## INTERFERON: FOR THE COLD AND CANCER?

### Intranasal leucocyte interferon: prophylaxis against rhinoviruses . . .

Interferon has shown consistent antiviral effects *in vitro* but less success in clinical studies, possibly because of rapid clearance, inactivation or incorrect dose.

26 volunteers received either intranasal recombinant leucocyte A interferon (rIFN-$\alpha$A; Roche) $10 \times 10^6$ U/day (in 2 divided doses) for 4 days, or placebo, and 2 hours after the second dose were inoculated with rhinovirus type 13. There was no difference in infection *rates* between the 14 subjects receiving interferon (71.4%) and the 12 receiving placebo (83%), but interferon significantly suppressed symptoms of illness: 1 was ill on interferon (7.1%) compared with 8 (66.7%) on placebo. There were significantly lower symptom scores on interferon (4.2) than on placebo (21.2) and nasal secretion was reduced over 3 days (0.6g *vs* 8.4g on placebo). On interferon there was a significant reduction in frequency of virus isolations and virus shedding. One patient on interferon experienced mild myalgia for 1 week.

Two tolerance studies were also carried out. 19 volunteers received $10 \times 10^6$ U/day (in 2 divided intranasal doses) and 10 received $5 \times 10^6$ U once daily. 11 subjects on $10 \times 10^6$ U/day experienced nasal congestion, 2 on $5 \times 10^6$ U/day had mild nasal congestion. Five subjects on $10 \times 10^6$ U/day showed bloody mucus and erosion of the nasal mucosa. None of 20 subjects taking placebo had any symptoms.

The side effects make prophylaxis for minor self-limiting infections unwarranted, but the positive clinical results suggest that if alternative doses or schedules can reduce the side effects, interferon has potential for long term prophylaxis against respiratory viruses.

Samo, T.C. et al.: Journal of Infectious Diseases 148: 535 (Sep 1983)

### . . . and coronaviruses . . .

After rhinoviruses, the second most common cause of colds are the coronaviruses. Using the same interferon as in the above trial, 83 volunteers received approximately $4 \times 10^6$U tid for 4 days (mean total actually used, $3.53 \times 10^7$ U) or placebo. 70 of these (35 on interferon, 35 on placebo) were challenged with coronavirus 229E about 4 hours after the fourth dose. The other 13 were challenged with saline.

Two significant colds occurred among the interferon users, while the other 33 had minimal or no symptoms. 13 of the placebo users had significant colds. On interferon, 9 subjects had a rise in antibody titre and virus was isolated in 12. On placebo, 20 had a rise in antibody titre and virus was isolated in 30. None of the subjects challenged with saline but receiving interferon showed any reaction to the interferon.

Clearly, interferon works prophylactically against coronaviruses, but this would mean exposure of at risk patients to long term interferon use. Therapeutic studies are therefore under way.

Higgins, P.G. et al.: Antimicrobial Agents and Chemotherapy 24: 713 (Nov 1983)

### . . . and a tolerance study

52 healthy adults received either human leucocyte interferon (HuIFN-$\alpha$2; Sch 30,500; Schering Corp) $8.4 \times 10^6$ U/day, or placebo, intranasally (2 sprays per nostril, bid) for 28 days each. The total interferon dose received was $2.35 \times 10^8$U.

In monitoring 5 nasal, 3 respiratory and 6 systemic symptoms, interferon produced significantly longer periods of nasal burning, sore throat and hoarseness (0.6-1.9 days, mean) compared with placebo (up to 0.7 days) which, however produced significantly more headache. The magnitude of these differences was small and may have been partly affected by 2 subjects who were eventually withdrawn because of respiratory infection. Nevertheless, histopathological examinations showed that interferon produced more mucosal irritation (dry mucous membranes, crusting, friability, bloody mucus) with inflammation and ulceration and submucosal lymphocytic and mononuclear cell infiltrates.

All symptoms had subsided within 8 weeks of stopping administration.

Thus '**. . . long term or indefinite administration of intranasal HuIFN-α2 at the dosages used in this study is not a feasible strategy for prophylaxis of respiratory viral infections. Alternative methods of administration . . . will have to be considered.**'

Hayden, F.G. et al.: Journal of Infectious Diseases 148: 914 (Nov 1983)

### But lymphoblastoid interferon is disappointing in AML

14 patients with acute myelogenous leukaemia, who had relapsed or failed to obtain remission on standard chemotherapy, received human lymphoblastoid interferon (Hu IFN-$\alpha$N; Wellcome) $100 \times 10^6$ U/m$^2$/day for 7 days by continuous IV infusion.

Four patients were unevaluable. One patient showed decreased bone marrow infiltration from 33% to 5% blasts, plus complete clearing from the blood, and another showed a reduction from 10% to <5%. But neutropenia and thrombocytopenia persisted in both, and the decreased infiltration lasted only 6 weeks and 3 months, respectively. The remaining 8 patients showed no change in marrow morphology and blast count increased in 5.



0156-2703/83/1210-0004/0$01.00/0 

Hepatic dysfunction occurred in 9 patients, and all patients experienced pyrexia, anorexia, fatigue and, 'flu-like symptoms. Peak serum levels of interferon reached 800 U/ml. Even at this maximum tolerated dose, the results were 'impressively negative'.

Rohatiner, A.Z.S. et al.: Cancer Chemotherapy and Pharmacology 11: 56 (No 1, 1983)