

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

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1 Title

2	Assessment of Nivolumab in HIV-Infected Patients with Advanced Non-Small Cell
3	Lung Cancer after Prior Chemotherapy. The IFCT-1602 CHIVA2 Phase 2 Clinical
4	Trial
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- **52** *Word count: 1230*

53 Key Points

- 54 *Word count: 99*
- Question: Is nivolumab treatment safe and effective in HIV-infected patients with pretreatedadvanced non-small cell lung cancer (NSCLC)?
- 57 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.
- 59 Disease control rate was 62.5% at 8 weeks. Most treatment-related adverse events were of
- 60 grade 1 and 2. One patient had a treatment-related serious adverse event. HIV viral load
- 61 remained undetectable (or controlled) throughout the study.
- 62 Meaning: Patients with controlled HIV infection can benefit from nivolumab treatment for
- 63 pretreated advanced NSCLC. Studies in first-line settings are required in this population.

64 Abstract

- 65 *Word count: 299*
- 66 **Importance:** Therapies targeting immune checkpoints, such as the programmed cell death 1
- 67 (PD-1) receptor, have become the standard-of-care for patients with non-small cell lung
- 68 cancer (NSCLC), but people living with HIV (PLWH) were excluded from these studies.
- 69 Objective: To evaluate the efficacy and tolerability of nivolumab in PLWH with advanced70 NSCLC.

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

73 Setting: National multicenter prospective study.

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

76 Intervention: Nivolumab was administered in second or third line, as monotherapy

intravenously at 3 mg/kg every 2 weeks, until disease progression or limiting toxicity.

Main Outcomes and Measures: The primary endpoint was disease control rate, evaluated
using the Response Evaluation Criteria in Solid Tumors, version 1.1. Adverse events were
graded using the National Cancer Institute Common Terminology Criteria for Adverse
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 treatment was 3.5 months (range: 0.5-26.5). The median follow-up was 23.6 months. Disease 84 control rate was 62.5% for 15 evaluable patients at 8 weeks (2 with partial response, 8 with 85 86 stable disease, and 5 with disease progression). Twelve (75%) patients had treatment-related adverse events, which were mild or moderate, except for one patient experiencing severe 87 pruritus, onycholysis, and pemphigoid. There were no opportunistic infections or unexpected 88 89 immune-related events. HIV viral load was stable during treatment. An increase in proliferating CD8+ and CD4+ T-cells was observed after 3 nivolumab cycles in a subgroup 90 of 9 patients. 91

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

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

96 Abbreviations: AE: adverse event; C: cycle; (c)ART: (combined) antiretroviral therapy;

97 CI: confidence interval; CTLA-4: cytotoxic T-lymphocyte-associated protein 4;

98 DCR: disease control rate; HIV: human immunodeficiency virus; IC: immune checkpoint;

99 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;

101 PFS: progression free survival; PLWH: people living with HIV; TIM-3: T-cell

102 immunoglobulin and mucin domain-containing protein 3; VL: viral load.

103 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.

110 Cancer therapy targeting immune checkpoint (IC) pathways, including the programmed cell 111 death 1 (PD-1) receptor/programmed cell death ligand (PD-L)1/2 pathway, has become the 112 standard-of-care for non-small cell lung cancer (NSCLC) in the general population, initially 113 as second-line, then as first-line treatment in patients with PD-L1 expression on \geq 50% of 114 tumor cells, and in combination with chemotherapy in all patients, except those with 115 oncogene-driven NSCLC³. However, PLWH were excluded from these clinical trials due to

- 116 concerns that T-cell stimulation may reactivate HIV infection or exacerbate immune
- 117 responses to HIV-related opportunistic infections⁴.

118 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.
- 120 PD-1/PD-L1 blockade facilitates latency reversal in cells from ART-treated individuals,
- 121 leading to increased virus production⁶. It also restores specific CD8⁺ and CD4⁺ T-cell
- 122 functions i.e. cytokine and cytotoxic molecules' production and cell proliferation^{7,8}.
- 123 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,
- 126 but no phase 2 trial had been conducted in this setting.
- 127 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
- 129 platinum-based doublet chemotherapy.

130 Methods

Sixteen patients with combined (c)ART-controlled HIV-1 infection (VL <200 copies/mL), 131 regardless of their CD4⁺ T-cell count, and histologically/cytologically proven NSCLC stage 132 IIIB or IV at diagnosis or after relapse post-surgery were included. Patients had received at 133 134 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 135 intravenously over 30 minutes at 3 mg/kg every 2 weeks, until disease progression or limiting 136 137 toxicity. The protocol was approved by an independent ethics committee and the French health authorities (ANSM). Written informed consent was obtained from each patient. 138

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).

146 **Results**

147 Sixteen patients were enrolled between December 2017 and July 2019 (eFigure 1,

148 Supplement 3). Baseline characteristics are presented in **Table 1** and eTable 1, Supplement 3.

149 Fourteen (88%) patients were men, median age was 58 years (range: 44-71), and 16 (100%)

150 were smokers. Ten (63%) patients had adenocarcinoma. PD-L1 expression was negative in

151 9/14 (64%) tumors and positive in 5/14 (36%) tumors, with 3 expressing PD-L1 on \geq 50% of

152 cells. Median CD4⁺ T-cell count was 385 cells/µL (range: 187-778) and HIV-VL was

153 25 copies/mL (range: 0-44). Patients received nivolumab as second- (69%) or third-line

154 (31%) treatment for a median duration of 3.5 months (range: 0.5-26.5). The median

155 follow-up was 23.6 months (95% confidence interval [CI95%]: 13.9-30).

156 DCR was 62.5% (CI95%: 39-86%) for 15 evaluable patients at 8 weeks, including 2 patients

157 with partial response, 8 with stable disease, and 5 with progressive disease. Median PFS and

158 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

160 partial response, 3 were stable, 4 progressed, and 1 was not determined. Among

161 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 162 patient experiencing grade 3 pruritus, onycholysis, and pemphigoid (Table 2). The AE of 163 pemphigoid (grade 2) was also reported as serious. No opportunistic infections or unexpected 164 immune-related events were observed. There were no significant changes in CD4⁺ and CD8⁺ 165 T-cell counts, and HIV-VL was globally stable during nivolumab treatment (Figure 1). 166 167 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 168 CD4+Ki67+ T-celles at C3 compared to C1 (p=0.0313) (eFigure 3, Supplement 3). These 169 changes were not associated with better tumor response, since among 4 patients with the 170 highest proportion of CD8⁺Ki67⁺ T-cells, tumor progression occurred in 2 cases. 171 PD-1 was almost undetectable on CD4⁺ and CD8⁺ T-cells from C2 onwards, suggesting high 172 receptor occupancy, whereas T-cell immunoglobulin and mucin domain-containing protein 3 173 (TIM-3) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) expression significantly 174 increased at C3 on CD4⁺ (p=0.031) and CD8⁺ (p=0.015) T-cells, respectively (eFigure 3, 175 Supplement 3). Notably, most of the patients with TIM-3 or CTLA-4 upregulation at C3 were 176 progressing (3/4 and 3/3 patients, respectively). 177

178 **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. Mosttreatment-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.

194 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.

200 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.

206 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,

- as monotherapy or in combination with chemotherapy or a second ICI. Since the strength of
- our conclusions was limited by the small sample size, we endorse recent recommendations to
- extend inclusion criteria to patients with controlled HIV infection in future trials 15 .

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215 and design: French Cooperative Thoracic Intergroup (IFCT). Acquisition, analysis, or

216 *interpretation of data*: IFCT. *Drafting of the manuscript*: Scinopsis Medical Writing. *Critical*

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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.
- 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.
- 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.
- 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.
- 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.

- 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.
- 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.
- 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 cancera phase 1 study. *JAMA Oncol.* 2019;5(9):1332-9.
- 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.
- 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.
- 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	Patient
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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) °
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).

No. $(\%)^{a}$ (n = 16)							
Type of adverse event	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	3 (19)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	
administration site conditions							
Asthenia	3 (19)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	
General physical health	1 (6)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	
deterioration							
Xerosis	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	
Musculoskeletal and connective	3 (19)	1 (6)	2 (13)	0 (0)	0 (0)	0 (0)	
tissue disorders	a (10)			0. (0)	0. (0)	0. (0)	
Arthralgia	3 (19)	1 (6)	2 (13)	0 (0)	0(0)	0 (0)	
Skin and subcutaneous tissue	3 (19)	2 (13)	0 (0)	1 (6)	0 (0)	0 (0)	
disorders	2 (10)	2 (12)	0.(0)	1.00	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	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	
disorders	1 (()	1 (()	0 (0)	0.(0)	0.(0)	0 (0)	
	1(6)	1(6)		0(0)	0(0)	0(0)	
Weight despected	1(6)		1(0)				
Weight decreased	1(6)		$\frac{1}{0}$	0(0)	0(0)	0(0)	
Vietabolism and nutrition	1 (0)	1 (0)	U (U)	0(0)	0(0)	U (U)	
UISOFUETS Hyperkalamia	1 (6)	1(6)	0.(0)	0.(0)	0.(0)	0(0)	
Nomena austern discorders	1(0)	$\frac{1}{0}$	1 (6)				
Tremor	1(0)		1 (0)				
Tremor	1 (0)	0(0)	1 (0)	0(0)	0(0)	0(0)	

Table 2. Adverse Events Related to Treatment

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.





A) CD4⁺ T-cells







