(6/28) of the patients with an elevated AP and normal bone scan developed soft tissue metastases within 9 months after nephrectomy and died subsequently. They had prolonged elevated AP levels until death.

In the group of patients with a positive bone scan (8), 5 complained of skeletal pain. The painful locations were confirmed on the bone scan. In the group of patients with a normal bone scan, there was no patient with complaints of skeletal pain as a presenting or associated symptom.

AP is a mixture of iso-enzymes which are mainly produced in the intestine, liver, placenta, kidney and bone. In bone, it is produced by osteoblasts and excreted in the bile. Elevated AP is present during pregnancy, in growing children and in patients with bone disease and hepatobiliary disease. AP as a prognostic marker for disease progression in RCC is controversial. An explanation for the high rate (90%) of patients with an elevated AP and normal bone scan might be the association of RCC with paraneoplastic syndromes. Few tumours are association with such a diversity of paraneoplastic syndromes as RCC, and the incidence of these systemic features in RCC patients is relatively high. Elevated AP was reported in 14.7% (64/434) of RCC patients and abnormal liver function tests (Bilirubin, SGOT, SGPT and SAP) in 15% (60/400) [5]. This syndrome of elevated liver function tests is associated with reversible non-metastatic hepatic dysfunction and is referred to as Staufer syndrome. The aetiology is unknown and, in the absence of hepatic metastases, these abnormal liver function tests revert to normal after nephrectomy. In the future, it may be helpful to determine the AP iso-enzymes to increase the sensitivity of AP, especially the bone specific fraction which is produced by osteoblasts. Another useful approach to determine whether an elevated AP level reflects hepatic or bone disease is to measure a related enzyme, 5-'nucleotidase, which is produced by hepatic canalicular microvilli but is not found in bone.

A routine pre-operative bone scan in RCC patients without skeletal pain is not indicated. In RCC patients, the chance of having bone metastases at presentation is small, even with an elevated AP, and these metastases are often symptomatic. AP is often elevated without evidence of (bone) metastases and can normalise after nephrectomy. The only indication for a bone scan in staging RCC patients is, therefore, skeletal pain.

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Thyroid Cancer: Different Outcomes to Chemotherapy According to Tumour Histology

L. Biganzoli, V. Gebbia, L. Maiorino, P. Caraci and A. Iirillo

I.T.M.O., Division of Medical Oncology B, Istituto Nazionale per lo Studio e la Cura dei Tumori, Via Venezian 1, 20133 Milan, Italy

IN THE MANAGEMENT of thyroid carcinoma, doxorubicin alone, or in combination with cisplatin, is considered the most active regimen, although it gives unsatisfactory response rates with significant side-effects [1–3]. Epirubicin is endowed with a spectrum of activity similar to doxorubicin and an equivalent response rate with less cardiotoxicity and acute myelosuppression [4, 5]. Carboplatin produces less nephrotoxicity, neurotoxicity and vomiting than cisplatin [6, 7].

In an attempt to identify a well tolerated regimen which does not affect patients' quality of life, the association of epirubicin 75 mg/m^2 given by i.v. (intravenous) bolus on day 1, and carboplatin 100 mg/m^2 by 30 min infusion on days 1–3, repeated every 28 days, was proposed as first-line chemotherapy to patients aged $\leq$ 70 years, ECOG performance status $\leq$ 2, affected by histologically proven thyroid carcinoma (except medullary) not suitable for surgery or radioactive iodine. Eight cycles were planned except for the cases showing progressive disease. Response and toxicity were evaluated according to WHO-UICC criteria [8].

20 patients entered the study: all were suitable for the evaluation of response and toxicity. 10 patients were male and 10 female, the median age was 64 years (range 35–70), ECOG performance status was 0 in 8 patients and 1 in 12. Sites of disease were thyroid (8 patients), local relapse (7), regional nodes (12), distant nodes (3), lung (12) and bone (1). 12 patients were pretreated with locoregional surgery, 5 with radioactive iodine and 2 with radiotherapy. A total of 83 cycles of chemotherapy have been delivered, with a median of four cycles per patient (range 1–8). Treatment was well tolerated. No cases of grade 4 toxicity occurred; grade 3 anaemia occurred in 15% of patients, leucopenia was observed in 5% and nausea/vomiting in 5%. Alopecia was complete in 7 patients.

2 male patients achieved complete responses both lasting 12+ months: they were 70 years old with disease limited to the regional nodes, and in one case, local relapse. In these cases, the time to the best response was 5 and 3 months, respectively. One patient achieved a partial response lasting 4 months; 7 patients had stable disease for a median duration of 9 months (range

Correspondence to E. Bajetta.
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Table 1. Responses according to histological type

Tumour type (No. pts)	Tumour responses (%) CR	PR	NC	PD
Anaplastic (11)	2 (18)	-	1 (9)	8 (73)
Non-anaplastic (9)	-	1 (11)	6 (67)	2 (22)

CR, complete remission; PR, partial remission; NC, no change; PD, progressive disease.

4–20). 10 patients progressed and 50% of these had clear disease progression after only one cycle of chemotherapy. Table 1 shows antitumour activity according to the histological type. Median survival was 2 months (range 0.5–17+) in patients with anaplastic carcinoma and 22 months (range 3–38+) in the non-anaplastic carcinoma.

The association of epirubicin and carboplatin was well tolerated, but an overall response rate of 15% calls for a need to identify new drugs or new approaches for the treatment of thyroid carcinoma, especially considering that such tumours comprise different morphologies, natural histories and prognoses [9, 10]. Consequently, it is important to consider the histological type. In our analysis, we considered two different subgroups, anaplastic and non-anaplastic tumours, which showed different relationships with chemotherapy.

It appears that chemotherapy did not impact on the natural history of non-anaplastic carcinomas because 67% of treated patients had stable disease, with a median duration of 10 months (range 4–20) and a median survival of 22 months (range 12+–38+), and no complete remissions were obtained in this subgroup of patients. However, patients with anaplastic carcinoma might benefit from chemotherapy as suggested by the 2 complete remissions lasting more than 1 year in this study, with a median survival of 2 months. Nevertheless, in the same group, 45% of patients experienced early progression, with a median survival of 41 days (range 13–58).

Therefore, there is a need to select patients with non-anaplastic carcinoma avoiding treatment of asymptomatic cases with indolent disease. Clinical and biological prognostic factors for response must be identified for anaplastic carcinomas because of their bimodal response to treatment.

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Phase II Study of Intensive CEV (Carboplatin, Epirubicin and VP-16) Plus G-CSF (Granulocyte-colony Stimulating Factor) in Extensive Small Cell Lung Cancer

C. Gridelli,[1] F. Perrone,[3] M. D'Aprile,[4] A. Rossi,[2] S. Palmeri,[5] C. Curcio,[6] E. Veltri,[4] G. Ianniello,[7] V. Lorusso,[8] G. Palmieri,[2] L. Rinaldi,[1] S. De Placido,[2] C. Gallo[3] and A.R. Bianco[2] on behalf of GOCSI Gruppo Oncologico Centro-Sud-Isole

[1]Divisione di Oncologia Medica B, Istituto Nazionale Tumori, Napoli; [2]Cattedra di Oncologia Medica, Facoltà di Medicina, Università "Federico II", Napoli; [3]Centro Elaborazione Dati Clinici del Mezzogiorno, CNR-ACRO; [4]Divisione di Oncologia Medica, Ospedale "S Maria Goretti", Latina; [5]Cattedra di Oncologia Medica, Policlinico "Giaccone", Palermo; [6]Divisione di Chirurgia Toracica, Ospedale "Ascalesi", Napoli; [7]Servizio di Oncologia Medica, Ospedale Civile "G. Rummo", Benevento; and [8]Divisione di Oncologia Medica, Istituto Nazionale Tumori, Bari, Italy

THE DOSE intensity of chemotherapy seems to be crucial in a number of responsive tumours [1]. Earlier studies on high dose

Correspondence to C. Gridelli.
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