Interferon alfa-n1 in the Treatment of Refractory Genital Warts: Results of a Multistudy Program. P.K. Weck and D.A. Buddin, Burroughs Wellcome Co., Res. Triangle Park, NC, U.S.A.

A progression of controlled clinical trials utilizing interferon alfa-n1 (Wellferon) was conducted in patients with resistant or recurrent genital warts. The goal of this program was to identify tolerable and effective systemic doses for recalcitrant disease. To date, seven studies are completed. Evaluation of numbers and bidimensional measurements of lesions has allowed calculation of complete (CR) and partial (PR) clearance rates across different studies.

	Females		Males	
Dose/Schedule	CR	PR	CR	PR
5 MU/m^2 daily x 28 then t.i.w. x 2	25%	69%	-	-
3 MU/m^2 daily x 14 then t.i.w. x 4	12%	60%	6%	44%
1 MU/m^2 daily x 14 then t.i.w. x 4	14%	53%	-	-

Interferon associated side effects are dose-related, subside on repeated dosing, and make 5 MU/m^2 an unacceptable dose for this patient population. Fever and headache occur in 80-90% of patients upon first exposure. Clinical laboratory alterations, such as reduced WBC counts and elevated LFTs, are transient with no significant clinical sequelae. These findings indicate that systemic interferon alfa-n1 is effective and acceptable alternative therapy for disease refractory to conventional treatment modalities.

Intravenous Ribavirin Therapy of Hemorrhagic Fever with Renal Syndrome (HFRS).
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A prospective, randomized, double-blind, placebo-controlled, clinical trial of intravenous ribavirin therapy of HFRS (33 mg/kg loading dose; 16 mg/kg every 6 hours for 4 days; 8 mg/kg every 8 hours for 3 days) was conducted in a nine-site study in Hubei Province, PRC. During two seasons, 244 patients met the study criteria for analysis (enrollment within 4 days of fever onset (extended to 7 days the second season) with clinical diagnosis serologically confirmed by IgM ELISA). Statistical analysis demonstrated random assignment of patients between treatment groups. Treatment reduced mortality from 10 of 118 in the placebo group to 3 of 126 in the ribavirin group ($p=0.041$ by Fisher's exact test). Patients treated by the fourth day of fever showed the most marked improvement, with 5-fold less risk of dying. Ribavirin treatment significantly reduced kidney damage, a major component of the disease, as assessed by decreased serum creatinine, proteinuria, edema, and hypertension. Ribavirin therapy also significantly decreased maximum WBC counts (prognostic for survival), and hemorrhagic manifestations (increased platelets, decreased petechiae and ecchymosis). Ribavirin significantly shortened hypotensive and oliguric phase duration, while resulting in an earlier onset of the recovery (polyuric) phase. The only significant side effect was a reversible anemia. Intravenous ribavirin therapy has provided the first proven effective drug therapy for early treatment of HFRS.