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Efficacy of Lopinavir/ritonavir (LPV/r) in Clinical Practice: an 18-Month observational prospective cohort (Kaleobs Cohort)

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Background

Kaletra®, (lopinavir/ritonavir, 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 analysis focused on the antiviral activity through 18 months.

Objectives

To assess, through an 18-Month (M) follow-up, the virological response and immune restoration with LPV/r-containing regimens in routine practice.

Methods

Study Design

Large observational cohort of 1315 adult HIV-infected patients treated for the first time by LPV/r and conducted in France in 181 investigating centers.
Follow-up was scheduled up to 18 months.
Patients were included between September 2002 and November 2003.

Patients

HIV-1 positive patients, currently treated by Kaletra® (lopinavir/ritonavir) Soft Gel Capsules (SGC) 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 were left to the judgment of each physician within the 18-month period.
Data collection for this analysis at baseline and during follow-up included demographic data, current ARV medications, physical examination, HIV RNA and CD4 count, genotype and clinical tolerability of treatment.

Statistical analysis

Description is based on mean and standard deviation for quantitative values.
Baseline characteristics are presented for the total number of patients included in the cohort.
Follow-up data are only presented for patients with M18 data (n=171).
Changes in laboratory parameters are compared during time and between the 3 groups using two factor analysis of variance for paired series.

Results

Baseline Cohort Characteristics

Patient Distribution and Baseline Characteristics

Figure 1: Patient Distribution (all patients)

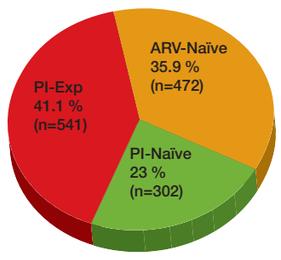


Table 1: Baseline Immunologic and Virologic Characteristics (all patients)

	ARV-Naïve	PI-Naïve	PI-Exp
% (n)	35.9 (472)	23 (302)	41.1 (541)
Mean (SD) baseline Viral Load (VL) (log copies/mL)	5.0 (+/-0.8)	4.0 (+/-1.1)	4.1 (+/-1.3)
Mean (SD) CD4+ count (cells/mm³)	153 (+/-146)	262 (+/-177)	287 (+/-236)

Protease Mutations at inclusion (all patients)

The median number of protease mutations at inclusion was 1 for PI-Naïve and 2 for PI-Exp.

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, 21.1% for PI-Naïve and 21.5% for PI-Exp.

Immunological and Virological Response

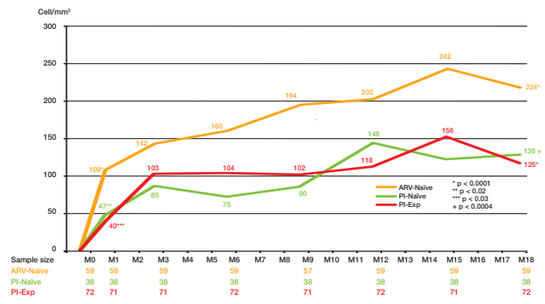
(Patient who completed the 18-month follow up, n=171)

CD4 Cell Count Response

Table 2. Baseline Immunologic and Virologic Characteristics

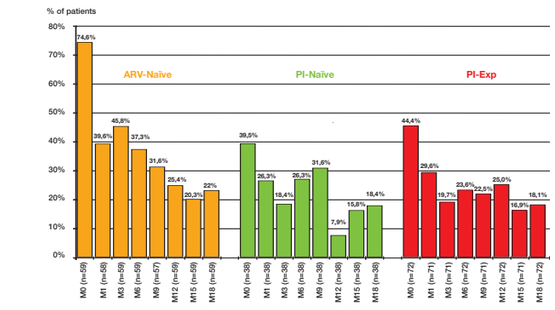
	ARV-Naïve	PI-Naïve	PI-Exp
Mean (SD) baseline viral load (VL) (log copies/mL)	5.0 (+/-0.8) n=57	3.9 (+/-1.3) n=38	3.9 (+/-1.4) n=70
Mean (SD) CD4+ count (cells/mm³)	129 (+/-108) n=59	293 (+/-184) n=38	266 (+/-225) n=72

Figure 2. CD4 Cell Count Mean Change from Baseline



A significant increase in CD4+ cells was observed since the first month and through M18 for each population: +224 CD4+ (n=59) for ARV-Naïve, +136 CD4+ (n=38) for PI-Naïve and +125 CD4 + (n=72) for PI-Exp patients.

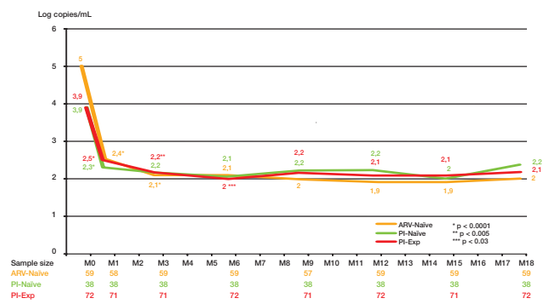
Figure 3. Evolution of the Percentage of Patients with CD4 Cell Count < 200



A decrease of the percentage of patients with immunodepression (Cell Count < 200) was observed in each group since the first month and through 18 months.
More than 78% of patients in each group present no immunodepression at M18.

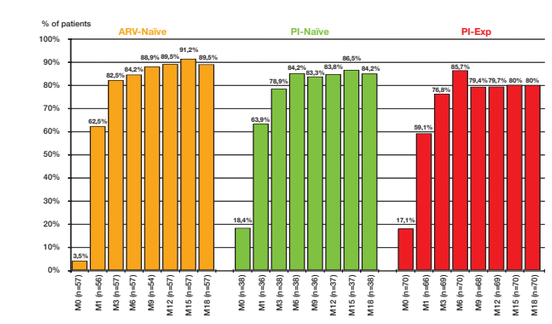
Virologic Response

Figure 4. Mean Viral Load Response



A significant decrease in VL was observed through M18 for each population: -3.0 log (n=60) for ARV-Naïve, -1.7 log (n=38) for PI-Naïve and -1.8 log (n=72) for PI-Exp patients.

Figure 5. Evolution of the Percentage of Patients with Undetectable Viral Load



An undetectable Viral load (VL < 2.6 Log copies/mL) was observed for 80% to 90% of patients according to the group at M18.

Tolerance and Clinical Outcome

Figure 6. Prevalence of Adverse Events at Each Visit (all patients)

More than 70% of patients show no clinical adverse event after 1 month of treatment in each group.
At Month 18, in at least 85% of patients in each group, no clinical adverse event was noted.
Most clinical adverse events (AE) (>76%) were gastro-intestinal (GI) and of mild to moderate intensity.

Table 3. Patient Disposition Through 18 Months (all patients)

Patients Included	**1315**	
Discontinuation	**201 (15,3%)**	
Discontinuation due to Adverse Events	**98 (48,8%)**	
Diarrhea		45 (22,4%)
Nausea / Vomiting		21 (10,4%)
Cephalia		1 (0,5%)
Others		30 (14,9%)
Discontinuation due to Failure	**3 (1,5%)**	
Others Reasons	**100 (49,7%)**	

Premature discontinuation occurred for 15.3% (201) patients, mainly related to AE (48.8%, n=98), GI for most of them (67.3%, n=66).

Conclusion

These results confirm the virological efficacy of LPV/r-containing regimens in ARV- or PI-Naïve and PI-Exp patients. Immune restoration was noted in all 3 populations. The benefit of ARV regimens including LPV/r (SGC) was sustained, as demonstrated in patients followed up to M18.
While complete data in this PMOS was less than anticipated, the findings are consistent with the virologic suppression and CD4+ T-cell outcomes in the published literature from clinical trials utilizing LPV/r SGC (1-3). In this PMOS the formulation of LPV/r taken by patients was the soft gelatin capsule. Recently in France a new formulation of LPV/r has replaced the SGC's.
The tablet formulation of LPV/r has advantages.
It can be taken without regards to meals and does not require refrigeration.
Therefore a future observational study of the tablet tolerance, virologic efficacy, and immune recovery is warranted.

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