

enabling confirmation of the diagnosis and commencement of adequate treatment. In patients clinically suspected of presenting with TB or with suggestive endoscopic lesions, a possible recommendation is the performance of a PCR study for *M. tuberculosis* in intestinal tissue because it favors rapid diagnosis and has a high diagnostic yield.

### Ethical considerations

The study was approved by the scientific ethics committee of the *Hospital Clínico Universidad de Chile* and the patient gave his written statement of informed consent. The authors declare that the present article contains no personal information that would enable patient identification.

### Financial disclosure

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### Conflict of interest

The authors declare that there is no conflict of interest.

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## What do we know about detectable viremia at the end of hepatitis C virus treatment and the subsequent sustained virologic response?<sup>☆</sup>



### ¿Qué sabemos acerca de la carga viral detectable al final del tratamiento de virus de hepatitis C con respuesta viral subsecuente?

The treatment of hepatitis C virus (HCV) infection with regimens based on second generation direct-acting antivirals

(DAAs) has been associated with high rates of sustained virologic response (SVR) and few secondary effects (1%). However, there is little information about the impact of detectable viral load on the SVR at the end of treatment with DAAs.<sup>1</sup> Thus, we refer to the case of a 49-year-old Mexican man that had a history of failed treatment in 2006 with pegylated interferon and ribavirin for 48 weeks. The liver biopsy taken at that time reported grade 2 fibrosis (METAVIR F2). In 2016, the patient received 12 weeks of paritaprevir/ritonavir/ombitasvir/dasabuvir (3 D), with complete adherence, and no significant adverse events. Viral load at the end of treatment was detectable (Abbott Real Time PCR assay [ART]), with SVR 3 months later (Table 1).

Previous analyses have reported a 5–7% detectable viral load at the end of treatment with SVR after different DAA regimens.<sup>1–4</sup> We found 6 reports in relation to that interesting phenomenon, which are summarized in Table 1. To explain the viremia at the end of treatment, some authors suggest a mechanism involving viral kinetics, in which

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**Table 1** Characteristics of patients with detectable viral load at the end of treatment and later sustained virologic response.

Reference	n Fibrosis	Genotype	Previous treatment	Detection	Treatment	Baseline	Week 4	EOT	SVR4	SVR12	SVR24
Ancha et al. <sup>8</sup>	5 Cirrhosis (n = 1)	1a (n = 4) 1b (n = 1)	Experienced (n = 2)	CTM	SOF/LDV – 12 weeks (n = 4)	-	-	<15–235 IU/mL	-	ND	ND
Maasoumy et al. <sup>2</sup>	471 Cirrhosis (n = 120)	1	Experienced (n = 231)	CTM ART	SOF/SIM – 12 weeks (n = 1) SOF/LDV ± RBV (8, 12, 24 weeks)	6.4 log 10 IU/mL	-	n = 33 18 IU (12–62)	-	ND (n = 32)	-
Malespin et al. <sup>4</sup>	5 Cirrhosis (n = 4)	1a (n = 3) 1a or 1b (n = 2)	Naïve (n = 2) Experienced (n = 3)	ART	SOF/SIM -12 weeks (n = 4)	-	-	EOT+	ND	ND	ND
Shteyer et al. <sup>3</sup>	1 - F2-F4 (Fibro-spect)	1b	-	ART	SOF/LDV – 12 weeks (n = 1)	Log 7.0	-	Log 1.0	ND <sup>a</sup>	ND	ND
Sidharthan et al. <sup>5</sup>	6 -	1	Naïve	ART	SOF/LDV – 6 weeks + GS-9669 (n = 5)	-	-	14–64 IU/mL	ND (n = 2) <sup>b</sup> 14 IU/ml (n = 1) <sup>c</sup>	ND (n = 2)	-
Childs-Kean and Hong <sup>1</sup>	5 Cirrhosis (n = 2)	1a	Naïve (n = 4) Experienced (n = 1)	ART	SOF/LDV – 6 weeks + GS-9451 (n = 1) 3D + RBV 12 weeks (n = 1)	2,000,000 and 7,000,000 IU/mL	780–49 IU/mL	25–13 IU/mL	23 IU/mL (n = 1) ND (n = 4)	ND	-
Current case <sup>c</sup>	1 F2 (Biopsy)	1b	Experienced (n = 1)	ART	SOF/LDV – 8 weeks (n = 3) SOF/LDV – 12 weeks (n = 1) 3D	802380 IU/mL Log 5.9	56 IU/mL Log 1.75	14 IU/mL Log 1.14	ND	ND	ND

3D: paritaprevir/ritonavir/ombitasvir/dasabuvir; ART: Abbott RealTime PCR assay; CTM: Cobas TaqMan HCV Test; EOT: end of treatment; ND: not detected; RBV: ribavirin; SOF/LDV: sofosbuvir/ledipasvir; SOF/SIM: sofosbuvir/simeprevir.

<sup>a</sup> Shteyer et al. describe cases of patients with acute hepatitis C.

<sup>b</sup> In Sidharthan et al., 2 patients achieved RNA < the detection limit at 8 weeks after treatment.

<sup>c</sup> Viral load measured using the Abbott m2000r Real-time System (Abbot Laboratories, Germany), with a detection threshold of 12 IU/mL.

noninfectious viral particles or defective virions can be detected transiently at the end of treatment.<sup>5</sup> In addition, HCV infection is known to affect cell immunity, and a decrease in viral load after an effective treatment could subsequently restore the immune mechanisms that enable the clearance of residual viruses at the end of antiviral therapy.<sup>1,4</sup> Strikingly, the majority of cases with positive viremia that later achieve SVR were described through the use of highly sensitive assays, such as real-time polymerase chain reaction.<sup>1,2</sup> HCV virion clearance occurs at a rate of 10–12 virions per day, but apoptosis of the infected cells has been observed to extend for more than 70 days.<sup>6</sup> We believe that our patient is not a case of a false positive, given that the viral loads were determined using the same method and they were not detectable 24 weeks after having finished treatment.

At present, predictors associated with detectable viral load at the end of treatment have not been reported. In the largest case series, conducted by Maasoumy et al.,<sup>2</sup> neither the baseline viral load nor the regimen utilized, were associated with said phenomenon. The available information suggests that having a detectable viral load at the end of treatment is not clinically relevant, given that almost all the patients in the case series cited above, reached SVR (Table 1). In the recommendations of the 2018 EASL guidelines,<sup>7</sup> the determination of viral load at the end of treatment is omitted, evaluating response 12 weeks later. That is based on the fact that efficacy of the DAA regimens is close to 100%.

### Ethical disclosures

Informed consent was requested from the patient to receive the treatment. The present scientific letter meets the current bioethical research norms and was authorized by the ethics committee of the *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán*. The patient cannot be recognized or identified through the images or data contained in the article.

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