

PROLONGED THERAPY WITH LOW-DOSE PEGINTERFERON FOR ADVANCED CHRONIC HEPATITIS C

Researchers conducted a prospective, multicenter randomized controlled trial of long-term peginterferon therapy in adults diagnosed with chronic hepatitis C who did not respond to initial antiviral treatment (peginterferon and ribavirin) to determine whether this treatment approach prevents progressive liver disease. Patients received either peginterferon alfa-2a (90 µg/wk; n = 517) for 3.5 years or no treatment (n = 533) and were stratified according to stage of fibrosis (622 with non-cirrhotic fibrosis and 428 with cirrhosis). All patients were seen at 3-month intervals, and they underwent liver biopsy at 1.5 and 3.5 years after randomization. The primary endpoint was progression of liver disease (as indicated by death, hepatocellular carcinoma, hepatic decompensation, or an increase in the Ishak fibrosis score of ≥ 2 points in those with bridging fibrosis at baseline). Levels of serum aminotransferases and serum hepatitis C virus RNA as well as histologic necroinflammatory scores all decreased significantly ($P < 0.001$) with treatment as compared with no treatment, but there was no significant difference between the groups in the rate of any primary outcome (34.1% in the treatment group versus 33.8% in the control group; hazard ratio, 1.01 [95% confidence interval, 0.81–1.27]; $P = 0.90$). More patients experienced at least 1 serious adverse event in the treatment group (38.6%) than in the control group (31.8%), but this difference was not significant ($P = 0.07$). Long-term therapy with peginterferon did not reduce disease progression in patients with chronic hepatitis C and advanced fibrosis who did not respond to prior antiviral treatment.

Di Bisceglie AM, Shiffman ML, Everson GT, et al; HALT-C Trial Investigators. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. N Engl J Med 2008;359:2429–41.

SKIN BIOPSY ANALYSIS USING PCR PROTOCOL FOR RABIES DETECTION IN HUMANS

Investigators determined the accuracy of a reverse-transcription, heminested polymerase chain reaction (RT-hnPCR) protocol for diagnosing rabies by comparing the results of RT-hnPCR obtained with use of biologic fluid specimens (saliva and urine) and skin biopsy specimens with the results obtained with use of the standard rabies diagnostic procedure performed with a postmortem brain biopsy specimen. The RT-hnPCR protocol was standardized at 3 participating centers in Cambodia, Madagascar, and France. Patients (n = 51) who were thought to have a diagnosis of rabies at hospital admission were prospectively enrolled from Cambodia, Madagascar, Senegal, and France, and baseline skin punch biopsies were obtained. During hospitalization, 425 skin, urine, and saliva samples were

collected from these patients. Ultimately, 43 patients (84%) were confirmed as having rabies, most of whom had a classic clinical presentation for encephalitic rabies. The data obtained indicate a high specificity (100%) of RT-hnPCR and a higher sensitivity ($\geq 98\%$) when RT-hnPCR was performed with skin biopsy specimens than when the test was performed with fluid specimens, regardless of when the sample was collected (ie, 1 day after symptom onset or just after death). Also, a sensitivity of 100% was obtained with the saliva sample when at least 3 successive samples per patient were analyzed. In suspected cases of rabies or encephalitis of unknown origin, skin biopsy specimens should be systematically collected and tested by RT-hnPCR immediately to confirm rabies; if the technique is not readily available locally, the samples should be tested retrospectively for epidemiologic purposes.

Dacheux L, Reynes J, Buchy P, et al. A reliable diagnosis of human rabies based on analysis of skin biopsy specimens. Clin Infect Dis 2008;47:1410–7.

HSV-2 SUPPRESSION DECREASES PLASMA HIV-1 LEVELS IN COINFECTED WOMEN

The authors conducted a randomized, double-blind, placebo-controlled crossover trial in adult women (Lima, Peru) who were coinfecting with herpes simplex virus type 2 (HSV-2) and HIV-1 and who were not receiving antiretroviral therapy to determine whether HSV-2 suppressive therapy would reduce plasma and genital HIV-1 levels. Patients (n = 20) received valacyclovir (500 mg twice daily) or placebo for 8 weeks, followed by a 2-week washout period, and then were switched to the alternate arm for 8 weeks. Plasma samples (obtained weekly) and endocervical swab specimens (obtained 3 times weekly) were collected for HIV-1 RNA polymerase chain reaction assay. Plasma HIV-1 levels were significantly lower during the valacyclovir arm of the study as compared with the placebo arm ($-0.26 \log_{10}$ copies/mL, a 45% decrease). Likewise, the cervical HIV-1 levels were significantly lower in the valacyclovir arm than in the placebo arm ($-0.35 \log_{10}$ copies/swab, a 55% decrease). Suppressive HSV-2 therapy may reduce HIV-1 viral copies, thus potentially reducing HIV-1 infectiousness and slowing HIV-1 disease progression.

Baeten JM, Strick LB, Luchetti A, et al. Herpes simplex virus (HSV)-suppressive therapy decreases plasma and genital HIV-1 levels in HSV-2/HIV-1 coinfecting women: a randomized, placebo-controlled, cross-over trial. J Infect Dis 2008;198:1804–8.

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