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Treatment of patients with chronic hepatitis C infection in Lombardia: a report by the Lombardia Hepatitis Network

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Abstract. The arrival of potent directly acting antivirals (DAAs) for the treatment of chronic Hepatitis C virus (HCV) infection was a challenge for the regional health system of the Lombardia Region. Lombardia represents roughly 8% of the Italian territory but includes nearly 16% of the Italian population. In 2014, nearly 37,600 HCV patients were routinely followed-up in liver centers across the region; nearly 16,000 were classified as having advanced fibrosis or cirrhosis (Metavir F3-F4). The creation of a regional network was necessary to ensure uniformity in treatment access and treatment management. The first database analysis of the Lombardia Hepatitis Network was conducted in January 2016, and included data on 2432 patients who had received treatment from December 2014 to December 2015. The most prevalent HCV genotypes were HCV-1 found in 63% and HCV-3 found in 17%. Overall 90.4% patients achieved an SVR, SVR rates were 92.9% in HCV-1, 89.3% in HCV-2, 81.1% in HCV-3 and 88.9% in HCV-4.

Key Words
Hepatitis, Cirrhosis, Lombardia.

Background

The arrival of potent directly acting antivirals (DAAs) for the treatment of chronic Hepatitis C virus (HCV) infection was a challenge for the regional health system of the Lombardia Region[1]. Lombardia represents roughly 8% of the Italian territory but includes nearly 16% of the population, which is mostly living in 3 macro-areas concentrated near Milan, Bergamo, and Brescia. To ensure that HCV patients were offered optimal access to treatment with DAAs in the years 2015-2016, at the end of 2014, the regional welfare system conducted a survey among expert hepatology centers scattered throughout the region to understand the epidemiology of HCV in Lombardia and to assess the number of patients currently followed at Liver centers that fell into the National criteria for reimbursement of DAAs.

The Lombardia Hepatitis Network

In 2014 nearly 37,600 HCV patients were routinely followed-up in liver centers across the region, nearly 16,000 were classified as having

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Table I. Characteristics that define an expert Liver Center.

Mandatory	1.	A multi-disciplinary team including an expert in liver diseases, a pathologist and a dedicated nurse. All experts need to have special knowledge in viral hepatitis.
	2.	A nominate Team cordinator
	3.	The nurse needs to have knowledge in patients education and managementof HCV patients
	4.	A local cohort of at least 500 patients
	5.	A local radiology unit
	6.	A local Endoscopy unit
	7.	A local Laboratory capable of performing virological test
	8.	A specialized outpatient unit
	9.	A local Pharmacy Unit
	10.	Link to a Regional Liver Transplant Center
Optional but recommended	11.	A multidisciplinary outpatient clinic to diagnosis and manage patients with liver diseases
	12.	Proven clinical or translational research activity on the field of viral hepatitis
	13.	A link to a Virology Laboratory
	14.	A laboratory with expertise in Drug Drug interactions

advanced fibrosis or cirrhosis (Metavir F3-F4). The next step was creating a network in the Lombardia Region that could guarantee immediate access to therapy and state of the art clinical management to this large group of patients. Seven local experts on the management of chronic HCV were asked to provide standardized guidelines for treatment and management of viral hepatitis C as well as defining the required criteria to be labeled as a DAA prescribing center.

Therapy recommendations were based on those provided by the Italian Association for the Study of the Liver (AISF), that regularly updates its treatment guidelines to follow those produced by the European Association for the Study of the Liver (EASL)[2]. The AISF guidelines take into account the Italian National Health system reimbursement rules when providing guidance on treatment options in Italy. The document produced by the local experts, defined Percorso Diagnostico Terapeutico Assistenziale (PDTA), did not only concentrate on treatment but also focused on diagnosis, management of patients with chronic HCV infection and outcome indicators[3]. Although none of its recommendations were based on pharmaco-economy principles, every approved regimen for the treatment of chronic hepatitis C that was considered to be optimal by the experts was followed by the full price for the Regional health system to highlight differences in costs between similar treatment options. Liver centers included in the Regional Network for HCV were asked to follow the PDTA treatment recommendations and regularly provide figures on treatment and sustained virological response (SVR) rates. Expert liver centers were required to have specific characteristics regarding the clinical know-how and cross-sectional expertise (Table I).

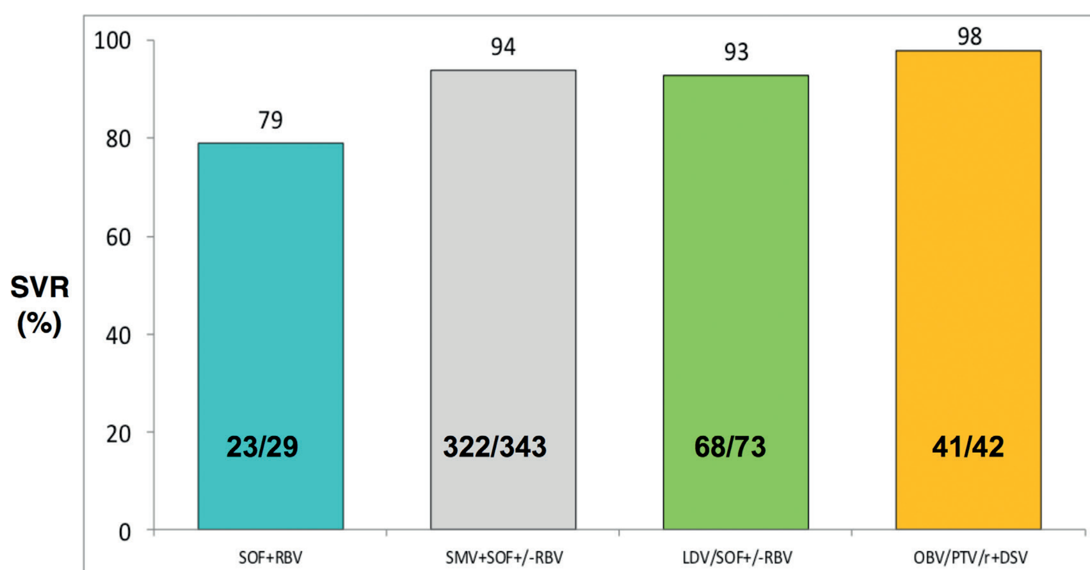

Figure 1. SVR rates in HCV-1 patients.

The first database analysis was conducted in January 2016, and included data on 2432 patients who had received treatment in Lombardia from December 2014 to December 2015. Nearly ¾ of the enrolled patients (74%) fell in the number 1 criteria for DAA reimbursement by AIFA, i.e., Child-Pugh A or B cirrhosis, while 14% of patients were classified as having F3 fibrosis. The most prevalent HCV genotypes were HCV-1 found in 63% and HCV-3 found in 17%. At the time of analysis 1534 patients had completed the treatment phase and 872 could be evaluated for SVR. By ITT analysis overall 90.4% (788/872) patients achieved an SVR, SVR rates were 92.9% in HCV-1 (498/536), 89.3% in HCV-2 (101/113), 81.1% in HCV-3 (116/143) and 88.9% in HCV-4 (71/80). In HCV-1 patients, the SVR rates were largely dependent on the use of EASL/AISF approved treatment regimens as they ranged from 98% with Paritaprevir/Ombitasvir/Dasabuvir ± Ribavirin to 79% in those who received the suboptimal combination of Sofosbuvir + Ribavirin (Figure 1). The same difference was seen in the overall cohort, since 93% of those who received an EASL/AISF endorsed regimen achieved an SVR compared to 87% of those who received suboptimal regimens (p=0.001). The use of suboptimal regimens was mostly dictated by urgent cases that could not await the introduction of DAA combinations for HCV-3 and HCV-1 decompensated patients, that were reimbursed in Italy only in the second quarter of 2015. This effect can be clearly seen when looking at the second update of the Lombardia Regional network which was performed in July 2016. In this case, more than 2293 patients were included in the SVR analysis. Overall 94.6% patients achieved an SVR, SVR rates were 97.4% in HCV-1a, 96.2 in HCV-1b, 94.9% in HCV-2, 86.6% in HCV-3 and 93.7% in HCV-4.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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