

HIV/HCV CO-INFECTION AT CROI 2014

HCV mono-infection and co-infection with HIV and HCV was a major feature at the 21st annual Conference on Retroviruses and Opportunistic Infections (CROI) held in Boston from March 3-6, 2014. The cure for HCV is literally around the corner. This article will cover HCV highlights at CROI for both co-infected and mono-infected people.

The biggest news for people co-infected is that so far the new Direct Acting Antiviral (DAA) drugs have the same effectiveness and side effects in co-infected people as they do in mono-infected people. This means that co-infected people should not have to wait to use the new interferon or interferon/ribavirin (inf/r) combination free DAAs when they are FDA approved later this year -- if they can afford them. This is a huge advance since the new DAA combinations studies in mono-infected people described at CROI have between a 90 to 100% cure rate which is measured by a sustained viral response (no rebounding viral load) 12 weeks after the completion of therapy (SVR 12), some with only 6 to 12 weeks of therapy and without the life-altering side effects that accompany traditional 48 weeks of inf/r treatment.

Studies of inf/r free DAA combinations in people with HCV alone are further along than studies in co-infected people. The latest co-infection results are from studies in patients still using inf/r containing regimens. But the effectiveness and similar side effect profiles in inf/r containing studies bodes well for the better tolerated DAA combinations in people also co-infected with HIV. Let's start with the co-infected studies and build to the really exciting latest mono-infected data.

Doug Dieterich from New York presented data from an open-label study of faldaprevir plus inf/r for 24 to 48 weeks in co-infected patients with no prior HCV treatment, (naïve patients), or in those who relapsed after completing prior HCV therapy, (relapsers). People who did well quickly were treated for only 24 weeks in what is called response guided therapy.

Although this study did include inf/r, the take home message is that it cured 83% of prior relapsers, 69% of treatment naïves and 71% of people with HCV genotype (GT) 1a, traditionally the hardest to treat HCV genotype. The side-effects experienced by co-infected people were also very similar to those in mono-infected patients.

The data was even better with simeprevir (Olysio), a next generation, FDA approved protease inhibitor (PI) plus inf/r in a mix of naïve and previously treated patients in a study again presented by Doug Dieterich. Simeprevir is dosed only once per day unlike earlier approved HCV PIs that require administration three times per day. Cure rates, which are now measured by a sustained viral response for 12 weeks after the completion of therapy (SVR12), were 74% overall and 89% in the response guided patients who because they initially did well on treatment, received only 24 weeks of therapy instead of 48 weeks of treatment. Side effects were also similar to those experienced by mono-infected patients, except for rash events which were higher in simeprevir patients.

The best results for co-infected patients were presented by Susanna York of North Carolina in a study of sofosbuvir (Sovaldi), plus ribavirin (RBV) but without interferon in naïve co-infected people with various HCV genotypes for 12 and 24 weeks. Sofosbuvir (SOF), arguably the most promising new DAA, and to date the most expensive, is FDA approved for mono-infected and co-infected patients. The cure rate for GT1 patients on SOF plus RBV was 76% and 88% in GT 2 patients, but only 67% of GT 3 patients after 12 weeks of therapy. SVR rates were higher with 24 weeks of therapy and were 92% for GT 2 and 94% for GT 3 patients. Side effects included fatigue, insomnia, headache and nausea, all RBV associated toxicities. While T-cell counts dropped, T-cell percentages, a more accurate measure of T-cell performance, remained the same.

SOF is also being studied with GS 5885, now known as ledipasvir (LDP), in a one pill, once a day fixed dose combination (FDC), in co-infected people. SVR 12 rates have been as high as 100% in mono-infected people on 12 weeks of treatment without the terrible inf/r associated side effects. Gilead, the manufacturer of the FDC, filed for FDA approval of SOF plus LDP in mono-infected patients with GT 1 on February 11, 2014.

Studies in mono-infected people presented at CROI on 12 weeks of therapy showed 67% of GT 1a treatment naïve patients on daclatasvir and simeprevir ± RBV, 90% SVR 12 rates in GT 1a people on daclatasvir, asunaprevir and BMS-791325, 99% in easier to treat GT 1b naïve patients on ABT450/r plus ABT333 ± RBV.

The most exciting HCV news was the data in mono-infected people, especially the 6 week versus 12 week data presented by Anita Kohl from the NIH. There was a 100% cure rate on 12 weeks of Gilead's SOF + LDP, a 95% cure rate on **6 weeks**

of SOF + LDP + GS 9669, a new non-nucleoside NS5B inhibitor and a 100% cure rate on **6 weeks** of SOF + LDP + GS9451, a new protease inhibitor. in mono-infected people. DAAs have revolutionized HCV treatment. One of the major questions remaining is whether people will be able to afford the new HCV treatments.