Table 1. Baseline characteristics and preliminary outcomes in patients with cirrhosis undergoing antiviral therapy

Baseline characteristics	
Total, n	58
Genotype, n (%) 1 2 3	 49 (84%) 5 (8%) 4 (7%)
Base viral log, mean (log 10)	2,294,785 (5.82)
Child-Turcotte-Pugh score, mean	7.44
Child-Turcotte-Pugh class, no (%) A B C	 20 (34%) 29 (50%) 9 (15%)
Serum albumin, mean (mg/dL)	3.3
Total bilirubin, mean (mg/dL)	1.6
International normalized ratio, mean	1.2
Treatment agents, n (%) SOF/SIM SOF/SIM/R SOF/R# SOF/LED	 27 (46%) 2 (3%) 26 (45%) 3 (5%)
Outcomes-related data	
End of Treatment Viral Clearance, n (%) Yes No Died Pending	Data available for 53 patients 45 (85%) 7 (13%) 1 (2%) 5
SVR4, n (%) Yes No Died Pending	Data available for 38 patients 23 (60%) 13 (34%) 2 (5%) 20
SVR12, n (%) Yes No Died Pending	Data available for 31 patients 16 (51%) 13 (42%) 2 (6%) 27

CTP: Child-Turcotte-Pugh, MELD: model of end-stage liver disease, R: ribavarin, SOF: Sofosbuvir, SIM: Simeprevir, LED: ledipasvir, SVR4. SVR12: sustained virologic response at 4 and 12 weeks after treatment completion # one patient initially started on SOF/R for 2 weeks and changed to SOF/SIM for remainder of treatment course

Tu1045

Effect of α-Fetoprotein Levels After Interferon Therapy on Regression of Liver Fibrosis in Chronic Hepatitis C Patient Who Achieved an SVR

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Objectives: Eradicating of chronic hepatitis C virus improves liver fibrosis and reduces incidence of decompensated liver disease and hepatocellular carcinoma in chronic hepatitis C patients. However, almost no reports have examined the factor associated with regression in liver fibrosis following an SVR. The aim of this study was to investigate the relationship between regression in fibrosis, as assessed by sequential biopsies, and clinical factors of patients who were achieved an SVR. ***Methods***: 163 patients (102 men, 61 women; 59.8 ± 9.5 years) who had achieved an SVR after interferon therapy were enrolled this study. To evaluate the change in fibrosis stage over time, the enrolled patients underwent an initial biopsy before therapy, and underwent a sequential biopsy after eradicating of HCV. The clinical factor associated with regression of liver fibrosis after eradicating of HCV in patients who were achieved an SVR was analyzed. ***Results***: The mean time interval between the sequential biopsies was 5.9 ± 1.9 years. Fibrosis stage regressed in 69 patients (39%), remained stable in 89 patients (55%) and progressed in 11 patients (6%). The mean fibrosis stage significantly decreased, from 2.15 ± 1.08 units to 1.80 ± 1.34 units ($P < 0.001$). Univariate analysis revealed that platelet counts, α-fetoprotein (AFP) levels, and γGTP levels at initial biopsy, ALT levels, platelet counts, AFP levels, and γGTP levels at second biopsy were significantly different between patients with regressed fibrosis and patients without regressed fibrosis. Logistic Regression analysis confirmed that lower AFP levels (Odds ratio [OR], 2.30; P=0.022), lower AST levels (OR, 2.27; P=0.019), and higher platelet levels (OR, 2.12; P=0.046) after eradicating of HCV were significant independent factor associated with regressed fibrosis after SVR. ***Conclusion***: AFP levels after interferon therapy were significantly correlated with regression of liver fibrosis in patients who had achieved an SVR.

Tu1046

Evaluation of the Role of the Immune Responses in Determining the Emergence of HCV Ns3 Resistance Mutations During Protease Inhibitor (PI) Therapy

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Background: The efficacy of protease inhibitor (PI)-drugs in HCV treatment is limited by the selection and expansion of drug resistant mutations. HCV replication is error-prone and genetic variability within the dominant epitopes ensures its persistence. The aim of this study is to evaluate the role of immune responses in the emergence of NS3 resistance mutations and to determine how variation in CTL epitopes selected by PI drug pressure affects persistence and failure of treatment during PI therapy. **Methods**: Patients were recruited from University of Cincinnati Hospital and Hepatology Clinics after informed consents and in agreement with the institution review board guidelines. 10 chronically HCV-infected subjects were treated with the boceprevir-based triple therapy. Viral RNA was tested for PI-resistance associated viral mutations (RAVs) using deep-sequencing (pyrosequencing) methods. PI-mutations were investigated at baseline and at 24 week post-treatment. HLA of the patients were determined and synthetic peptides were used to evaluate T cell responses, and HLA binding in responder and non-responder patients. **Results**: 8 of the patients were males and 2 females; 6 African-American and 4 Caucasian. SVR was achieved in 70% of patients, two patients were treatment non-responders and one was classified as a relapser. At baseline, the RAV proportion within individual patients was higher in those who achieved SVR (36 -90%) than NR (27-63%). In the relapsing patient the NS3 resistant variants; R155T and A156G were selected by PI drug pressure after 24 weeks of treatment. Both variants showed lower cell mediated immune response and HLA binding avidity suggesting a significant role of those two mutations in resistance development and relapse. In contrast to NR, significant strong cell-mediated immune responses were observed at the baseline among those who achieved SVR for all T cell epitopes tested. Moreover, despite increasing the cell-mediated immune response at week 24 in NR patients, it failed to control the development of overt drug resistance mutations. **Conclusion** We clearly identified significantly stronger baseline NS3-specific immune responses in the SVR group in comparison to NR which was associated with the outcome of boceprevir-based triple therapy. Although increases in the immune responses were observed in the NR patients to the mutants after treatment, they were unable to clear HCV infection. We also confirmed that the presences of pre-existent RAVs do not play a significant role on the outcome of anti HCV combined therapy.

Tu1047

Distribution of SNP Rs 738409 of PNPLA3 Gene and Its Association With Metabolic Syndrome in Mexican Population With Chronic HCV

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Introduction: Non-alcoholic hepatic steatosis is clinically important in patients with chronic HCV (hepatitis C virus) because it can accelerate the progression of hepatic fibrosis, reduce the of response rate to antiviral therapy and increase the incidence in hepatocellular carcinoma. Some variants on the patatin-like phospholipase-3 (PNPLA3) gene increases risk of steatosis and fibrosis progression in HCV infected patients. The PNPLA3 single nucleotide polymorphism (SNP) rs 738409 may play as a genetic predictor for steatosis and fibrosis. This gene is located on the long arm of chromosome 22 at band 13.31 (22q13.31). It encodes a membrane protein of with enzymatic activity and participates in the energy balance of adipocytes. **Objective**: Describe the SNP rs 738409 in PNPLA3 gene distribution in Mexican patients with chronic HCV, its response to treatment and association to metabolic syndrome. **Methods**: The blood of 85 subjects treated (ribavirin/*pegylated interferon alfa*-2a) for chronic HCV was analyzed. Clinical and biochemical data for metabolic syndrome were retrospectively collected. The gene genotype of SNP Rs738409 in PNPLA3 gene was determined according to the following sequence GGAGATAAGGCCACTGTAGAAGGG [C/G] ATGGGAAGCAGGAACATCCAAGGCCT in genomic DNA obtained from peripheral blood mononuclear cells. Real-time PCR and PCR-dissociation curves (PCR-TR Light-Cycler v2) were used. **Results**: The prevalence of metabolic syndrome was of 18% (n = 16). The most common cardiovascular risk factors in our population were [n = 55 (64.7%)], hypercholesterolemia [n = 42 (49.4%)], followed by overweight [n = 31 (36.4%)] and obesity [n = 19 (22.35%)]. Alterations in carbohydrate metabolism were also common, with an altogether prevalence of 37.6% (n= 32). The risk genotype (GG) associated with the development of hepatic steatosis, was founded in 4 patients (4.4%). The GG and GC genotypes had better response kinetics at treatment week 12. The CC genotype carriers maintained a higher viral load. In overall, presence of this polymorphism did not modify the viral response rate (VRR) as it was similar in the 3 groups. **Conclusions**: Metabolic disorders and cardiovascular risk factors were highly prevalent in our population. Hy*poalphalipoproteinemia* and weight problems were the most common risk factors. The data obtained from our sample suggest that SNP Rs738409 genotype GG in PNPLA3 gene is rare and doesn't seem to alter the VRR. The SNP rs738409 must be assessed in open population to determine the true prevalence and impact in our population. The high prevalence of metabolic disorders could negatively impact the VRR in our population.

Tu1048

Positivity Rates and Genotype Results in "Baby Boomers" Screened for HCV Following the 2012 CDC Call to Action: Results From a Nationwide Lab Test Database

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Purpose In August 2012, the Centers for Disease Control and Prevention (CDC) called for all Americans in the "Baby Boomer" generation (born 1945 - 1965) to have a one-time screening test for hepatitis C (HCV). We previously analyzed screening rates in >100,000 practices nationwide, and found that in the year following the CDC call, screening rates rose significantly (10%) in the Baby Boomer cohort, but also decreased significantly (10%) in the non-Baby Boomer cohort (screening rate/practice 4.17 vs. 4.58, $p<0.001$). In this study, we examined the positivity rates in screened patients, and viral genotypes found in HCV+ patients. Methods We defined the pre-call-to-action period as Aug 2011 - Jul 2012; the first year post-call as Aug 2012 - Jul 2013, and the second year post-call as Aug 2013 - Jul 2014. Using data from the nationwide Medivo Lab Exchange Database (Medivo Inc., NY, NY), we analyzed lab test results from 4,961,282 adults screened for HCV antibody (Ab) between Aug 2011 and Jul 2014; 1,529,916 (30.8%) were Baby Boomers and 3,431,366 (69.2%) were non-Baby Boomers. Logistic regression was performed to compare probability of having a + HCV antibody test among Baby Boomers vs. non-Baby Boomers in the year pre- CDC call to action and in years 1 and 2 post-call. Descriptive analytics was performed

on HCV+ patients' genotype test results. Results Overall, the HCV antibody positivity rate was 8.54%; 12.69% among Baby Boomers and a 4.4% among non-Baby Boomers. Logistic regression analysis showed that Baby Boomers were 250% more likely to have a + HCV antibody test (OR = 3.5, p < 0.001) than non-Baby Boomers. However, over time HCV positivity rates among Baby Boomers fell compared to non-Baby Boomers. Statistical analysis showed that in the first year post-call, Baby Boomers were 21% less likely to have a + HCV Ab result (OR = 0.79, p < 0.01), and in the second year post-call, Baby Boomers were 31% less likely (OR = 0.69, p < 0.01) to test + on HCV screening. (Table 1) Descriptive analysis of HCV genotype test results shows that between Aug 2011- Jul 2014, 208,685 of the HCV+ patients had HCV genotype testing; 76.38% had genotype 1, 10.92% had genotype 2, 10.90% had genotype 3 and 1.8% had other genotypes. (Table 2) Conclusions HCV positivity rates are significantly higher among Baby Boomers than among non-Boomers, but this rate is falling over time as more Baby Boomers are screened. Genotype testing shows that HCV genotype 1 continues to be the most common among US HCV+ patients. More study is needed to examine ongoing HCV screening and positivity rates across birth cohorts, and to determine if the population HCV genotype profile is changing over time.

Time Period	08/2011 – 07/2012 (Pre-Call to Action)		08/2012 – 07/2013 (Post-Call Yr 1)		08/2013 – 07/2014 (Post-Call Yr 2)	
	Baby Boomers	Non- Baby Boomers	Baby Boomers	Non-Baby Boomers	Baby Boomers	Non-Baby Boomers
Total # patients screened	448,403	1,215,084	514,535	1,082,248	566,888	1,134,034
# Patients tested HCV +	58,258	49,730	53,945	44,075	58,076	50,925
Positivity Rate	14.93%	4.27%	11.71%	4.25%	11.41%	4.70%

Table 1: HCV Screening Rates

Table 2: HCV Genotype Test Results

	Baby Boomers	Non Baby-Boomers
Genotype 1	104,032	44,703
Genotype 2	10,315	8,543
Genotype 3	13,524	7,005
Other Genotypes	2,245	1,156

Tu1049

Impact of HCV Testing in a Targeted Group of High Risk Individuals From the Community

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Background: Hepatitis C is the most common blood borne infection in the United States. Fifty to 75% of individuals living with HCV are unaware of their infection and fewer than 20% of those aware of their infection are engaged in subspecialty care. Many high risk individuals may not access primary care or if they do, may not be tested in accordance with CDC guidelines. This represents a missed opportunity given the recent approval of curative treatment for HCV. We aim to assess the demographic and socioeconomic factors associated with HCV seropositivity among patients diagnosed from community based testing program serving high-risk populations. **Methods**: Community based testing was conducted by two community based organizations. A baseline survey was utilized to assess general demographic information. The survey was administered after the patient had provided informed consent and a rapid HCV Oraquick antibody test was performed. **Results**: Nine hundred and eight patients were tested from June through November 2014, 10% of whom were HCV antibody positive. Of the 908 individuals tested, 41% of individuals were female, 73% were black, 12% were white, 10% Latino or Hispanic and 5% declined to answer or didn't know their race. Of the individuals identified as HCV antibody positive, 37% were female, 23% reported their race as black, 12% of individuals identified as Hispanic or Latino, 28% identified as white, and 37% declined to answer or didn't know their race. Notably, 37% of all HCV antibody positive individuals were born outside of the 1945-1965 birth cohort. Ninety percent of HCV antibody positive individuals had a history of drug use; of this group 43% had injected drugs, and 32% of those individuals admitted to sharing injection equipment. Among HCV antibody positive individuals, 77% stated they had medical insurance with 68% of those individuals stating that they had a primary care provider (PCP). Eighty-five percent of those individuals with a PCP had seen that provider in the past 12 months. Among the HCV antibody positive individuals, only 13% were aware of a previous HCV antibody positive diagnosis after being tested by their PCP. None of the HCV antibody positive individuals reported being engaged in HCV related medical care. **Conclusions**: Community based testing and linkage to care programs serving high risk individuals have the potential to engage individuals in subspecialty care, where the standard health care system may have failed to do so. Although many of the HCV positive individuals had attended primary care appointments within the past year, few had been previously tested by their PCP and none reported being engaged in HCV related subspecialty care. Community based testing and linkage to care programs are needed to ensure that high risk individuals receive the proper HCV testing and treatment.

Tu1050

Treatment and Outcomes of Chronic Hepatitis C (CHC) in the Elderly

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Background. Individuals with CHC in the U.S. are getting older. Elderly CHC patients may be at a higher risk for cirrhosis and hepatocellular carcinoma (HCC), but also non-hepatic comorbidities, which negatively impact their likelihood of receiving or responding to antiviral treatment. Alternatively, they may have less alcohol & drug use and greater willingness to start and adhere to treatment. However, there is little information on the clinical course or outcomes of CHC in the elderly. **Methods.** A retrospective cohort study using data from the VA HCV Clinical Case Registry in patients with CHC diagnosed (positive HCV RNA or HCV genotype test) between 10/1999 and 1/2009 who had at-least one year of follow up in the VA. The main exposures and outcomes were calculated for ages 20-49, 50-64, and 65-85 years (the elderly). The outcomes were incident HCC detected after the one year following the HCV index date, and death. The exposures were HCV treatment (pegylated interferon with or without ribavirin) and SVR (RNA test negative at least 12 weeks after the end of treatment). Logistic regression was used to examine the effect of age on receipt of antiviral therapy and Cox proportional hazards models to examine the effect of treatment receipt and SVR on time to HCC (and to death) adjusting for potential confounders. **Results.** We analyzed of 161,744 CHC patients; 97.1% were men and 47.8% white. The age distribution was 34.8% (20-49 yrs), 59.1% (50-64 yrs), and 6.0% (65-85 yrs). Elderly patients were significantly less likely to receive antiviral therapy (3.9% vs. 15.7%), but among those who received treatment, SVR was not different from the rest (33.5% vs. 32.6%). Elderly CHC patients had less alcohol use disorders, HIV and HBV, but more medical comorbidities than the overall group. Older patients were less likely to receive treatment after adjusting for these differences (adjusted OR: 0.38, 95% CI 0.33-0.44). The incidence of HCC was significantly higher among the elderly; 8.4 per 1000 person years (PY) compared with 2.6 and 5.7 per 1000 PY in the 20-49 and 50-64 age groups, respectively. Overall, HCC incidence was significantly lower among those treated with a SVR independent of age (adjusted HR 0.39, 95% CI 0.32-0.49). The overall mortality rate was also lower among those treated with SVR irrespective of age groups (adjusted HR: 0.33, 0.30-0.35). In analyses restricted to the elderly, treatment with SVR was associated with a reduction in mortality risk compared to treatment with no SVR (HR 0.53, 0.32-0.89). **Conclusions.** Elderly patients with CHC are more likely to develop HCC but are less likely to receive antiviral therapy than younger patients. When treated, elderly patients are as likely to achieve a SVR as younger patients. Receipt of curative treatment is associated with a benefit in reducing HCC and overall mortality irrespective of age.

Tu1051

Advanced Fibrosis Is Common in Individuals Whose Hepatitis C Has Not Been Diagnosed: Results From the National Health and Nutrition Examination Survey 2001-2012

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Background and Aims: Hepatitis C virus (HCV) infection is a global public health problem - while it is common, its consequences may be severe, including end stage liver disease and hepatocellular carcinoma. Moreover, most individuals with HCV remain asymptomatic, which makes the diagnosis difficult. With the hypothesis that individuals whose HCV is not diagnosed are less likely to have advanced fibrosis than those who have been diagnosed, we compare liver fibrosis between respondents to the National Health and Nutrition Examination Survey (NHANES) with diagnosed and undiagnosed HCV infection. **Methods:** Testing for HCV was incorporated in NHANES 2001-2012. In a subgroup of the respondents with HCV infection, follow-up questionnaires were administered. Awareness of HCV infection was assessed by the question whether they had known they had HCV before receiving a letter from NHANES. Liver fibrosis was estimated by the FIB-4 and APRI scores. Based on the published cut-off values for advanced fibrosis, the proportion of respondents with a high probability of advanced fibrosis was compared between respondents with known and undiagnosed HCV. **Results:** Out of 45,089 respondents of the NHANES survey, 591 tested positive for confirmatory anti-HCV antibody. There were 580 participants with complete laboratory data needed for the FIB-4 and APRI scores, of whom 227 had answered the awareness question in hepatitis C follow-up questionnaires. Slightly more than half (52.9%, n=120) knew that they had hepatitis C infection before the survey, whereas in the remainder (47.1%, n=107). HCV was only discovered from the survey. In the figure, the two groups were comparable with respect to age, aminotransferase and platelet counts. Men were less likely to be aware of their HCV status. BMI was higher in those with known diagnosed, the clinical significance of which is uncertain. The raw FIB-4 and APRI scores were similar between the two groups. Among the respondents with known HCV infection, the proportion with a high, intermediate, and low probability of advanced fibrosis was 12.5%, 33.3%, 54.2%, respectively. The corresponding data in those with undiagnosed HCV were 18.7%, 26.2%, 55.1%, respectively. A similar pattern was seen with the APRI score. **Conclusions:** While nearly half of survey respondents did not know of their HCV infection, nearly one every five had advanced fibrosis. Their liver fibrosis was no less advanced than in those whose HCV had been diagnosed prior to participation in the survey. These data further justifies the current recommendation for HCV screening in asymptomatic individuals.