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CLINICAL

Boceprevir for previously treated chronic hepatitis C virus genotype 1 infection

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SUMMARY

This paper reports the important results of the RESPOND-2 trial and is accompanied in the same issue by the report of the SPRINT-2 trial investigating the use of boceprevir for untreated chronic hepatitis C virus (HCV) genotype 1 infection. The RESPOND-2 trial recruited 403 patients who had either no response to interferon previously or had no circulating virus at the end of treatment but then relapsed within the first 24 weeks of stopping therapy.

Following randomisation all patients had a lead-in period of four weeks of pegylated (PEG-) interferon alpha-2b and weight-based ribavirin (800–1,400 mg). After the lead-in period three groups were treated in a 1:2:2 ratio. Group 1 received a further 44 weeks of PEG-interferon and ribavirin plus placebo. Group 2 received response guided therapy with boceprevir 800 mg three times daily plus PEG-interferon and ribavirin for 32 weeks if they had undetectable virus at weeks eight and 12. For individuals with detectable virus at week eight and undetectable virus at week 12, PEG-interferon and ribavirin were given for a further 12 weeks. Group 3 received 44 weeks of boceprevir 800 mg three times daily and PEG-interferon and ribavirin. Any patients with detectable virus at week 12 discontinued treatment.

The proportion of relapsers in each group was around 65% with around 20% in each group having significant fibrosis or cirrhosis. The viral load was high in over 80% of patients in all groups. The sustained virological response (SVR) was 21% in group 1, 59% in group 2 and 66% in group 3 which is a highly significant result for comparisons between the boceprevir groups and group 1 ($p<0.001$). Those with prior relapse had better response rates than those with prior non-response and patients who had a reduction in HCV RNA levels by greater than 1 log at week four (good response) had a substantially better outcome than those with a poor interferon response.

Viral breakthrough in the treatment arms, indicating probable resistance, was only 5%. There was an increase in anaemia in the treatment groups compared with group 1 (45% vs 20%). This however resulted in discontinuation in only 3% of group 3 patients.

OPINION

Chronic hepatitis C infection affects over 200 million people worldwide. It is the leading indication for liver transplantation both in the United States and Europe and has a prevalence in the United Kingdom of around 0.5%. It is estimated that half of the infected patients in Scotland remain undiagnosed.[2]

The treatment for the infection following its discovery in 1991 was initially standard interferon with very poor rates of SVR, which equates to a cure, in the order of 10%. The addition of daily ribavirin to standard interferon improved the SVR rates to around 30% for genotype 1, which is the most difficult genotype to treat. From early in the last decade the standard of care became PEG-interferon with ribavirin, which increased response rates to over 40% in genotype 1 and over 70% in genotypes 2 and 3.

Until this year there has been no real prospect of offering any realistic offer of cure to patients with genotype 1 infection who have failed treatment. The arrival of the protease inhibitors has very much heralded a real hope to these patients. There are now two protease inhibitors making their way to the market later this year. Telaprevir[3] and boceprevir add about an additional 20% response rate in the untreated genotype 1 patients, giving SVRs around 60% with a shortened duration of therapy (24 or 28 weeks as opposed to the present 48 weeks) but it is in the previously treated patients that the major improvement in outcome is seen. The huge increase of response rates by over 40% in this trial is a major step forward in the treatment of genotype 1 hepatitis C.

These drugs however will be expensive and along with the combination of PEG-interferon and ribavirin will be a challenging course of therapy for the patient and the treatment staff.

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