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Response to Piroth et al: Optimal duration of treatment for acute hepatitis C in HIV positive individuals?

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In a recent paper Piroth and colleagues report on the outcomes following treatment of acute hepatitis C in 40 HIV positive MSM, 38 of whom received combination therapy with pegylated interferon and ribavirin¹. The overall SVR rate of 82% is encouraging, especially given that 81% of their cohort had genotype (GT) 1 or 4 infection, and supports guidelines for recommending treatment in this setting². However, we question the conclusions the authors draw from their data regarding optimal duration of therapy.

The authors argue that those patients treated for longer than 28 weeks had a significantly greater SVR rate than those treated for less than 28 weeks (92% versus 64% respectively, $p=0.03$), and that the rate of SVR (25%) in those who did not achieve RVR but received <28 weeks of therapy merits extension to 48 weeks for all patients with non-RVR. The evidence for these specific recommendations however is weak and confused by how data from the 'null responder' group is dealt with in this non-randomised design. Five patients were reported as 'never responding' to therapy presumably defined as no RVR or EVR and ceased therapy before 28 weeks. In the analysis examining SVR rates the authors appear to have included these subjects in the group receiving less than 28 weeks (SVR 9/14, 64%) versus longer duration (SVR 23/25, 92%) resulting in the 'short arm' appearing to be inferior. In fact the true question to examine is how common relapse was in non-RVR subjects who then achieved EVR and were subsequently treated for less than 28 weeks. A high rate of relapse in this situation would suggest inadequate length of treatment course. In the HEPAIG study it appears that 13 non-RVR patients subsequently achieved EVR but only one of these was treated for < 28 weeks and this patient subsequently achieved SVR.

In the Australian Trial in Acute Hepatitis C 35 HIV positive MSM were treated with 24 weeks combination therapy with Pegylated interferon and ribavirin and RVR was achieved in 12 (34%)³. In the 23 non-RVR subjects, 3 had no EVR and were discontinued and of the remaining 20 (50% GT 1), only 3 (2 GT 1 and 1 GT 3) relapsed after treatment completion, demonstrating that 24 weeks of combination therapy was adequate in 85% of subjects with no RVR but EVR. Given the additional expense and toxicity of extending therapy to 48 weeks (we note the 40% use of growth factors in HEPAIG), the costs would outweigh any potential marginal benefit. The HEPAIG study recommendation is even less appealing given the likelihood of new therapies available for retreatment within the next few years for those who do relapse.

In summary we agree with the HEPAIG authors that combination therapy is optimal in this setting and that treatment should be discontinued in those with complete non-response at week 12. However, we believe their treatment duration recommendations are not based on available evidence and that this question therefore remains unanswered.

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