Poster # 140

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Efficacy and Tolerance of Lopinavir/ritonavir in Clinical Practice: An Observational Prospective Cohort of 1278 Patients

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Background

Lopinavir (LPV) is an HIV protease inhibitor (PI) co-formulated with ritonavir(r), which acts as a pharmacokinetic enhancer.
Marketed as Kaletra®, LPV/r has been extensively studied in both anti-retroviral naïve and experienced HIV-infected patients. Long-term data are available and show a potent antiviral effect and a good tolerance in clinical trials.
In order to assess the use of Kaletra® in routine practice, a large observational cohort, KALEOBS, has been set up to study short and long term tolerance, as well as antiviral activity.
This poster presents the intermediate analysis at Month 9.

Objectives

To study short and long-term tolerance of LPV/r-containing regimens, as well as antiviral activity, in routine practice.

Methods

Study Design

Large observational cohort of 1278 adult HIV-infected patients treated for the first time by LPV/r, currently ongoing in France in 181 investigating centers.
Follow-up is scheduled for 18 months. Patients were included between September 2002 and November 2003.

Patients

HIV-1 positive patients, currently treated by Kaletra® (lopinavir/ritonavir) for at least 1 month and no more than 3 months, and :

- either naïve of ARV (ARV-Naïve)
- or pre-treated without PI (PI-Naïve)
- or pre-treated with a first line PI (PI-Exp).

Follow-up

After an inclusion visit (M0), visit frequency was determined by standard of care (M1, M3, then every 3 months). Due to the observational character of this survey, data collection and follow-up are left to the judgment of each physician within the 18-month period.
Data collection at baseline and during follow-up includes demographic data, prior and current ARV medications, physical examination, HIV RNA and CD4 count, genotype, laboratory results (total cholesterol, HDL and LDL-cholesterol, triglycerides, glycemia), evaluation of compliance and tolerability of treatment.

Statistical analysis

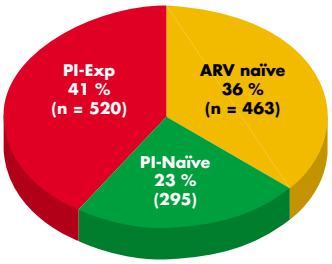
Description is based on mean and standard deviation for quantitative values.
Comparison of compliance and clinical and laboratory tolerability is performed using analysis variance for quantitative variable and the Chi^2 tests for qualitative variables.
Changes in CD4 count, viral load and laboratory parameters are compared during time and between the 3 groups using two factor analysis of variance for paired series.
Baseline characteristics are presented for the total number of patients included in the cohort. Follow-up data are only presented for patients who had completed their 5th visit at Month 9.

Results

Baseline Cohort Characteristics

Demographic and baseline characteristics (all patients)

Figure 1. Patient Distribution



According To Entry Critera (n = 1278)

Table 1. Baseline Characteristics

	ARV-Naïve n = 463 (36 %)	PI-Naïve n = 295 (23 %)	PI-Exp n = 520 (41 %)
Mean age (years)	39	40	41
Gender (% male)	69.6 %	66.8 %	74.2 %
CD4 count (cells/mm³) Mean (± SD) < 200	154 (± 154) 68.4 %	287 (± 235) 43.4 %	262 (± 178) 40.0 %
HIV RNA (log_{10} copies/mL) Mean (± SD) > 5 log	5.0 (± 0.8) 59.3 %	4.0 (± 1.3) 22.9 %	4.1 (± 1.2) 27.6 %
Total median number of PI mutations at baseline	/	1	2

Demographic and baseline characteristics were similar between entry criteria groups. A more advanced immuno-virological profile is observed for ARV-Naïve compared to PI-Naïve and PI-Exp patients.

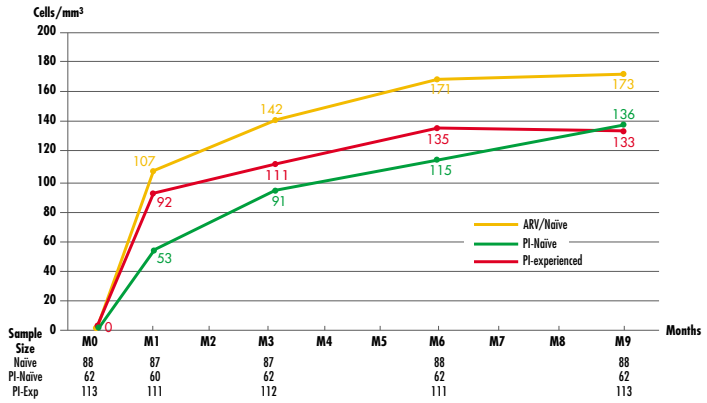
Antiretroviral Regimens Combined with LPV/r (all patients)

For the 3 populations, AZT+3TC are the most frequently antiretroviral drugs combined with LPV/r at inclusion : in 66.7 % of the cases for ARV-Naïve, 20.50 % for PI-Naïve and 21.60 % for PI-Exp.

Imunological and virological response

CD4 Cell Count Response

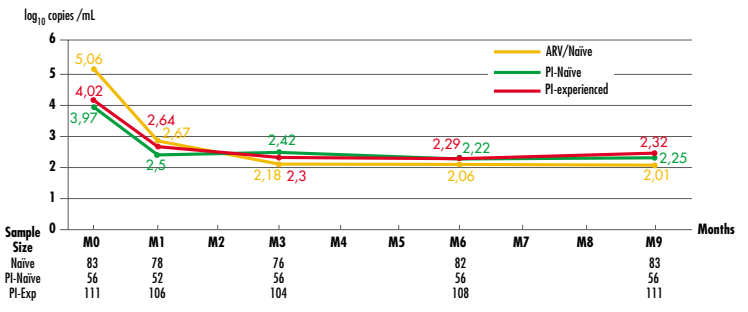
Figure 2. CD4 Cell Count Mean Change from Baseline



Significant increase of CD4 is observed for the 3 populations (p <0.0001) since the 1st month of treatment and sustained during 9 months.

Virologic Response

Figure 3. Mean Viral Load Evolution



Significant decrease in viral load through 9 months is observed for each population: - 3.0 log (n = 83) for ARV-Naïve (p < 0.0001); - 1.7 log (n = 56) for PI-Naïve (p < 0.0001); - 1.7 log (n = 111) for PI-Exp (p < 0.0001).
For each population, more than 75% of patients demonstrate HIV-RNA < 400 copies/mL since month 3 to month 9.

Clinical outcome

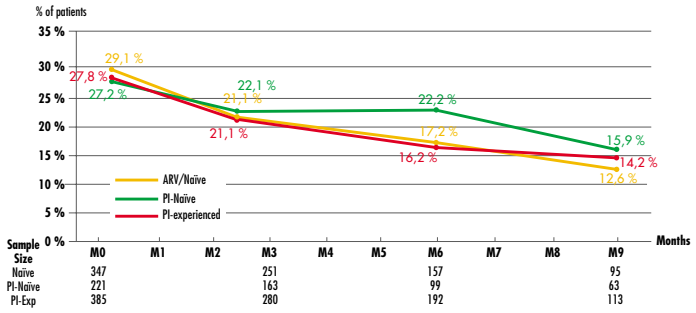
Table 2. Patient Disposition Through Month 9

Patients Included	**1278**	
Discontinuation prior to 9 Months	**114**	
Discontinuation due to Adverse Events	**63**	
Diarrhea		31
Nausea/vomiting		13
Cephalgia		1
Others		18
Premature Discontinuation due to Failure	**2**	
Other reasons	**49**	
(no available information: monitoring in progress)		

Premature discontinuation occurred for 8.9% of patients (n=114), mainly related to adverse events (55%, n=63), GI for most of them (69.8%, n=44)

Clinical safety: adverse events

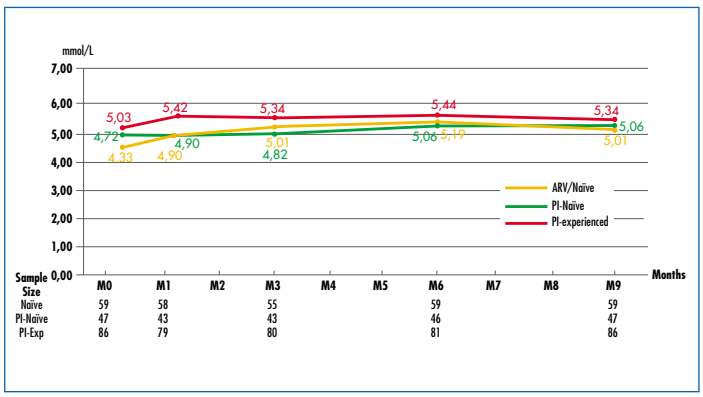
Figure 4. Prevalence of Adverse Events



More than 70 % of patients show no clinical adverse event after 1 month of treatment in each group. At Month 9, nearly 85 % of patients in each group show no clinical adverse event. Adverse events are for most of them (> 88%) gastro-intestinal.

Biological safety: total cholesterol, triglycerides, HDL-c and LDL-c

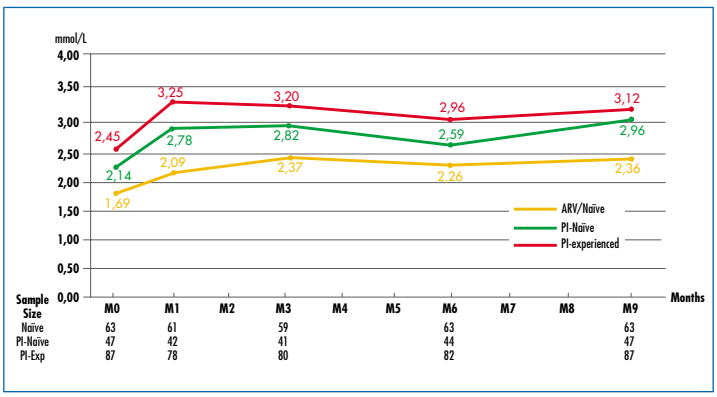
Figure 5. Mean Total Cholesterol Evolution



Mean change from baseline to 1 month in TC:

+0.57 mmol/L for ARV-Naïve (n=58) p < 0.0001
+0.18 mmol/L for PI-Naïve (n=43) p=ns
+0.39 mmol/L for PI-Exp (n=79) p < 0.04

Figure 6. Mean Triglycerides Evolution



Mean change from baseline to 1 month in TG:

+0.40 mmol/L for ARV-Naïve (n=61) p < 0.006
+0.64 mmol/L for PI-Naïve (n=42) p < 0.04
+0.80 mmol/L for PI-Exp (n=78) p < 0.0001

Table 3. Distribution of Total Cholesterol and Triglycerides Values at Month 9

	ARV-Naïve	PI-Naïve	PI-Exp
Total Cholesterol mmol/L (g/L)	n=59	n=47	n=86
< 6.45 (< 2.5)	88.1 %	89.4 %	82.6 %
> 6.45-7.74 (> 2.5-3.0)	11.9 %	8.5 %	15.1 %
> 7.74 (> 3.0)	0%	2.1 %	2.3 %
Triglycerides mmol/L (g/L)	n=63	n=47	n=87
< 2,28 (< 2)	61.9 %	59.6 %	41.4 %
> 2,28-4,56 (> 2-4)	30.2 %	21.3 %	41.4 %
> 4,56 (> 4)	7.9 %	19.1 %	17.2 %

Figure 7. Mean LDL-Cholesterol Evolution

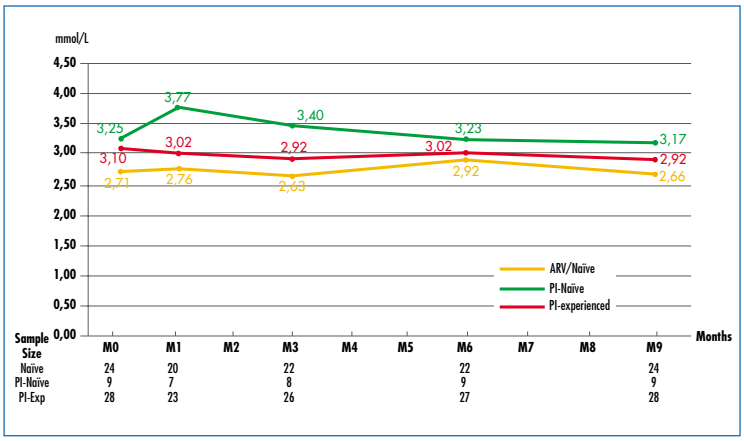
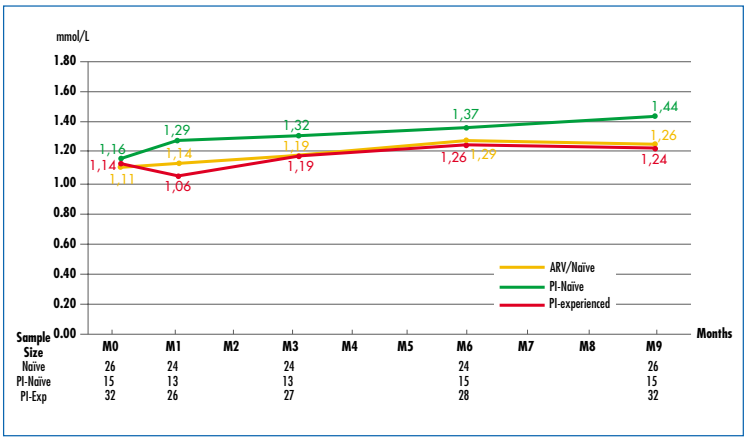


Figure 8. Mean HDL-Cholesterol Evolution



After a significant increase within the first month, total cholesterol (TC) and triglycerides (TG) remained stable in the 3 populations up to 9 months.
No significant increase of LDL-cholesterol nor decrease of HDL-cholesterol were observed in the 3 populations from month 3 to month 9.

Conclusions

KALEOBS represents one of the largest Kaletra® antiretroviral cohort of HIV-infected patients followed in routine practice.

Through 9 months, both ARV-naïve and experienced patients exhibited a good immunologic and virologic response, with more than 75% of patients demonstrating HIV-RNA < 400 copies/mL in the 3 populations.

LPV/r was well tolerated as indicated by the low rate of cohort discontinuation due to adverse events.

KALEOBS show modest effects of LPV/r on lipid levels. After a significant increase within the first month, total cholesterol (TC) and triglycerides (TG) remained stable in the 3 populations up to 9 months.

Acknowledgements

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References

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