IFCT-1001 CHIVA trial : A phase II study of carboplatin (Ca) plus pemetrexed (P) followed by maintenance P as first-line therapy for Human Immunodeficiency Virus positive (HIV+) infected patients (pts) with advanced non-squamous non-small cell lung cancer (NS-NSCLC).

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A. Lavole, P. Tomasini, C. Hermant, I. Monnet, L. Kiakouama-Maleka, X. Quantin, L. Taillade, H. Lena, P. Fraisse, H. Janicot, C. Audigier-Valette, A. Makinson, A. Langlais, MP. Lebitasy, F. Morin, J. Cadranel

French Cooperative Thoracic Intergroup (IFCT); Hôpital Tenon, AP-HP and Faculté de Médecine Pierre et Marie Curie, Université Paris VI, Paris, France; AP-HM Hôpital Nord, Marseille, France; CHU of Toulouse, Toulouse, CHI of Creteil, Creteil, France; HCL Hôpital Croix-Rousse, Lyon, France; Centre Hospitalier Universitaire Montpellier, Montpellier, France; AP-HP Groupe Hospitalier Pitié-Salpétrière, Paris, France; Centre Hospitalier Universitaire, Hopital Pontchaillou, Rennes, France; Hopitaux Universitaires Strasbourg, Strasbourg, France; CHU, Clermont Ferrand, France; Service de Pneumologie - CH Toulon, Toulon, France; CHU, Montpellier, France; IFCT, Paris, France; Intergroupe Francophone De Cancerologie Thoracique (IFCT), Paris, France

BACKGROUND

- The use of tritherapy in developed countries starting in 1996 led to a considerable reduction in AIDS mortality due to opportunistic infections and AIDS-defining cancers. However, increased life expectancies were accompanied by a diversification of the causes of death in HIV-infected individuals. In 2010 cancer represented 34% of the causes of death in France and lung cancer was the first cause of mortality by cancer.
- The prognosis of LC is worse in HIV-positive individuals. Some authors suggest that these poor outcomes may be related to interactions and additive toxicities of the cytotoxic and antiretroviral drugs. It is also likely that the disease is particularly aggressive. Recommendations for treatment of advanced NSCLC are lacking in this population, as HIV seropositivity is an exclusion criteria from most trials.
- We conducted a multicenter phase II trial to evaluate the efficacy and safety of CaP induction followed by P maintenance, in HIV associated advanced NS-NSCLC.

METHODS

Four cycles of CaP were administered, followed by P until progression in controlled patients with PS ≤ 2 after induction.

The primary endpoint was a ≥ 30% disease control rate (DCR) after 12 weeks.

Secondary endpoints were objective response rate, progression-free (PFS) and overall survival (OS), as well as the incidences of adverse events (AE) and opportunistic infections.

Statistics : Fleming (1 step) alpha=5%, beta=95% p0=30%, p1=50%, H0 : p ≤ p0=30% versus H1 : p ≥ p1

KEY INCLUSION CRITERIA

- Age ≥ 18 years ≤ 75 years,
- WHO performance status: 0, 1 or 2
- NSCLC histologically (highly recommended) and/or cytologically confirmed, stage III (non-irradiable or inoperable) or stage IV (according to 2009 TNM classification), with other than predominantly squamous histology
- **HIV seropositivity (previous or inaugural), irrespective of CD4 count or viral load**
- Weight loss ≤ 10% of total body weight in the month before inclusion
- Creatinine clearance (MDRD) ≥ 45 mL/min

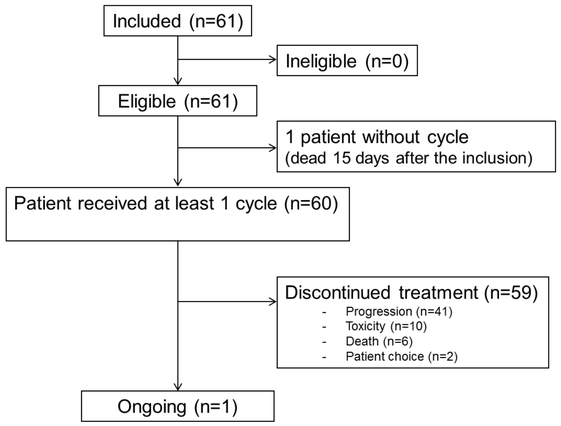
PATIENT CHARACTERISTICS

	ALL (N=61) N (%)
Sex	
Male	46 (75.4)
Female	15 (24.6)
Age	
Median	52.9
Range	[36.6-67.5]
Smoking status	
Current	54 (88.5)
Former	3 (4.9)
Never	4 (6.6)
Pack-years smoked	
Median	36.0
Range	[4.0-120.0]
PS	
0	17 (27.9)
1	33 (54.1)
2	11 (18.0)
Histology	
Adenocarcinoma	56 (91)
Others	5 (9)
Stage	
III	6 (9.8)
IV	55 (90.2)

	ALL (N=61) N (%)
Median known duration of HIV infection	
Median	20.69
Range	[0.1-29.0]
Nadir CD4+ T-cell count	
Median	163.00
Range	[1.0-822.0]
CD4+ T-cell count	
Median	418.00
Range	[18.0-1230.0]
HIV Viral load (VL)	
Median	39.00
Range	[0.0-95499.0]
AntiRetroviral Therapy (ART)	
No	2 (3.6)
Yes	53 (96.4)
Cotrimoxazole	
No	49 (80.3)
Yes	12 (19.7)

	ALL (N=61) N (%)
Cancer History	
Yes	**9 (14.8)**
Non Hodgkin lymphoma	2
Hodgkin lymphoma	2
Kaposi	1
Anal	0
Others	4
Infections	
Yes	**43 (70.5)**
Toxoplasma	5
Pneumocystis jiroveci pneumonia	8
Mycobacteriosis (tuberculosis et no tuberculosis)	9
Hepatitis B	7
Hepatitis C	24
Others	9
Comorbidities	
Yes	**31 (50.8)**
Arterial hypertension	10
Dyslipidaemia	10
Diabetes	3
Cardiopathy	9
Others	16

FLOW-CHART



OVERVIEW OF TOXICITIES (cycle 1 to 4)

	ALL (N=60)
Any AE, any grade (N,%)	59 (98.3%)
Any AE, grade 3 - 4 (N,%)	36 (60.0%)
Any AE, grade 5 ‡ (N,%)	2 (3.3%)

‡ Sepsis

	Any grade (N=60)	Grade 3 - 4 (N=60)
Hematological AEs	57 (95.0%)	36 (60.0%)
Anaemia	52 (86.7%)	18 (30.0%)
Neutropenia	47 (78.3%)	32 (53.3%)
Thrombocytopenia	42 (70%)	21 (35.0%)
Febrile neutropenia	4 (6.7%)	4 (6.7%)

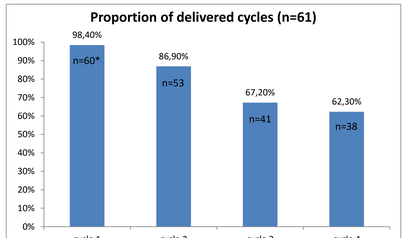
	Any grade (N=60)	Grade 3 - 4 (N=60)	Grade 5 (N=60)
Asthenia	40 (66.7%)	10 (16.7%)	0 (0%)
Nausea	28 (46.7%)	3 (5%)	0 (0%)
Vomiting	15 (25%)	3 (5%)	0 (0%)
Diarrhoea	7 (11.7%)	1 (1.7%)	0 (0%)
Anorexia	19 (31.7%)	2 (3.3%)	0 (0%)
Weight decreased	9 (15%)	0 (0%)	0 (0%)
Sepsis	3 (5.0%)	1 (1.7%)	2 (3.3%)
Neuropathy peripheral	3 (5.0%)	0 (0%)	0 (0%)
Alopecia	3 (5%)	0 (0%)	0 (0%)
Renal failure	4 (6.7%)	0 (0%)	0 (0%)

No fatal event during the maintenance by pemetrexed

EFFICACY

	N=61	
Disease Control (DC)	**31 (50.8%)**	**IC95% [38.3%-63.4%]**
Partial Response (PR)	18 (29.5%)	
Stable Disease (SD)	13 (21.3%)	

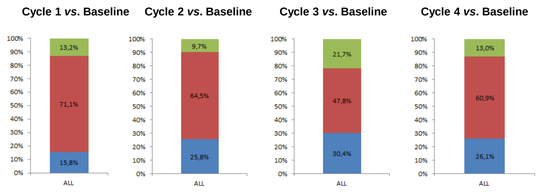
DRUG DELIVERY



Maintenance by pemetrexed:
30 patients (49.2%), 3.7 cycles (mean), range : 1-13

QUALITY OF LIFE (QoL)

LCSS questionnaire (Global Quality of Life)

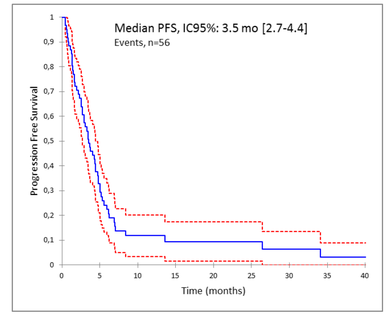


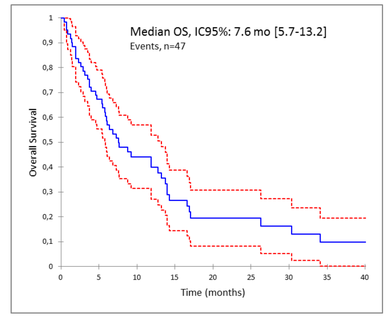
P = 0.33 between C1 and C4

Declined — average score increased by 10 points from baseline
Stable
Improved — average score decreased by 10 points from baseline

SURVIVAL

Median follow-up : 26.5 months (30-NOV-2015)





CONCLUSIONS

1/ Four cycles of CaP induction, followed by P maintenance, were effective and reasonably well-tolerated in first-line therapy of HIV-infected patients with NE-NSCLC

2/ Any opportunist infection was observed

3/ Overall survival was shorter than in general population whereas HIV infected patients have a good immunovirological control. There is an urgent unmet need for investigation of others therapies, particularly immune-based therapies targeting the immune checkpoints.

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