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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.

1. Gottlieb JA, Hill CS Jr, Ibanez ML, Clark RL. Chemotherapy of thyroid cancer: an evaluation of experience with 37 patients. *Cancer* 1972, **30**, 848–853.
2. Shimaoka K, Schoenfeld DA, DeWys WD, Creech RH, De Conti R. A randomized trial of doxorubicin versus doxorubicin plus cisplatin in patients with advanced thyroid carcinoma. *Cancer* 1985, **56**, 2155–2160.
3. Williams SD, Birch R, Einhorn LH. Phase II evaluation of doxorubicin plus cisplatin in advanced throid cancer: a Southeastern Cancer Study Group Trial. *Cancer Treat Rep* 1986, **70**, 405–407.
4. Cerosimo RJ, Hong WK. Epirubicin: a review of the pharmacology, clinical activity and adverse effects of an adriamycin analogue. *J Clin Oncol* 1986, **4**, 425–429.
5. Martoni A, Giovanni M, Tomasi L, *et al.* Therapeutic efficacy and tolerability of 4' epidoxorubicin in patients with advanced solid tumors. *Cancer Chemother Pharmacol* 1984, **12**, 179–182.
6. Van Echo DA, Egorin MJ, Aisner J. The pharmacology of carboplatin. *Semin Oncol* 1989, **16** (Suppl. 5), 1–6.
7. Muggia FM. Overview of carboplatin: replacing, complementing and extending the therapeutic horizons of cisplatin. *Semin Oncol* 1989, **16** (Suppl. 5), 7–13.
8. *WHO/UICC Handbook for Reporting Results of Cancer Treatment.* WHO offset Publication No 48. Geneva, World Health Organization, 1979.
9. McKenzie AD. The natural history of thyroid cancer: a report of 102 cases analysed 10–15 years after diagnosis. *Arch Surg* 1971, **102**, 274–277.
10. Byar DP, Green SB, Dor P, *et al.* A prognostic index for thyroid carcinoma. A study of the E.O.R.T.C. Thyroid Cancer Cooperative Group. *Eur J Cancer* 1979, **15**, 1033–1041.

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