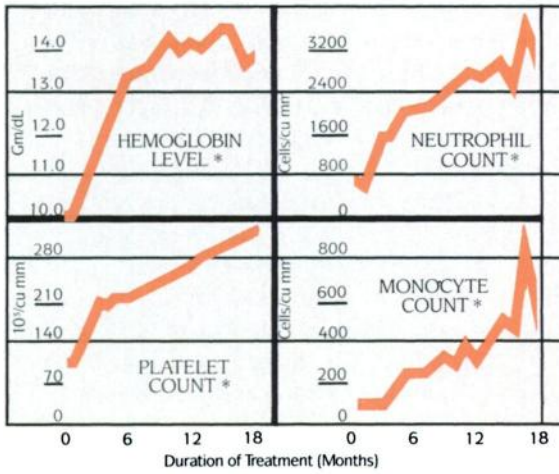
In hairy cell leukemia

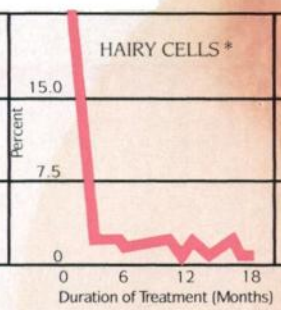
Restore normal patterns

Normalize blood parameters



- Virtually all patients benefit: 89% improved, 11% stabilized.
- Effective in all stages of disease.

Reduce tumor burden



- As blood parameters normalize, there is a concurrent decrease in peripheral blood hairy cells.

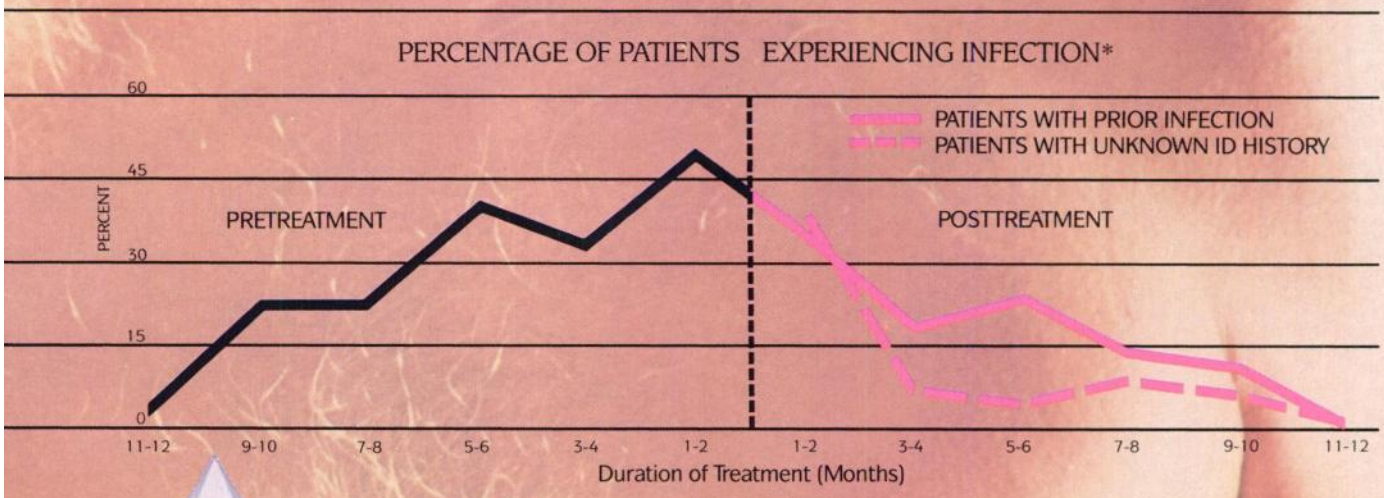
The Roferon-A multicenter study consisted of 96 patients, all of whom were evaluated for safety. Seventy-five patients were evaluable for efficacy. Of these, 57 had prior splenectomy and 18 had not; many were pancytopenic and transfusion-dependent. Of the 21 patients not evaluable for efficacy, 16 were not on drug long enough for efficacy evaluation at the time of data analysis, 2 were removed for administrative reasons, and 3 were removed for preexisting intercurrent illness.

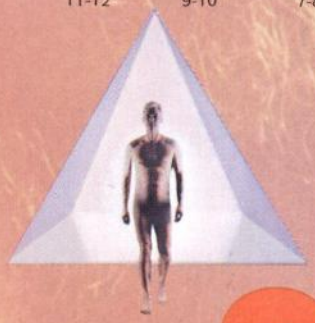
*Multicenter Study, Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

ROCHE® Leading the way in biotherapeutics

Virtually eliminate opportunistic infections

- Key disease-fighting elements are restored with normalization of blood counts.





Increase survival

- Statistically increased survival compared to a historical control group

SC/IM

ROFERON®-A

BRAND OF Interferon alfa-2a, recombinant/Roche

Please see summary of product information on following page.

ROFERON®-A
Interferon alfa-2a, recombinant/Roche

Before prescribing, please consult complete product information, a summary of which follows:

CONTRAINDICATIONS: Hypersensitivity to alfa interferon, mouse immunoglobulin or any component of the product.

WARNINGS: Administer only under guidance of qualified physician. (See DOSAGE AND ADMINISTRATION.) Appropriate management of therapy and its complications is possible only when adequate diagnostic and treatment facilities are readily available.

Use with caution in patients with severe preexisting cardiac disease, severe renal or hepatic disease, seizure disorders and/or compromised CNS function.

Because of the possibility of severe or even fatal adverse reactions, inform patients of both benefits and risks.

Use with caution in patients with cardiac disease or *any* history of cardiac illness. No direct cardiotoxic effect has been demonstrated, but it is likely that acute, self-limited toxicities (*i.e.*, fever, chills) frequently associated with administration may exacerbate preexisting cardiac conditions. Rarely, myocardial infarction has occurred.

Exercise caution in administration to pa.ients with myelosuppression.

CNS adverse reactions included decreased mental status, exaggerated CNS function, dizziness. More severe obtundation and coma rarely observed. Most of these abnormalities were mild and reversible within a few days to three weeks upon dose reduction or discontinuation of therapy. Careful periodic neuropsychiatric monitoring of all patients recommended.

Leukopenia and elevation of hepatic enzymes occurred frequently but were rarely dose-limiting. Thrombocytopenia occurred less frequently. Proteinuria and increased cells in urinary sediment were also seen infrequently. Rarely, significant hepatic, renal and myelosuppressive toxicities were noted.

PRECAUTIONS: *General:* When considering for chemotherapy, evaluate need and usefulness of the drug against risk of adverse reactions. Most adverse reactions are reversible if detected early. If severe reactions occur, reduce dosage or discontinue drug and take appropriate corrective measures. Reinstitute therapy with caution and with adequate consideration of the further need for the drug and alertness to possible recurrence of toxicity.

The minimum effective dose in hairy cell leukemia not established.

Information for Patient: Caution patients not to change brands of Interferon without medical consultation, as a change in dosage may result. Inform patients regarding potential benefits and risks. If home use is desirable, give instructions on appropriate use, including review of the Patient Information Sheet. Patients should be well hydrated, especially during initial stages of treatment.

Laboratory Tests: Complete blood counts and liver function tests should be performed prior to therapy and at appropriate periods during therapy. Since responses are not generally observed for one to three months after treatment initiation, very careful monitoring for severe depression of blood cell counts is warranted during the initial phase.

Patients who have preexisting cardiac abnormalities and/or are in advanced stages of cancer should have electrocardiograms taken prior to and during treatment.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Carcinogenesis: Roferon-A has not been tested for carcinogenic potential. *Mutagenesis:* A. Internal studies. Ames test results revealed no evidence of mutagenicity. Human lymphocyte cultures were treated *in vitro* at noncytotoxic concentrations. No increase in chromosomal damage noted. B. Published studies. No published studies on mutagenic potential. However, a number of studies on the genotoxicity of human leukocyte interferon have been reported. A chromosomal defect has been reported after the addition of human leukocyte interferon to lymphocyte cultures from a patient suffering from a lymphoproliferative disorder. Other studies have failed to detect chromosomal abnormalities following treatment of lymphocyte cultures from healthy volunteers with human leukocyte interferon. Protection from chromosomal aberrations produced by gamma rays observed in primary chick embryo fibroblasts. *Impairment of Fertility:* Nonpregnant female rhesus monkeys treated at doses of 5 and 25 million IU/kg/day have shown menstrual cycle irregularities, including prolonged or shortened menstrual periods and erratic bleeding; these cycles were considered to be anovulatory. Monkeys returned to a normal menstrual rhythm following discontinuation of treatment.

Drug Interactions: Not fully evaluated.

PREGNANCY: Pregnancy Category C. Safe use in human pregnancy not established. Therefore, use during pregnancy only if potential benefit justifies potential risk to fetus. Primate studies showed dose-related menstrual irregularities and an increased incidence of spontaneous abortions. Decreases in serum estradiol and progesterone concentrations reported in women treated with human leukocyte interferon. Therefore, fertile women should not receive Roferon-A unless they are using effective contraception during therapy. Male fertility and teratologic evaluations have yielded no significant adverse effects.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

ROFERON®-A
Interferon alfa-2a, recombinant/Roche

Pediatric Use: Safety and effectiveness in children under 18 not established.

ADVERSE REACTIONS: The following data on adverse reactions are based on the SC or IM administration of Roferon-A as a single agent for the treatment of 63 patients with hairy cell leukemia during investigational trials in the U.S.

Flu-like syndromes consisting of fatigue (89%), fever (98%), chills (64%), myalgias (73%), headache (71%) occurred in the majority of patients and tended to diminish with continuing therapy. Other side effects such as anorexia (46%), nausea (32%), emesis (10%), diarrhea (29%), dizziness (21%), rash (18%), change in taste (13%), dryness or inflammation of the oropharynx (16%), dry skin or pruritus (13%), weight loss (14%) were observed with moderate frequency. Less commonly, diaphoresis (8%), paresthesias (6%), numbness (6%), partial alopecia (8%), reactivation of herpes labialis (8%), transient impotence (6%), arthralgias (5%) were also observed. Rarely (<3%), CNS effects including decreased mental status, depression, visual disturbances, sleep disturbances, nervousness, as well as cardiac adverse events, including hypertension, chest pain, arrhythmias, palpitations, were reported. Adverse experiences which occurred rarely and may have been related to underlying disease included epistaxis, bleeding gums, ecchymosis, petechiae. Miscellaneous adverse events, such as night sweats, urticaria, conjunctivitis, inflammation at the site of injection, were also rarely observed.

Roferon-A has also been evaluated for the treatment of many other types of cancer under investigation in the U.S. These studies generally utilized higher doses (12 to 50 million IU/m²). All of the above adverse reactions which occurred in patients with hairy cell leukemia were also observed in patients receiving higher doses. The incidence of most adverse reactions was similar between the two groups, but tended to be more severe in the higher dosage group. Additional adverse effects which occurred in these patients included confusion (10%), hypotension (6%), lethargy (3%), edema (3%). Adverse experiences occurring in less than 1% of these patients and observed only in patients with malignancies other than hairy cell leukemia are as follows: *GI:* abdominal fullness, hypermotility, hepatitis; *CNS:* gait disturbance, poor coordination, hallucinations, syncope, seizures, encephalopathy, psychomotor retardation, coma, stroke, transient ischemic attacks, aphasia, aphonia, dysarthria, dysphasia, forgetfulness, amnesia, sedation, apathy, anxiety, emotional lability, irritability, hyperactivity, involuntary movements, claustrophobia, loss of libido; *Peripheral Nervous System:* muscle contractions; *Cardiovascular:* congestive heart failure, pulmonary edema, myocardial infarction, Raynaud's phenomenon, hot flashes; *Pulmonary:* bronchospasm, tachypnea; *Miscellaneous:* excessive salivation, flushing of skin.

Abnormal Laboratory Test Values: The percentages of abnormal laboratory test values seen in 1019 patients evaluated in overall safety trials (including hairy cell leukemia patients) are: *Hematologic:* leukopenia (69%), neutropenia (58%), thrombocytopenia (42%), decreased hemoglobin (6.3%), decreased hematocrit (12.5%); mean time to nadir: WBC—22 days, platelets—17 days. *Hepatic:* SGOT (78%), alkaline phosphatase (48%), LDH (47%), bilirubin (31%). *Renal/Urinary:* BUN (10%), serum creatinine (10%), uric acid (15%), proteinuria (25%). *Other Tests:* hypocalcemia (51%), elevated serum glucose (39%), elevated serum phosphorus (17%).

Neutralizing antibodies were detected in approximately 27% of all patients (3.4% for hairy cell leukemia patients). No clinical sequelae of their presence have been documented. Antibodies may occur spontaneously in certain clinical conditions.

DOSAGE AND ADMINISTRATION: Hairy Cell Leukemia—The dose of Roferon-A is 3 million IU daily for 16 to 24 weeks, administered as an SC or IM injection. SC administration is particularly advisable for, but not limited to, thrombocytopenic patients (platelet count <50,000) or for patients at risk for bleeding. The recommended maintenance dose is 3 million IU, 3 times/week. Dosage reduction by one-half or withholding of individual doses may be needed when severe adverse reactions occur. The use of doses higher than 3 million IU is not recommended. Treatment should be continued for 6 months before determining whether to discontinue therapy in nonresponding patients. The optimal duration of treatment has not been determined in responding patients. If severe reactions occur, modify dosage (50% reduction) or temporarily discontinue therapy until adverse reactions abate. The need for dosage reduction should take into account the effects of prior X-ray therapy or chemotherapy that may have compromised bone marrow reserve.

HOW SUPPLIED: Roferon-A Injectable Solution: Vials containing 3 million IU Interferon alfa-2a, recombinant/Roche (3 million IU/mL). Boxes of 10 (NDC 0004-1987-01). Roferon-A Injectable Solution: Vials containing 18 million IU Interferon alfa-2a, recombinant/Roche (3 million IU/0.5 mL). Boxes of 1 (NDC 0004-1988-09). Roferon-A Sterile Powder for Injection: Vials containing 18 million IU Interferon alfa-2a, recombinant/Roche, with accompanying diluent. Boxes of 1 (NDC 0004-1993-09). For reconstitution, storage and handling directions, see complete product information.

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

P.I. 1086

The promise fulfilled

Restore quality to life

- Performance status greatly improved
- 86% of patients gained up to 10% of, or maintained, their total body weight

Common side effects usually self-limiting and manageable

Initial side effects, such as fever, chills, myalgias, headache and fatigue, are self-limiting and generally manageable. Myelosuppression, which can occur early in the treatment course, warrants close clinical and laboratory observation and is usually alleviated by dose reduction or temporary discontinuation of drug. Roferon-A should be used with caution in patients with severe preexisting cardiac disease, severe renal or hepatic disease, seizure disorders and/or compromised central nervous system function. Persistent fatigue is found to be less troublesome with *p.m.* or *h.s.* administration.

SC/IM fixed dosing simple enough for self-administration

Ready-to-Use Injectable Solution

No mixing or reconstitution necessary

3 million IU vial (3 million IU/mL)

18 million IU vial (3 million IU/0.5 mL)

Sterile Powder for Injection

18 million IU vial (3 million IU/0.5 mL)

3 mL diluent for reconstitution

Must be refrigerated at temperatures of 36° to 46°F (2° to 8°C). At no time should Roferon-A Ready-to-Use Injectable Solution remain unrefrigerated for more than 24 hours. The Sterile Powder for Injection should not remain unrefrigerated for more than 48 hours. Once the powder is reconstituted, it should be refrigerated and must be used within 30 days. Do not freeze or shake.

SC/IM

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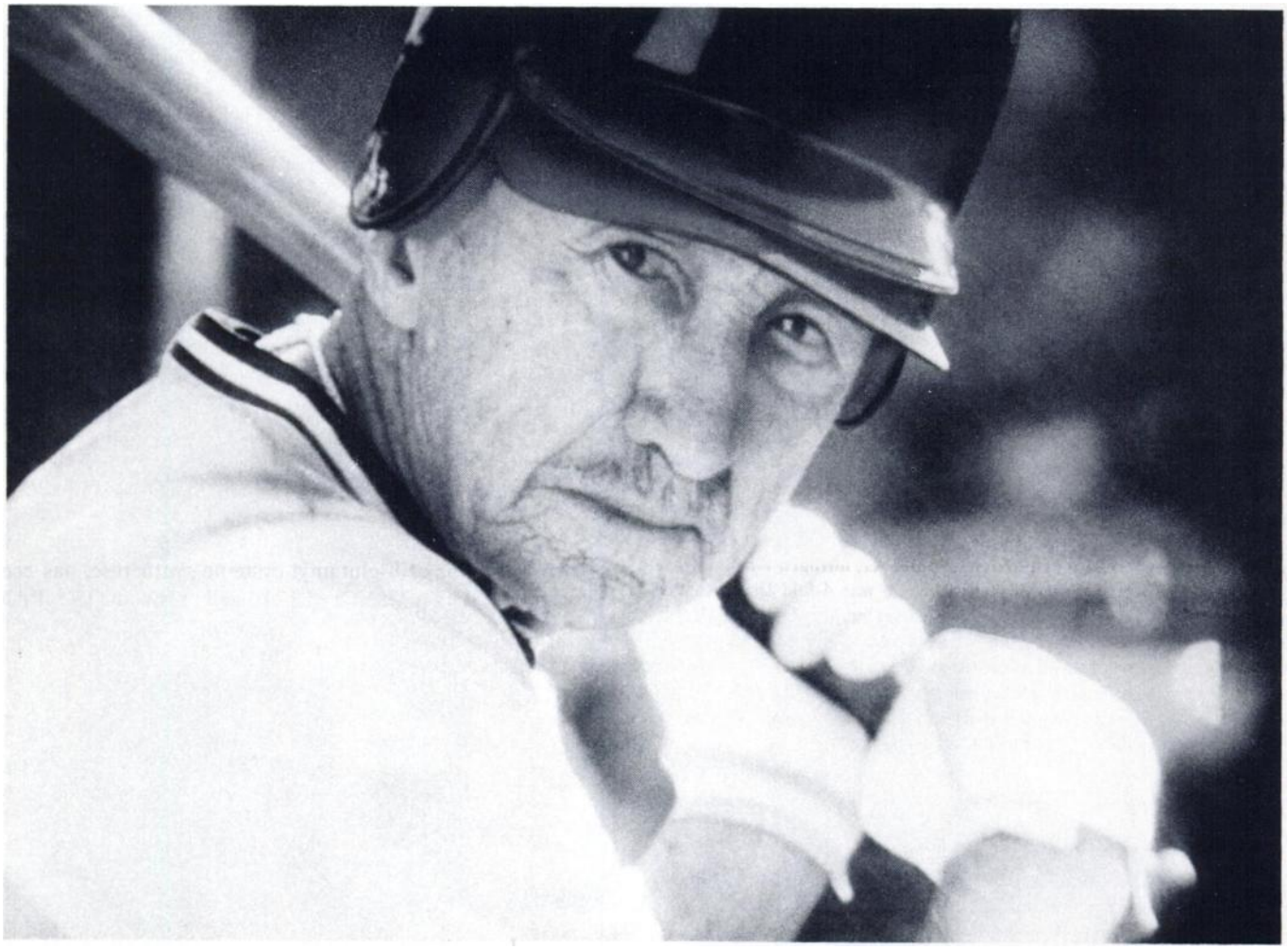
The fourth modality

Please see summary of product information on adjacent page.

This space contributed as a public service.

$500,000,000 OF RESEARCH HELPED CLIFF SHAW PLAY BASEBALL AT AGE 85.



In November 1973, Cliff Shaw was stricken with cancer.

Fortunately, it was detected early enough. And with surgery, Cliff was able to continue living a healthy, active life.

There was a time when such a diagnosis was virtually hopeless.

But today, cancer is being beaten. Over the years, we've spent $500,000,000 in research. And we've made great strides against many forms of cancer.

With early detection and treatment, the survival rate for colon and rectal cancer can be as high as 75%. Hodgkin's disease, as high as 74%. Breast cancer, as high as 90%.

Today, one out of two people who get cancer gets well. It's a whole new ball game.

AMERICAN CANCER SOCIETY®

Help us keep winning.