# Hepatitis C Virus Clearance in Older Adults

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**OBJECTIVES:** To determine whether older adults with the hepatitis C virus (HCV) achieve a sustained viral response (SVR) after treatment with direct-acting antiviral therapy.

**PARTICIPANTS:** Individuals aged 80 and older with chronic HCV infection (N = 253; n = 213 with cirrhosis, n = 40 with advanced fibrosis).

**MEASUREMENTS:** We investigated the efficacy, safety, and global clinical effect of treatment with different combinations of direct antiviral agents (DAAs). Participants with cirrhosis were staged according to Child-Pugh-Turcotte class, Model for End-Stage Liver Disease score, and the D'Amico staging system. The type and number of comorbidities at baseline and hepatic and nonhepatic events during follow-up were registered.

**RESULTS:** Ninety-five percent of participants with cirrhosis and 95% of those with advanced fibrosis attained SVR. The rate was independent of sex, HCV genotype, and treatment schedule. During a mean follow-up of 14 ± 4 months (range 5–23 months), 34 events occurred in 27 participants: 10 hepatocellular carcinomas, 12 hepatic decompensations, 9 nonhepatic events, 3 deaths. Multivariate analysis of risk factors for experiencing adverse events during follow up showed that participants in D'Amico Stages 4 and 5, with a baseline serum albumin level of 3.5 mg/dL or less, and 3 or more comorbidities were the most at risk.

**CONCLUSION:** In a real-world setting, DAAs are safe and effective in older adults with HCV-related advanced fibrosis or cirrhosis. Individuals with preserved albumin synthesis and fewer than 3 comorbidities at baseline have the most to gain from long-term DAA therapy. **J Am Geriatr Soc 66:85–91, 2018.**

**Key words: direct-acting antivirals; HCV; chronic hepatitis; octogenarians**

New epidemiological data indicate that the prevalence of hepatitis C virus (HCV) infection is almost null in young and middle-aged individuals and is peaking in older adults (≥70).[1] In a recent Italian survey, HCV prevalence was 0.2% in subjects younger than 30 and 6.0% in those aged 70 and older.[2] The current prevalence places particular argument in decision-making when prescribing antiviral treatment to elderly adults because it is unknown whether it can improve their natural history. Elderly adults with chronic hepatitis C infection are more likely than younger individuals to have progressed to the cirrhotic stage and to be at risk of liver-related complications.[3,4] HCV clearance is essential to improve the natural history of the disease in the general population,[5,6] but data on likelihood of reducing liver-related complications and increasing life expectancy after sustained viral response (SVR) in elderly adults are limited.[7–10] The combination of advanced liver disease and older age makes an individual vulnerable, and people with this combination are likely to have extrahepatic comorbidities (e.g., cardiac and renal disease)[11]; these individuals may achieve a substantial increase in life expectancy despite an expected high rate of SVR.[12,13] Although they have a good safety profile, new interferon-free direct antiviral agent (DAA) regimens are expensive, and the treatment of elderly adults should be assessed according to an individualized cost-effectiveness approach to overall health.[12] The approach suggested for antiviral HCV treatment with DAAs in individuals aged 70 and older is to limit it to those with no major comorbidities, an estimated

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Metavir liver fibrosis score of F2 to F4, and a life expectancy of longer than 1 year.[7]

What constitutes an elderly population needs to be defined, varying from 60 and older to 80 and older.[4,7–12] Age itself is not a predictor of a negative response to the new DAAs. Even if real-world observational studies have increased the number of elderly adults treated with the new DAAs,[7–12] few individuals aged 80 and older have been enrolled in Phase III registration trials.[11,12] Even in these experiences, scanty information on whether successful viral treatment in old-old adults with HCV decreases mortality is available. Long-term follow-up studies have indicated that definitive HCV clearance can regress the extent of hepatic fibrosis and reduce the risk of cirrhosis-related complications, including hepatocellular carcinoma (HCC).[12,13] In addition, after viral clearance, favorable outcomes for extrahepatic events such as end-stage renal failure and cardiovascular events have been also documented.[14] These studies had individuals younger than 70 as their target population, which limits the generalizability of their conclusions to older adults. In very old adults, multiple comorbidities, multidrug consumption, and drug-drug interactions makes questionable the beneficial effect of HCV clearance. The evaluation of life expectancy based on liver disease with respect to that based on comorbidities can be considered useful criteria to identify suitable candidates for the highly effective oral antiviral drugs. With aging, the progression of liver fibrosis, and the presence of non-liver-related morbidities could make HCV clearance useless .[7,15] The aim of this study was to determine whether HCV clearance with new DAAs in individuals aged 80 and older, despite liver disease and multiple comorbidities, would reduce hepatic and extrahepatic events or mortality.

## PARTICIPANTS AND METHODS

### Study Design

From May 2015 to December 2016, 2,612 individuals with HCV infection and severe liver disease received treatment at collaborating Italian centers; information on the main characteristics of the cohort has been published previously.[16] Records of individuals aged 80 and older were extracted from the original database, and the individuals were followed up with during and after an antiviral course with the new DAAs. The Ethics Committee of the Coordinating Centre in San Giovanni Rotondo, Italy, approved the study. Selection criteria were aged 80 and older, no evidence of active HCC on imaging, and serum ribonucleic acid (HCV RNA) for HCV identified using polymerase chain reaction. Exclusion criteria were human immunodeficiency virus co-infection, an estimated glomerular filtration rate of less than 15 mL/min, and current hepatic decompensation unresponsive to appropriate treatment. The following parameters were noted: albumin, international normalized ratio, bilirubin, platelet count, creatinine, serum HCV RNA level, and HCV genotype. Comorbidities were recorded and classified according to a previously developed method.[17] Similarly, co-administered drugs were listed, and interaction with the intended DAAs was carefully checked by consulting the Liverpool HEP drug interactions guidance.[18]

### Definition and Staging of Cirrhosis

The definition of portal hypertension was in accordance with the Baveno VI Consensus Workshop[19] and included esophageal varices at endoscopy, ultrasound evaluation for collateral blood circulation, liver stiffness of 20 kPa or greater, and a platelet count of less than 150,000/μL.

Participants were considered to have cirrhosis if had esophageal varices on endoscopy, evidence of cirrhosis, portal hypertension, or ascites on ultrasound; a FibroScan (Hepatic elastography) liver stiffness value of 14.0 kPa or greater; or irregular surface of liver on ultrasound. Participants with a liver stiffness value of less than 14 kPa, no previous hepatic decompensation, and no irregular liver surface on ultrasound were considered to have advanced fibrosis (Metavir Class F3). Child-Pugh-Turcotte (CPT) class and MELD score were calculated using site-derived laboratory parameters. Participants with cirrhosis were further stratified into five classes according to a previously developed method[20] (Stage 1: compensated cirrhosis without portal hypertension; Stage 2 compensated cirrhosis with portal hypertension; Stage 3: history of variceal bleeding, Stage 4: previous, single episode of ascites or encephalopathy in the absence of esophageal bleeding; Stage 5: multiple, recurrent episodes of decompensation).

### Treatment

The attending clinician selected the therapy schedule as determined according to viral genotype and subtype, as suggested by the Italian Association for the Study of the Liver.[21] Participants with cirrhosis were offered treatment whether or not they had experienced previous decompensation events that needed to be controlled before starting DAAs. Side effects that appeared during the antiviral treatment were categorized according to Common Terminology Criteria for Adverse Events version 4.0.[22] After completion of the antiviral regimen, all participants were regularly followed up with monthly ambulatory visits and telephone interviews.

### Primary Outcomes

The primary goal of the present study was to evaluate the global clinic effect of therapy in very old adults and to determine whether achieving viral clearance would prevent the onset of unfavorable clinical events and improve overall survival. We evaluated onset of hepatic decompensation, new HCC or other neoplasias, clinical events requiring hospitalization, and death. Secondary outcomes included viral clearance in terms of SVR at week 12 (SVR12), and pre- and posttreatment variations in biochemical parameters.

### Data Analysis

Participant baseline characteristics were assessed according to standard descriptive statistics. Categorical variables were reported as percentages, and the chi-square test (or Fisher exact test, when needed) was used to compare differences in rates of SVR12. Continuous variables were expressed as means ± standard deviations and median

with interquartile ranges. To compare variables at baseline and at the end of follow-up, the McNemar test was used for categorical variables and the Wilcoxon signed-rank test for continuous variables. The Kaplan-Meier method was used to estimate overall cumulative incidence of events. Time to the first clinical event (months from starting treatment to the first event of HCC, hepatic decompensation event, nonhepatic event, or death) was evaluated using the survival with Kaplan–Meier method. Differences between subgroups (sex, SVR12, genotype, CPT, stage of cirrhosis,[20] albumin, bilirubin, international normalized ratio, estimated glomerular filtration rate, pretherapy status, comorbidities, drugs) were assessed using the log-rank test. Variables with $P < .05$ were entered into Cox multivariate regression models to identify the independent prognostic factors for the occurrence of unfavorable events All analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL).

The variables that were significant ($P < .05$) on univariate analysis were tested using multivariate Cox regression analysis, and the results were expressed in terms of hazard ratios (HRs) and 95% confidence intervals (CIs). All tests were two-sided, and all $P$-values <.05 were considered significant.

## RESULTS

Two hundred fifty-three individuals aged 80 and older met the inclusion criteria; the mean age was 82.5 (range 80–88), and 132 (52%) were male. Forty had advanced fibrosis (16%), and the remaining 213 (94%) had liver cirrhosis. Thirty-three with cirrhosis recalled single or multiple events of liver decompensation (15.5%). At the pretreatment evaluation, 36 (17%) were staged in CPT Class B or C, 14 (7.5%) had a MELD score greater than 16, and 37 (17%) were D'Amico Stage 3 to 5. The distribution of HCV genotypes was as follows: 1A in 3 patients (1%), 1B in 164 (65%), 2 in 80 (32%), and 4 in 6 (2%). Ninety patients (35.6%) had no comorbidities at the baseline evaluation, 131 (54.9%) had one or two, and 24 (9.5%) had 3 or more. The most frequent comorbidities were diabetes mellitus, hypertension, and history of cardiovascular disease or cerebrovascular accidents.

### Treatment Response

The overall SVR12 was 94.9%. Participant and virus characteristics that may have affected the outcome of therapy are shown in Table 1; no influence of sex, age, number of comorbidities, number of co-prescribed drugs, or failed previous antiviral treatment was seen. As to degree of liver impairment, participants in compensated (Stages 1 and 2) or decompensated (Stages 3 to 5) stages of the D'Amico system were equally responsive. A marginal lower response rate was documented in the 11 participants with CPT Class C. Response rates according to HCV genotype, presence of liver cirrhosis, and antiviral treatment schedule are given in Supplementary Table S1; no difference between the subgroups was noted.

Careful pretreatment evaluation of drug-drug interactions and good management of incipient side effects enabled treatment to be completed in all participants with multiple comorbidities. The most commonly used medications were angiotensin-converting enzyme inhibitors, beta-blockers, angiotensin II receptor blockers, and calcium antagonist receptors for individuals with hypertension; insulin or repaglinide in association or not with metformin for diabetes mellitus, and aldosterone blockers and furosemide for individuals with congestive heart failure. Sixty-two percent of participants with two or more comorbidities were undergoing platelet antiaggregant treatment with acetylsalicylic acid, and 2% of them were treated with

**Table 1. Baseline Characteristics and Sustained Viral Response (SVR) of Individuals with Hepatitis C Virus Infection After Treatment with Direct-Acting Antivirals**

| Characteristic | All, N = 253 | SVR, n = 240 (94.9%) | P-Value |
|---|---|---|---|
| | n (%) | | |
| Sex | | | |
| Male | 132 (52) | 125 (95) | .90 |
| Female | 121 (48) | 115 (95) | |
| Genotype | | | |
| 1a | 3 (1) | 3 (100) | .91 |
| 1b | 164 (65) | 155 (95) | |
| 2 | 80 (32) | 76 (95) | |
| 4 | 6 (2) | 6 (100) | .97 |
| Advanced fibrosis | 40 (16) | 38 (95) | |
| Cirrhosis | 213 (84) | 202 (95) | |
| D'Amico cirrhosis stage | | | |
| 1–2 | 176 (83) | 166 (94) | .61 |
| 3–5 | 37 (17) | 36 (97) | |
| Child-Pugh-Turcotte class | | | |
| A | 177 (83) | 167 (94) | .19 |
| B | 30 (14) | 30 (100) | |
| C | 6 (3) | 5 (83) | |
| Albumin, g/dL | | | |
| >3.5 | 192 (76) | 181 (94) | .70 |
| 2.8–3.5 | 55 (22) | 53 (96) | |
| <2.8 | 6 (2) | 6 (100) | |
| International normalized ratio | | | |
| ≤1.7 | 242 (96) | 230 (95) | .38 |
| >1.7 | 11 (4) | 10 (91) | |
| Bilirubin, mg/dL | | | |
| <2 | 236 (93) | 225 (95) | .21 |
| 2–3 | 13 (5) | 11 (85) | |
| ≥3 | 4 (2) | 4 (100) | |
| Estimated glomerular filtration rate, mL/min per 1.73 $m^2$ | | | |
| 15.1–30.0 | 2 (1) | 2 (100) | .46 |
| 30.1–60.0 | 127 (50) | 118 (93) | |
| 60.1–90.0 | 103 (41) | 99 (96) | |
| 90.0 | 21 (8) | 21 (100) | |
| Pretherapy status | | | |
| Naïve | 161 (64) | 154 (96) | .45 |
| Treatment experienced | 92 (36) | 86 (93) | |
| Ribavirin[a] | | | |
| Without | 95 (55) | 93 (98) | .04 |
| With | 78 (45) | 71 (91) | |
| Number of comorbidities | | | |
| 0 | 90 (36) | 89 (99) | .07 |
| 1–2 | 139 (55) | 128 (92) | |
| ≥3 | 24 (9) | 23 (96) | |
| Number of medications | | | |
| 1 | 130 (51) | 122 (94) | .45 |
| ≥2 | 123 (49) | 118 (96) | |

[a]Genotype 2 excluded.

**Table 2. Biochemical Parameters and Child-Pugh-Turcotte Classes Before and After Therapy with Direct Antiviral Agents in 213 Individuals Aged 80 and Older with Cirrhosis**

| Parameter | Baseline | 3-Month Follow-Up | P-Value |
|---|---|---|---|
| Albumin, g/dL (n = 158) | | | |
| >3.5 | 118 (75) | 141 (89) | <.001 |
| 2.8–3.5 | 35 (22) | 13 (8) | |
| <2.8 | 5 (3) | 4 (3) | |
| International normalized ratio (n = 157) | | | |
| ≤1.7 | 148 (94) | 148 (94) | .10 |
| 1.7–2.2 | 6 (4) | 2 (1) | |
| >2.2 | 3 (2) | 7 (5) | |
| Bilirubin, mg/dL (n = 165) | | | |
| <2.0 | 151 (91) | 157 (95) | .06 |
| 2.0–3.0 | 11 (7) | 5 (3) | |
| ≥3.0 | 3 (2) | 3 (2) | |
| Creatinine, mg/dl, mean ± SD, median (IQR) (n = 158) | 0.87 ± 0.22, 0.81 (0.70–1.00) | 0.90 ± 0.20, 0.90 (0.76–1.00) | .002 |
| Platelets, μL, mean ± SD, median (IQR) (n = 167) | 114 ± 56, 108 (81–138) | 122 ± 49, 119 (90–149) | <.001 |
| Child-Pugh-Turcotte class, n (%) (n = 153) | | | |
| A | 131 (86) | 140 (91) | .18 |
| B | 16 (10) | 10 (7) | |
| C | 6 (4) | 3 (2) | |

SD = standard deviation; IQR = interquartile range.

dual antiplatelet therapy (clopidogrel plus acetylsalicylic acid); 2 participants were given vitamin K antagonists.

### Treatment Safety

Two participants, one in CPT Class A5 and the other in D'Amico Stage 1,[20] withdrew from treatment because of dizziness or irritability. Twenty-seven participants (10.7%) complained of 51 side effects during treatment, which are listed in Supplementary Table S2; half of the side effects were classified as serious (Grades 3 and 4). The most frequent events were anemia (21.6%) and cutaneous rush and pruritus (17,6%), which were observed in participants who were administered ribavirin; reduction or withdrawal of ribavirin alleviated these complaints.

### Posttherapy Follow-Up Data

After completion of treatment, all participants, regardless of whether they had achieved SVR12, were regularly followed up for a mean of 14 ± 4 months (range 5–23 months). Comparing pre- and posttherapy parameters of liver function (Table 2), amelioration in serum albumin, creatinine, and platelet counts was seen. In addition, at the 3-month posttreatment evaluation, the number of individuals with cirrhosis in CPT Class A increased substantially, from 86% at baseline to 91%.

The time-course of adverse events during follow up is given in Figure 1; of the cohort of 253 individuals aged 80 and older, 27 (10.7%) manifested one or more events during the observation period, and the rest maintained compensated liver cirrhosis. Of 34 total events, 12 episodes were secondary to hepatic failure (9 ascites decompensation, 2 spontaneous bacterial peritonitis, 1 hepatic encephalopathy), 9 to extrahepatic disease (3 acute heart failure, 1 depression with an organic mental disorder, 1 hip fracture and immobilization syndrome, 1 cerebral hemorrhage, 1 breast cancer, 2 cases of severe anemia in participants with chronic kidney failure); in addition, there were 10 new cases of HCC and 3 deaths. The events occurred more frequently in individuals with D'Amico Stage 3 or 5 cirrhosis, with 17 events in 37 participants, versus 16 events in 176 participants in Stages 1 and 2; in those in CPT classes B and C, with 17 events in 36 participants, versus 16 events in 177 participants in Class A; in those with a MELD score of 16 or greater, with 8 events in 14 participants, versus 23 events in 239 participants with a score less than 16; in participants with baseline total bilirubin value of 2 mg/dL or greater, with 12 events in 17 participants, versus 22 events in 236 participants with baseline bilirubin of less than 2 mg/dL; in participants with serum albumin of 3.5 g/dL or less, with 23 events in 61 participants, versus 11 events in 192 participants with serum albumin greater than 3.5 g/dL. Only one participant with advanced fibrosis had an extrahepatic cardiopulmonary event associated with severe anemia; this participant had diabetes mellitus and hypertension and had a previous heart failure event (Supplementary Table S3). Supplementary Figures S1 to S4 show the cumulative incidence of events according to liver impairment (D'Amico stage and CPT class), baseline albumin levels, and comorbidities. In the advanced stages of liver impairment, we observed events in 41% of participants with D'Amico Stages 4 and 5, in 42% of those with CPT Class C, in 27.8% of those with serum baseline albumin level of 3.5 g/dL and less, and in 37% of those with 3 of more comorbidities.

Upon multivariate analysis, having 3 or more comorbidities (relative risk (RR) = 6.17, 95% CI = 2.51–14.52), a baseline albumin level of 3.5 g/dL or less (RR = 2.85, 95% CI = 1.12–7.04), and D'Amico Stage 4 or 5 liver impairment (RR = 3.77, 95% CI = 1.57–9.04) were independent risk factors for occurrence of events. We also considered the combination of baseline albumin level and number of comorbidities to provide clinicians with a simple, useful tool for antiviral treatment in individuals aged

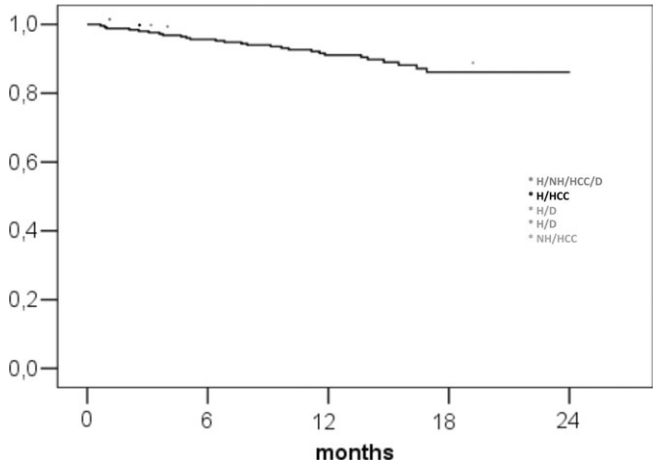


**Figure 1.** Overall incidence of events in 253 individuals aged 80 and older with hepatitis C virus infection. H = hepatic events; NH = nonhepatic events; HCC = hepatocellular carcinoma; D = death.

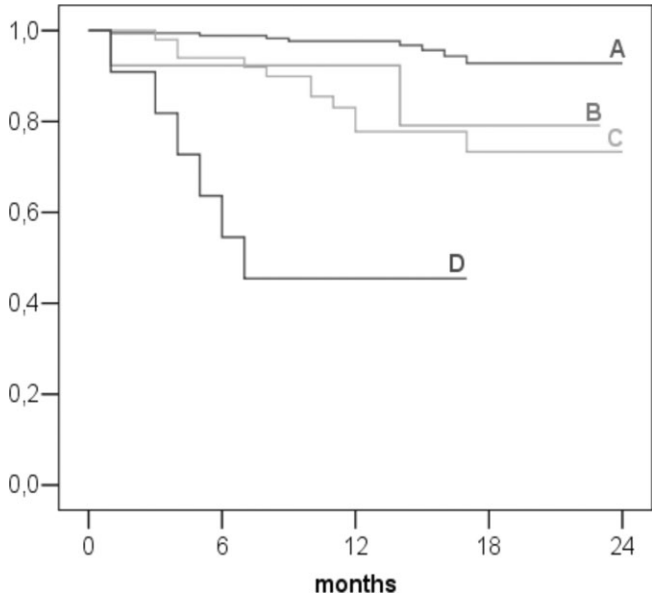


**Figure 2.** Overall incidence of events stratified according to baseline serum albumin level and number of comorbidities. (A) Low-risk group: baseline serum albumin level >3.5 g/dL and <3 comorbidities. Intermediate-risk group: (B) baseline serum albumin level >3.5 g/dL and ≥3 comorbidities and (C) baseline albumin serum level ≤3.5 g/dL and <3 comorbidities. (D) High-risk group: baseline serum albumin level ≤3.5 g/dL and ≥3 comorbidities.

80 and older. The combination of these two simple parameters allowed us to stratify the population into four subgroups of participants with different cumulative risks of incidence of events (6.2% 19.2%, 25.8%, 54.5%, respectively), so we can assume that the subgroup of participants with a lower cumulative incidence have a lower risk of experiencing an event, the subgroups with a risk of 19.2% and 25.8% have an intermediate risk, and the group with a risk of 54% have a higher risk of experiencing an event and concerns individuals aged 80 and older with cirrhosis and a baseline serum albumin level of 3.2 g/dL or less and 3 or more comorbidities (Figure 2, Supplementary Table S4).

## DISCUSSION

Elderly adults with chronic HCV infection are more likely to develop cirrhosis and HCC and several non-liver-related comorbidities, including diabetes mellitus and kidney and cardiovascular disease, that decrease overall survival.[4] In the interferon era, antiviral treatment has been prescribed reluctantly because of it low efficacy and side effects.[23,24]

Current HCV treatment with DAAs regimens is more efficient and better tolerated than interferon-based therapies, and the number of elderly adults who will receive anti-HCV treatment is likely to increase.[25–27] Its safety profile and the more effective DAA regimens received Food and Drug Administration approval for use in all individuals regardless of age.[28] The question is whether viral clearance in advanced age is cost effective, considering the degree of liver impairment, comorbidities, and life expectancy in elderly adults.

Although several studies have documented an overall survival benefit for individuals with HCV who achieved SVR,[15,29,30] none questioned whether this paradigm is applicable also in individuals aged 80 and older, who are normally underrepresented in registration clinical trials.

The current study provides evidence supporting positive clinical outcomes after therapy with DAAs in individuals aged 80 and older with HCV infection. In the entire cohort of 253 participants, 213 of them with cirrhosis, 86.6% of the overall population was free of events 23 months after HCV clearance. The cumulative incidence of events was higher in participants with D'Amico Stage 4 or 5, in those in CPT Class B or C, in those with a MELD score of 16 or greater, and in those with 3 or more comorbidities and a baseline albumin level of 3 g/dL or less. During clinical observation after SVR, 10.6% of participants had first events, 44.7% of which were not liver related. Our analysis found that the benefit was more robust in a subset of participants and that improvement in the quality of life was observed only in these participants. The influence of serum albumin level and the presence and number of comorbidities were most predictive of performance and possible influences of antiviral treatment. Participants with fewer than 3 comorbidities and albumin levels in the normal range had a high rate of cumulative survival (93.2%) and the lowest rate of cumulative events (6.8%). In these participants, obtaining SVR, we observed a decrease in fatigue and a feeling of relief regarding the state of their health. Cumulative survival (45.5%) and cumulative events (54.5%) were significantly worse for individuals with albumin serum levels of 3.5 g/dL or less and three or more comorbidities; in this subset of participants, in spite of obtaining SVR, no changes were observed in perception of quality of life. This is statistically a significant difference can be used to make a decision whether to treat or not elderly patients with HCV infection and liver cirrhosis. Based on these findings, we suggest the following approach for the treatment of individuals aged 80 and older with liver cirrhosis secondary to chronic HCV infection. For those with fewer than three comorbidities and good liver function (serum albumin level >3.5 g/dL), there is the possibility of offering treatment.

Alternatively, in those with low serum albumin and 3 or more comorbidities, treatment is marginally effective, which needs to be communicated to the individual. For the remaining two categories of individuals falling between these two extremes, consideration about treatment needs to be discussed before a final decision is made.

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**Conflict of Interest**: None.

**Author Contributions**: Angelo Andriulli is the guarantor of this article and contributed to the conception of scope and protocol; provided supervision, coordination and guidance for collaborating, peripheral centers; conceived and implemented the analysis plan, and drafted the initial and final manuscript. Antonio Massimo Ippolito, Angelo Iacobellis, Anna Grazia Niro, Michele Milella, Vincenzo Messina, Fabio Conti, Filomena Morisco, Michele Barone, Antonio Patrizio Termite, and Giuseppina Brancaccio were responsible for data acquisition and take responsibility for the integrity of the data and the accuracy of the analysis. Maria Rosa Valvano completed the statistical analysis, extracted and tabulated the data, and drafted the tables and figures. All authors provided the Coordinating Center with an electronic report of the participant input process and reviewed and approved the final draft.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Cumulative incidence of events by D'Amico staging system.

**Figure S2.** Cumulative incidence of events by Child-Pugh–Turcotte.

**Figure S3.** Cumulative incidence of events by baseline serum albumin level.

**Figure S4.** Cumulative incidence of events by comorbidities.

**Table S1.** The effectiveness of the antiviral therapies in 253 octogenarian patients with HCV infection by treatment schedules for all genotype and for all degree of liver impairment.

**Table S2.** the adverse events observed during antiviral treatment.

**Table S3.** The clinical outcome of HCV elderly patients at follow up.

**Table S4.** the risk of developing hepatic and non-hepatic events (the 253 octogenarian patients were stratified by baseline level of serum albumin and number of comorbidities).

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