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The HCV Sicily Network: a web-based model for the management of HCV chronic liver diseases

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Abstract. – OBJECTIVE: Epidemiological studies report that in Sicily reside about 30,000 citizens with a diagnosis of chronic hepatitis due to HCV. The availability of direct antiviral action (DAA) is a real therapeutic breakthrough, but the high cost of the therapeutic regimes limits their use and forced the National Health System to establish clinical priority for the treatment.

MATERIALS AND METHODS: The HCV Sicily Network is a web-based model of best medical practice, which was designed to improve the management and the treatment of HCV chronic hepatitis and cirrhosis.

The network includes 41 centers and 84 gastroenterologists or infectivologists connected by a web platform that recorder the diagnosis and the clinic priority for the therapy.

RESULTS: From March 2015 to September 2016, 9,965 patients (57% male, mean age 61 years, 34% with age over 70 years) have been recorded in the web platform, 3,319 patients completed the treatment, and 1,754 completed the 12 weeks of follow-up. The Sustained Virological Response (SVR) was achieved in 1,541 patients (87.8%), while 136 patients (7.7%) 77 patients (4.5%) experienced a virological relapse during the 12 weeks of follow-up.

CONCLUSIONS: The HCV Sicily Network is an excellent system for the Regional Department of Health that can have a real estimation of patients that received an efficacy, but high-cost therapy.

Key Words:
Web-based network, Hepatitis C virus, Direct antiviral agent drugs (DAA).

***Partecipant to resist - HCV (rete Sicilia selezione terapia - HCV)**

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Introduction

The hepatitis C virus (HCV) infection is still a relevant health public issue in Sicily, where live about 5 millions of citizens. Epidemiological studies report that in Sicily reside about 30,000 citizens with a diagnosis of chronic hepatitis due to HCV. The availability of new drugs with direct antiviral action (DAA) is a real therapeutic breakthrough, but the high cost of the therapeutic

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Table I. Clinical criteria for the priority treatment with DAAs defined by AIFA.

Group 1: Patients with Child-Pugh A or B cirrhosis or HCC with complete response to surgical or locoregional therapies; Group 2: Patients with recurrent HCV hepatitis after liver transplantation; Group 3: Patients with chronic hepatitis with severe extrahepatic manifestations HCV-related (cryoglobulinemia syndrome with organ damage, B-cell lymphoproliferative diseases); Group 4: Patients with METAVIR F3 fibrosis; Group 5: Patients on waiting list for liver transplantation because of cirrhosis and MELD score less than 25 points and/or HCC within Milan criteria with the possibility of a waiting list for at least 2 months; Group 6: Patients with HCV chronic hepatitis, who received solid organ or bone marrow transplantation.

regimes limits their use and forced the National Health System to establish clinical priority for the treatment.

To achieve an ethical and social project and to properly allocate economic resources for useful treatment of hepatitis C must promote the interests of the individual patient and the best benefit for the health organization.

These values can be guaranteed through the good clinic practice, effectiveness and transparency of procedures and evidence-based therapeutic decisions. The pharmacological innovation has to be accompanied to carry forward this program by an important technical innovation, represented by the realization of modern informatics systems that allow to monitor patients and therapies and to recorder disease outcomes, which in the future will permit to have information to health program based on precision medicine[1].

The aims of the HCV Sicily Network are to identify patients with HCV chronic diseases who live in Sicily, to define the stage of disease and to allocate patients in the drug regimes in accordance with the guidelines. In Sicily, the synergy between health institutions and physicians has been the basis for designing this new model for integrated management of chronic liver disease due to HCV infection (Figure 1).

Figure 1. The key points of integrated management of HCV chronic diseases.

Materials and Methods

The HCV Sicily Network is a web-based model of best medical practice, which was designed to improve the management and the treatment of chronic hepatitis and cirrhosis. The Health Program of Sicily has predicted the networks integrate assistance, which through the Information and Communication Technology (ICT) can improve the medical care of the citizens, the health efficiency and the physicians' skills. The website www.registrohcvsicilia.it represents the communication tool, which includes citizens, physicians and stakeholders allowing to guarantee the access to diagnosis and available antiviral therapies (Figure 2). The network includes 41 centers (Figure 3) and 84 gastroenterologists or infectivologists connected by a web platform that recorded the diagnosis and the clinic priority for the therapy decided by AIFA (Agenzia Italiana del Farmaco) (Table I).

The web platform also has an informatics agenda that guarantees the fibroscan booking, essential investigation to identify patients with treatment priorities and the therapies booking from Spoke to Hub centers, which can prescribe antiviral therapies.

Results

From March 2015 to September 2016, 9,965 patients (57% male, mean age 61 years, 34% with age over 70 years) have been recorded in the web platform. Of these 9,965 patients, 5,294 patients (53%) had the priority criteria for the treatment as defined by AIFA and 4,616 patients (32% with

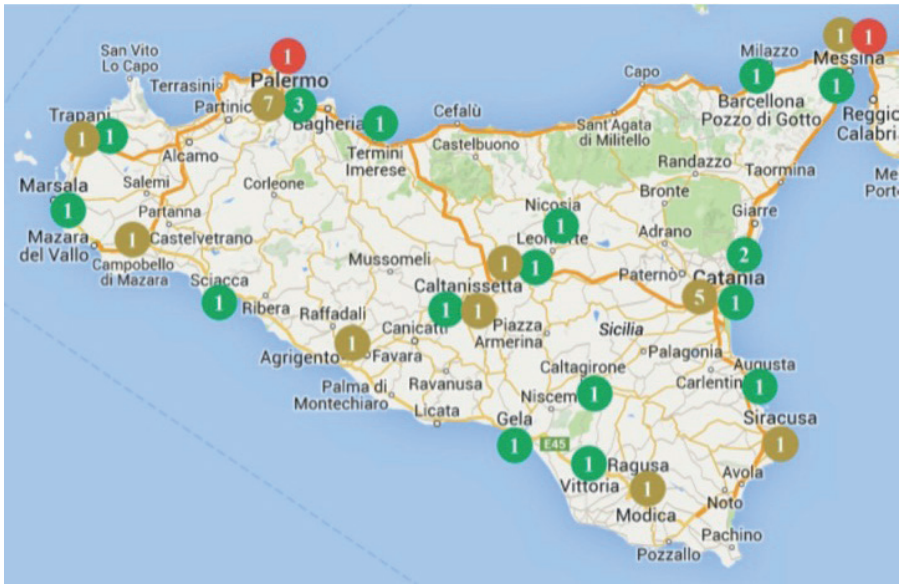

Figure 2. The SPOKE and HUB centers of resist - HCV.

F3 fibrosis, 59% with Child-Pugh A cirrhosis and 9% with Child-Pugh B cirrhosis) started the therapy with DAA drugs.

Table II reported the distribution of HCV genotypes and the diagnosis of liver disease according to age.

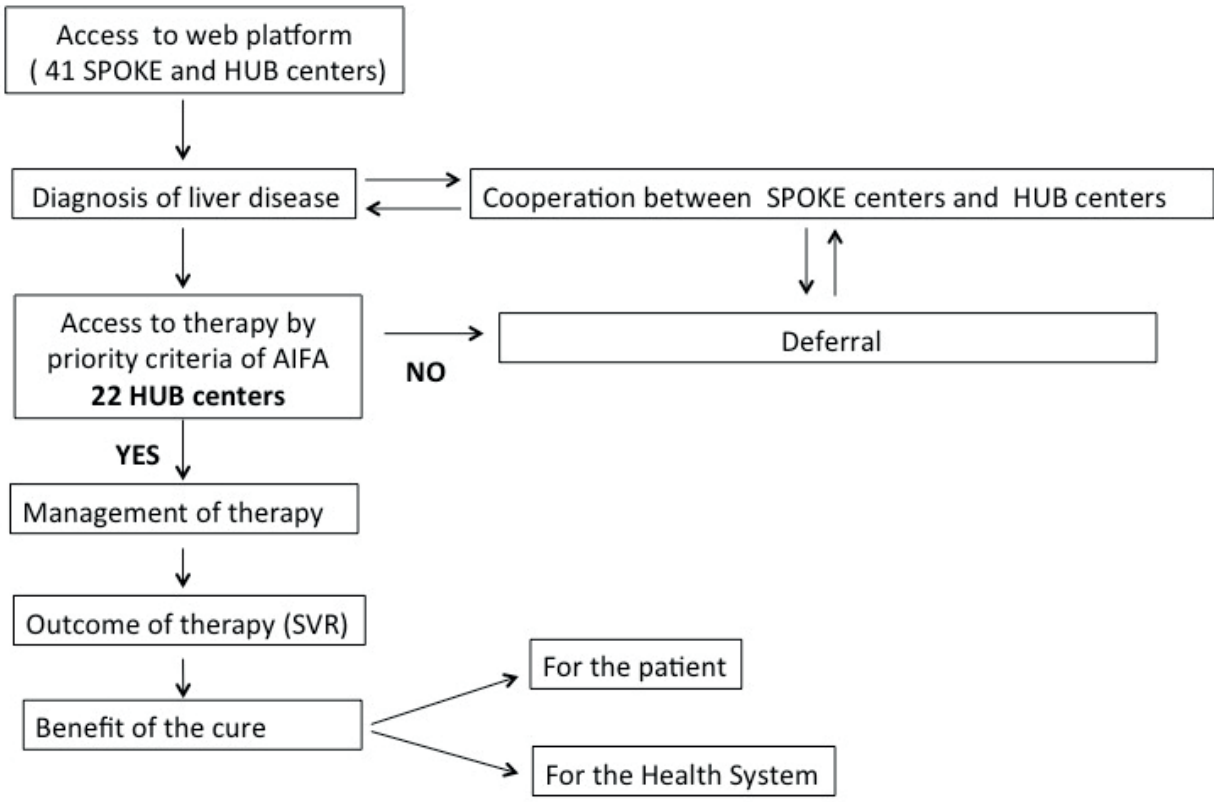

Figure 3. The points of clinical management of resist - HCV.

Table II. HCV genotypes distribution and diagnosis of liver disease according with age of patients.

	Overall	Males	Females	Diagnosis
Age > 80 years	**280**	**148 (53%)**	**132 (47%)**	
Genotypes				
- 1a	8 (2.8%)	3 (2%)	5 (4%)	Chronic hepatitis : 32%
- 1b	212 (75%)	115 (77%)	97 (74%)	Cirrhosis: 65%
- 2	46 (14.4 %)	24 (16.2%)	22 (16.6%)	HCC: 2%
- 3	0	0	0	
- 4	4 (1.4%)	3 (2%)	1 (0.7%)	
- Others/mixed	10	4	6	
Age 70- 80 years	**2113**	**1031 (49%)**	**1082 (51%)**	
Genotypes				Chronic hepatitis: 39.7%
- 1a	64 (3%)	25 (2.4%)	39 (3.6%)	Cirrhosis: 58%
- 1b	1748 (82%)	862 (83.6%)	886 (81.8%)	HCC: 2.3%
- 2	242 (11.5%)	122 (11.8%)	120 (11%)	
- 3	9 (0.4%)	5 (0.4%)	4 (0.4%)	
- 4	47 (2.2%)	20 (2.0%)	27 (2.6%)	
- Others/mixed	12	6	6	
Age 60- 70 years	**1995**	**1147 (54%)**	**964 (46%)**	
Genotypes				Chronic hepatitis: 51.3%
- 1a	124 (6.2%)	66 (5.7%)	58 (6.2%)	Cirrhosis: 47.3%
- 1b	1549 (77%)	780 (68%)	769 (80%)	HCC: 1.4 %
- 2	193 (9.7%)	105 (9.2%)	88 (9.3%)	
- 3	41 (2%)	27 (2.3%)	14 (1.4%)	
- 4	73 (3.6%)	44 (3.8%)	29 (3%)	
- Other/mixed	15	9	6	
Age 50- 60 years	**1516**	**1014 (67%)**	**502 (33%)**	
Genotypes				Chronic hepatitis: 57%
- 1a	245 (16%)	193 (19%)	52 (10%)	Cirrhosis: 42%
- 1b	819 (54%)	484 (47%)	335 (67%)	HCC: 1%
- 2	80 (5.3%)	37 (3.6%)	43 (8.5%)	
- 3	266 (17.5%)	224 (22%)	42 (8.5%)	
- 4	99 (6.5%)	72 (7.2%)	27 (5.4%)	
- Others/mixed	7	4	3	
Age < 50 years	**1203**	**840 (70%)**	**363 (30%)**	
Genotypes				
- 1a	235 (19.5%)	181 (21%)	54 (15%)	Chronic hepatitis: 73%
- 1b	580 (48%)	351 (42%)	229 (63%)	Cirrhosis: 26%
- 2	67 (5.5%)	44 (5.2%)	23 (6.3%)	HCC: 1%
- 3	261 (21.6%)	221 (26%)	40 (15%)	
- 4	51 (4.2%)	35 (4.1%)	16 (4.4%)	
- Others/mixed	9		1	

At September 2016, 3,319 patients completed the treatment and 1,754 completed the 12 weeks of post-therapy observation (Figure 4).

The rate of patients with F3 chronic hepatitis was 27.2%, 56.3% of patients had a diagnosis of Child-Pugh A cirrhosis and 16.9% of patients had a diagnosis of Child-Pugh B cirrhosis (Table III).

By intention to treat analysis, 92.3% of treated patients obtained a virological response at the end of therapy. Only 135 patients (7.7%) didn't obtain a virological response: 23 patients died because of liver or no liver-related causes, 45 were drop-out, 59 discontinued the treatment because of adverse events and only 8 patients were virologic non-responders. The Sustained Virological Response (SVR) was achieved in 1,541 patients (87.8%), while 77 patients (4.5%) experienced a virological relapse during the 12 weeks of follow-up after the end of therapy (Figure 5).

Table III. Clinical features of 1.745 patients treated between March and December 2015.

	Chronic hepatitis (F3) 475 (27.2%)	Child-Pugh A cirrhosis 983 (56.3%)	Child-Pugh B cirrhosis 296 (16.9%)
Mean age (years)	62.2	65.6	65.7
Age ≥ 70	143 (31%)	415 (42%)	133 (45%)
Men (%)	259 (56%)	573 (58%)	179 (66%)
Previous therapy (%)			
- Naïve	217 (46%)	383 (39%)	131 (44.%)
- Experienced	247 (54%)	600 (61.%)	167 (56%)
Esophageal Varices (%)		364 (37.1%)	78 (26.3%)
- F0		378 (38.4%)	190 (64.2%)
- F1-F3		241 (24.5%)	30 (10%)
- not done			
Previous HCC	1 (0.2%)	26 (2.2%)	44 (14.8%)
Comorbidities	89 (19.1%)	265 (27%)	95 (32.4%)
- Diabetes	161 (34.6%)	429 (43.6%)	117 (39.5%)
- Arterial hypertension	10 (2.1%)	24 (2.4%)	14 (3.3%)
- Stage-3 kidney disease	16 (3.4%)	48 (4.6%)	11 (7.3%)
- Hearth disease	50 (10.7%)	103 (11.1%)	37(12.5%)
- Depression			
- HIV co-infection	29 (6.2%)	30 (4.5%)	9 (3.0%)
Genotypes (%)	50 (10.7%)	74 (7.5%)	23 (7.7%)
- 1a	318 (68.5)	726 (74%)	212 (74.6%)
- 1b	47 (10.1%)	83 (8.4%)	29 (9.8%)
- 2	21 (4.6%)	65 (6.6%)	21(7.1%)
- 3	27 (5.8%)	34 (3.4%)	12 (4.5%)
- 4	1	1	1
- Others			

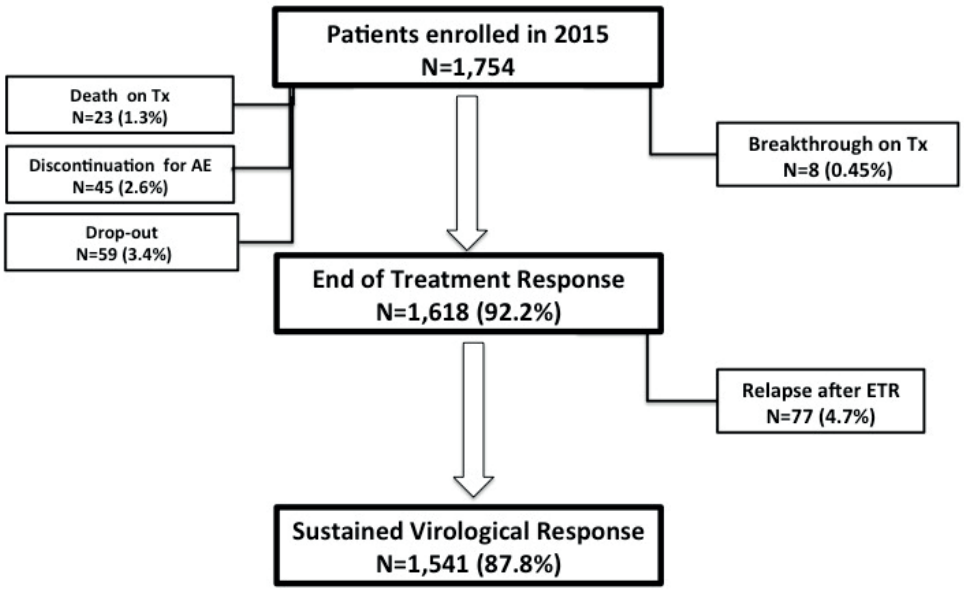

Figure 4. The algorithm of the patients included in the resist - HCV.

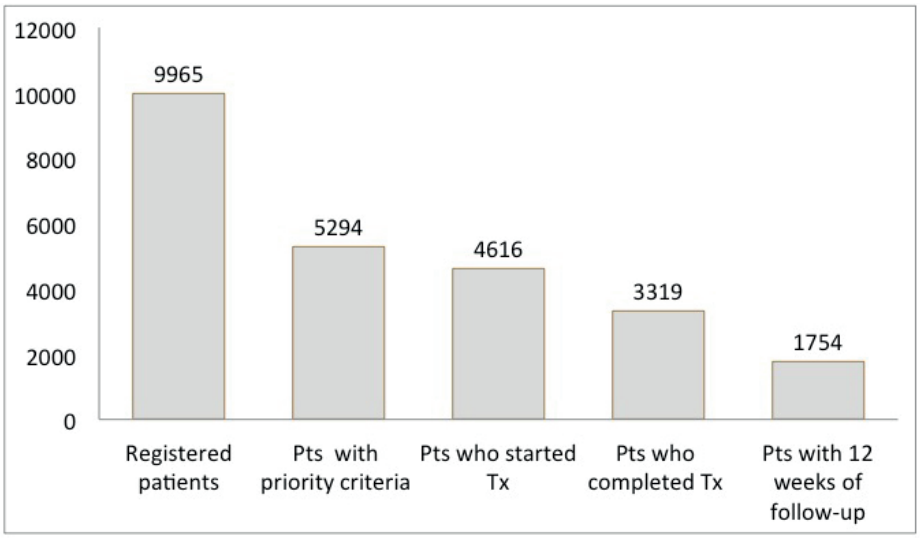

Figure 5. The results (End of Treatment Response and Sustained Virological Response) of therapy in patients who concluded the therapy and follow-up (Intention to treat analysis).

Discussion

The EASL and AASLD guidelines[2,3] recommended therapy with DAAs for all patients with a chronic liver disease related to HCV infection, but in Italy, the AIFA indicated some clinical priority criteria for the treatment of patients.

The HCV Sicily Network is a web-based model that consents the transparent and appropriation management of therapy with DAAs as indicate by AIFA and provides real-time results to the regional health organization and the scientific community.

The HCV Sicily Network is an extraordinary system for the Regional Department of Health that can have a real estimation of patients that received an efficacy, but high-cost therapy.

This network provides with high precision and continually all the data on the efficacy and tolerability of antiviral therapies in a very large cohort of patients treated in all centers of Sicily. At the same time continue the follow-up of patients who have not the priority for the treatment criteria.

Conclusions

The work will consent to upload also the epidemiologic estimates of virus C infections in Sicily and to evaluate the natural disease history in the next years to the light of eradication obtained with new DAAS.

Conflicts of interest

The authors declare no conflicts of interest.

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