

Should patients with hepatitis C genotype 2/3 infection who are slow responders to PEG-interferon and ribavirin have treatment duration extended from 24 to 32-36 weeks?

A 'before and after' study

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Introduction

Approximately 30% of patients with genotype 2 or 3 (GT2/3) hepatitis C virus infection (HCV) do not achieve rapid virological response (RVR) with standard pegylated (PEG) interferon and ribavirin treatment. It is unclear if these "slow responders" benefit from extending treatment duration beyond the standard 24 weeks^{1,2,3}. In 2009, the Viral Hepatitis Service at John Hunter Hospital introduced a protocol to extend the standard PEG-interferon / ribavirin treatment duration to 32-36 weeks for G2/3 patients who were considered slow responders, i.e. HCV not detected at week 8 or week 12 of treatment, in the hope of improving rates of sustained virological response (SVR).

Aim

To assess the value of extending treatment in slow responding G2/3 patients.

Method

In this 'before and after' study, we analysed prospectively collected data to compare the Control Group: non-cirrhotic, slow responder (i.e. negative RVR) G2/3 patients treated prior to the lengthened treatment protocol change to the Extended Group: non-cirrhotic, slow responder (i.e. negative RVR) G2/3 patients who received 32-36 weeks of treatment, with the primary outcome measure being SVR 24 weeks following treatment completion (SVR24). Null responders (i.e. virus detected at week 12) had all treatment ceased and were excluded from analysis.

Extended group inclusion criteria

All patients since August 2009 who were HCV detected at week 4 and received extended treatment of 32 - 36 weeks.

- Genotype 2 or 3
- Patients treatment was extended to 24 weeks PEG-Interferon / Ribavirin treatment from the **date of virus not detected** (week 8 or 12 of Rx).
- Non-cirrhotic, as defined by:
 - Liver biopsy, or
 - Fibroscan, or
 - CT, or
 - Clinical assessment
- Compliant with the length of treatment
- Non-responders and patients in retreatment were not included in the study.

Results

Nine eligible patients were treated prior to the protocol change (standard duration, 24 weeks) and 17 were treated after (extended duration, 32-36 weeks).

The standard duration treatment group did not significantly differ from the extended treatment duration group in terms of mean age, gender, mean weight, proportion with Genotype 3, mean viral load, and mean ribavirin dose ($p > 0.05$ for all of these comparisons). See table below.

Patient participation in extended treatment was informed and voluntary. Treatment was well tolerated, with no patients stopping treatment early due to adverse effect.

The SVR24 rate was higher in the extended duration group (15/17, 88%) than the control group (5/9, 55%, $p = 0.06$) receiving standard treatment, and the relapse rate was significantly lower (12% vs. 55%, $p = 0.02$).

Table 1. Comparison of variables and outcomes between the Extended Group and the Control Group

		Extended Group (n=17)	Control Group (n=9)
Mean	Age ¹	45.1 years	48.2 years
	Weight ¹	78.4kg	76.9kg
	Ribavirin dose ¹	14.1mg/kg	13.5mg/kg
	HCV Viral load ¹	6.2	6.4
Sex	Male ¹	9	6
	Female ¹	8	3
Genotype	2 ¹	6	1
	3 ¹	11	8
Response	SVR24 ²	15 (88%)	4 (44%)
	Relapse ³	2 (12%)	5 (55%)

1. $p > 0.05$, 2. $p = 0.06$, 3. $p = 0.02$

Conclusion

As PEG-Interferon / Ribavirin will remain standard treatment for G2/3 patients for the short-term future, patients with G2/3 HCV who fail to achieve an RVR with PEG-interferon and ribavirin may benefit from an extension of treatment duration from 24 to 32-36 weeks.

A limitation of the study was the small control group, due to week 4 PCR tests not being conducted routinely prior to April 2007.

Larger studies are needed to confirm these findings and to reconcile them with conflicting studies in the literature.

Control group inclusion criteria

All patients April 2007 to July 2009 who were HCV detected at week 4 and received standard treatment of 24 weeks.

- Genotype 2 or 3
- Hepatitis C virus detected at week 4 of treatment.
- Non-cirrhotic, as defined by:
 - Liver biopsy, or
 - Fibroscan, or
 - CT, or
 - Clinical assessment
- Compliant with the length of treatment
- Non-responders and patients in retreatment were not included in the study.

References

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