Immune Checkpoint Inhibitors in Solid Tumor Patients with Chronic Hepatitis C Virus Infection: A Prospective Case-series

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BACKGROUND

- Immune checkpoint inhibitors are a novel class of targeted therapy that activate T cell-mediated tumor cell death.
- Controversies exist about the safety and efficacy of immunotherapy in patients with chronic viral infections affecting T cells, such as hepatitis C virus (HCV).

AIM

- Herein, we analyzed the effect of immune checkpoint inhibitors on HCV viremia and HCV-related hepatic outcome.

METHODS

- HCV-infected patients with solid tumors seen at MD Anderson Cancer Center (11/2012 - 9/2018) were enrolled in a prospective observational study, and monitored for the development of HCV reactivation, hepatitis flare and HCV-associated hepatitis.

DEFINITIONS

- HCV reactivation: HCV-RNA ≥1 $\log_{10}$IU/mL over baseline.
- Hepatitis flare: alanine transaminase increase to ≥3 times upper limit of normal.
- HCV-associated hepatitis: HCV reactivation and hepatitis flare, while on cancer treatment.

RESULTS

- During the study period, 223 chronically infected patients with solid tumors were enrolled in the prospective observational study.
- Out of the 223 patients, 18 (8%) received immune checkpoint inhibitors.
- Only 7 patients returned for regular monitoring (Table 1).
- These 7 cases were followed for a median duration of 9 months (interquartile range, 5-12 months).

Table 1. Patients' Characteristics, Treatment Received and Outcomes

Patient	Age, y	Sex	HCV genotype	Prior AVT	Cirrhosis	Type of Cancer	Immunotherapy	HCV reactivation	Hepatitis flare
1	60	Male	3	IFN	Yes	HCC	Pembrolizumab	No	Yes [a]
2	67	Male	1a	No	Yes	HCC	Nivo + Ipi	No	Yes [b]
3	52	Male	1a	No	No	Melanoma	Nivo + Ipi	No	Yes [c]
4	57	Male	3	IFN+RBV	No	Melanoma	Pembrolizumab	No	No
5	55	Male	1a	No	No	Melanoma	Ipi	Yes [d]	Yes [d]
6	56	Male	2	No	Yes	Lung	Nivo	No	No
7	58	Male	2	No	No	Lung	Atezolizumab [e]	No	Yes

Abbreviations: AVT, antiviral treatment; IFN, interferon; Ipi, ipilimumab; Nivo, nivolumab; RBV, ribavirin

[a] Drug-induced liver injury

[b] After partial hepatectomy.

[c] Negative infectious work-up including hepatitis A, B, E, cytomegalovirus, and herpes simplex virus.

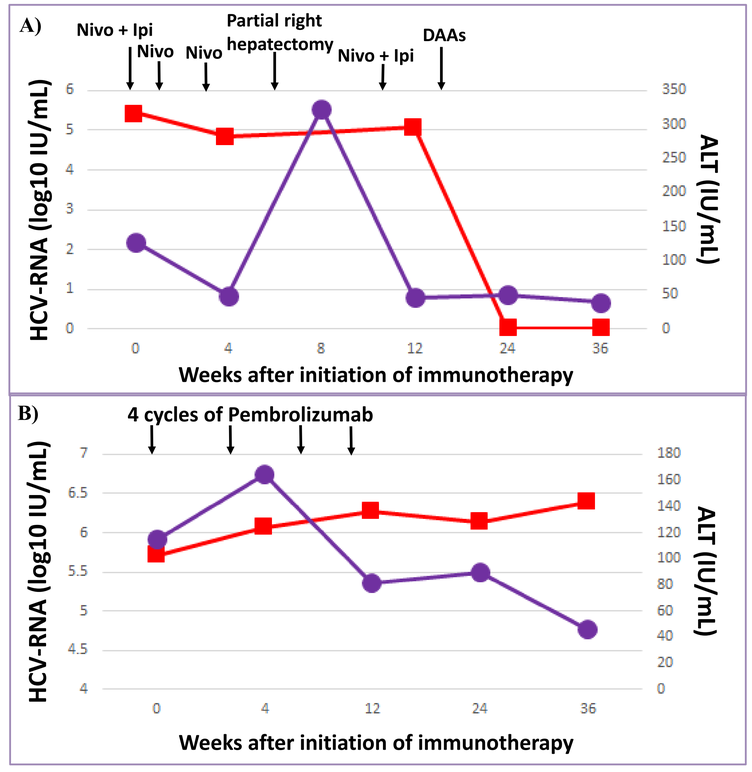
[d] Six months after completing immunotherapy.

[e] Received concomitant chemotherapy (paclitaxel and carboplatin).

- None of the patients had HCV reactivation or HCV-associated hepatitis while receiving immune checkpoint inhibitors. HCV reactivation was detected in one patient, six months after completing immunotherapy, and after starting high dose steroids for brain metastasis (Patient 5, table 1).
- Immune checkpoint inhibitors were discontinued in one patient (14%) due to hepatitis flare unrelated to HCV (Patient 3, table 1).
- Illustrative changes in HCV RNA and ALT in 2 patients receiving immune checkpoint inhibitors are shown in Figure 1.

RESULTS

Figure 1. Changes in HCV RNA and ALT in 2 Patients. A) Patient with HCC treated with Nivolumab + Ipilimumab. B) Patient with melanoma treated with Pembrolizumab.



Abbreviations: ALT, alanine aminotransferase; DAA, direct-acting antivirals; HCC, hepatocellular carcinoma; HCV, hepatitis C virus: Ipi, ipilimumab; Nivo, nivolumab.

CONCLUSION

The use of immune checkpoint inhibitors is not associated with HCV reactivation or HCV-associated hepatitis in patients with solid tumors.