7. Miller AB, Hoogtrstaen B, Staquet M, Winkler M. Reporting results of cancer treatment. *Cancer* 1981, 47, 207–214.
8. Gehan EA. The determination of the number of patients required in a preliminary and a follow-up trial of a new chemotherapeutic agent. *J Chron Dis* 1961, **13**, 146–153.
9. Muggia FM. Clinical activity in other tumors. In McGuire WP, Rowinsky EK, eds. *Paclitaxel in Cancer Treatment*. New York, Marcel Dekker, 1995, 329–338.

European Journal of Cancer Vol. 32A, No. 10, pp. 1823–1824, 1996.
Copyright © 1996 Elsevier Science Ltd. All rights reserved
Printed in Great Britain
0959–8049/96 $15.00 + 0.00

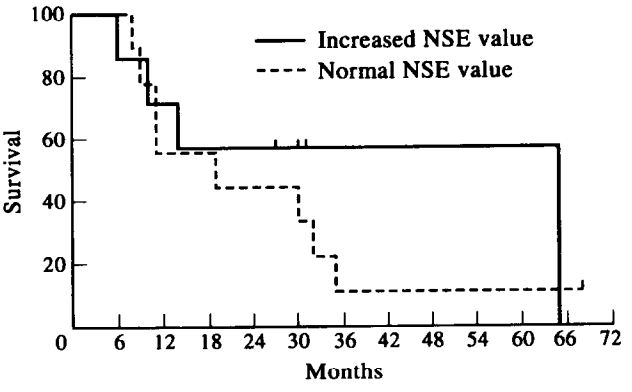

Figure 1. Overall survival according to initial NSE (neuron-specific enolase) value.

PII: S0959-8049(96)00165-7

Serum Neuron-specific Enolase (NSE) as a Tumour Marker for the Ewing's Sarcoma Family of Tumours

K. Fizazi, A. Le Cesne, N. Dohollou, S. Affaied, M. Spielmann and T. Le Chevalier

Department of Medical Oncology, Institut Gustave-Roussy, rue Camille Desmoulins, 94805 Villejuif, France

EWING'S SARCOMA and peripheral primitive neuroectodermal tumours (PNET) have recently been included in what has been designated the 'Ewing's sarcoma family of tumours' [1], because they share a common molecular pattern. Clinical features have recently been described in adults and they do not seem to differ from those found in children [2]. No serum tumour marker is currently available. These neoplasms commonly express neural differentiation: neuron-specific enolase (NSE) expression, as assessed by immunohistochemical analysis, is found in 15–58% of lesions [3–7]. However, controversial data exist concerning the prognostic value of NSE: Pinto and coworkers [3] reported a better outcome for patients with NSE expression, whereas other authors have not confirmed these results [4–6].

We assessed serum NSE in a series of 21 consecutive adult patients with Ewing's sarcoma or PNET, homogeneously treated in our institution. 13 were male and 8 were female. Ages ranged from 17 to 34 years (median: 21 years). 16 patients had localised disease, whereas 5 had metastases at presentation. 12 patients had Ewing's sarcoma of bone; 1, Ewing's sarcoma of soft tissue; 7, neuroepithelioma and 1, Askin's tumour.

Serum NSE was elevated (> 12.5 ng/ml) prior to therapy in 11 patients (52%), i.e. 7 of 16 patients with localised disease (44%) and 4 of 5 with metastatic disease (80%). Treatment consisted of neoadjuvant chemotherapy combining doxorubicin, ifosfamide, vindesine and cisplatinum, followed by surgery when possible, or radiotherapy. Of 11 patients, 9 with initially elevated NSE (82%) achieved a clinical response to primary chemotherapy. Of these 9, 7 had localised disease. In contrast, only 4 of 10 patients (40%) with initially normal serum NSE responded to therapy ($P < 0.2$).

After primary chemotherapy serum NSE was normal in 17 patients (81%) of whom 14 had localised disease. The remaining 4 patients with elevated serum NSE during the course of chemotherapy had a very poor outcome since all died within the first year of diagnosis. The number of cases with data available on histological response or serum NSE at relapse was insufficient for analysis. Overall survival curves of patients with localised disease according to initial serum NSE were calculated using the Kaplan–Meier method and are presented in Figure 1. Patients with initially raised NSE seemed to fare better long-term. However, statistical significance was not reached ($P = 0.54$), possibly because the number of cases was too small.

In conclusion, serum NSE is elevated prior to therapy in approximately 50% of patients with neoplasms belonging to the Ewing's sarcoma family of tumours. This tumour marker seems to be more frequently elevated in cases of metastatic disease and usually normalises during therapy. Patients with localised disease and elevated serum NSE are likely to achieve a better response to chemotherapy, although statistical significance was not reached in our experience. These findings require further studies for definitive conclusions.

Correspondence to K. Fizazi.
Received 10 Apr. 1996; accepted 23 Apr. 1996.

1. Horowitz ME, Malawer MM, Delaney TF, Tsokos MG. Ewing's sarcoma family of tumors: Ewing's sarcoma of bone and soft tissue and the peripheral primitive neuroectodermal tumors. In Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 2nd ed. Philadelphia, JB Lippincott, 1993, 162–165.
2. Fizazi K, Dohollou N, Spielmann M, *et al.* Adults with Ewing's sarcoma: a retrospective study of 146 cases. *ECCO* 8, 1995, 250.
3. Pinto A, Grant LH, Hayes FA, Schell MJ, Parham DM. Immunohistochemical expression of neuron-specific enolase and Leu 7 in Ewing's sarcoma of bone. *Cancer* 1989, **64**, 1266–1273.
4. Daugeard S, Kamby C, Sunde LM, Myhre-Jensen O, Schiodt T. Ewing's sarcoma. A retrospective study of histological and immunohistochemical factors and their relation to prognosis. *Virchows Arch A Pathol Anat Histopathol* 1989, **414**, 243–251.
5. Carter RL, al Sams SZ, Corbett RP, Clinton S. A comparative study of immunohistochemical staining for neuron-specific enolase, protein gene product 9.5 and S-100 protein in neuroblas-

toma, Ewing's sarcoma and other round cell tumours in children. *Histopathology* 1990, **16**, 461–467.
6. Fellinger EJ, Garin-Chesa P, Glasser DB, Huvos AG, Rettig WJ. Comparison of cell surface antigen HBA 71 (p30/32 MIC2), neuron-specific enolase, and vimentin in the immunohistochemical analysis of Ewing's sarcoma of bone. *Am J Surg Pathol* 1992, **16**, 746–755.
7. Dierick AM, Roels H, Langlois M. The immunophenotype of Ewing's sarcoma. An immunohistochemical analysis. *Pathol Res Pract* 1993, **189**, 26–32.

Acknowledgement—We thank Lorna Saint Ange for editing the manuscript.

European Journal of Cancer Vol. 32A, No. 10, pp. 1824–1825, 1996.
Copyright © 1996 Elsevier Science Ltd. All rights reserved
Printed in Great Britain
0959–8049/96 $15.00 + 0.00

PII: S0959-8049(96)00179-7

Transaxillary Access to Perform Hepatic Artery Infusion (HAI) for Secondary or Primitive Hepatic Tumours

C. Zanon[1] and M. Grosso[2]

[1]Service of Oncological Surgery, University of Turin; and [2]Institute of Radiology, University of Turin, Ospedale S. Giovanni Battista c.so Dogliotti 8, 10128 Turin, Italy

HEPATIC ARTERY infusion (HAI) to effect regional chemotherapy for metastases of colorectal cancer was first used at the beginning of 1980 with unexpected findings in terms of responses related to systemic chemotherapy. However, various trials have not been able to demonstrate a definite improvement in survival [1–5].

Recently, new clinical studies with new therapeutic protocols (HAI, HAI + systemic chemotherapy) [6–11] and new proposals to use HAI as an adjuvant or neoadjuvant [12–14], either in surgical or cryosurgical treatment, have renewed interest in this form of treatment for hepatic neoplasia and in particular, for hepatic metastases of colorectal tumours.

One of the main obstacles to the use of HAI is the fact that, in cases of metachronous metastases (the majority), regional chemotherapy is only possible after surgical intervention to isolate the gastroduodenal artery and the positioning of the tip of the catheter of the Port in the hepatic artery, with consequential creation of a subcutaneous pocket containing the Port. Based on the preliminary work of Japanese authors form the University of Chiba [15], who conceived the introduction of their own catheter coated with heparin on slow release, accessed by the left axillary artery and using a subcutaneous Port (carried out under local anaesthesia), we have conceived a system of introduction similar to theirs for the use of HAI, but using catheters already on the market for others uses.

Before the intervention, the patients were subjected to sonography of the superior and inferior abdomen and of the thorax, scintigraphy of the bones, colonscopy, a CT-scan with arteriography, all to exclude extrahepatic localisations of the neoplasm with consequential contra-indication to HAI, and to have a radiologically clear view of the flow of the hepatic artery that usually presents anatomical variations in some patients.

Our catheters and the Ports were implanted under local anaesthesia. The left axillary artery was punctured laterally approximately 2 cm from the border of the first rib with the help of colour doppler ultrasonography to avoid further puncturing of the same artery. After a suitable guidewire was been introduced, a Headunter catheter of 5 F allowed us to reach the hepatic artery, when necessary, embolising with Gianturco coils, the gastroduodenal artery or anomalous right or left hepatic arteries emergent of the aorta, the superior mesenteric artery or the left gastric artery, to avoid systemic diffusion of the drugs. After positioning the Headunter catheter and having threaded a suitable guidewire, we introduced a catheter of 5,8–6 F perfecting with the aid of a contrast agent the position of the catheter, noting the diffusion of the agent to all sections of the liver. Finally, a subcutaneous pocket was created under the clavicle with an incision of the skin as an inverted T to contain a Port or an Infusaid system. The catheter was filled with a solution containing 2000 U/l of Heparin. The patient was discharged the same day with a prescription for Enoxaparina 2000 U/l or Fragmin 2500 U/l every day.

Patients were examined routinely for both the response of the tumour and the functioning of the catheters, with a determination every 15 days of Dd, CRP, T.Bil, Gamma GT, ALP, AST, ALT, Na, K, Ca, Mg, leucocytes cont, Ht, PTL and a scintigraphy with marked albumin to verify the distribution of the drug in the liver. The patient was asked not to lift the left arm for a week.

Currently, we have implanted 12 catheters using this method in patients with hepatic metastases from a colorectal tumour. All function perfectly. The age range of the patient is 48–76 years. The Karnofsky Performance Status was above 60% for all. There have been no complications due to the method. The operations were conducted in day surgery and no conversion to an ordinary recovery has been necessary. In case of occlusion, dislocation or infection of the catheter, it could be replaced thus permitting the constant efficiency of the HAI. We removed the gallbladder in every patient who underwent rectocolectomy for colorectal cancer, to avoid chemical cholecystitis during chemotherapy. Given the low toxicity of the method and the possibility of substitution, we believe such a route of access should be followed in cases of synchronous metastases of colorectal cancer or in other tumours such as primitive tumours of the liver as suggested by the Japanese group [15].

Correspondence to C. Zanon at Cattedra di Chirurgia Generale-Servizio, di Chirurgia Esofaged ed Oncologica dell'Università di Torino, C.so Dogliotti 14, 10126 Torino, Italy.
Received and accepted 10 Apr. 1996.

1. Chang AE, Schneider PD, Sugarbaker PH, *et al.* A prospective randomized trial of regional vs systemic continuous 5-FU chemotherapy in the treatment of colorectal metastases. *Ann Surg* 1987, **206**, 685–693.