

# EFFICACY OF TRIPLE THERAPY WITH THYMALFASIN (THYMOSIN ALPHA 1) IN COMBINATION WITH PEGINTERFERON ALFA-2A AND RIBAVIRIN FOR THE TREATMENT OF HCV NONRESPONDERS

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## ABSTRACT

### BACKGROUND:

Approximately 55% to 60% of treatment-naïve patients fail to achieve a sustained virologic response (SVR) with interferon and ribavirin therapy.<sup>1</sup> Only 11% of nonresponders achieve a SVR when retreated with peginterferon alfa-2a (PEG-IFN  $\alpha$ -2a) plus ribavirin.<sup>1</sup> The low rate of sustained virologic response after retreatment with current therapies underscores the need for new therapeutic options and more efficacious treatment strategies.

Thymalfasin (thymosin alpha 1; T $\alpha$ 1) is a 28-amino acid peptide that has shown efficacy in the treatment of chronic hepatitis C virus (HCV). Investigative studies including treatment-naïve patients have shown that thymalfasin plus interferon alfa (IFN- $\alpha$ ) improved HCV RNA viral clearance compared to IFN- $\alpha$  therapy alone,<sup>2,3</sup> and thymalfasin has an excellent safety profile.

### OBJECTIVE:

This study investigated the effects of thymalfasin in combination with PEG-IFN  $\alpha$ -2a and ribavirin as retreatment for patients who failed to respond to a previous 6-month course of interferon plus ribavirin therapy.

### METHODS:

The patients in this study had chronic viral hepatitis C and did not respond to prior combination therapy of standard IFN- $\alpha$ /ribavirin administered for at least 6 months. In this open-label study, all subjects were assigned to receive treatment with thymalfasin (1.6 mg twice a week), PEG-IFN  $\alpha$ -2a (180  $\mu$ g once a week), and ribavirin (800 mg to 1,000 mg/day) for 48 weeks. All patients had positive HCV RNA by PCR analysis, abnormal levels of ALT, compensated hepatic disease, and liver biopsy with chronic damage. A change from positive to negative HCV RNA or the reduction by more than 2 log<sub>10</sub> of the initial viral load was considered an early viral response (week 12). At the end of treatment (week 48), or at the end of follow up (week 72), a viral response was defined as an undetectable viral load (<600 IU/mL).

### RESULTS:

Thirty patients from Mexico were included (9 men, 21 women), average age was 57 (range 27 to 64), all with positive viral load, 19 with values >500,000 IU/mL; 11 were infected with genotype 1a, 15 with genotype 1b, and 4 with genotype 2. Twenty-eight patients completed 48 weeks of therapy and 2 completed only 24 weeks due to side effects. Early viral response was observed in 56.6% of patients at week 12 and 50% at week 24. End-of-treatment response at week 48 was 50% and 21.4% achieved a sustained virologic response at week 72. Among genotype 1 patients, 25% experienced sustained viral response at week 72. Two patients stopped the treatment in week 24 after testing positive for HCV RNA. The 4 patients with genotype 2 were all positive at week 72. Normalization of ALT levels was observed in 27.5% of patients at week 12, 27.5% at week 24, 53.2% at week 48, and 25% at week 72. A reduction of the dose of PEG IFN  $\alpha$ -2a was required in 32.1% at week 48 and 25% required dose reduction of ribavirin. Thymalfasin was well tolerated, without side effects or a need to reduce the dose.

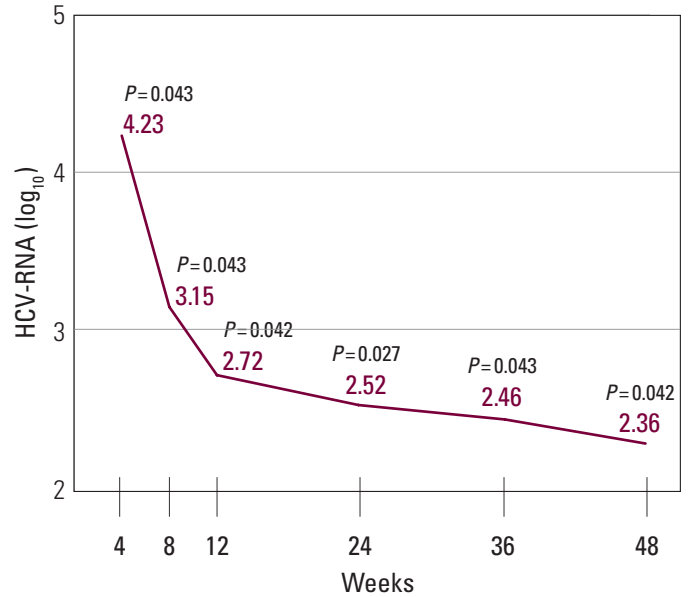
### CONCLUSION:

For difficult-to-treat HCV patients, triple therapy with thymalfasin, PEG IFN  $\alpha$ -2a, and ribavirin offers advantages for the retreatment of patients who previously failed treatment with IFN- $\alpha$  plus ribavirin. A large, randomized study evaluating the efficacy and safety of this triple therapy regimen is needed to confirm these promising results.

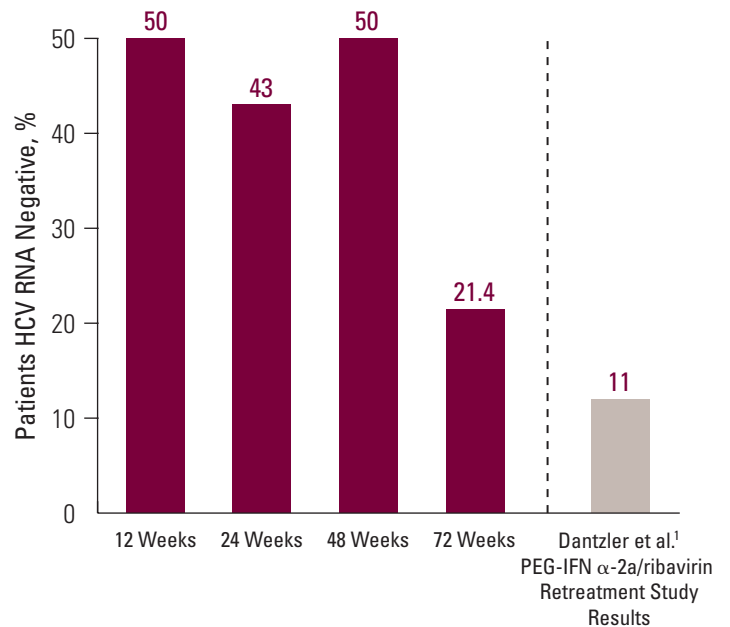
## BASELINE PATIENT CHARACTERISTICS

PATIENT CHARACTERISTICS	Mean (Range)
Age (y)	57 (27-64)
Gender (male/female)	9/21
Hispanic	30 (100%)
Genotype 1a, 1b	26
Genotype 2	4
<b>Baseline laboratory results</b>	
ALT (IU/mL)	89 ± 69
AST (IU/mL)	85 ± 79
Albumin (mg/dL)	3.9 ± 0.6
Bilirubin (mg/dL)	0.9 ± 0.3
Hemoglobin (g/dL)	15.5 ± 1.4
White blood (count/mm <sup>3</sup> )	6203 ± 1815
Neutrophils (count/mm <sup>3</sup> )	3349 ± 726
Platelet (x103/mm <sup>3</sup> )	205 ± 98
<b>HCV RNA level by PCR</b>	
<500,000 IU/mL	11
>500,000 IU/mL	19

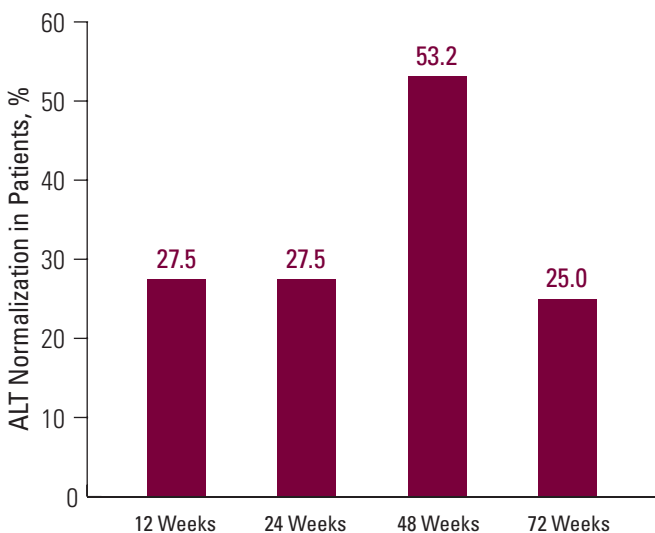
## HCV KINETICS DURING TRIPLE THERAPY



## HCV RNA CLEARANCE RATES AT 12 WEEKS, 24 WEEKS, END-OF-TREATMENT (48 WEEKS), AND AT 72 WEEKS WITH TRIPLE THERAPY



## ALT NORMALIZATION



## REFERENCES:

- Dantzer TE, Lawitz EJ. Treatment of chronic hepatitis C in nonresponders to previous therapy. *Curr Gastro Rep.* 2003;5:78-85.
- Moscarella S, Buzzelli G, Romanelli RG, et al. Interferon and thymosin combination therapy in naïve patients with chronic hepatitis C: preliminary results. *Liver.* 1998;18:366-369.
- Sherman KE, Sjogren M, Creager RL, et al. Combination therapy with thymosin α1 and interferon for the treatment of chronic hepatitis C infection: a randomized, placebo-controlled double-blind trial. *Hepatology.* 1998;27:1128-1135.