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Efficacy and safety of dual boosted PI regimen without RT inhibitors

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Objective: To evaluate the efficacy and tolerability of dual boosted PI regimens in HIV-1 infected patients with resistance mutations or intolerance to reverse transcriptase inhibitors (RTI).

Design and methods: Prospective open-label study. Inclusion criteria were :

- Treatment experienced patients (pts)

- Virological failure with resistance in RT gene (VF)

- Intolerance to RTI (Intol) with mitochondrial toxicity (24/41), lipodystrophy (12/41) and concomitant anti-VHC treatment (PEG-INF+ribavirine) (7/41) and intolerance to NNRTI (3/41).

They started on dual boosted PI regimen without RTI. VL and CD4 count were performed at week 4 and then every 3 months.

Genotypic resistance test (GRT) was performed at baseline and PI trough concentrations (C_{min}) were measured twelve +/- 2 hours after last intake at W4.

The primary endpoint was the percentage (%) of patients with VL<400 cp/mL at W24 according to both intent-to-treat (ITT) and on-treatment (OT) analysis.

Baseline characteristics

Number of patients	82 (41 pts per group)
Female/male	22/60
AIDS	24 (29%)
Co-infection HCV	21 (26%)
HBV	3
HCV+HBV	3

	VF	Intol
Median age (years)	39 [23-56]	44 [38-50]
Median CD4 count	240.10 ⁶ cells/L	294.10 ⁶ cells/L
Range	[36-548]	[27-1012]
Median HIV RNA	12700 copies/mL	200 copies/mL
Range	[304-750 000]	[200-182290]*
No prior PI exposure	1 [0-5]	2 [0-5]
No prior NRTI exposure	5 [3-7]	5 [0-7]
No prior NNRTI exposure	1 [0-2]	1 [0-2]
No PI naive pts	10	7

* 12 pts in Gp2 were in treatment interruption before inclusion

Genotypic resistance testing performed in 44/53 pts showed at least one PI primary resistance mutation in 32% pts. All PI combinations they received were in adequacy with GRT.

Patients disposition : Two pts were lost to follow-up and 1 pt died. 4 pts discontinued study regimen before W24 (VF=3 and Intol=1) and 7 pts experienced virological failure at W24 (VF=5 ; Intol=2).

Dual PI Regimens were : All PI regimens were boosted by RTV 100 mg bid.

SQV 800mg +	LPV 400 mg bid (n=33)	IDV 400mg +	LPV 400 mg bid (n=25)
	or		or
	IDV 400 mg bid (n=4)		APV 600 mg bid (n=14)
or	APV 600 mg bid (n=2)	LPV 400mg +	APV 600 mg bid (n=1)
	or		or
	ATV 300 mg qd (n=2)		ATV 300 mg qd (n=1)

Pharmacological results : Median C_{min} were adequate at W4 in the three most frequent regimens and relationship between C_{min} and % of virologic success at W24

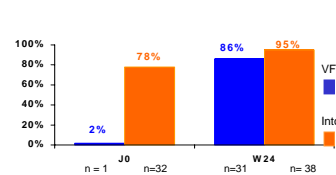
C _{min} dual PI regimen		VL < 400 cp/mL n (%)	AE n (%)
A: n=25	SQV + LPV	25 (76 %)	2 (6%)
Median C_{min}	408 ng/mL 4494 ng/mL		
Adequate range >100 ng/mL	[3000-7000 ng/mL]		
B: n=14	IDV + LPV	21 (84 %)	3 (12%)
Median C_{min}	251 ng/mL 6194 ng/mL		
Adequate range [150-500 ng/mL]	[3000-7000 ng/mL]		
C: n=9	IDV + APV	13 (93 %)	2 (14%)
Median C_{min}	375 ng/mL 1872 ng/mL		
Adequate range [150-500ng/mL]	[1250-3000 ng/mL]		

→ The proportion of patients with PI C_{min} above the minimal of adequate range is 88%, 79% and 100% in A, B, C respectively.

Tolerance : No serious adverse events (AE) were observed. Eight pts (9%) switched for another dual PI regimen mainly for gastrointestinal intolerance grade < 3 (5 pts : A=2;B=2;C=1) or dyslipidemia (1 pts : A=0;B=0;C=1) with a sustained virologic success.

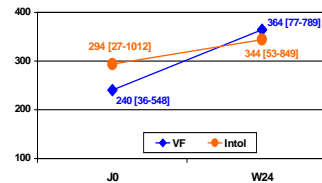
Only 3 pts with AE had PI C_{min} above the maximal of adequate range.

Proportion of patient with viral load <400 copies/mL (OT)



78% (28/41) of pts in Intol sustained a VL<400cp/mL between baseline and W24

Median increase of CD4 (OT)
CD4 .10⁶ cells/mL [range]



% of pts <400 at W24 : - ITT: 68% (36/53 pts)
- OT: 79% (38/48 pts)
Median decrease of HIV RNA of -1.59 log₁₀ [-3.72 ; 1.08]

Median increase of CD4 at W24
• VF = + 61 [-145;+463] .10⁶ cells/mL
• Intol = +73 [-390;+239] .10⁶ cells/mL

Conclusions : Exclusive dual boosted PI regimen is an effective and safe antiretroviral therapy.

Overall, proportion of patients with HIV RNA < 400 copies/mL at W24

■ In ITT = 84% CI₉₅ [76-92%] (69/82)

■ On treatment = 91% CI₉₅ [84-97%] (69/76)

■ Median decrease of HIV RNA of -1.59 log₁₀ copies/mL in pts with detectable VL at baseline

■ Median increase of CD4 = + 61 .10⁶ cells/mL in VF and + 73.10⁶ cells/mL in Intol

■ Overall, 88% of patients had adequate PI C_{min}

■ Adverse events occurred in 9 % of patients

Furthermore, interest of this dual PI regimen particularly in patients with no options among the two remaining RT inhibitors classes.