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Clinical Outcomes of Checkpoint Inhibitor Therapy in People with HIV: A Single-Center Case Series

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Further evidence for the general safety and tolerability of immune checkpoint inhibitors in terms of both HIV- and non-HIV-related outcomes

Introduction

- Immunotherapeutic agents, particularly immune-checkpoint inhibitors (ICI), have transformed the treatment landscape for advanced malignancies.
- Such therapies could considerably benefit people with HIV (PWH), yet PWH have often been excluded from ICI trials such that data regarding ICI safety in PWH are limited.
- Despite the exclusion of PWH from most clinical trials, retrospective studies have shown a safety profile of ICIs among PWH comparable to that among patients without HIV.
- Viral reactivation and blips have also been theorized and observed among PWH after ICI, a phenomenon which necessitates further investigation.
- We performed a retrospective cohort analysis of all PWH who received ICI in clinical practice at one academic medical center which serves a large number of PWH.

Methods

1) We systematically identified all PWH with advanced cancer who received ICIs from January 2000 to December 2018 at the University of California, San Francisco Medical Center.
2) Three reviewers independently collected data on demographics, HIV history, and HIV and hematologic parameters. We cataloged overall outcomes (death, anti-tumor efficacy) and non-HIV adverse events (infectious and auto-immune).

Included: All patients with an ICD-10-coded diagnosis related to HIV infection who had documented administration of at least one of 7 ICIs:
- PD-1 inhibitors: atezolizumab, avelumab, durvalumab
- PD-L1 inhibitors: cemiplimab, nivolumab, pembrolizumab
- CTLA-4 inhibitor: ipilimumab

Excluded: 5 patients who were receiving ICIs as part of a clinical trial

Definitions:
- Treatment episode: A discrete period of time on a particular ICI or combination of ICIs (i.e. ipilimumab and nivolumab)
- Viral blip: Increase in plasma HIV RNA from “not detected” to any level of “detected” within one year of ICI initiation

Results

25 patients identified with 29 treatment episodes

No significant change in plasma HIV RNA levels, CD4⁺ T-cell count, CD8⁺ T-cell count, or CD4⁺ / CD8⁺ ratio

Viral blips in 5/19 (26%) of treatment episodes

Most common adverse events were diarrhea (n=7) and rash (n=5)

Five deaths within one month of ICI initiation, all attributed to progressive malignancy

Table 1: Baseline characteristics of 25 patients with HIV who received checkpoint inhibitor therapy

Demographic characteristics	N=25
Age at drug initiation (years)	59.2 (54.5 – 63.2)
Sex, [n (%)]	
Male	23 (92.0)
Female	2 (8.0)
Race, [n (%)]	
White	19 (76.0)
Black	2 (8.0)
Native Hawaiian or Other Pacific Islander	1 (4.0)
Asian	1 (4.0)
Other/unknown	2 (8.0)
Ethnicity, [n (%)]	
Hispanic/Latino	2 (8.0)
Not Hispanic/Latino	22 (88.0)
Unknown	1 (4.0)
HIV disease history characteristics	
HIV risk factor, [n (%)]	
MSM	17 (68.0)
Injection Drug Use	2 (8.0)
Heterosexual intercourse	3 (12.0)
Not specified in medical record	4 (16.0)
Duration of HIV infection at ICI initiation (years), n=20	28.3 (16.3 – 32.1)
Nadir CD4⁺ T-lymphocyte count (cells/µl), n=16	95 (35.5 – 250)
Co-infection history, [n(%)]	
History of any opportunistic infection	11 (44.0)
Pneumocystis jirovecii Pneumonia	4 (16.0)
Kaposi’s Sarcoma	4 (16.0)
CMV retinitis	2 (8.0)
Mycobacterium avium complex infection	1 (4.0)
Oral Candidiasis	1 (4.0)
Other/unspecified	6 (0.24)
Positive hepatitis B core antibody	17 (68.0)
Positive hepatitis C antibody	3 (12.0)

Table 2: Adverse events following 29 treatment episodes, by type (number of episodes)

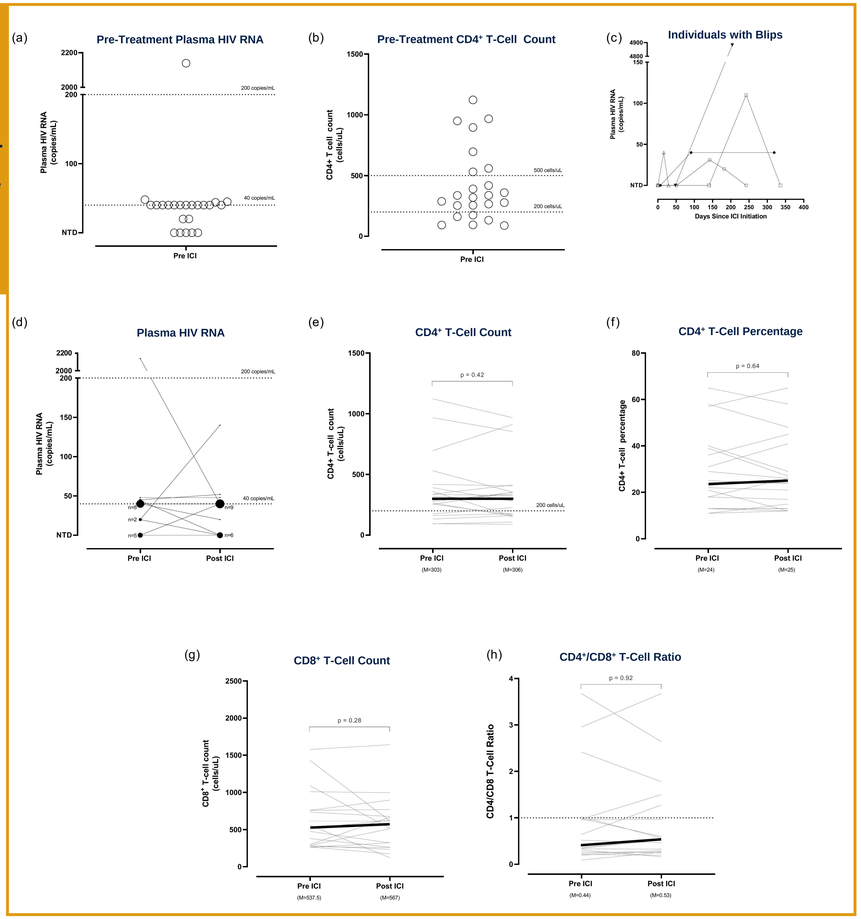
Systemic	Sepsis (2), unspecified fever (2), severe fatigue (2), acute DVT of leg (1), anasarca (1)
Pulmonary	Pneumonia (2)
Gastrointestinal/Hepatic	Diarrhea (7), hepatitis (1), hepatomegaly (1), ascites with normal LFTs (1)
Genitourinary	UTI (3), AKI (2), autoimmune orchitis (1)
Neurological	Macular degeneration (1), distal sensorimotor demyelinating neuropathy (1), encephalopathy with myoclonic jerks (1), AMS (3)
Endocrine	Adrenal insufficiency (1)
Dermatological	Diffuse rash (3), pruritic rash (2)
Death during treatment	n = 5

DVT, deep venous thrombosis; LFTs, liver function tests; UTI, urinary tract infection; AKI, acute kidney injury; AMS altered mental status

Figure 1: Changes in HIV parameters associated with checkpoint inhibitor therapy.

Symbols represent unique individuals in (c).

Thick line represents the change in median M between the two time points in (e), (f), (g), and (h).



Summary

- ICI therapy was not associated with loss of virologic control nor with a significant change in CD4⁺ T-cell count, CD8⁺ T-cell count, or CD4⁺/CD8⁺ ratios. We observed a frequency of viral blips within the range observed in the published literature for PWH on ART (10-30%) and the range for PWH receiving ICI (0-33%).
- Other studies of ICIs in PWH have shown similar types and frequencies of adverse events, with the most common being fatigue, rash, gastrointestinal toxicities, and pyrexia. These rates have been similar to those without HIV.

Implications

For clinical practice:
- In general, ICIs do not appear to be associated with major HIV-related or non-HIV-related adverse events.

For investigation:
- This study contributes to the growing evidence supporting the inclusion of PWH in future clinical trials of ICI therapy.
- While we did not see an increased rate of viral blips on routine clinical testing, our findings corroborate the safety and tolerability of ICIs in future studies of these agents as potential HIV therapeutics, for example as agents that may reverse HIV latency.

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