TG plus FA either high or low dose [7–10] have been reported.

In September 1991, a phase II trial of outpatient oral chemotherapy for patients with metastatic colorectal carcinoma was initiated. Chemotherapy consisted of: TG 1200 mg/day and FA 45 mg/day, in 3 oral daily fractions on days 1–21, every 28 days. Treatment was continued until progression or unacceptable toxicity.

36 patients were included in this study. Patient characteristics were as follows: Mean age at diagnosis was 62.4 years (range 34–75 years); 20 patients were male and 16 female; median Zubrod performance status was 1; location of disease: unresectable primary tumour 13%, locoregional relapse 47% and metastatic disease 50%; previous adjuvant chemotherapy had been given to 11% of patients. A total of 257 cycles of chemotherapy were administered (mean 7.1 cycles/patient).

Overall toxicity was moderate (grades III–IV WHO): nausea/vomiting 2.7% patients, mucositis 5.5%, diarrhoea 5.5%. Epigastric discomfort was experienced by 27.7%. There were no neutropenic fever episodes, red cell transfusion or toxic deaths. A 33% reduction of TG and FA dose was scheduled for patients with epigastric discomfort (12% of patients) and for diarrhoea in 15% of patients. Therapy was stopped in a patient for unacceptable epigastric discomfort.

The overall response rate was 15/36 (41.6%; 95% confidence interval, 25–57%): no complete responses, 15 partial responses, 11 had no changes and 10 had progressive disease. The median response duration was 8 months. The median survival time was 10 months, 1-year survival 45%, 2-year survival 17% and 4-year survival 5.7%. The median follow-up was 10.5 months (range 2–50) and the median time to progression 6 months.

It is remarkable that toxicity with this schedule of treatment was moderate, consisting mostly of gastrointestinal symptoms, mostly epigastric discomfort (27% of patients). This toxicity is comparable to that reported in other studies [7, 9, 10], even though a high incidence of epigastric discomfort has not been previously reported. This schedule shows a satisfactory response rate (41.5% RR). Survival is comparable to that of other palliative chemotherapy schedules in advanced colorectal cancer. Survival was significantly longer in responders than in non-responders (Mantel–Haenszel test: $Z = 3.01$, $P < 0.01$).

For the afore-mentioned reasons, it is concluded that this schedule of outpatient oral therapy with TG and FA is moderately effective in palliation for advanced colorectal cancer patients with mild toxicity. Response and survival are comparable to those reported with standard intravenous chemotherapy.

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Sjögren's Syndrome and Multiple Myeloma

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SJÖGREN SYNDROME (SS) is an autoimmune disease characterised by the presence of at least two of the following: keratoconjunctivitis sicca, xerostomia and any one of the autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, scleroderma and primary biliar cirrhosis. B-cell lymphoma is an occasional complication of SS, macroglobulinaemia develops in some patients [4]. Most of the reported monoclonal gammopathies in Caucasian patients with SS involve the IgM class [5]. Non-IgM monoclonal gammopathies in patients with SS is infrequent. Here we describe a Spanish patient with SS associated with multiple myeloma.

A 65-year-old woman was admitted to our hospital for xerostomia and xeropthalmia. Examination revealed keratoconjunctivitis sicca by the Schirmer-I-test (bilateral eyes: 1

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mm/5 min) and the Rose Bengal staining test [2]. Salivary flow was decreased markedly. Sequential scintigraphy of salivary glands showed no active concentration of technetium during a 60 min period. Sialography showed globular sialectasis. Lip biopsy revealed lymphocyte and plasma cell infiltration and acinar atrophy in the minor salivary glands. Laboratory studies disclosed leucocytopenia, positive rheumatoid factor (1:320), positive antinuclear antibody (1:1200) with a speckled pattern and positive anti-SS-B (1:4). A monoclonal spike was discovered in the gamma-region of the serum. Immunoelectrophoresis identified the monoclonal component as IgG. Serum Ig determination revealed IgG: 3.8 g/l, IgA: 0.12 g/l and IgM: 0.08 g/l. Bone marrow aspiration showed plasma cell infiltration (22%), and X-ray examination showed lytic defect in cranial bone. Chemotherapy with prednisone and melphalan was not effective.

Hyperimmune reaction has been assumed to play an important role in the lymphomagenesis in SS. SS patients have been recognised to have a high incidence of benign monoclonal gammopathy in the serum or urine [6, 7], although multiple myeloma is very rare [8]. Osserman and associates [9] have observed that chronic inflammation may represent a stimulus in the development of multiple myeloma. The exact mechanism remains under speculation. The same immunological disorder may play a role in the pathogenesis of monoclonal gammopathy in SS.

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Vinorelbine in Pregnancy

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FETAL TOXICITY of chemotherapy given during pregnancy is clearly dependant of the time of treatment. Early administration of cytotoxic agents is associated with an increased number of fetal malformations, often with compromised fetal viability. Doxorubicin and vinca alkaloids are considered to be less teratogenic than other agents when used in the first trimester [1]. Exposure in the subsequent two-thirds of gestation does not lead to an increased risk of abnormality. However, low birth weight, intra-uterine growth retardation, premature birth or common toxic side-effects can also be observed. Anthracyclines, antimetabolites, vinca alkaloids are drugs commonly used in breast cancer. Myelosuppression and myocardial necrosis have been described with anthracyclines [2, 3]. Vinca alkaloids seem to be relatively safe: vinblastine as single agent has been used in all trimesters of pregnancy without producing any teratogenic or deleterious effect. Only 2 cases of transient neonatal pancytopenia with vincristine have been observed [1]. No case of 5-fluorouracil toxicity when administered after the first trimester has been reported.

We treated 3 pregnant breast cancer patients with a combination of 5-fluorouracil (5-FU) and vinorelbine (V) [4]. Patients and tumour characteristics are shown in Table 1.

Patient 1 (35 years of age; T3 N0 M0 tumour; 24 weeks pregnant when given chemotherapy) received 2 courses of 5-FU 500 mg/m^2 daily for 5 days and V 30 mg/m^2 days 1 and 5. Because of progression, she subsequently received 6 courses of epidoxorubicin 75 mg/m^2 and cyclophosphamide 1 200 mg/m^2 at 14 day intervals. Patient 2 (33 years of age; T3 N0 M0 tumour; 29 weeks pregnant when given chemotherapy) received 2 courses of 5-FU 500 mg/m^2 daily for 5 days and V 20 mg/m^2 days 1 and 5, and one course with increased doses: 5-FU 750 mg/m^2 daily ×5 days, V 25 mg/m^2 days 1 and 5. Patient 3 (28 years of age; local recurrence; 28 weeks pregnant when given chemotherapy) received 3 courses of 5-FU 750 mg/m^2 daily for 5 days and V 30 mg/m^2 days 1 and 5. Delivery occurred at 34 weeks (caesarian section), 37 weeks (spontaneous) and 41 weeks (spontaneous), respectively. The characteristics of 3 newborns are depicted in Table 1. The only toxic effect that could be attributed to chemotherapy is anaemia at day 21 in case 1; in this case, the mother received

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