Anti-Cancer Drugs 2000, **11,** pp. 707–708

Case report

Biliary tract cancer: our experience with gemcitabine treatment

Francesco Verderame,[1] Pietro Mandina,[2] Francesco Abruzzo,[2] Michele Scarpulla[2] and Roberto Di Leo[1]

[1]Division of Internal Medicine, Service of Oncology and [2]Division of General Surgery, Azienda Ospedaliera 'Ospedali Civili Riuniti', 92019 Sciacca (Ag), Italy.

Biliary tract cancers are uncommon tumors, with a poor prognosis because most patients present an invasive cancer at diagnosis that makes them inoperable. Chemotherapy is a palliative treatment, but single drugs or combination schedules have demonstrated a response rate of 14–18%, with a duration of response of 8.5 months. We report a single center experience with gemcitabine in the treatment of patients with advanced biliary tract cancers. We report on four cases of chemonaive patients with advanced biliary tract cancers treated with gemcitabine 1 g/m q days 1, 8 and 15. After three cycles of treatment we observed one partial response and three stable disease (according to WHO criteria), with an increase in performance status and a complete relief of pain in all patients. The median time to progression observed was 10.7 months. Although this experience is limited to a small number of patients, it shows that gemcitabine appears to be worthy of clinical research in this neoplastic pathology and makes the drug a particularly interesting agent for investigation in patients with biliary tract malignancies. [© 2000 Lippincott Williams & Wilkins.]

Key words: Biliary tract cancer, gallbladder carcinoma, gemcitabine

Introduction

Biliary tract cancers are relatively uncommon tumors in western countries accounting for less than 1% of deaths from cancer in the US. However, it is a leading cause of cancer death in women in Chile and other Latin American countries, and it is increasing (11.6 to 16.2 deaths per 100 000 population for 1982 and 1991, respectively).[1] Because of their high mortality, these cancers represent a significant health problem.[2] Patients with gallbladder carcinoma are curable if at diagnosis the tumor is confined to the mucosa or muscular layer of the organ (T1 tumor, Stage 1, AJCC).[3] Unfortunately, at diagnosis most of the patients present with invasive, inoperable cancer, thus permitting only palliative treatment. Generally, the median survival from diagnosis is about 4 months. Five-year survival did not exceed 3% in the largest series of patients with inoperable gallbladder and bile duct cancer studied.[4] Although chemotherapeutic management of biliary tract cancer has rarely been studied systematically because of inadequate numbers of patients at separate institutions, responses to chemotherapy are generally uncommon and brief in duration.[5] Both single-agent and combination chemotherapeutic trials have demonstrated a response rate of 14–18% with a median duration of response of 8.5 months. The most effective agents studied are 5-fluorouracil and adriamycin.[4]

Based on (i) the poor experience in the management of biliary tract cancer, (ii) the published data indicating the efficacy of gemcitabine in patients with pancreatic cancer,[6] and (iii) the common embryologic origin of the exocrine pancreas and the gallbladder, we initiated a trial with gemcitabine in all patients that arrived at our center with a histologic diagnosis of biliary cancer.

Case reports

From July 1996 to September 1998, we enrolled four patients with a diagnosis of adenocarcinoma of the biliary tract. Of these, three had carcinoma of the gallbladder (two women and one man) and the other had a cholangiocarcinoma (a woman). The median age of the patients was 63 years (57–76). Two of the patients with a diagnosis of gallbladder carcinoma had undergone exploratory laparotomy that indicated

Correspondence to F Verderame, Oncology Service, Azienda Ospedaliera 'OCR', Via Figuli 2, 92019 Sciacca (Ag), Italy.
Tel: (+39) 925 962281; Fax: (+39) 925 21241;
E-mail: vrdonc@libero.it

inoperable cancer with peritoneal effusions. The third patient presented with numerous liver metastases upon computed tomography (CT) scan. At presentation, they had hyperbilirubinemia (2–4 times the normal range), and high alkaline phosphatase (440, 560, 890 and 1050 UI/l), γ-GT (720, 940, 1230 and 1520 UI/l) and Ca 19.9 levels (119, 230, 420 and 560 mU/l). The patient with cholangiocarcinoma was diagnosed with a needle liver biopsy. This patient had undergone a gastrectomy for a MALToma 2 years before this evaluation and an intrahepatic mass was revealed during the follow-up.

After laparatomy with extended cholecystecomy and hepaticojejunostomy, all the patients with gallbladder cancer were treated with gemcitabine 1 g/m^2 over 30 min weekly for 3 weeks followed by 1 week of rest. After three cycles, all patients underwent a re-evaluation and presented with an increased performance status, a complete relief of pain and a good quality life. After three courses of treatment, a CT scan showed a partial response in the patient with cholangiocarcinoma and a stable disease (according to WHO criteria) in the other three patients (a 25% decrease of disease maximum diameters in a patient and no change in the other two patients). The cholestatic index of all the patients was reduced. Bilirubinemia fell in the normal range, the alkaline phosphatase range was 90–410 UI/l, while the γ-GT range was 70–570 UI/l. The Ca 19.9 level fell within the normal range (25 mU/l) in the patient with cholangiocarcinoma and was reduced by 45% of the initial value in the other patients (103, 189 and 240 mU/l). All patients continued treatment with the prescribed schedule with no adverse events and good quality of life until clinical progression. Median time to progression for all patients was 10.7 months (range 7–15). At the time of disease progression, the performance status dramatically worsened for all patients and all died within 25 days (15–40 days).

The role of medical treatment in advanced biliary tract cancer is still unclear, because there is a lack of clinical trials with large numbers of patients. In our experience, gemcitabine given as palliative treatment in chemonaive patients revealed good tolerability and was an effective drug in the management of biliary tract cancer. Although our experience is limited to a small number of patients, all of the patients had clinical and objective responses (reduction or stable disease) with good control of symptoms for a longer time as compared to studies using other agents. This experience and published data[3,7] show that gemcitabine appears to be worthy of clinical research in this neoplastic pathology, and makes the drug a particularly interesting agent for investigation in patients with biliary tract malignancies.

References

1. De Aretxabala X, Roa I, Araya JC, *et al*. Gallbladder cancer in Chile. *Cancer* 1992; **69**: 60–5.
2. Nagornay DM, McPherson GAD. Carcinoma of the gallbladder and extraepatic bile ducts. *Semin Oncol* 1988; **15**: 106–15.
3. Castro MP. Efficacy of gemcitabine in the treatment of patients with gallbladder carcinoma. A case report. *Cancer* 1998; **82**: 639–41.
4. Falkson G, MacIntyre JM, Moertel CG. Eastern Cooperative Group experience with chemotherapy for inoperable gallbladder and bile duct cancer. *Cancer* 1984; **54**: 965–9.
5. Douglass H, Tepper J, Leichman L. Neoplasm of the gallbladder. In: Holland JF, Frei E, Bast RC, Kufe DW, Morton DL, Weilchselbaum RR, eds. *Cancer medicine*, 3rd edn. Philadelphia, PA: Lea & Febiger 1993: 1448–54.
6. Moore M. Activity of gemcitabine in patients with advanced pancreatic carcinoma: a review. *Cancer* 1996; **78** (3 suppl): 633–8.
7. Gallardo J, Fodor M, Gamargo C, *et al*. Efficacy of gemcitabine in the treatment of patients with gallbladder carcinoma. *Cancer* 1998; **83**: 2419–20.

(Received 3 May 2000; revised form accepted 18 July 2000)