If there had been any question over whether the two hepatitis C projects nearing US launch would be used together on approval, today there should be no doubt. The combination of Gilead Sciences’ sofosbuvir with Johnson & Johnson’s simeprevir achieved a greater than 90% viral suppression rate in patients who have previously failed to clear their disease on an interferon-based therapy.

The fact that the regimen did so without an assist from ribavirin is even better news, since eliminating its risk of anaemia is recognised as big an improvement as removing the flu-like symptoms associated with interferon. Given that the data presented at AASLD are phase II, and the FDA will almost surely not sanction the combination yet, it is probable that physicians will want to reserve the new treatment for advanced patients with few options.

Without explicitly endorsing off-label use of the two agents together, Ira Jacobson, a Cornell University medical professor who presented the Cosmos trial data at AASLD, said, “It has occurred to many clinicians that approval of these two agents will represent the first time that physicians and patients will have access to agents in these two classes together.

“All of us want to help our patient to the maximum extent possible, so it’s not difficult to imagine extrapolating from these data and considering the application of this regimen even in the absence of additional data to patients in particular need.”

Beat and raise?

With a 90% viral suppression rate four weeks after the end of treatment, expectations were already sky high. The big question was whether the cure rate would hold or even improve, and whether the ribavirin is necessary to achieve these rates.

The sofosbuvir-simeprevir combination did not disappoint. The first cohort to complete the 12 weeks of follow-up after the end of treatment consisted of genotype 1 patients who had not responded to prior interferon with little to no fibrosis. The non-ribavirin arms both achieved sustained viral response (SVR) of 93%, regardless of whether patients underwent 12 or 24 weeks of treatment. With 24 weeks of treatment, the arm with ribavirin had an SVR rate of 79%, and in the 12-week arm the SVR was 96%.

“There is no incremental benefit going to 24 weeks,” Fred Poordad, a San Antonio University of Texas medical professor, said of the Cosmos data in a review of ongoing phase II trials. “I wonder if ribavirin would add an incremental benefit.”

Dr Jacobson also presented interim results on patients with advanced fibrosis or cirrhosis that were no less encouraging. Four weeks after the end of a 12-week treatment regimen patients taking the new antivirals together were hitting 100% viral suppression, and 96% if ribavirin was added to the mix. 100% of patients who had never received an interferon-based treatment had viral suppression, with the only relapse in that liver-disease cohort having been a single patient taking ribavirin.

How important is ribavirin to hep C treatment? It certainly made interferon better, but the side effects, particularly anaemia, required careful management and caused occasional discontinuations, said Gregory Fitz, internal medicine department chair at the University of Texas Southwestern and AASLD’s president.

“If these other agents can avoid that toxicity I think having regimens that are both interferon and ribavirin-free is a step forward,” Dr Fitz said.

Sofosbuvir and simeprevir, now called Sovriad after approval in Japan, have both received unanimous support from FDA advisory committees. Sovriad is due a US decision by November 28 and sofosbuvir by December 6.

After the data release yesterday afternoon, shares in J&J’s partner Medivir, which licensed out the protease inhibitor in 2004, were up 6% to SEK84 today.
With the growing chatter about the sofosbuvir-simeprevir combination, some other very positive developments in hepatitis C were lost in the noise, but were no less significant. Bristol-Myers Squibb reported positive phase II data from its combination of daclatasvir, asunaprevir and BMS-791325, with 12-week SVR above 90% in genotype 1 – the only weakness being response in cirrhotics in one of two dosing groups.

Gilead reported data on the use of sofosbuvir and ribavirin in pre and post-liver-transplant genotype 1 patients, a population in particular need of treatment options; this showed that a 12-week regimen before transplant achieved a post-transplant viral suppression rate of 64%. A 24-week course to treat infection relapse following liver transplant achieved viral suppression in 77% of patients four weeks after the end of treatment.

And in genotype 2 and 3 patients, sofosbuvir with an interferon and ribavirin backbone achieved a 96% viral suppression rate in genotype 2 and 83% in genotype 3.

Two years ago, Incivek and Victrelis marked a step forward, improving cure rates and reducing the time some patients needed to take interferon and ribavirin. It now looks as though physicians within a month might be able to start recommending a regimen free of both of these mainstay treatments, and many appear ready to do so in patients who are running short of options.

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