

Supplemental online content for:

Effect of Hepatitis C Virus Infection in Patients With Cancer: Addressing a Neglected Population

Harrys A. Torres, MD; Parag Mahale, MBBS, MPH; Boris Blechacz, MD; Ethan Miller, MD; Ahmed Kaseb, MD; H. Franklin Herlong, MD; Nathan Fowler, MD; Ying Jiang, MS; Issam I. Raad, MD; and Dimitrios P. Kontoyiannis, MD

J Natl Compr Canc Netw 2015;13:41–50

- **Expanded Table 1:** General Characteristics of Patients With Proven HCV Infection (N=642)
- **Expanded Table 3:** Treatment Outcomes of Patients With Cancer Who Underwent Treatment for HCV Infection (N=78)
- **eTable 1:** The Final Cox Proportional Hazards Regression Model to Determine the Relationship Between HCV Treatment After Cancer Diagnosis and Progression to Cirrhosis
- **eTable 2:** The Final Cox Proportional Hazards Regression Model to Determine the Relationship Between HCV Treatment After Cancer Diagnosis and Progression to Portal Hypertension

Expanded Table 1 General Characteristics of Patients With Proven HCV Infection (N=642)	
Characteristic	Result
Sex, n (%)	
Female	206 (32)
Male	435 (68)
Mean age (y) ± SD	58.3 ± 9.4
Race or ethnicity, n (%)	
Non-Hispanic white	414 (65)
Black	110 (17)
Hispanic	66 (10)
Asian	30 (5)
Middle Eastern	15 (2)
Native American	2 (1)
Risk factors for HCV infection, n/total (%)	
Illicit drug use	246/409 (60)
Blood transfusion (before 1992)	136/409 (33)
Tattoos	108/409 (26)
Incarceration	41/409 (10)
Multiple sexual partners	32/409 (8)
Occupational exposure	15/409 (4)
Military service	9/409 (2)
Sharing used needles for vaccination	4/409 (1)
Baseline liver biopsy, METAVIR stage, n/total (%)^a	
Unknown	45/206 (22)
0 (no fibrosis)	14/206 (7)
1 (periportal fibrotic expansion)	21/206 (10)
2 (periportal septae)	40/206 (19)
3 (portocentral septae)	46/206 (22)
4 (cirrhosis)	40/206 (19)
Baseline cirrhosis, n (%) ^a	73 (17)
Baseline portal hypertension, n (%)^a	31 (8)

(continued on next page)

Abbreviations: HCV, hepatitis C virus.

Hepatitis B exposure: hepatitis B core antigen positivity; hepatitis B infection: hepatitis B surface antigen positivity.

^aFor those with data available.

^bSolid and hematologic malignancies.

Expanded Table 1 General Characteristics of Patients With Proven HCV Infection (N=642) (cont.)

Characteristic	Result
Cancer type, n%	
Hematologic	173 (27)
Leukemia	41 (6)
Lymphoma	106 (17)
Hodgkin lymphoma	8 (1)
Non-Hodgkin's lymphoma	98 (15)
Diffuse large B-cell lymphoma	51 (8)
Multiple myeloma	19 (3)
Other hematologic tumor	7 (1)
Solid tumor	462 (72)
Hepatocellular carcinoma	166 (26)
Other gastrointestinal tumor	63 (10)
Breast cancer	42 (7)
Prostate cancer	36 (6)
Lung cancer	27 (4)
Mixed tumor ^b	7 (1)
Disease status,^a n/total (%)	
Complete remission	223 (35)
Partial remission	14 (2)
Stable disease	96 (15)
Progressive disease	295 (46)
Hematopoietic stem cell transplant, n/total (%)	40 (23)
Autologous	26 (65)
Allogenic	13 (33)
Both	1 (2)
Mean baseline body mass index (kg/m²) ± SD	27.4 ± 6.1
Basal HCV viral load >600,000 IU/mL	298 (69)
Mean baseline serum cholesterol (mg/dL) ± SD	167.1 ± 40.5
Mean baseline serum triglycerides (mg/dL) ± SD	150.5 ± 98.9
Coinfection,^a n (%)	
Hepatitis B	197 (39)
Exposure	7 (1)
Infection	10 (2)
HIV	

Abbreviations: HCV, hepatitis C virus.

Hepatitis B exposure: hepatitis B core antigen positivity; hepatitis B infection: hepatitis B surface antigen positivity.

^aFor those with data available.

^bSolid and hematologic malignancies.

Expanded Table 3 Treatment Outcomes of Patients With Cancer Who Underwent Treatment for HCV Infection (N=78)

Characteristic	SVR (n=27)	Non-SVR (n=51)	P Value
Age, y (mean ± SD)	58.6 ± 1.9	59.4 ± 1.0	.37
Male sex, n/total (%)	12/27 (44)	33/51 (65)	.09
Race or ethnicity, n/total (%)			.02
Non-Hispanic white	19/27 (73)	28/51 (55)	
Black	1/27 (4)	15/51 (29)	
Hispanic	2/27 (8)	4/51 (8)	
Middle Eastern	0/27 (0)	2/51 (4)	
Asian	4/27 (15)	2/51 (4)	
Cancer type, n/total (%)			.24
Hematologic	9/27 (33)	22/51 (43)	
Acute myeloid leukemia	0/9 (0)	2/22(9)	
Acute lymphocytic leukemia	0/9 (0)	1/22 (5)	
Chronic myeloid leukemia	1/9 (11)	0/22 (0)	
Chronic lymphocytic leukemia	0/9 (0)	2/22 (9)	
Hodgkin lymphoma	0/9 (0)	1/22 (5)	
Non-Hodgkin's lymphoma	7/9 (78)	13/22 (59)	
Diffuse large B cell	3/7 (43)	5/13 (38)	
Marginal zone B cell	2/7 (29)	3/13 (23)	
Mantle cell	1/7 (14)	1/13 (8)	
Lymphoplasmacytic	1/7 (14)	0/13 (0)	
Mycosis fungoides	0/7 (0)	2/13 (15)	
Follicular	0/7 (0)	1/13 (8)	
Peripheral T cell	0/7 (0)	1/13 (8)	
Multiple myeloma	1/9 (11)	3/22 (14)	
Solid tumor	18/27 (67)	29/51 (57)	
Breast cancer	6/18 (33)	4/29 (14)	
Prostate cancer	2/18 (11)	3/29 (10)	
Lung cancer	2/18 (11)	1/29 (3)	
Colorectal cancer	1/18 (6)	3/29 (10)	
Skin cancers	1/18 (6)	7/29 (24)	
Melanoma	0/1 (0)	3/7 (43)	
Basal cell carcinoma	0/1 (0)	2/7(29)	
Squamous cell carcinoma	1/1 (100)	2/7 (29)	
Cancers of oropharynx & larynx	1/18 (6)	4/29 (14)	
Glioblastoma	1/18 (6)	0/29 (0)	
Meningioma	1/18 (6)	1/29 (3)	
Pancreatic cancer	1/18 (6)	0/29 (0)	
Penile cancer	1/18 (6)	0/29 (0)	
Ovarian cancer	1/18 (6)	0/29 (0)	
Hepatocellular carcinoma	0/18 (0)	3/29 (10)	
Bone cancer	0/18 (0)	1/29 (3)	

(continued on next page)

Expanded Table 3 Treatment Outcomes of Patients With Cancer Who Underwent Treatment for HCV Infection (N=78) (cont.)			
Characteristic	SVR (n=27)	Non-SVR (n=51)	P Value
Duodenal cancer	0/18 (0)	1/29 (3)	
Thyroid cancer	0/18 (0)	1/29 (3)	
HSCT, n/total (%)	2/9 (22)	7/22 (32)	.92
Autologous	2/2 (100)	4/7 (57)	
Allogeneic	0/2 (0)	3/7 (43)	
Radiotherapy, n/total (%)	13/27 (48)	14/51 (27)	.06
Chemotherapy, n/total (%)^a	17/27 (63)	40/51 (78)	.23
Alkylating agents	11/17 (65)	17/40 (43)	
Monoclonal antibodies	9/17 (53)	15/40 (38)	
Rituximab	5/9 (56)	10/40 (25)	
Platinum analogues	7/17 (41)	10/40 (25)	
Systemic corticosteroids	7/17 (41)	11/40 (28)	
Taxanes	7/17 (41)	5/40 (13)	
Antimetabolites	6/17 (35)	18/40 (45)	
Pyrimidine analogs	3/6 (50)	15/18 (83)	
Folic acid antagonist	2/6 (33)	1/18 (6)	
Purine analogues	1/6 (17)	2/18 (11)	
Topoisomerase inhibitors	6/17 (35)	20/40 (50)	
Vinca alkaloids	6/17 (35)	8/40 (20)	
Chemotherapy-modulating agent	1/17 (6)	0/40 (0)	
Endocrine/Hormonal agents	1/17 (6)	2/40 (5)	
Immunomodulators	1/17 (6)	2/40 (5)	
Proteasome inhibitor	1/17 (6)	1/40 (3)	
Targeted therapy	1/17 (6)	8/40 (20)	
Miscellaneous agents (hydroxyurea)	1/17 (6)	0/40 (0)	
HCV genotype, n/total (%)^b			<.001
1	1/17 (6)	26/36 (72)	
2	10/17 (59)	7/36 (20)	
3	4/17 (23)	3/36 (8)	
6	2/17 (12)	0/36 (0)	
Baseline cirrhosis, n/total (%)^b	2/23 (9)	9/42 (21)	.30
Basal HCV RNA >600,000 IU/mL^b	11/17 (65)	36/48 (75)	.42
Mean baseline BMI (kg/m²)^b ± SD	26.5 ± 1.1	27.9 ± 1.0	.47
Concomitant chemotherapy, n/total (%)	3/27 (11)	4/51 (8)	1.0
Trastuzuma ^b	2/3 (67)	1/4 (25)	
Tamoxifen	1/3 (33)	1/4 (25)	
Letrozole	0/3 (0)	1/4 (25)	
TACE ^c	0/3 (0)	1/4 (25)	
Baseline laboratory values, ± SD^b			
Aspartate aminotransferase (IU/L)	46.7 ± 6.1	77.6 ± 9.6	.006

(continued on next page)

Expanded Table 3 Treatment Outcomes of Patients With Cancer Who Underwent Treatment for HCV Infection (N=78) (cont.)

Characteristic	SVR (n=27)	Non-SVR (n=51)	P Value
Alanine aminotransferase (IU/L)	43.3 ± 7.2	71.1 ± 9.1	.009
Prothrombin time (s)	13.5 ± 0.7	13.8 ± 0.6	.67
International normalized ratio	1.3 ± 0.2	1.2 ± 0.1	.95
Alkaline phosphatase (IU/L)	97.3 ± 7.8	120.3 ± 11.1	.41
Total bilirubin (mg/dL)	0.6 ± 0.1	0.7 ± 0.1	.69
Albumin (g/dL)	4.1 ± 0.1	3.8 ± 0.1	.14
Hemoglobin (g/dL)	12.8 ± 0.4	13.4 ± 0.3	.22
WBC count (cells/mcL)	11,300 ± 2700	6700 ± 600	.05
Absolute neutrophil count (cells/mcL)	5761 ± 953	3504 ± 306	.007
Absolute lymphocyte count (cells/mcL)	2864 ± 649	2349 ± 435	.24
CD4 count (cells/mcL)	853.1 ± 176.7	710.1 ± 167.5	.38
Coinfection, n (%)^b			
Hepatitis B exposure/infection	10 (43)	20 (45)	1.0
HIV infection	3 (4)	7 (5)	1.0
HCV treatment			
Monotherapy with IFN, n (%)	7 (26)	5 (10)	.06
Combination therapy, ^d n (%)	20 (74)	46 (90)	
Mean treatment duration (wk) ± SD^b			
Genotype 1 ^e	–	24.3 ± 18.7	
Genotype 2 or 3	24.9 ± 7.4	9.6 ± 8.7	
Treatment interruption, n/total (%)^b			
	3/19 (16)	35/39 (90)	<.0001
Toxicity from HCV treatment, n (%)^b			
	19 (70)	31 (61)	.40

Abbreviations: BMI, body mass index; HCV, hepatitis C virus; HSCT, hematopoietic stem cell transplant; IFN, interferon; pegIFN, pegylated interferon; SVR, sustained virologic response; TACE, transcatheter arterial chemoembolization.

Hepatitis B exposure: hepatitis B core antigen positivity; hepatitis B infection: hepatitis B surface antigen positivity.

^aA patient may have received more than one type of chemotherapeutic agent

^bFor those with data available.

^cTACE was performed using doxorubicin.

^dIn patients with SVR, includes standard IFN + ribavirin (n=3 [11%]), pegIFN alfa 2a + ribavirin (n=15 [56%]), and pegIFN alfa 2b + ribavirin (n=2 [7%]). In patients without SVR, includes standard IFN + ribavirin [n=13 (25%)], pegIFN alfa 2a + ribavirin (n=27 [53%]), pegIFN alfa 2b + ribavirin (n=5 [10%]), and pegIFN alfa 2a + ribavirin + nitazoxanide (n=1 [2%])

^eThe treatment duration was unavailable for the only cancer survivor with a genotype 1 infection who experienced SVR.

eTable 1 The Final Cox Proportional Hazards Regression Model^a to Determine the Relationship Between HCV Treatment After Cancer Diagnosis and Progression to Cirrhosis

Variable	Hazard Ratio	Standard Error	P Value	95% CIs for Hazard Ratio	
				Lower Limit	Upper Limit
HCV treatment	0.66	0.28	.33	0.28	1.52
ANC <1000 cells/mcL	5.16	3.71	.02	1.26	21.15
WBC <4000 cells/mcL	5.33	2.64	.001	2.01	14.09
AST >46 IU/L	3.23	1.51	.01	1.30	8.06
ALP >126 IU/L	3.04	1.13	.003	1.47	6.33

Abbreviations: ALP, alkaline phosphatase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; HCV, hepatitis C virus.
^aFinal model was determined by Akaike information criteria and *P* values for statistical significance.

eTable 2 The Final Cox Proportional Hazards Regression Model^a to Determine the Relationship Between HCV Treatment After Cancer Diagnosis and Progression to Portal Hypertension

Variable	Hazard Ratio	Standard Error	P Value	95% CI for Hazard Ratio	
				Lower Limit	Upper Limit
HCV treatment	0.23	0.15	.02	0.06	0.82
Albumin <4.0 g/dL	5.83	3.02	.001	2.11	16.08
ANC <1000 cells/mcL	4.39	3.52	.065	0.91	21.16
AST >46 IU/L	3.00	1.91	.08	0.86	10.43

Abbreviations: ANC, absolute neutrophil count; AST, aspartate aminotransferase; HCV, hepatitis C virus.
^aFinal model was determined by Akaike information criteria and *P* values for statistical significance.