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Intralesional Recombinant α_{2a} Interferon Therapy in Superficial Transitional Cell Carcinoma of the Bladder

Savino M. Di Stasi, Antonio Tabilio, Guido Virgili, Giuseppe Vespasiani, Massimo Porena and Francesco Micali

EXPERIMENTAL [1–3] and clinical [4–7] studies carried out in the last few years have demonstrated that interferons (IFN) are active against bladder transitional cell carcinoma (TCC). Intravesically instilled IFN have proved to be as therapeutically efficacious as the more commonly used cytotoxic agents and bacillus Calmette–Guerin in superficial TCC of the bladder, particularly in carcinoma *in situ* [6, 7]. Tarry *et al.* [8] recently investigated the therapeutic potential of intralesional IFN in artificially induced murine TCC. Tumour incidence and volume were significantly lower in IFN-treated mice than in control mice and no IFN-alpha (IFN-α) treated mouse manifested toxicity.

We evaluated the tolerability, toxicity and therapeutic efficacy of recombinant IFN-α_{2a} (rIFN-α_{2a}), administered by intralesional injection, in 15 patients with endoscopically and ultrasonographically measurable unifocal papillary superficial TCC of the bladder (Table 1). Informed consent was obtained from all patients before they entered the trial. Tumours were diagnosed and staged by suprapubic and transurethral ultrasonographies, cystoscopy and intravenous urography. Histological diagnosis of TCC was obtained before beginning treatment.

rIFN-α_{2a} was delivered endoscopically at dose rate of 3×10^6 IU, weekly for 4 consecutive weeks (total dose 12×10^6 IU). 4 weeks after the last intralesional rIFN-α_{2a} injection, patients were restaged, maximum lesion diameters documented and transurethral resection (TUR) for residual tumour performed. No further treatment was given. Patients were carefully checked for intolerance and rIFN-α_{2a}-induced toxicity throughout treatment. Blood samples were taken for radioimmunoassay of serum IFN-α at time 0, 8, 16 and 24 h of each treatment. Immunophenotypic studies were carried out on the peripheral blood lymphocytes with monoclonal antibodies CD3, CD4, CD8, CD14, CD20 and CD56. Cell infiltrates in the TUR specimens and an equal number of control patients not treated with rIFN-α_{2a} were stained with CD3, CD4, CD8 and CD20. Response to intralesional rIFN-α_{2a} was classified on the basis of ultrasound, endoscope and pathological findings and according to the Memorial Sloan–Kettering Cancer Center Response Criteria [9].

Table 1. Intralesional IFN: patients' data

Eligible	15
Males/females	9/6
Mean age (yr)	64.4 (range 49–85)
First tumours	11
Recurrent tumours	4
Stage	
Ta	13
T1	2
Grade	
G1	12
G2	3

1 patient (7%) achieved complete remission (CR), 6 (40%) partial remission (PR), 6 (40%) minor remission (MR) and 2 (13%) stabilisation of disease (SD). The overall response rate was therefore 47%. All objective remissions (CR+PR) were recorded in patients with tumours 20 mm or less. Locoregional and systemic tolerability to intralesional rIFN-α_{2a} therapy was satisfactory. All patients completed the therapy. An influenza-like syndrome and slight dysuria were documented after every rIFN-α_{2a} administration. Radioimmunoassay for serum IFN-α showed that mean maximum plasma concentrations of 15.1 IU (range 13.5–17) were reached 8 h after each administration. The immunological findings suggested that the antitumour effects of rIFN-α_{2a} are not mediated through the immune system (data not shown). Intralesional injection of rIFN-α_{2a} is therapeutically efficacious for treating papillary lesions in patients with superficial TCC of the bladder. Even high doses of rIFN-α_{2a} injected directly into the bladder will cause only minimal side-effects. Our results and these from animal studies indicate that the intralesional injections of IFN are more efficacious when the tumour is small.

Correspondence to S.M. Di Stasi.
S.M. Di Stasi, G. Virgili, M. Porena and F. Micali are at Department of Urology; A. Tabilio is at Institute of Haematology, Perugia University, Policlinico Monteluce, 06100 Perugia; and G. Vespasiani is at Institute of Urology, L'Aquila University, L'Aquila, Italy.
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