

Respuesta Virologica temprana para Tratamiento HCV predice Respuesta Sostenida en Pacientes coinfectados HCV/HIV.

Early Virologic Response for HCV Treatment Predicts Sustained Response in HCV/HIV Coinfected Patients. *Dr. Chung and Dr. Kuritzkes. ACTG. 16th Conference on Retroviruses and Opportunistic Infections (CROI): Abstract 103LB. Presented February 10, 2009.*

February 24, 2009 (Montreal, Canada) — Early virologic response (EVR) to treatment for hepatitis C (HCV) is equally predictive of sustained virologic response (SVR) in patients coinfecting with HIV as it is in patients with HCV mono-infection. The finding was presented here at the 16th Conference on Retroviruses and Opportunistic Infections.

Chronic HCV infection carries a substantial long-term risk of liver disease; coinfection with HIV can accelerate that disease progression up to 4-fold. Coinfection also has been associated with suboptimal response to therapy and with a longer duration of therapy to improve rates of SVR.

The SLAM-C trial (AIDS Clinical Trial Group [ACTG] A5178) examined use of the standard of care regimen of PEG-interferon (PEG) combined with ribavirin (RBV) in 330 HCV/HIV coinfecting patients.

Step 1 of the trial was a 12-week lead in of PEG (180 µg/week) plus weight-based RBV treatment (1200 mg/day for patients weighing >75 kg, 1000 mg/day for patients weighing ≤75 kg). Of 330 who entered step 1, 183 (55%) experienced EVR; 169 (51%) of them chose to move on to step 3. The remainder (167 patients [44%]) who did not experience EVR enrolled in step 2, maintenance dosing of PEG, which was reported last year.

In step 3, 169 patients who achieved a week 12 EVR (≥ 2 log decline or HCV RNA < 600 IU/mL) continued on the initial regimen for 72 weeks, with 24 weeks of follow-up once the course of treatment was completed. HCV genotypes 1 and 4 predominated (78%), and data were available for analysis on 146 patients.

Principal investigator Raymond Chung, MD, from Massachusetts General Hospital in Boston, reported that 51% of those who enrolled in step 3 achieved an SVR. "Taken as a function of the overall denominator of those who entered into step 1, this was a 25% overall SVR. If you look at [baseline] treatment-naive subjects, that was a 31% SVR."

Achieving a complete EVR (HCV RNA <600 IU/mL) at week 12, rather than a 2-log decline but still above that threshold, was a strong predictor of who would achieve an SVR (45 [64%] of 70 patients). In contrast, only 3 (13%) of 24 patients had an SVR if HCV RNA was above that level at week 12.

Toxicity, clinical events, fatigue, and quality of life were leading causes of discontinuation of treatment. However, 62 patients (66%) who achieved an EVR at week 12 completed the full course of therapy, with a 60% SVR. Predictors of SVR included no previous HCV treatment ($P = .0028$), HCV genotypes 2 and 3 ($P = .0006$), and achieving a complete EVR ($P < .0001$).

Dr. Chung said they did not have data on patients' prior use of interferon therapy and why they might have stopped or failed treatment; the initial focus of the study was the step 2 evaluation of maintenance therapy. Growth factors were allowed in this study, "but many sites chose not to use them," he said.

Recent studies in HCV mono-infected patients have shown that EVR response at week 4 or week 8 can be at least as predictive of SVR as week 12 response. Dr. Chung said they did not have samples from those time points and hoped that future studies in coinfecting patients might explore those earlier marks.

Daniel Kuritzkes, MD, from Brigham and Women's Hospital in Boston, Massachusetts, told Medscape *HIV/AIDS* that one of the most important things from the earlier reported data from this trial "is that weight-based dosing of ribavirin is very important and improved substantially the response rates for genotype 1A compared to what had been seen in the previous study that Ray did with the ACTG."

"The newer data tell us that you really can use early virologic markers to determine in which patients is it worth continuing" the course of treatment," Dr. Kuritzkes said. He called it an admittedly mixed message to the patient because one has suggested the regimen in the hope that it will work; but at least the early marker can reduce futile efforts in treating patients who will not respond well.

Expanding beyond the immediate data he said, "Part of the dilemma we have at the moment is that we are on the cusp of getting really interesting small molecules into the clinic. That makes you a little more conservative as a clinician. If a patient has the luxury of waiting, should I try to convince them to go on to

interferon/ribavirin today, or wait a year or two and get treated with something that might have a better virologic response."

Dr. Kuritzkes acknowledged that interferon likely would continue to be a part of any HCV regimen for the next decade, and perhaps ribavirin as well. But hopefully there will be a better rate of sustained virologic response with use of the new drugs in development.

The study was funded by the ACTG. Dr. Chung and Dr. Kuritzkes have disclosed no relevant financial relationships.

16th Conference on Retroviruses and Opportunistic Infections (CROI): Abstract 103LB. Presented February 10, 2009.