



Assessment of nivolumab in HIV-Infected patients with advanced non-small cell lung cancer after prior chemotherapy. The IFCT-1602 CHIVA2 phase 2 clinical trial

Armelle Lavole, Julien Mazieres, Sophie Schneider, Solenn Brosseau, Lize Kiakouama, Laurent Greillier, Amelie Guihot, Baptiste Abbar, Marine Baron, Alain Makinson, et al.

► To cite this version:

Armelle Lavole, Julien Mazieres, Sophie Schneider, Solenn Brosseau, Lize Kiakouama, et al.. Assessment of nivolumab in HIV-Infected patients with advanced non-small cell lung cancer after prior chemotherapy. The IFCT-1602 CHIVA2 phase 2 clinical trial. Lung Cancer, 2021, 158, pp.146-150. 10.1016/j.lungcan.2021.05.031 . hal-03524445

HAL Id: hal-03524445

<https://inria.hal.science/hal-03524445>

Submitted on 2 Aug 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Title

Assessment of Nivolumab in HIV-Infected Patients with Advanced Non-Small Cell Lung Cancer after Prior Chemotherapy. The IFCT-1602 CHIVA2 Phase 2 Clinical Trial

Armelle Lavole MD¹, Julien Mazieres MD, PhD², Sophie Schneider MD³, Solenn Brosseau MD⁴, Lize Kiakouama MD⁵, Laurent Greillier MD, PhD⁶, Amelie Guihot MD⁷, Baptiste Abbar MD⁷, Marine Baron MD⁸, Alain Makinson MD⁹, Alexandra Langlais¹⁰, Franck Morin¹¹, Jean-Philippe Spano MD, PhD¹², Jacques Cadranel MD, PhD¹

Authors' affiliations

¹ Service de Pneumologie et Oncologie Thoracique, AP-HP, Hôpital Tenon and GRC #04 Therascan, Sorbonne Université, Paris, France,

² Thoracic Oncology Department, Toulouse University Hospital, Université Paul Sabatier, Toulouse, France,

³ Pneumology, Centre Hospitalier de la Côte Basque, Bayonne, France,

⁴ Thoracic Oncology Department, Bichat-Claude Bernard Hospital, AP-HP, Paris, France,

⁵ Pneumology, Hôpital de la Croix-Rousse, Lyon, France,

⁶ Aix Marseille Univ, APHM, INSERM, CNRS, CRCM, Hôpital Nord, Multidisciplinary Oncology and Therapeutic Innovations Department, Marseille, France

⁷ Immunology, Hôpital de La Pitié-Salpêtrière, Paris, France,

⁸ Hematology, Sorbone University, Hôpital de La Pitié Salpêtrière, Paris, France,

⁹ Infectious and Tropical Diseases, CHU Montpellier, Montpellier, France,

¹⁰ Biostatistics, French Cooperative Thoracic Intergroup, Paris, France,

¹¹ Clinical Research Unit, French Cooperative Thoracic Intergroup, Paris, France,

¹² Medical Oncology, Hôpital de La Pitié Salpêtrière, Paris, France

On behalf the French Cooperative Thoracic Intergroup (IFCT)

26 **Conflict of Interest Disclosures:** Armelle Lavole reports non-financial support from Bristol
27 Myers Squibb, outside the submitted work. Julien Mazières reports grants and personal fees
28 from Roche, grants and personal fees from Astra-Zeneca, grants and personal fees from
29 Pierre Fabre , personal fees from Merck Sharp and Dohme, personal fees from Bristol Myers
30 Squibb, personal fees from Hengrui, personal fees from Daiichi, personal fees from
31 Boehringer, personal fees from Takeda, personal fees from Pfizer, outside the submitted
32 work. Laurent Greillier reports personal fees and non-financial support from Abbvie,
33 personal fees and non-financial support from Bristol Myers Squibb, personal fees and non-
34 financial support from Boehringer Ingelheim, personal fees and non-financial support from
35 Astra Zeneca, personal fees and non-financial support from Roche, personal fees and non-
36 financial support from Novartis, personal fees and non-financial support from Merck Sharp
37 and Dohme, personal fees and non-financial support from Pfizer, personal fees and non-
38 financial support from Takeda, outside the submitted work. Jean-Philippe Spano reports
39 personal fees from Roche, personal fees from Merck Sharp and Dohme, personal fees from
40 Astra Zeneca, personal fees from Leopharma, personal fees from Mylan, personal fees from
41 Biogaran, personal fees from Novartis, personal fees from Daiichi Sankyo Oncology,
42 personal fees from Pfizer, grants from Bristol Myers Squibb, non-financial support from
43 Incyte, personal fees from Pierre Fabre Oncology, grants from MSD Avenir, personal fees
44 from Lilly, personal fees from Gilead, grants from INCA, outside the submitted work. Marine
45 Baron reports personal fees from Janssen, outside the submitted work. Jacques Cadranel
46 reports personal fees from AstraZeneca, personal fees from Roche , personal fees from Merck
47 Sharp & Dohme , personal fees from Bristol-Myers Squibb, outside the submitted work.
48 Sophie Schneider, Solen Brosseau, Lize Kiakouma, Amélie Guihot, Baptiste Abbar, Alain
49 Makinson, Alexandra Langlais, and Franck Morin have nothing to disclose.

Address for correspondence: Dr Armelle LAVOLE, Service de Pneumologie - AP-HP
Hôpital Tenon, 4 rue de la Chine 75020 PARIS (France) Email: armelle.lavole@aphp.fr

Word count: 1230

Key Points

Word count: 99

Question: Is nivolumab treatment safe and effective in HIV-infected patients with pretreated advanced non-small cell lung cancer (NSCLC)?

Findings: In this nonrandomized, open-label, phase 2 study of 16 patients with HIV infection and previously treated advanced NSCLC, nivolumab was well-tolerated and beneficial. Disease control rate was 62.5% at 8 weeks. Most treatment-related adverse events were of grade 1 and 2. One patient had a treatment-related serious adverse event. HIV viral load remained undetectable (or controlled) throughout the study.

Meaning: Patients with controlled HIV infection can benefit from nivolumab treatment for pretreated advanced NSCLC. Studies in first-line settings are required in this population.

Abstract

Word count: 299

Importance: Therapies targeting immune checkpoints, such as the programmed cell death 1 (PD-1) receptor, have become the standard-of-care for patients with non-small cell lung cancer (NSCLC), but people living with HIV (PLWH) were excluded from these studies.

Objective: To evaluate the efficacy and tolerability of nivolumab in PLWH with advanced NSCLC.

71 Design: The CHIVA2 study was a nonrandomized, open-label, phase 2 clinical trial in
72 PLWH with previously treated advanced NSCLC.

73 Setting: National multicenter prospective study.

74 Participants: patients had viral load of <200 copies/mL, regardless of their CD4+ T-cell
75 count.

76 Intervention: Nivolumab was administered in second or third line, as monotherapy
77 intravenously at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity.

78 **Main Outcomes and Measures:** The primary endpoint was disease control rate, evaluated
79 using the Response Evaluation Criteria in Solid Tumors, version 1.1. Adverse events were
80 graded using the National Cancer Institute Common Terminology Criteria for Adverse
81 Events, version 4.0.

82 **Results:** Sixteen patients with advanced NSCLC were enrolled: 14 (88%) were men, median
83 age was 58 years (range: 44-71), and all were smokers. The median duration of nivolumab
84 treatment was 3.5 months (range: 0.5-26.5). The median follow-up was 23.6 months. Disease
85 control rate was 62.5% for 15 evaluable patients at 8 weeks (2 with partial response, 8 with
86 stable disease, and 5 with disease progression). Twelve (75%) patients had treatment-related
87 adverse events, which were mild or moderate, except for one patient experiencing severe
88 pruritus, onycholysis, and pemphigoid. There were no opportunistic infections or unexpected
89 immune-related events. HIV viral load was stable during treatment. An increase in
90 proliferating CD8+ and CD4+ T-cells was observed after 3 nivolumab cycles in a subgroup
91 of 9 patients.

Conclusions and Relevance: Second/third-line nivolumab treatment was well-tolerated and beneficial in PLWH with NSCLC. Future trials should investigate immune checkpoint inhibitors in first-line settings.

Trial Registration: EudraCT.ema.europa.eu registration number: 2016-003796-22

Abbreviations: AE: adverse event; C: cycle; (c)ART: (combined) antiretroviral therapy; CI: confidence interval; CTLA-4: cytotoxic T-lymphocyte-associated protein 4; DCR: disease control rate; HIV: human immunodeficiency virus; IC: immune checkpoint; ICIs: immune checkpoint inhibitors; NSCLC: non-small cell lung cancer; OS: overall survival; PD-1: programmed cell death 1 receptor; PD-L1: programmed cell death ligand 1; PFS: progression free survival; PLWH: people living with HIV; TIM-3: T-cell immunoglobulin and mucin domain-containing protein 3; VL: viral load.

Introduction

Antiretroviral therapy (ART) has significantly extended life expectancy for people living with human immunodeficiency virus (HIV) infection (PLWH). In parallel, mortality due to non-acquired immune deficiency syndrome-defining cancers, particularly lung cancer, has risen¹. In these patients, immunosuppressive cancer therapies such as chemotherapy and radiotherapy can cause an initial decline in CD4⁺ T-cell counts, which is associated with an increased mortality hazard².

Cancer therapy targeting immune checkpoint (IC) pathways, including the programmed cell death 1 (PD-1) receptor/programmed cell death ligand (PD-L)1/2 pathway, has become the standard-of-care for non-small cell lung cancer (NSCLC) in the general population, initially as second-line, then as first-line treatment in patients with PD-L1 expression on $\geq 50\%$ of tumor cells, and in combination with chemotherapy in all patients, except those with oncogene-driven NSCLC³. However, PLWH were excluded from these clinical trials due to

concerns that T-cell stimulation may reactivate HIV infection or exacerbate immune responses to HIV-related opportunistic infections⁴. *In vitro* studies show that HIV-infected memory CD4⁺ T-cells preferentially express PD-1, suggesting that IC inhibitors (ICIs) could reinvigorate the CD4⁺ T-cell HIV reservoir⁵. PD-1/PD-L1 blockade facilitates latency reversal in cells from ART-treated individuals, leading to increased virus production⁶. It also restores specific CD8⁺ and CD4⁺ T-cell functions i.e. cytokine and cytotoxic molecules' production and cell proliferation^{7,8}. Retrospective studies have shown that ICIs are generally well-tolerated in PLWH with advanced stage NSCLC, with no or transient effects on HIV viral load (VL) observed^{4,9}. At the time of initiating this trial, only case reports and studies in small cohorts were reported, but no phase 2 trial had been conducted in this setting. We conducted a phase 2 prospective study to investigate the tolerability and efficacy of nivolumab, a fully human anti-PD-1 antibody, in PLWH with advanced NSCLC, after prior platinum-based doublet chemotherapy.

Methods

Sixteen patients with combined (c)ART-controlled HIV-1 infection (VL <200 copies/mL), regardless of their CD4⁺ T-cell count, and histologically/cytologically proven NSCLC stage IIIB or IV at diagnosis or after relapse post-surgery were included. Patients had received at least one prior platinum-based doublet chemotherapy regimen. Full inclusion and exclusion criteria are provided in the trial's protocol ([Supplement 1](#)). Nivolumab was administered intravenously over 30 minutes at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity. The protocol was approved by an independent ethics committee and the French health authorities (ANSM). Written informed consent was obtained from each patient.

The primary endpoint was disease control rate (DCR) at 8 weeks. Secondary endpoints included progression free survival (PFS) and overall survival (OS). Adverse events (AEs) were graded using the National Cancer Institute Common Terminology Criteria for AEs v4.0. Phenotypes of T-cell activation/proliferation were explored in a subgroup of 9 patients at baseline, at cycle (C) C2, C3, C9, C15, C27, and C51, and at the end of treatment. The complete study objectives, assessments, and statistical analyses are provided in the eMethods ([Supplement 2](#)).

Results

Sixteen patients were enrolled between December 2017 and July 2019 (eFigure 1, [Supplement 3](#)). Baseline characteristics are presented in **Table 1** and eTable 1, [Supplement 3](#). Fourteen (88%) patients were men, median age was 58 years (range: 44-71), and 16 (100%) were smokers. Ten (63%) patients had adenocarcinoma. PD-L1 expression was negative in 9/14 (64%) tumors and positive in 5/14 (36%) tumors, with 3 expressing PD-L1 on $\geq 50\%$ of cells. Median CD4⁺ T-cell count was 385 cells/ μ L (range: 187-778) and HIV-VL was 25 copies/mL (range: 0-44). Patients received nivolumab as second- (69%) or third-line (31%) treatment for a median duration of 3.5 months (range: 0.5-26.5). The median follow-up was 23.6 months (95% confidence interval [CI95%]: 13.9-30).

DCR was 62.5% (CI95%: 39-86%) for 15 evaluable patients at 8 weeks, including 2 patients with partial response, 8 with stable disease, and 5 with progressive disease. Median PFS and OS were 3.4 months (CI95%: 1.8-5.6, n=14) and 10.9 months (CI95%: 2.2-not reached, n=10), respectively (eFigure 2, [Supplement 3](#)). Among 9 PD-L1-negative patients, 1 had a partial response, 3 were stable, 4 progressed, and 1 was not determined. Among 5 PD-L1-positive patients, 1 had a partial response and 4 were stable.

Twelve (75%) patients had treatment-related AEs, mostly of grade 1 and 2, except for one patient experiencing grade 3 pruritus, onycholysis, and pemphigoid (**Table 2**). The AE of pemphigoid (grade 2) was also reported as serious. No opportunistic infections or unexpected immune-related events were observed. There were no significant changes in CD4⁺ and CD8⁺ T-cell counts, and HIV-VL was globally stable during nivolumab treatment (**Figure 1**).

In the 9 patients selected for exploratory studies, there was a significant increase in the proportion of CD8⁺Ki67⁺ T-cells at C3 compared to C1 (p=0.047) and in the proportion of CD4⁺Ki67⁺ T-cells at C3 compared to C1 (p=0.0313) (eFigure 3, [Supplement 3](#)). These changes were not associated with better tumor response, since among 4 patients with the highest proportion of CD8⁺Ki67⁺ T-cells, tumor progression occurred in 2 cases. PD-1 was almost undetectable on CD4⁺ and CD8⁺ T-cells from C2 onwards, suggesting high receptor occupancy, whereas T-cell immunoglobulin and mucin domain-containing protein 3 (TIM-3) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) expression significantly increased at C3 on CD4⁺ (p=0.031) and CD8⁺ (p=0.015) T-cells, respectively (eFigure 3, [Supplement 3](#)). Notably, most of the patients with TIM-3 or CTLA-4 upregulation at C3 were progressing (3/4 and 3/3 patients, respectively).

Discussion

In this phase 2 prospective study, the only one focusing on NSCLC, nivolumab was not associated with HIV-VL rebound, replication blip, or unexpected treatment-emergent safety signals, in agreement with two other prospective studies in ART-controlled PLWH with solid tumors^{10,11}. Efficacy findings (62.5% DCR at 8 weeks, 3.4 months PFS, and 10.9 months OS) are consistent with phase 3 studies in the general population³ and better than in real-life settings in the same regional population of NSCLC¹². Patients with PD-L1-positive tumors

seemed to respond better, although this should be confirmed in a larger cohort. Most treatment-related AEs were mild or moderate. As previously observed^{7,8}, PD-1 blockade rapidly induced peripheral CD8⁺/CD4⁺ T-cell activation, which may reflect a boost in T-cell immunity against the tumor and/or the HIV infection (tissue biopsies were unavailable at this stage to confirm this). However, only 2/4 patients with increased peripheral T-cell counts were responders, supporting preliminary data that suggest independent immune responses elicited by viral infections and within the tumor microenvironment, and imply that antitumor and antiviral treatments may be safely combined¹³. TIM-3 and CTLA-4 were significantly upregulated on CD4⁺ and CD8⁺ T-cells, respectively, at C3. This seemed to be associated with tumor progression, suggesting a compensatory mechanism whereby alternative ICs are upregulated following PD-1/PD-L1 blockade, thus inhibiting antitumoral T-cell responses. Upregulation of alternative ICs has been observed *in vitro* on activated CD4⁺ T-cells and regulatory T-cells in the presence of cancer cells in the context of ICIs¹⁴.

Limitations

Our study is limited by the small sample size, which was due to difficulties in recruiting patients with the rare HIV-NSCLC combination, the study independent data monitoring committee recommended that patient inclusion be stopped in January 2020. The use of ICIs as first-line standard-of-care also rapidly evolved during this trial and led to the premature discontinuation of the study.

Conclusions

In summary, nivolumab treatment after prior chemotherapy was well-tolerated and beneficial in PLWH with advanced NSCLC. Future studies should investigate first-line immunotherapy,

209 as monotherapy or in combination with chemotherapy or a second ICI. Since the strength of
210 our conclusions was limited by the small sample size, we endorse recent recommendations to
211 extend inclusion criteria to patients with controlled HIV infection in future trials¹⁵.

Acknowledgments

Author contributions: Armelle Lavole had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* French Cooperative Thoracic Intergroup (IFCT). *Acquisition, analysis, or interpretation of data:* IFCT. *Drafting of the manuscript:* Scinopsis Medical Writing. *Critical revision of the manuscript for important intellectual content:* Armelle Lavole, Jacques Cadranet, and Amelie Guihot. *Statistical analysis:* IFCT. *Obtained funding:* IFCT. *Administrative, technical, or material support:* IFCT. *Study supervision:* IFCT.

Funding/Support: This study was funded by the Intergroupe Francophone de Cancérologie Thoracique (IFCT) and by Bristol-Myers Squibb and was sponsored by the IFCT. The study is part of the National OPDIVIH research program granted by the ANRS. *Partnerships:* CancerVIH Group, ANRS, and Oncovihac cohort.

Role of the Funder/Sponsor: The sponsor was involved in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, and approval of the manuscript; and in the decision to submit the manuscript for publication. Bristol-Myers Squibb had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the participating patients and their families as well as the study teams involved in the trial, the clinical research assistants, study coordinators and IFCT operations staff. We also thank the T4/T8 department and Christophe Parizot for his help with the biological part of the study and all the participating investigators: Dr Armelle Lavole (Paris – Tenon), Pr Julien Mazieres (Toulouse – CHU), Dr Sophie Schneider (Bayonne – CH), Dr Solenn Brosseau (Paris – Bichat), Pr Jean-Philippe Spano (Paris - Pitié-Salpêtrière), Dr Lize Kiakouama-Maleka (Lyon - Croix-Rousse), Pr Laurent Greillier

237 (Marseille – APHM). Medical writing assistance was provided by Dr Leonarda Di Candia
238 (Scinopsis, France) and funded by the IFCT.
239 **Additional Information:** None.

References

1. Rubinstein PG, Aboulafia DM, Zloza A. Malignancies in HIV/AIDS: from epidemiology to therapeutic challenges. *AIDS*. 2014;28(4):453-65.
2. Calkins KL, Chander G, Joshu CE, Visvanathan K, Fojo AT, Lesko CR, et al. Immune status and associated mortality after cancer treatment among individuals with HIV in the antiretroviral therapy era. *JAMA Oncol*. 2020 Feb 1;6(2):227-235.
3. Xia L, Liu Y, Wang Y. PD-1/PD-L1 blockade therapy in advanced non-small-cell lung cancer: current status and future directions. *Oncologist*. 2019;24(Suppl 1):S31-S41.
4. Ostios-Garcia L, Faig J, Leonardi GC, Adeni AE, Subegdjo SJ, Lydon CA, et al. Safety and efficacy of PD-1 inhibitors among HIV-positive patients with non-small cell lung cancer. *J Thorac Oncol*. 2018;13(7):1037-42.
5. Chomont N, El-Far M, Ancuta P, Trautmann L, Procopio FA, Yassine-Diab B, et al. HIV reservoir size and persistence are driven by T cell survival and homeostatic proliferation. *Nat Med*. 2009;15(8):893-900.
6. Fromentin R, DaFonseca S, Costiniuk CT, El-Far M, Procopio FA, Hecht FM, et al. PD-1 blockade potentiates HIV latency reversal ex vivo in CD4(+) T cells from ART-suppressed individuals. *Nat Commun*. 2019;10(1):814.
7. Trautmann L, Janbazian L, Chomont N, Said EA, Gimmig S, Bessette B, et al. Upregulation of PD-1 expression on HIV-specific CD8+ T cells leads to reversible immune dysfunction. *Nat Med*. 2006;12(10):1198-202.
8. Day CL, Kaufmann DE, Kiepiela P, Brown JA, Moodley ES, Reddy S, et al. PD-1 expression on HIV-specific T cells is associated with T-cell exhaustion and disease progression. *Nature*. 2006;443(7109):350-4.

9. Cook MR, Kim C. Safety and efficacy of immune checkpoint inhibitor therapy in patients with HIV infection and advanced-stage cancer: a systematic review. *JAMA Oncol.* 2019;5(7):1049-54.
10. Gonzalez-Cao M, Morán T, Dalmau J, Garcia-Corbacho J, Bracht JWP, Bernabe R, et al. Assessment of the feasibility and safety of durvalumab for treatment of solid tumors in patients with HIV-1 infection: the phase 2 DURVAST study. *JAMA Oncol.* 2020;6(7):1063-7.
11. Uldrick TS, Gonçalves PH, Abdul-Hay M, Claeys AJ, Emu B, Ernstoff MS, et al. Assessment of the safety of pembrolizumab in patients with HIV and advanced cancer- a phase 1 study. *JAMA Oncol.* 2019;5(9):1332-9.
12. Costantini A, Corny J, Fallet V, Renet S, Friard S, Chouaid C, et al. Efficacy of next treatment received after nivolumab progression in patients with advanced nonsmall cell lung cancer. *ERJ Open Res.* 2018 Apr 20;4(2):00120-2017.
13. Pinato DJ, Kythreotou A, Mauri FA, Suardi E, Allara E, Shiner RJ, et al. Functional immune characterization of HIV-associated non-small-cell lung cancer. *Ann Oncol.* 2018;29(6):1486-8.
14. Saleh R, Toor SM, Khalaf S, Elkord E. Breast cancer cells and PD-1/PD-L1 blockade upregulate the expression of PD-1, CTLA-4, TIM-3 and LAG-3 immune checkpoints in CD4(+) T cells. *Vaccines (Basel).* 2019 Oct 12;7(4):149.
15. Kim ES, Bruinooge SS, Roberts S, Ison G, Lin NU, Gore L, et al. Broadening eligibility criteria to make clinical trials more representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement. *J Clin Oncol.* 2017;35(33):3737-44.

Figure Legends

Figure 1. Peripheral CD4⁺ and CD8⁺ T-cell Count and HIV Viral Load.

A, B) Overall, peripheral CD4⁺ T-cells (A) and CD8⁺ T-cells (B) (counts/mm³) did not change significantly from baseline (BS) to the end of treatment (EoT). **C)** Peripheral viral load remained stable during the study. Data are depicted for n=16 patients. BS: baseline; C: cycle; EoT: End of Treatment.

Tables

Table 1. Baseline Characteristics of the Patients

Characteristic	No. (%) ^a (n = 16)
Age, median (range), years	58 (44-71)
Sex	
Male	14 (88)
Female	2 (13)
Smoking	
Yes	16 (100)
No	0 (0)
Pack per year, median (range)	40 (13-90)
ECOG performance status	
0-1	12 (75)
2	4 (25)
No. of prior cancer therapies	
1	11 (69)
≥2	5 (31)
Histology	
Adenocarcinoma	10 (63)
Unspecified NSCLC	1 (6)
Squamous cell carcinoma	5 (31)
Stage	
IIIB	1 (6)
IVA	4 (25)
IVB	11 (69)
PD-L1 ^b	
<1%	9 (64)
1-49%	2 (14)
≥50%	3 (21)
Duration of HIV infection, median (range), years	24 (3-39)
CD4 ⁺ T-cell count, median (range), cells/mm ³	385 (187-778)
Nadir CD4 ⁺ T-cell count, median (range), cells/mm ³	274 (32-778) ^c
HIV viral load, median (range), copies/mL	25 (0-44)
History of cancer	6 (38)
AIDS-related	1 (6)
Non-AIDS-related	5 (31)
History of infection	11 (69)
AIDS-related infections	3 (19)
Hepatitis B	2 (13)
Hepatitis C	3 (19)
Others	8 (50)
Comorbidities ^c	
Yes	8 (53)
No	7 (47)

Abbreviations: AIDS, acquired immune deficiency syndrome; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; NSCLC, non-small cell lung cancer; PD-L1, programmed cell death ligand 1.

^a Percentages are rounded off.

^b Data were available for n=14 patients (biopsies were not collected for 2 patients).

^c Data were available for n=15 patients (one patient missing/unknown).

Table 2. Adverse Events Related to Treatment

Type of adverse event	No. (%) ^a (n = 16)					
	Grade					
	Any	1	2	3	4	5
Any	12 (75)	4 (25)	7 (44)	1 (6)	0 (0)	0 (0)
Serious ^b	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Gastrointestinal disorders	7 (44)	4 (25)	3 (19)	0 (0)	0 (0)	0 (0)
Diarrhea	3 (19)	3 (19)	0 (0)	0 (0)	0 (0)	0 (0)
Nausea	3 (19)	1 (6)	2 (13)	0 (0)	0 (0)	0 (0)
Aphthous ulcer	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Constipation	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Dry mouth	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Stomatitis	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Vomiting	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Endocrine disorders	4 (25)	3 (19)	1 (6)	0 (0)	0 (0)	0 (0)
Hyperthyroidism	2 (13)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)
Hypothyroidism	2 (13)	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)
General disorders and administration site conditions	3 (19)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)
Asthenia	3 (19)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)
General physical health deterioration	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Xerosis	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Musculoskeletal and connective tissue disorders	3 (19)	1 (6)	2 (13)	0 (0)	0 (0)	0 (0)
Arthralgia	3 (19)	1 (6)	2 (13)	0 (0)	0 (0)	0 (0)
Skin and subcutaneous tissue disorders	3 (19)	2 (13)	0 (0)	1 (6)	0 (0)	0 (0)
Pruritus	3 (19)	2 (13)	0 (0)	1 (6)	0 (0)	0 (0)
Alopecia	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Alopecia areata	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Madarosis	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Onycholysis	1 (6)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)
Pemphigoid	1 (6)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)
Rash	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Blood and lymphatic system disorders	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Anemia	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Investigations	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Weight decreased	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Metabolism and nutrition disorders	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Hyperkalemia	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Nervous system disorders	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Tremor	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)

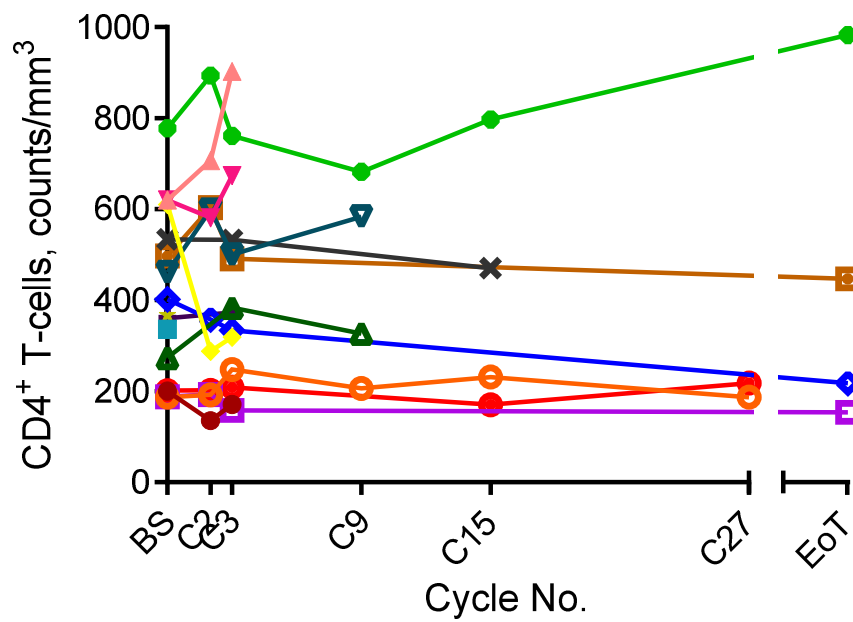
Abbreviations: AE, adverse event; SAE, serious adverse event.

^a Percentages are rounded off and may not sum up to the total exactly.

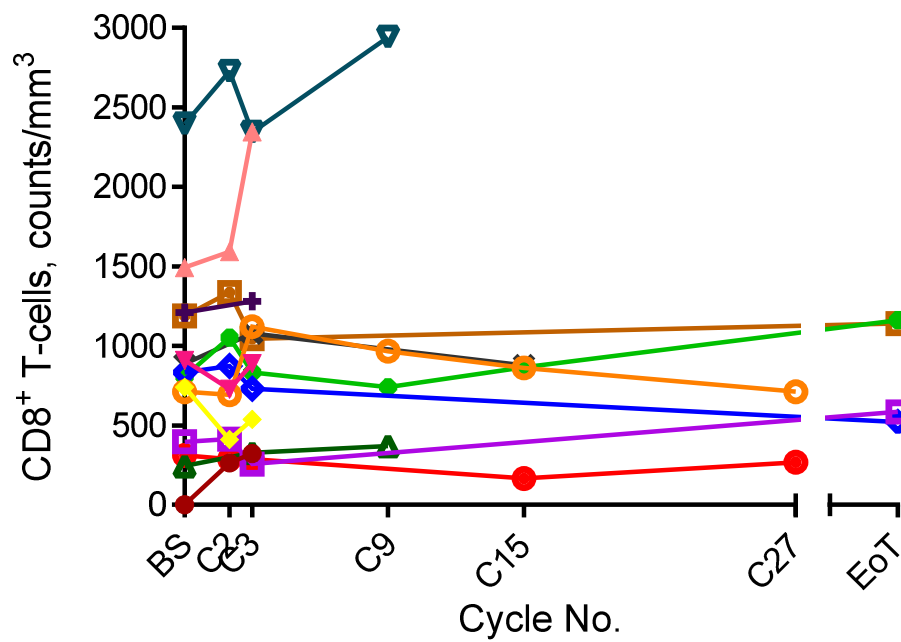
^b SAE's grades are presented as assessed when the event was declared as serious. Grades for the AE's preferred term represent the worst grade for each event.

Figure 1. Peripheral CD4⁺ and CD8⁺ T-cell Count and HIV Viral Load.

A) CD4⁺ T-cells



B) CD8⁺ T-cells



C) Viral load

