observed in previously untreated patients (18%; 95% confidence interval 5–33%) whose primary disease site was in the bile ducts. The responding lesions' sites included the liver (1), the lung (1) and the primary site (3). The median time to progression was 3 months (range 1–11); median survival in the patients as a whole was 8 months (range 1–16 months). The side-effects were manageable and always reversible. The single significant side effect was diarrhoea which was observed in 57% of cases (grade 3–4 in 22%). The median time to recovery was 7 days; in 2 cases, the side-effects persisted for more than 10 days. Hospitalisation was necessary in only one case. Although no anti-emetic prophylaxis was used, mild or moderate nausea or vomiting was observed in only 6 cases. Other toxicities included grade 1–2 abdominal pain which was observed in 30% of cases, and grade 1 hand–foot syndrome which was recorded in 25% of patients.

The activity of systemic chemotherapy in biliary tract cancer has rarely been evaluated in a large number of patients, the largest study available in the literature involving 30 patients treated with mitomycin-C [10]. The present report provides interesting data on the possibility of oral palliative chemotherapy in unresectable biliary tract cancer. Although moderate, the response rate observed in previously untreated patients (18%) is in line with the results reported in the literature [3, 4, 10] and, moreover, was observed in an adequate number of patients. It is worth noting that all the objective remissions in our series of patients were obtained in patients with primary bile duct disease, whereas no remission was observed in those with gall bladder carcinoma. However, although interesting, these data require confirmation in a larger group of patients because the small number of patients with primary gall bladder cancer in this series does not allow any definite conclusions to be drawn. Moreover, given the paucity of series reported in the literature, no data are available concerning any possible different chemosensitivity of these tumours. In summary, given the moderate activity and absence of myelotoxicity, the possibility of more complex regimens combining the proposed schedule with other drugs will be investigated in future trials.

1. Buskirk SJ, Gubderson LL, Adson MA, *et al.* Analysis of failure following curative irradiation of gallbladder and extraphepatic bile duct carcinoma. *Int J Radiat Oncol Biol Phys* 1984, **10**, 2013–2023.
2. Dees CD, Zapolanski A, Cooperman AM, Hermann RE. Carcinoma of the bile ducts. *Surg Gynecol Obstet* 1980, **51**, 193–198.
3. Harvey JH, Smith FP, Schein PS. 5-fluorouracil, mytomicin and doxorubicin (FAM) in carcinoma of the biliary tract. *J Clin Oncol* 1984, **2**, 1245–1248.
4. Falkson G, MacIntyre JM, Moertel CG. Eastern Cooperative Oncology Group experience with chemotherapy for inoperable gallbladder and bile duct cancer. *Cancer* 1984, **54**, 965.
5. Armstrong RD, Diasio RB. Metabolism and biological activity of 5-deoxy-5-fluorouridine, a novel fluoropyrimidine. *Cancer Res* 1980, **40**, 3333–3338.
6. Fujitah H. Pharmacokinetics of orally administed 5 deoxy-5 fluorouridine. *J Int Med Res* 1988, **14** (suppl 3), 13–15.
7. Alberto P, Winkelmann JJ, Paschoud N, *et al.* Phase I study of oral doxifluridine using two schedules. *Eur J Cancer Clin Oncol* 1989, **25**, 905–908.
8. Advanced Colorectal Cancer Meta-Analysis Project. Modulation of fluorouracil by leucovorin in patients with advanced colorectal cancer. Evidence in terms of response rate. *J Clin Oncol* 1992, **10**, 896–903.
9. Straw JA, Szapary D, Wynn WT. Pharmacokinetics of the diastereoisomers of leucovorin after intravenous and oral administration to normal subjects. *Cancer Res* 1984, **44**, 3114–3119.
10. Taal BG, Audisio RA, Bleiberg H, *et al.* Phase II trial of mytomicin C in advanced gallbladder and biliary tree carcinoma. An EORTC Gastrointestinal Tract Cancer Cooperative Group Study. *Ann Oncol* 1993, **4**, 607–610.

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Long-term Survival in a Patient with Rosai–Dorfman Disease Treated with Interferon-α

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Sinus histiocytosis with massive lymphadenopathy (SHML, Rosai–Dorfman syndrome) is a rare tumorous disorder of unknown aetiology that is usually regarded as benign [1, 2]. Involvement of aberrant immune responses to viral infections, i.e. Epstein-Barr virus or human herpes virus-6 has been suggested [3, 4]. We observed a 40-year-old patient who presented in 1980 with extranodal nasal manifestation of Rosai–Dorfman disease. Cervical and mediastinal lymphadenopathy and extranodal skin eyelid and larynx tumours developed that were resected. Steroid therapy in 1983 did not prevent recurrent eyelid and larynx manifestation. Subsequently, the patient showed a partial response to CHOP chemotherapy [5]. However, in 1984, clinical and radiological restaging revealed progressive disease, when a skin biopsy showed criteria of malignancy [4, 5]. Therefore, from 1985 to 1990, the patient received three cycles of 36 miu interferon-α2a three times a week for 3–4 months. He experienced three complete remissions of all neoplasia that lasted 13–21 months. However, weight loss, depression, leucopenia and cardiac arrythmia were observed as severe therapeutic side effects. In 1991, conservative left lateral cervical dissection had to be performed owing to a recurrent laryngeal tumour. Since 1992, multiple tumour manifestations in the thyroid gland, subglottis and skin indicated massive progressive disease. In 1993, a new 4 month interferon-α trial with reduced dosage (6 miu 3 times a week) resulted in partial response, but had to

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be stopped because of side-effects. However, due to a slowly progressive thyroid gland tumour long-term low dose interferon treatment with 3 miu 3 times a week was started, which was well tolerated.

The 15 year follow-up shows the clinical course of the rare extranodal Rosai–Dorfman syndrome that progressed under immunosuppressive and cytostatic therapy. High dose interferon treatment resulted in longlasting complete remissions, but was accompanied by severe side-effects. To conclude, interferon-α may be a therapeutical strategy in progressive Rosai–Dorfman syndrome presenting with clinical or histological signs of malignancy.

1. Maennle DL, Gierson HL, Gnarra DG, Weisenburder DD. Sinus histiocytosis with massive lymphadenopathy: a spectrum of disease associated with immune dysfunction. *Pediatr Pathol* 1991, **11**, 399.
2. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. *Arch Pathol* 1969, **87**, 63.
3. Levine PH, Jahan N, Murari P, Manak M, Jaffe ES. Detection of human herpes virus 6 in tissues involved by sinus histiocytosis with masive lymphadenopathy (Rosai–Dorfman disease). *J Infect Dis* 1992, **166**, 291.
4. Harley EH. Sinus histiocytosis with massive lymphadenopathy (Rosai–Dorman disease) in a patient with elevated Epstein–Barr virus titers. *J Natl Med Assoc* 1991, **83**, 922.
5. Foucar E, Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. An analysis of 14 deaths occurring in a patient registry. *Cancer* 1984, **54**, 1834.

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Anaphylactic Reaction after a First Filgrastim (Granulocyte-colony Stimulating Factor) Injection

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WE REPORT the first case of anaphylactic reaction after a first dose of filgrastim (Neupogen®, Amgen, Bâle, Switzerland). A 55-year-old female patient was admitted to Hôtel-Dieu Hospital in March 1995, for the treatment of an unknown primary adenocarcinoma. She had no particular previous history except an urticarian eruption after rifampicin and a generalised eruption after azithromycin. She received a regimen of cisplatin, etoposide and ifosfamide associated with Mesna for 3 consecutive days.

Concurrent medications were ondansetron, dexamethasone, clorazepam, alprazolam and zopiclone. To prevent neutropenia, the patient received a single intravenous filgrastim injection (300 μg) on day 4, and 5 min later, developed breathlessness with tachycardia and hypotension (70–0 mmHg), acute bronchospasm, diarrhoea and a vomiting episode. This life-threatening accident was resolved after injection of epinephrine, methylprednisone, salbutamol and macromolecular infusion. Because the reintroduction of all other concurrent therapeutics except filgrastim did not produce any allergic reaction, and according to the chronology, we believe that filgrastim had a causal role.

Allergic reaction with anaphylactic shock after a reinjection with granulocyte-colony stimulating factor has been described [1]. However, we were surprised that this reaction occurred after the first administration of the drug in this case, and may be explained if the causal agent was an excipient previously received by the patient. Filgrastim is contraindicated in patients with known hypersensitivity reactions to products derived from *Escherichia coli*, but this patient did not receive prior biological agents.

In allergic patients, filgrastim should be administered under medical care.

1. Jaiyeslmi I, Giraly S, Wood J. Subcutaneous granulocyte colony stimulating factor and acute anaphylaxis. *N Engl J Med* 1991, **325**, 587.

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