European Journal of Cancer Vol. 30A, No. 11, pp. 1727–1728, 1994.

0959–8049/94 $7.00 + 0.00

News

Second European Conference on Medicines Research: Perspectives in Clinical Trials

This conference will be held on 5-6 December 1994 in Brussels and aims to review progress, needs and opportunities in all areas relating to multicentre randomised controlled clinical trials in obstetrics, perinatology, paediatrics, neonatology and geriatrics. For further information contact Janie Wardle, PO Box 806, Cottenham, Cambridge CB4 4RT, U.K. Tel. 0954 252516, Fax 0954 252517.

Second International Symposium on Drug Resistance in Leukaemia and Lymphoma

This conference will be held in Amsterdam, Holland on 6–8 March 1995, the subject of which will be the clinical relevance of studies on drug resistance in both childhood and adult leukaemia and lymphoma. The aim is to review the current knowledge as well as to indicate future directions of studies on *in vitro* drug resistance and mechanisms of resistance for several classes of chemotherapeutic drugs in leukaemia and lymphoma. For further information contact Dr R. Pieters, Free University Hospital, Department of Paediatrics, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. Tel. 20 444 2420, Fax 20 444 2422.

The 8th Paediatric Tumours Congress and New Trends in Medicine 1995

This will be held on 1–5 May 1995 at Cukurova University Medical Faculty, Balcali, Adana, Turkey. For further information contact the Secretary of Congress, Assoc. Prof. Dr Atila Tanyeli, Department of Paediatric Oncology, Cukurova University, Medical Faculty, Adana, Turkey. Tel. 0322 3386060/3116, Fax 0322 3386906.

Letters

0959-8049(94)00192-8

Salivary Glands Enlargement in Association With Cytosine Arabinoside Application in Patients With Acute Myeloid Leukaemia

P. Cetkovský and V. Koza

CYTOSINE ARABINOSIDE (AraC), an effective antineoplastic agent, can produce a number of adverse reactions [1,2]. Recently published case reports have described acute bilateral parotitis during chemotherapy for acute leukaemias using regimens containing continuous infusion of AraC [3,4]. We report two examples of this rare complication of AraC.

A 36-year-old male with acute myeloid leukaemia (AML), received remission induction chemotherapy consisting of daunomycin (60 mg/m^2/day on days 1–3) and AraC (200 mg/m^2/day in continuous infusion on days 1–7). On day 5 of the therapy, the patient noted swelling in the parotid and submandibular regions associated with pain and tenderness. Salivary secretion was not altered, and examination of the ears, nose, throat and oral cavity revealed no abnormalities apart from parotid and submandibular gland swelling.

The serum amylase level was increased 4-fold. Chemotherapy was completed in 2 days, and the swelling, pain and raised amylase level disappeared promptly after discontinuation of the cytotoxic treatment. The patient received further treatment on day 21 with AraC (1000 mg/m^2/day in 6-h infusion on days 1–6) and idarubicin (12 mg/m^2/day on days 1–3). During and after this regimen, no swelling or discomfort in salivary glands was observed.

The second patient, a 16-year-old male suffering from AML received the same remission induction regimen. On day 4 he developed acute bilateral painful enlargement of the parotid and submandibular glands. The serology for mumps virus was negative and clinical examination of the ears, nose, throat and oral cavity revealed no pathology. The serum amylase level was increased 6-fold and normalised within 1 week. After discontinuation of the therapy, the discomfort disappeared but the swelling was present until day 20, when it spontaneously resolved in 2 days. On day 25, the patient received a first post-remission course consisting of AraC and mitoxantrone. There was no enlargement of salivary glands.

Correspondence to P. Cetkovský
The authors are at the First Department of Medicine, Division of Haematology, Charles University Teaching Hospital, alej Svobody 80, 323 18 Plzeň (Pilsen), Czech Republic.
Received 23 Feb. 1994; accepted 28 Mar. 1994.

A small portion of the patients receiving AraC experience painful enlargement of the salivary glands. In contrast to previous reports the two patients reported here experienced swelling and pain in both the parotid and submandibular salivary glands. Salivary glands enlargement occurred only in association with continuous infusion of standard dose of AraC and was not observed in the same patients after application of AraC in intermediate dose, in spite of the expectation that toxicity would be dose related.

1. Lokich JJ, Chawla PL, Jaffe N, Frei E III. Phase I evaluation of cyclocytidine (NSC-145668). *Cancer Chemother Rep* 1975, **59**, 389–393.
2. Peters WG, Colly LP, Willemze R. High-dose cytosine arabinoside : pharmacological and clinical aspects. *Blut* 1988, **56**, 1–11.
3. Humphries JE, Lee JT. Acute bilateral parotitis during chemotherapy for acute lymphoblastic leukemia. *Acta Haematol* 1992, **88**, 55–56.
4. Shpilberg O, Ra'anani P, Ben-Bassat I, Ramot B. Recurrent bilateral parotitis in acute myeloid leukemia. *Acta Haematol* 1991, **86**, 56.

European Journal of Cancer Vol. 30A, No. 11, pp. 1728–1729, 1994.

0959–8049/94 $7.00 + 0.00

0959-8049(94)00249-5

Low-dose BCG in Superficial Bladder Cancer With Strain Connaught Canada—as Effective as Strain Pasteur Paris?

D. Mack and J. Frick

Bacillus Calmette Guerin (BCG) intravesical therapy represents a major advance in the treatment of superficial transitional cell carcinoma (STCC) of the bladder. The high-grade stage T1 lesion (high-risk cancer) treated by transurethral resection alone is reported to progress to muscle invasion in 30 to 50% of patients. At present the optimal dose and treatment schedule remain to be defined, but treatment-related toxicity is significant. Therefore, as suggested by Pagano's group, we used BCG at a lower dose than previously reported, and also tested BCG Connaught Canada.

Therapy consisted of six weekly instillations of 75 mg BCG strain Pasteur Paris (3.75×10^8 colony-forming units, CFU) in 32 patients. Subsequently, the Pasteur strain was not available in Austria, and so another 25 patients entered into the study were treated with 27 mg BCG strain Connaught Canada (3×10^8 CFUs) to evaluate the feasibility, response and toxicity of BCG immunotherapy for patients with high risk STCC (Table 1).

Of 32 eligible patients in the Pasteur group, 84.4% had a complete response after the initial cycle with low-dose BCG and had stable disease. Similar results were achieved in the Connaught group: of 25 eligible patients, 84% had complete responses (Table 1). Mean follow-up was 30 months. Toxicity included profound local reactions, such as severe dysuria, frequency and gross haematuria. No systemic reactions except fever were seen; none of the patients needed INH (isonicotinic acid hydrazide). All reactions were treated symptomatically and were similar in both groups.

Table 1. Tumour stage/grade of 32 patients treated with BCG Pasteur and 25 patients treated with BCG Connaught in relation to response.

	Pasteur BCG		Connaught BCG	
Stage/grade	Response	No response	Response	No response
T1 II m	3	0	3	0
T1 II + TIS	4	0	1	0
T1 III s	0	0	3	0
T1 III m	11	1	9	1
T1 III + TIS	7	2	3	2
TIS	2	2	2	1
Total	27 (84.1%)	5	21 (84%)	4

m, multiple; s, solitary.

Morales and colleagues were the first to successfully use intravesical BCG for prophylaxis and therapy [1]. Later, Herr concluded that BCG produced a higher, more durable response rate than other intravesical agents and is the intravesical agent of choice for initial therapy of superficial bladder cancer [2]. BCG of various strains applied in different schedules yields a high response rate in STCC of the bladder [3].

However, the optimal dose of BCG treatment is presently unknown. In his first clinical trial of BCG, Morales and colleagues administered an arbitrary dose of 120 mg BCG Armand-Frappier [1]. This dose of 120 mg or an equivalent has been used by most investigators in subsequent studies. In 1988 Pagano and associates were the first to present results using a lower BCG treatment dose with the Pasteur Paris strain [4].

Akaza used BCG Tokyo 172 in a randomised study comparing an 80-mg dose with 120 mg [5]. All these studies clearly indicated that the lower dose of BCG was associated with decreased rates of both local and systemic side-effects. According to Pagano's results, we also used a low dose Pasteur BCG regimen in our STCC patients but we also used the Connaught strain. Until now, no data existed on the use of low-dose treatment with strain Connaught Canada. Mori and colleagues reported the effectiveness of BCG-Connaught with a total dose of 9.0×10^8 CFUs per instillation [6]. We used BCG-Connaught at one third of this dosage (3.0×10^8 CFUs). 21/25 patients showed response after the completion of the initial cycle. 4 patients did not respond and underwent more invasive therapy. None of our patients had tumour progression or metastasis. All patients showed irritative symptoms such as frequency, dysuria, gross haematuria.

This study suggests that low-dose BCG with strain Connaught Canada is as effective as low-dose BCG with strain Pasteur Paris. It is necessary to carry out several dose-finding studies with different strains. The fundamental aim of an adjuvant treatment-concept for STCC should be for maximum efficacy with the lowest morbidity and costs.

Correspondence to D. Mack.
The authors are at the Department of Urology, General Hospital Salzburg, Müllner Hauptstrasse 48, A-5020 Salzburg, Austria.
Revised 23 May 1994; accepted 24 June 1994.