patients discontinued GLN early, 2 (14%) because of nausea, 1 for psychological problems, and withdrew from the study. Of the 11 evaluable patients (6 M, 5 F, age range 25–54 years), 5 (45%) continued GLN until neutrophil recovery (median 31 days, range 27–39); 6

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