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Assessment of the Safety of Pembrolizumab in Patients With HIV and Advanced Cancer—A Phase 1 Study

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IMPORTANCE Anti–PD-1 (anti–programmed cell death 1) and anti–PD-L1 (anti–programmed cell death ligand 1) regimens are preferred therapies for many cancers, including cancers associated with HIV. However, patients with HIV were excluded from most registered trials.

OBJECTIVE The primary objective was to evaluate the safety of pembrolizumab in people with HIV and advanced cancer; the secondary objective was to evaluate tumor responses.

DESIGN, SETTING, AND PARTICIPANTS Open-label, nonrandomized, phase 1 multicenter study conducted at 7 Cancer Immunotherapy Trials Network sites. Patients with HIV and advanced cancer as well as a CD4 count greater than or equal to 100 cells/μL, antiretroviral therapy (ART) for 4 or more weeks, and an HIV viral load of less than 200 copies/mL were eligible. Exclusion criteria included uncontrolled hepatitis B or C infection, active immunosuppressive therapy, or a history of autoimmune disease requiring systemic therapy.

INTERVENTIONS Pembrolizumab, 200 mg, administered intravenously every 3 weeks for up to 35 doses in 3 CD4 count–defined cohorts. Participants continued ART.

MAIN OUTCOMES AND MEASURES Safety and tolerability were assessed using current NCI Common Terminology Criteria for Adverse Events. Immune-related adverse events grade 2 or higher were considered immune-related events of clinical interest (irECI). Tumor responses were evaluated using standard tumor-specific criteria.

RESULTS Thirty participants (28 men and 2 women; median [range] age, 57 [39-77] years) were enrolled from April 2016 through March 2018; 6 had Kaposi sarcoma (KS), 5 had non-Hodgkin lymphoma (NHL), and 19 had non–AIDS-defining cancers. Safety was observed over 183 cycles of treatment with pembrolizumab. Most treatment-emergent adverse events at least possibly attributed to pembrolizumab were grade 1 or 2 (n = 22), and 20% (n = 6) were grade 3. The irECI included hypothyroidism (6 participants), pneumonitis (3 participants), rash (2 participants), an elevated aminotransferase/alanine aminotransferase level (1 participant), and a musculoskeletal event (1 participant). One participant with pretreatment KS herpesvirus (KSHV) viremia developed a polyclonal KSHV-associated B-cell lymphoproliferation and died. HIV was controlled in all participants. Increases in CD4 count were not statistically significant (median increase, 19 cells/μL; $P = .18$). Best tumor responses included complete response (lung, 1 patient), partial response (NHL, 2 patients), stable disease for 24 weeks or more (KS, 2 patients), stable disease for less than 24 weeks (15 patients), and progressive disease (8 patients); 2 patients were not evaluable.

CONCLUSIONS AND RELEVANCE Pembrolizumab has acceptable safety in patients with cancer, HIV treated with ART, and a $CD4^+$ T-cell count of greater than 100 cells/μL but may be associated with KSHV-associated B-cell lymphoproliferation. Clinical benefit was noted in lung cancer, NHL, and KS. Anti–PD-1 therapy is appropriate for US Food and Drug Administration–approved indications and clinical trials in this population.

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Supplemental content

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In the era of effective antiretroviral therapy (ART) for HIV, people living with HIV remain at an increased risk of developing a range of cancers, most commonly B-cell non-Hodgkin lymphoma (NHL), Kaposi sarcoma (KS), lung cancer, squamous cell skin cancer, head and neck squamous cell carcinoma, classic Hodgkin lymphoma (cHL), and hepatocellular carcinoma (HCC).[1-4] Indeed, cancer is a leading cause of death for the more than 37 million people worldwide living with HIV.[5,6] For several HIV-associated cancers, treatment outcomes in select patients are comparable to those in the general population. However, lack of knowledge about the use of cancer therapies in patients with HIV, health care disparities,[7] and biologic factors, including advanced HIV-associated immunosuppression,[8-10] may affect outcomes. Immunotherapy may be beneficial for treating HIV-associated cancers; however, people living with HIV have been often excluded from cancer clinical trials that test novel agents.[11]

Programmed cell death 1 (PD-1) is a checkpoint molecule that negatively regulates antigen receptor signaling of T cells, including CD8+ effector T cells.[12,13] Pembrolizumab is a humanized IgG4 monoclonal antibody designed to block the interaction between PD-1 and its ligands, PD-L1 (programmed cell death ligand 1) and PD-L2. Monoclonal antibodies targeting PD-1 and PD-L1 are revolutionizing the approach to treatment of many cancers. To date, pembrolizumab and 5 other monoclonal antibodies targeting PD-1 or PD-L1 have been approved by the US Food and Drug Administration (FDA) for 15 distinct cancers.

The adverse event (AE) profile of checkpoint inhibitors targeting PD-1/PD-L1 has been evaluated in the general population with cancer,[12,14-16] but has not been previously studied prospectively in people living with HIV. Immune-related AEs (irAEs) related to anti–PD-1 therapy occur in fewer than 30% of patients with cancer, and are generally mild to moderate, with skin, musculoskeletal, gastrointestinal, and endocrine irAEs being the most common. These irAEs are generally managed with steroids or hormone replacement.[17] It is unknown whether anti–PD-1 therapy has an acceptable safety profile in people with HIV. Potential concerns have included administration in the setting of increased expression of PD-1 in HIV infection that is inversely correlated with CD4+ T-cell count,[18-20] unknown effects in the setting of HIV-associated perturbations in T-cell repertoires,[21] and concerns about unmasking opportunistic infections.[22] Likewise, the activity of anti–PD-1 therapy in this patient population with immune compromise is understudied.

Prospective anti–PD-1 safety data are required to guide the treatment of patients with HIV and cancer with what is now standard-of-care immunotherapy and to inform HIV-related eligibility criteria for future immuno-oncology studies. We hypothesized that anti–PD-1 therapy would be safe and active in people with cancer and HIV that is well controlled on ART.

Key Points

Question Is anti–PD-1 (anti–programmed cell death 1) therapy safe to administer in people with HIV with a range of CD4+ T-cell counts and cancer?

Findings In this multicenter, open-label, nonrandomized, phase 1 study of 30 participants with HIV, a CD4 count of greater than 100 cells/μL, and advanced cancer, pembrolizumab had an acceptable safety profile, although an unexpected treatment-emergent adverse event of Kaposi sarcoma herpesvirus-associated polyclonal B-cell lymphoproliferation was noted. Clinical benefit was observed in participants with Kaposi sarcoma, primary effusion lymphoma, diffuse large B-cell lymphoma, and lung cancer.

Meaning Anti–PD-1 therapy is appropriate for US Food and Drug Administration–approved indications and clinical trials in people with HIV.

Methods

Trial Oversight

We conducted an investigator-initiated multicenter phase 1 trial in 7 medical centers in the United States. The trial protocol is available in Supplement 1. The trial was coordinated by the Cancer Immunotherapy Trials Network (CITN) and sponsored by the National Cancer Institute Cancer Therapy Evaluation Program and Merck & Co, Inc. The protocol was approved by the Fred Hutchinson Cancer Research Center's Institutional Review Board and participating site institutional review boards. It was performed in accordance with the principles of the Declaration of Helsinki. All participants provided written informed consent. Participants were accrued from April 2016 to January 2018.

Trial Population

Patients with HIV and metastatic or locally advanced cancer for which no standard therapy exists, previous therapy failure due to disease progression or relapse, or who were ineligible to receive standard therapy were screened for additional eligibility criteria. Tumor-specific criteria were listed for non–small cell lung cancer, NHL, cHL, KS, HCC, and melanoma. HIV-associated eligibility criteria required a CD4 count greater than or equal to 100 cells/μL (if <200 cells/μL, a CD4 to CD8 ratio >0.4 was required), effective ART for at least 4 weeks with an HIV viral load of less than 200 copies/mL, and no symptomatic AEs higher than grade 1 according to the Common Terminology Criteria for Adverse Events (CTCAE) attributed to ART. Participants had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1 and disease measurable or assessable by tumor-specific criteria. Laboratory criteria included an absolute neutrophil count of greater than 500/μL, a platelet count greater than 50,000/μL, hemoglobin level greater than 9 g/dL, total bilirubin less than 1.5 × upper limit of normal (ULN) (<5 times ULN and direct bilirubin <0.7 mg/dL allowed for patients on atazanavir ART), aspartate and alanine aminotransferase levels less than 2.5 times ULN, creatine kinase level less than 5 times ULN, serum creatinine level less than 2.5 times ULN, and thyrotropin (TSH) within institutional normal limits. Key exclusion criteria included cirrhosis with a Child-Pugh score of B or C, uncontrolled hepatitis B or C infection (detectable hepatitis B virus DNA or hepatitis C virus RNA by polymerase chain reaction), active immunosuppressive therapy, or history of autoimmune disease requiring systemic therapy. A complete list of eligibility criteria is provided in the protocol in Supplement 1.

Baseline demographics, including self-reported race and ethnicity, were obtained. Patients were accrued into 1 of 3 $CD4^+$ T cell–based cohorts (up to 12 patients per cohort) to evaluate safety across a range of CD4 counts: cohort 1, 100 to 199 $CD4^+$ T cells/μL; cohort 2, 200 to 350 $CD4^+$ T cells/μL; and cohort 3, greater than 350 $CD4^+$ T cells/μL.

Trial Procedures

The trial was open-labeled and nonrandomized, evaluating pembrolizumab (MK-3475), 200 mg, administered intravenously every 3 weeks for up to 35 doses with continued ART. Safety monitoring occurred on all cycles. Adverse events were graded and attributions were assigned using CTCAE v4.0 until January 29, 2018, and then v5.0 was used. Management of irAEs included withholding pembrolizumab and administration of corticosteroids based on AE severity following standard protocol guidelines. Thyrotropin was measured, and participants who developed hypothyroidism were initiated on levothyroxine. Unacceptable AEs were defined as any grade 3 or 4 AE that required withholding pembrolizumab. Zero or 1 unacceptable AE in the first 6 participants in each cohort were required to expand each cohort from 6 to 12 patients. The HIV viral load and CD4 counts were measured over the first 3 cycles, then every 3 cycles.

Objective responses and disease progression were monitored by appropriate imaging or measurement methods at 9-week intervals during the first year of treatment and 12-week intervals during the second year. Treatment beyond progression was allowed with repeat imaging 4 to 6 weeks later to confirm progressive disease (PD) in select patients following standard guidelines. Treatment for patients who achieved stable disease (SD) or better could continue for up to 2 years. Drug administration was discontinued for confirmed PD, unacceptable AEs, intercurrent serious illness, investigator's decision, consent withdrawal, or completion of 2 years of therapy.

Trial End Points

The primary objective was to assess safety and tolerability of pembrolizumab in patients with HIV on ART with locally advanced or metastatic cancer, as measured using CTCAE criteria. Immune-related AEs of grade 2 or higher were considered immune-related events of clinical interest (irECI). The HIV viral load and CD4 counts were monitored longitudinally. Participants who had HIV RNA detected but less than 400 copies/mL during the study did not require a change of ART based on the US Department of Health and Human Services HIV treatment guidelines. The secondary objective was to obtain preliminary insights into clinical benefit (eg, tumor shrinkage or stabilization ≥24 weeks) in this patient population. Solid tumor responses were assessed by Response Evaluation Criteria In Solid Tumors v1.1,[23] lymphoma responses by the refined Lugano classification lymphoma response criteria,[24] and KS by modified AIDS Clinical Trial Group criteria.[25]

Statistical Analysis

The safety population included all participants who received at least 1 dose of pembrolizumab (n = 30). After completion of accrual to cohorts 2 and 3 and when all on-treatment patients had received at least 2 cycles of pembrolizumab, the database was locked on March 9, 2018. Baseline characteristics were tabulated and summarized. All observed AEs were tabulated and treatment-emergent AEs (TEAEs) at least possibly attributed to pembrolizumab, all serious AEs (grades 3-4), as well as irECI were recorded. With an initial sample size of 6 participants in a specific cohort and a true unacceptable AE rate of 30%, there was a 58% chance of observing at least 2 unacceptable AEs in each cohort. Post hoc evaluation of antithyroid antibodies (antithyroid peroxidase or antithyroglobulin) was performed to evaluate the sensitivity and specificity of standard cutoff values at baseline for subsequent development of hypothyroidism during the study. Changes in CD4+ T-cell counts from baseline to time of best response were evaluated by Wilcoxon signed rank test. Given the diversity of tumor types, there was no prespecified statistical plan for activity analysis. Statistical analyses were performed from January 2019 to March 2019 using SAS (version 9.4).

Results

Participant Characteristics

From April 2016 through March 2018, 30 participants were enrolled, with 6 participants in cohort 1 and 12 each in cohorts 2 and 3 (eTable 1 in Supplement 2). The median (range) age was 57 (39-77) years; 28 (93%) participants were men and 2 (7%) were women. Eighteen (60%) participants were white, 9 (30%) were black or African American, 2 (7%) were Native American or Native Hawaiian, and 2 (7)% did not report race. Three (10%) participants identified as Hispanic or Latino. Overall, the median CD4 count was 285 cells/μL (range, 132-966 cells/μL). Twenty-six participants had an undetectable HIV viral load and 4 had low-level HIV viremia, with less than 200 copies/mL at study entry. Sixteen (53%) patients had an ECOG PS of 0, and 14 (47%) had an ECOG PS of 1. Eleven (37%) had AIDS-defining cancers, including KS (6) and NHL (5). Nineteen (63%) had non–AIDS-defining cancers, the most common being anal cancer (6) and advanced squamous cell carcinoma of the skin (3). Participants were heavily pretreated; 19 (63%) had received previous radiation therapy, and the median number of prior systemic therapies was 2 (range, 0-8).

Treatment

Safety was observed over the course of 183 cycles in 30 participants. The median number of cycles was 5 (range, 1-32). At the time of analyses, 4 participants continued to receive therapy.

Safety Outcomes

Treatment-emergent AEs at least possibly attributed to pembrolizumab that occurred in at least 5% of participants are listed in the **Table**. A full list of all TEAEs at least possibly attributed to pembrolizumab is included in eTable 2 in Supplement 2. Most TEAEs were grade 1 or 2 (n = 22), with 6 (20%) being grade 3. The most common AEs, occurring in at least 20% of participants included anemia (13), fatigue (10), nausea (7), and hypothyroidism (8). Most grade 3 TEAEs were hematologic and did not meet criteria for irECI. Serious AEs (eTable 3 in Supplement 2) were

Table. Treatment-Emergent Adverse Events at Least Possibly Related to Pembrolizumab, Worst per Patient

	No. (%)			
Event[a]	Grade 1	Grade 2	Grade 3	Total
Any	6 (20)	16 (53)	6 (20)	29 (97)
Blood and lymphatic system disorders				
Anemia	4 (13)	5 (17)	4 (13)	13 (43)
Endocrine disorders				
Hypothyroidism	2 (7)	6 (20)	0	8 (27)
Gastrointestinal disorders				
Abdominal pain	4 (13)	0	0	4 (13)
Nausea	6 (20)	1 (3)	0	7 (23)
Vomiting	3 (10)	0	0	3 (10)
General disorders and administration site conditions				
Fatigue	7 (23)	3 (10)	0	10 (33)
Fever	1 (3)	2 (7)	0	3 (10)
Localized edema	0	2 (7)	0	2 (7)
Pain	1 (3)	1 (3)	0	2 (7)
Infections and infestations				
Soft-tissue infection	0	1 (3)	1 (3)	2 (7)
Laboratory test results				
Alanine aminotransferase increased	2 (7)	0	1 (3)	3 (10)
Alkaline phosphatase increased	4 (13)	2 (7)	0	6 (20)
Aspartate aminotransferase increased	3 (10)	0	1 (3)	4 (13)
Blood bilirubin increased	0	1 (3)	0	2 (7)
CD4 lymphocytes decreased	0	1 (3)	1 (3)	2 (7)
Creatine phosphokinase increased	1 (3)	1 (3)	0	2 (7)
Lymphocyte count decreased	3 (10)	2 (7)	1 (3)	6 (20)
Neutrophil count decreased	0	2 (7)	1 (3)	3 (10)
Platelet count decreased	1 (3)	1 (3)	0	3 (10)
Metabolism and nutrition disorders				
Anorexia	2 (7)	0	0	2 (7)
Hyponatremia	2 (7)	0	0	2 (7)
Musculoskeletal and connective tissue disorders				
Pain in extremity	0	3 (10)	0	3 (10)
Nervous system disorders				
Headache	2 (7)	0	0	2 (7)
Respiratory, thoracic, and mediastinal disorders				
Cough	3 (10)	0	0	3 (10)
Dyspnea	0	1 (3)	0	2 (7)
Pneumonitis	1 (3)	3 (10)	0	4 (13)
Skin and subcutaneous tissue disorders				
Dry skin	3 (10)	1 (3)	0	4 (13)
Pruritus	5 (17)	0	0	5 (17)
Maculopapular rash	3 (10)	1 (3)	0	4 (13)

[a] Occurring in 5% or more participants.

generally attributed to complications of progressive cancer. All TEAEs are noted in eTable 4 in Supplement 2. Thirteen irECI were observed, including hypothyroidism (6), pneumonitis (3), rash (2), an elevated aminotransferase/alanine aminotransferase level (1) (eFigure 1 in Supplement 2), and a musculoskeletal event (1). Hypothyroidism was effectively managed with levothyroxine in all participants. Post hoc analysis of baseline antibodies against thyroglobulin or thyroperoxidase were below the lower limit of normal in all but 1 participant who was on baseline levothyroxine. Standard cutoff values were not sensitive for predicting subsequent hypothyroidism.

Unexpectedly, 1 heavily pretreated participant with KS and a prior history of elevated peripheral blood mononuclear cell-associated KSHV and KSHV-associated inflammatory cytokine syndrome[26] developed marked KSHV viremia and inflammatory symptoms and died. An autopsy showed severe diffuse KSHV-associated polyclonal B-cell lymphoproliferation in the lymph nodes, spleen, lungs, and kidney (eFigure 2 in Supplement 2).

CD4 and HIV Monitoring

Clinical CD4 and HIV RNA monitoring were performed during the study (**Figure 1**). From baseline to the time of best response, $CD4^+$ T cells had a median increase of 19 cells/μL (P = .18) and 152 cells/μL in participants with SD for 24 weeks or more (P = .13). Detectable HIV viremia at less than 400 copies/mL was noted in 7 participants during at least 1 visit. All participants were on ART and none met the US Department of Health and Human Services criteria for uncontrolled HIV. One participant observed on the study for 31 cycles of pembrolizumab therapy developed persistent low-level HIV viremia (<400 copies/mL) of unclear clinical significance (Figure 1B) but maintained stable CD4 counts.

Responses

Protocol-defined clinical benefit was noted in 5 (17%) participants across all 3 cohorts. Best responses included a sustained complete response in 1 participant with lung cancer, partial response in 2 participants with NHL, 1 participant with diffuse large B-cell lymphoma, 1 participant with primary effusion lymphoma (eFigure 3 in Supplement 2), and sustained SD for 24 weeks or more in 2 participants with KS. Best responses in participants not meeting the criteria for clinical benefit included SD for less than 24 weeks (13), refined Lugano classification immune response 3[24] (ie, decreasing size of target lesions meeting criteria for SD but with increasing fluorodeoxyglucose avidity of unclear significance in 1 lymph node) (2), and PD (8); 2 participants were not evaluable (**Figure 2**). One participant with HCC metastatic to bones did not meet the criteria for a partial response based on measurements of small liver lesions but did have resolution of bone pain and a decrease in alpha-fetoprotein from more than 20 000 ng/mL to 10 ng/mL. This participant was taken off the study after 11 cycles of therapy due to a more than 20% increase in the size of 2 small liver lesions (alpha-fetoprotein increased to 20 ng/mL). The patient subsequently received local therapies for the liver lesions and continued to have sustained control of bone metastases without additional systemic cancer therapy for 36 months since enrolling on the study.

Figure 1. CD4 and HIV Monitoring

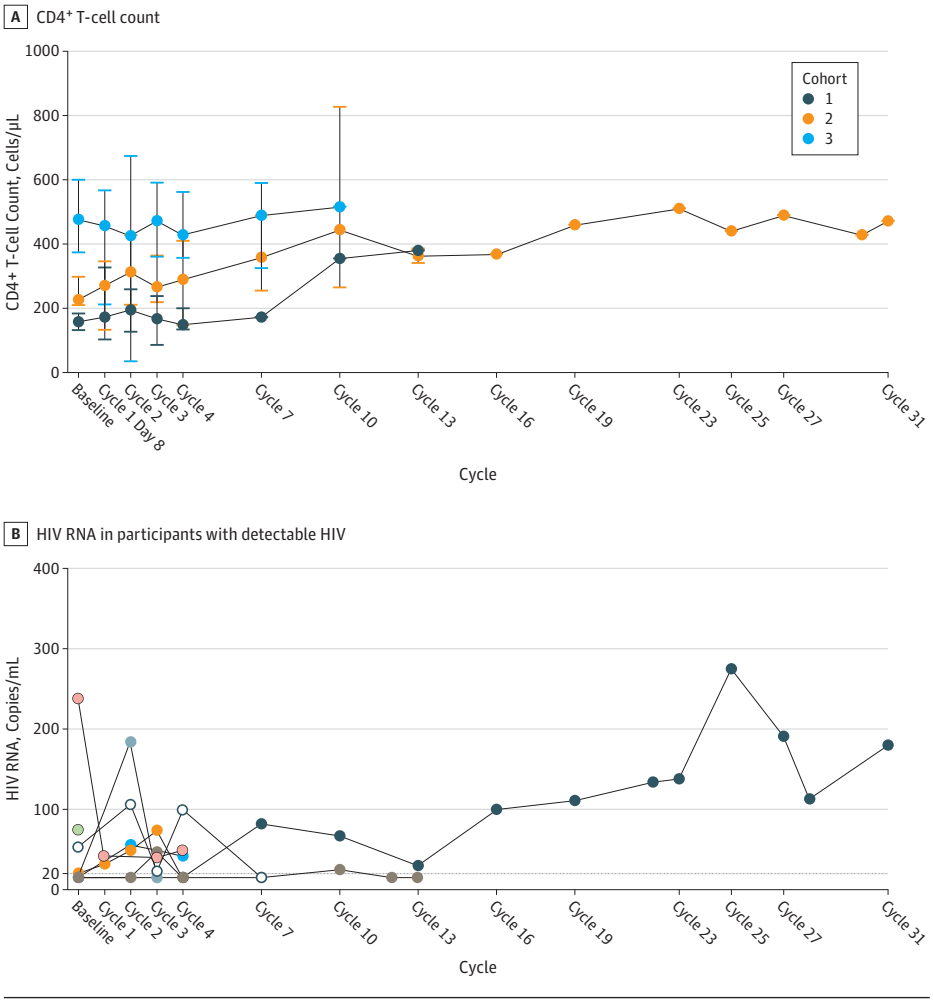


Figure 1 shows CD4+ T-cell counts (median and range) over time on pembrolizumab (A) and the HIV RNA levels in 7 participants (B). Lines represent the 7 (23%) participants with HIV viremia detected at least once during the study. Blips were defined as a detectable HIV viral load of less than 400 copies/mL. The lower limit of detection is 20 copies/mL.

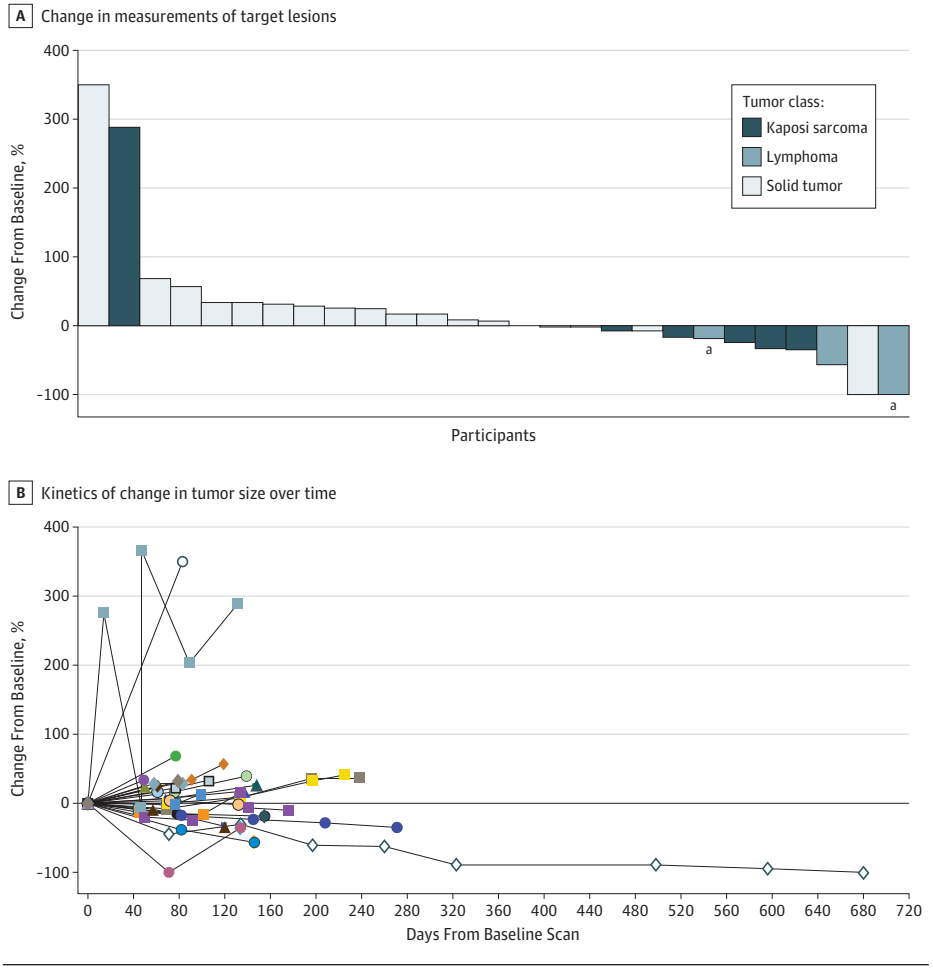
Discussion

Checkpoint inhibitors provide an important treatment option for people with HIV and cancer. Anti–PD-1/PD-L1 therapy has been approved for a variety of cancers that occur with increased incidence in people with HIV, including lung cancer,[27,28] squamous cell skin cancer,[29] cervical cancer,[30,31] HCC,[32] cHL,[33] head and neck squamous cell carcinoma[34] and Merkel cell carcinoma.[35] However, the safety of this therapy in people with HIV has not been previously explored prospectively. The current study has demonstrated that pembrolizumab has a similar AE profile for people with HIV and advanced cancer who have suppressed HIV on ART to that observed in published studies of participants without HIV.[15,16] The proportion of grade 3 and 4 irECI was generally similar to that previously described in patients receiving anti–PD-1 therapy for FDA-approved indications. The commonest irECI was hypothyroidism, which was noted in 6 (20%) participants and was successfully managed through monitoring of TSH and administration of levothyroxine using routine guidelines.[17]

Through prospective evaluation in participants with HIV, the current study demonstrates that pembrolizumab monotherapy does not appear to have a detrimental effect on CD4+ T-cell counts. In the setting of relapsed and refractory cancers, CD4+ T-cell counts tended to increase during the study, although the increases were not statistically significant. Additionally, HIV viral loads remained suppressed below the limit of detection on commercial assays in 23 (77%) participants, and low-level viremia, generally blips less than 400 copies/mL (of no clinical significance), was noted in only 7 patients. No participant required a change of ART. Correlative studies evaluating the effects of pembrolizumab on HIV latency reversal and measures of persistence are ongoing.

One hesitation in testing anti–PD-1 or anti–PD-L1 therapy in patients with HIV and cancer has been a concern that these patients would not have sufficient underlying T-cell immunity to benefit from therapy. However, although the focus of this trial was safety, the responses in several tumor types across all 3 cohorts were also documented, including 2 AIDS-defining cancers, KS and NHL. Kaposi sarcoma is a highly immune-responsive tumor that is sometimes managed with ART alone,[9,36] although additional therapy is often needed. Retrospective reports have

Figure 2. Characteristics of Tumor Responses to Pembrolizumab



A, Maximum percent change of the sum of the measurements of target lesions from baseline based on tumor specific measurement criteria. B, Kinetics of change in tumor size over time.
[a]Participants whose best response was refined Lugano classification immune response 3.[24] For Kaposi sarcoma, the numbers of nodular lesions were used.

described responses to anti–PD-1 therapy in HIV-associated and endemic KS.[37,38] Prospective evaluation is warranted to evaluate the efficacy of anti–PD-1 monoclonal antibodies for KS. To date, tumor regression was noted in 5 of 6 participants with relapsed or refractory KS, although this did not meet criteria for partial response at the time of analysis. To better define anti–PD-1 activity in KS, the CITN-12 study team continues participant enrollment in a phase 1b cohort to evaluate pembrolizumab as a first-line systemic therapy in addition to ART for HIV-associated KS. Additionally, data from the present study demonstrated meaningful activity against primary effusion lymphoma, a KSHV-associated cancer with few good treatment options (eFigure 3 in Supplement 2). Although anti–PD-1 therapy may be promising in KSHV-associated cancers, a previously undescribed KSHV-associated B-cell lymphoproliferation was observed in a patient with KS and a history of circulating cell-associated KSHV that was at least possibly attributable to pembrolizumab.

Initial CITN-12 KS eligibility criteria include at least 3 months on ART, the timeframe in which patients with KS are at the greatest risk of immune reconstitution inflammatory syndrome.[39] Because death from generalized polyclonal KSHV-associated B-cell lymphoproliferation potentially represents KSHV-multicentric Castleman disease (MCD), the protocol was amended to exclude patients with a history of KSHV-MCD in the last 5 years. In patients with KS and unexplained symptoms concerning for KSHV-MCD, an assessment of KSHV viral load and a computed tomography scan are warranted, and enlarged lymph nodes should be biopsied. In general, KSHV-MCD is successfully managed with rituximab,[40,41] which should be considered if KSHV-MCD is observed in the setting of anti–PD-1 therapy.

Limitations

To our knowledge, this is the first and largest prospective study evaluating the safety of anti–PD-1 therapy in people with HIV and cancer; however, the phase 1 design and sample size did not allow for a formal comparison of rates of specific AEs, such as hypothyroidism, with those noted in the general population. Because this was not a randomized study, we were unable to compare TEAE rates associated with the use of pembrolizumab vs alternative cancer interventions or observation alone in this population. Lastly, although the present study demonstrated that pembrolizumab had activity in several cancers, the study did not have enough participants with any given tumor to accurately estimate response rates or to compare response rates with those of people with the same cancers but no HIV.

Conclusions

Data from the present study strongly support the use of monoclonal antibodies targeting the PD-1 pathway in people with HIV on ART and CD4+ T-cell counts of more than 100 cells/μL for FDA-approved cancer indications. These data also demonstrate the feasibility of including patients with HIV in immunotherapy trials with appropriate eligibility criteria and study design.[11] Tumor regression in participants with a range of tumor types and CD4 counts supports activity of anti–PD-1 therapy in people with HIV. Evaluation of pembrolizumab as a first-line systemic therapy for HIV-associated KS is ongoing.

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Other: Sznol.
Other—patient enrollment, scientific input, correlative studies: Emu.

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