THE LOPSAQ STUDY: 48-WEEK ANALYSIS OF A BOOSTED DOUBLE PROTEASE INHIBITOR (PI) REGIMEN CONTAINING LOPINAVIR/RITONAVIR (LPV/R) PLUS SAQUINAVIR (SQV) WITHOUT ADDITIONAL ANTIRETROVIRAL THERAPY

Poster THPE 0135

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Background: The virological, immunological and clinical responses to the boosted double PI regimen combination of LPV/r (400/100 mg BID) and SQV (1000 mg BID) without reverse transcriptase inhibitors (RTI) over 48 weeks in HIV-positive patients who have few viable RTI treatment options.

Methods: Cohort study of 128 heavily pre-treated patients who were experiencing therapy failure on their current regimen due to resistance or systemic toxicities.

Patients with PI resistance mutations or RTI-toxicity underwent a structured treatment interruption (STI) (n=76) until virus reverted to genotypic susceptibility or until resolution of toxicity symptoms.

Response was defined as viral load <400 copies/ml at week 48.

Baseline Characteristics	Number (%[a])
Total number	128 (100)
Female	24 (19)
Age at baseline[b] (years) [median (range)]	41 (22–67)
CD4 count at baseline (cells/mm³) [median (range)]	172 (2–998)
HIV RNA at baseline log₁₀ (copies/ml) [median (range)]	5.06 (<1.3-6)
Reasons for switch to saquinavir/lopinavir/ritonavir:	
Toxicity or non-virologic	49 (38.3)
Resistance, virologic failure	72 (56.2)
Both	7 (5.5)
Years of ART [mean (range)]	6.3 (0,1–14)
Number of previous antiretroviral drugs [median (range]	9 (2–15)

[a]Unless otherwise specified; [b]start of SQV/LPV/r therapy

Baseline Characteristics (con't)	Number (%[a])
Previous PIs taken	
Lopinavir/r	22 (17)
Saquinavir	50 (39)
Amprenavir	13 (10)
Indinavir	79 (62)
Nelfinavir	48 (38)
Ritonavir	79 (62)
PI-naive patients	22 (17)
Number of antiretroviral drugs in last regimen [median (range)]	3 (1–7)
Last regimen was PI-sparing	86 (67)
Pre-study STI > 4 weeks	76 (59)
Number of previous PIs [median (range)]	2 (0–6)

Week 48 Results, all pts. (1)

	N
• On treatment at week 48:	78/128
• Discontinuation before week 48:	50/128
• Lost to follow up:	5
• Therapy changes:	45
- 11 due to virologic failure	
- 27 due to non-virologic reasons	
- 5 due to both	
- 2 not documented	

Week 48 Results (2)

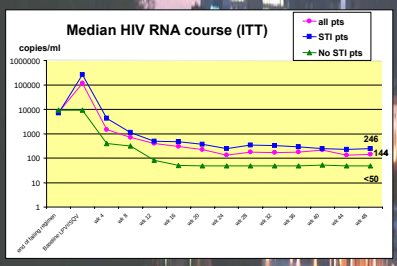
Non-virologic reasons for DC	N
Dose change	10
Diarrhoea	5
Patient choice	4
Lipodystrophy	3
Therapy interruption > 4 weeks	2
Gastrointestinal Disturbances	2
Others	5
Exitus	1
Total	32

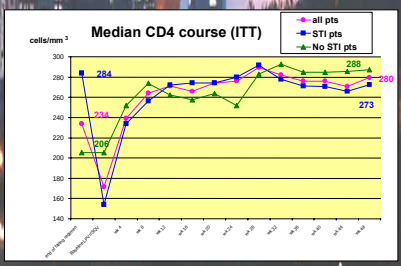
Week 48 Results (3)

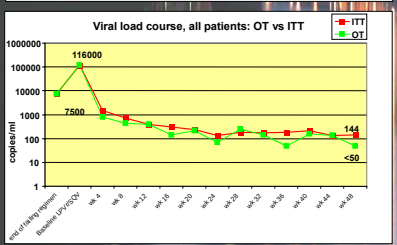
Median CD4 change from baseline (OT):	118 cells/mm³
Median VL change from baseline (OT):	-115856 copies/ml (-2,6 log)
Median follow up:	62 weeks (range: 4-219)
Median VL nadir:	<50 copies/ml
Median time to VL nadir:	14 weeks
Median time needed to <400 copies for pts >=400 copies (112/127) at BI	11 weeks (85/112)

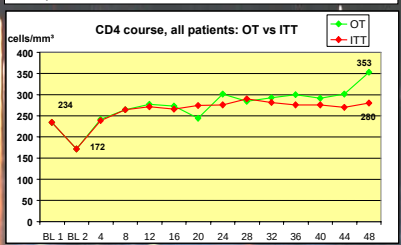
Week 48 Results (4)

	N
VL rebound (1 log change from nadir confirmed 2x):	14
VL rebound (above 5000 copies/ml from nadir confirmed 2x):	16
Fall back below 5000 copies/ml after rebound:	2









Factors associated with achieving a virological response on boosted lopinavir + saquinavir therapy in univariable analysis:

	< 400 copies at week 48 ITT analysis (n=78)	≥ 400 copies at week 48 ITT analysis (n=50)	*P-value*
	[median, (range)]	[median, (range)]	
HIV RNA at baseline (log₁₀ copies/ml)	4.81, (1.28-6.00)	5.29, (1.28-6.00)	0.002
CD4 count at baseline (cells/mm³)	203, (15-998)	90, (2-555)	<0.001
No. of antiretroviral drugs previously taken	8, (3-14)	10, (2-15)	0.003
No. of PIs previously taken	2, (0-6)	3, (0-6)	0.006
No. of PI mutations at end of last regimen	1, (0-8)	2, (0-11)	0.043
Previous saquinavir exposure [n (%)]	23 (29%)	27 (54%)	0.009
Previous lopinavir exposure [n (%)]	8 (10%)	14 (28%)	0.015
Previous ritonavir exposure [n (%)]	42 (54%)	37 (74%)	0.026

In a multivariable analysis, the only factors independently associated with virological response were higher CD4 count at baseline (*p=0.003, OR=0.21, 95% CI=0.076 – 0.594*) and lower number of drugs previously taken (*p=0.003, OR=1.275, 95% CI=1.085 – 1.498*).

Conclusions:

The combination of LPV/r and SQV without RTIs is a potential option as salvage therapy for patients experiencing therapy failure due to resistance or RTI toxicity.

This regimen may not be suitable for patients with very low baseline CD4 cell counts, very broad antiretroviral therapy experience or extensive PI resistance mutations.