LETTER

Low-dose oral interferon α possibly retards the progression of idiopathic pulmonary fibrosis and alleviates associated cough in some patients

Idiopathic pulmonary fibrosis (IPF) has no effective treatment and a relatively short life expectancy after diagnosis. Interferon α (IFNα) inhibits the growth of proliferating fibroblasts.[1] IFNα also inhibits the production of collagen by fibroblasts independently of its effect on fibroblast replication.[2] Biological activity of low-dose IFNα by oromucosal administration has been reported in several species including man,[3] despite the expected rapid inactivation by digestive enzymes.[4]

We therefore tested the effect of oral administration of very low doses of IFNα on the progression of IPF. Twelve of 20 patients with IPF aged 50–82 years (mean 67) completed treatment for at least 12 months with IFNα administered by lozenge (150 IU) taken three times each day. IPF was diagnosed according to the diagnostic criteria set forth by the American Thoracic Society. Three subjects had lung biopsies and all subjects had high resolution CT prior to entry into the study. All subjects had had significant loss of function documented by pulmonary function tests on entry with the average baseline forced vital capacity (FVC) being 57.0% of predicted with a range of 36.7–73.4%. The subjects were seen by a physician in the clinic on days 7, 14, 30, 60 and 90 after the start of treatment, and then at regular 3 month intervals. Serial blood work, pulmonary function tests (PFTs) and CT scans were obtained at regular intervals. The other eight subjects were excluded because of non-compliance, progression of IPF, transfer to another research study, or failure to begin or complete treatment. Autopsy on the three subjects who died during treatment was consistent with deaths resulting from progression and/or complications of severe IPF.

Clinical data on the 12 subjects who completed at least 1 year of treatment are summarised in table 1. All subjects tolerated treatment well. Using the criteria from the International Consensus Statement, FVC was stable in 10 subjects (12 evaluable), and O_2 saturation postexercise was stable or improved in nine subjects (11 evaluable) over a 12-month period. High resolution CTs (HRCTs) showed no evidence of progression after 1 year in seven subjects (11 evaluable) and only slight progression in the other four. Two subjects followed for 36 and 57 months showed stability on the PFTs and no progression on the HRCT.

Five of the six subjects with chronic cough on entry reported an overall improvement within 2–3 weeks after starting treatment. Five of these subjects who completed the validated Leicester Cough Questionnaire had a significant improvement in their total score.[5] Detailed methodology, results and other supplemental data are available online on the journal website for review.

Our study, designed as a proof of concept study, was limited by a small number of subjects and by not being placebo controlled. Treatment with low-dose, oral IFNα appeared to stop or delay progression in most subjects and markedly improved the IPF-associated cough in this uncontrolled single arm study. The potential efficacy of this low-cost, well-tolerated regimen needs to be validated in a larger double-blinded placebo-controlled trial.

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Lorenz O Lutherer,[1] Kenneth M Nugent,[1] Byron W Schoettle,[1] Martin J Cummins,[2] Rishi Raj,[1] Surinder S Birring,[3] Cynthia A Jumper[1]

[1]Departments of Internal Medicine and Physiology, Texas Tech University Health Sciences Center, Lubbock, Texas, USA; [2]Amarillo Biosciences, Amarillo, Texas, USA; [3]Department of Respiratory Medicine, King's College Hospital, Denmark Hill, London, UK

Correspondence to Rishi Raj, Pulmonary, Critical Care and Sleep Medicine, Texas Tech University Health Sciences Center, 3601 4th Street, Stop 9410, Lubbock, TX 79430-9410, USA; rishi.raj@ttuhsc.edu

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Ethics approval This study was conducted with the approval of the Institutional Review Board of the Texas Tech University Health Sciences Center Lubbock Campus.

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Table 1 Outcomes for FVC (% predicted), O_2 saturation postexercise (%) and HRCT for two successive 6 month periods and 1 year based on the International Consensus Statement criteria*

Subject	Baseline FVC	6 months FVC	12 months FVC	Outcomes By period†	Baseline O_2 Sat	6 months O_2 Sat	12 months O_2 Sat	Outcomes By period†	Progression On HRCT
1	49.80	52.50	52.20	S–S–S	75	75	75	S–S–S	None
3	36.70	38.50	41.80	S–S–S	85	78	82	W–I–S	None
4	73.40	70.30	72.70	S–S–S	99	96	97	S–S–S	None
5	59.00	59.80	51.00	S–W–S	61	63	60	I–S–S	Slight§
8	72.60	69.10	67.40	S–S–S	91	93	92	I–S–S	Slight
11	47.30	37.70	37.40	W–S–W	‡				‡
12	66.00	78.80	72.30	I–S–S	83	83	82	S–S–S	None
15	54.00	63.40	56.70	I–W–S	80	74	65	W–W–W	Slight
16	43.10	40.00	40.00	S–S–S	67	82	77	I–W–I	Slight
18	68.30	62.20	59.70	S–S–S	83	82	73	S–W–W	None
19	63.90	59.60	48.10	S–W–W	86	91	86	I–W–S	None
20	49.80	49.50	45.70	S–S–S	85	81	83	W–S–S	None

*Stable defined as a value less than a ±10% change for FVC and less than a ±4% point change for O_2 saturation post-exercise. Values at the end of the first period were used as baseline for the second period. One-year outcomes based on ±changes of <19 and 8% for FVC and O_2 saturation, respectively, comparing 12 month values with baseline.
†Outcomes are indicated by: I=improved, S=stable and W=worse for the first 6 month period, the second 6 month period and 1 year in that order.
‡Subject unable to perform 6 min walk due to physical disability and baseline HRCT lost.
§Slight progression reflects a change due to a very minimal increase in disease or a technical factor of lung image when comparing 12 month scan with baseline scan.
FVC, forced vital capacity; HRCT, high resolution CT.

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