PE13/33

Treatment of HCV With Pegylated Interferon+Ribavirin (PegRB) in Coinfected Patients Receiving Lopinavir/r as Monotherapy (LPV/r-MT) or Triple Therapy (LPV/r-T): Final Analysis of the PEKARI Study (GESIDA 5506)

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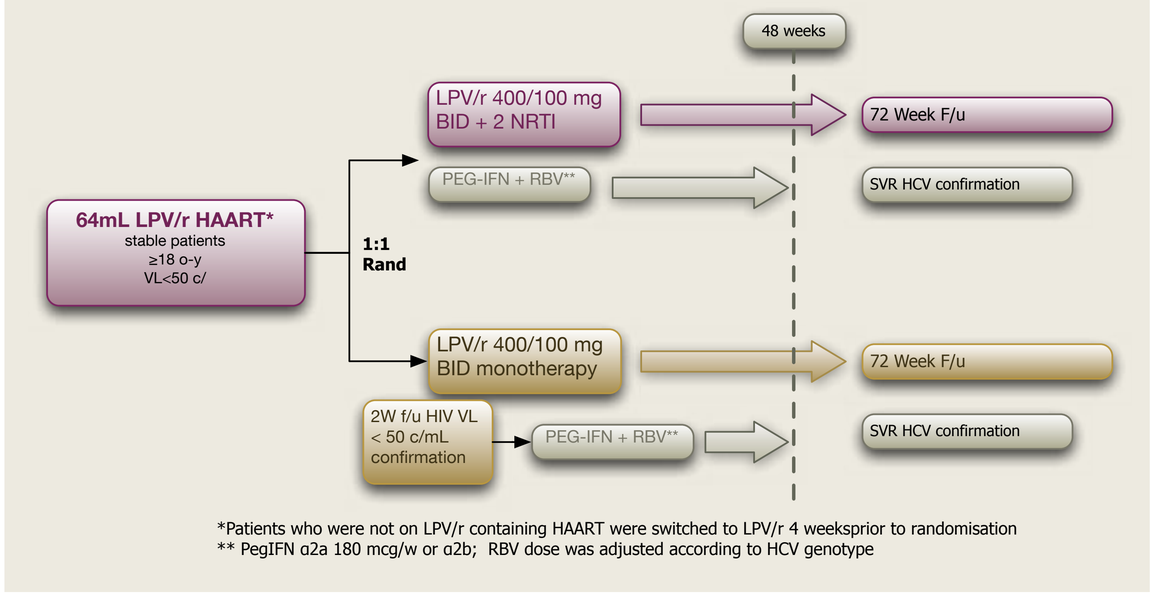
OBJECTIVES

- **Primary:** To assess the efficacy of antiretroviral therapy (ART) taken as LPV/r-MT or LPV/r-T in combination with PegRB in HIV/HCV-coinfected patients. Efficacy was defined as a sustained virological response to HCV treatment and control of HIV infection.
- **Secondary:** To evaluate tolerability, safety, adherence, CD4 count, and HIV control in both arms.

STUDY DESIGN:

- Phase IV, randomized, comparative, multicenter (14 sites) nationwide pilot study of HIV/HCV-coinfected patients who initiate treatment with PegRB. Patients had been taking stable ART (3 months) and had an HIV viral load <50 copies/mL (6 months prior to inclusion). The study lasted 72 weeks after the start of treatment for HCV. Patients on LPV/r-T for ≥4 weeks were randomized (1:1) to withdraw their nucleoside analogs (LPV/r-MT) or maintain the current LPV/r-T regimen. Treatment of HCV was started with PegRB (LPV/r-MT patients, ≥2 weeks after randomization), provided HIV-RNA was <50 copies/mL (Figure 1).

FIGURE 1.
Trial design



*Patients who were not on LPV/r containing HAART were switched to LPV/r 4 weeksprior to randomisation
** PegIFN α2a 180 mcg/w or α2b; RBV dose was adjusted according to HCV genotype

Table 1.
Inclusion-exclusion criteria

Inclusion criteria	Exclusion criteria
Liver biopsy confirming the presence of chronic hepatitis performed not more than 1 year prior to inclusion	Switch of protease inhibitor for suspected virological failure;
Uninterrupted antiretroviral therapy for the previous 6 months with LPV/r+2 NRTIs/NtA for a minimum of 4 weeks.	Psychiatric illness or active substance abuse that would prevent adherence to the protocol (except cannabis or methadone maintenance therapy authorized by the investigator).
No active opportunistic infection within 30 days before the baseline visit.	Pregnancy or breastfeeding.
Karnofsky index ≥70	Hepatitis B infection and treatment with tenofovir and lamivudine
Abstinence from alcohol and other drugs and herbal preparations unless authorized by the investigator.	
No drugs that are contraindicated with LPV/r.	
Commitment to using a reliable contraceptive method approved by the investigator (women of childbearing age).	

RESULTS

- Mean age of the 62 patients (31/arm) was 44.3±5.6 years. The female/male ratio was 1/3, 85.5% had acquired HIV infection through injection drug use, and 29% were AIDS stage C. Baseline characteristics were similar in both arms, except for prevalence of HCV genotypes 1 and 4 (54.9% and 16.1% in LPV/r-MT and 60% and 3.3 % in LPV/r-T) and advanced fibrosis (F3-F-4) (46.7% LPV/r-MT vs 31% LPV/r-T) (Table 1).

Table 2.
Baseline characteristics

	PegIFN+RBV	
	LPV/r (n=31)	LPV/r+2 NRTI (n=31)
Male, n (%)	19 (61.3)	25 (80.6)
Mean age, y	44.2	44.5
Current or past IV drug use, n (%)	29 (93.5%)	24 (77.4%)
Median time of HIV infection, y	17.3	14.6
Median nadir CD4, cells/mm3	156	157
Median time of HCV infection, y	14.2	12.1
Median HCV RNA, log10 IU/mL	6.6	6.2
Median CD4 baseline, cells/mm3	646	493
AIDS, n %	19 (61.3%)	24 (77.4%)
Median time on HAART, y	9.5	8.0
HCV genotype, n (%)	1: 17 (54.9%)	1: 18 (60%)
	3: 9 (29.0%)	3: 11 (36.7%)
	4: 5 (16.1%)	4: 1 (3.3%)
Fibrosis stage (FibroScan). N (%)	F0-1: 9 (31.0%)	F0-1: 12 (41.4%)
	F2: 6 (20.7%)	F2: 7 (24.1%)
	F3/F4 : 14 (48.2%)	F3/F4: 10 (34.5%)

- At week 12, HCV viral load fell >2 log in 71% of LPV/r-MT patients and 55% of LPV/r-T patients (p=NS). The sustained virological response rate (undetectable HCV at week 24 post-treatment) was 35% in LPV/r-MT and 45% in LPV/r-T (p=0.4) (Table 2). Regarding HIV control, a viral blip was detected in 7 patients on LPV/r-MT and in 6 on LPV/r-T. One patient taking 1 LPV/r-MT had virological failure without resistance mutations (Table 3). No significant differences were found for immune control, adverse effects, adherence, or quality of life.

Table 3.
Virological response

		LPV/r-MT		LPV/r-T	
	Total	31	100%	31	100%
Week 4	<50	9	29%	10	32.3%
Week12	<50	14	45.2%	16	51.6%
Week 24	<50	18	58.1%	17	54.8%
week 48	<50	14	45.2%	15	48.4%
Week 72 or premature stop	<50	11	35.5%	14	45.2%

Table 4.
Incidence of blips and virologic failure in both study arms.

		LPV/r-MT		LPV/r-T	
Blip	VL>50	7	22.6%	6	19.4%
	VL<50	24	77.4%	25	80.6%
	Total	31	100%	31	100%
Virological failure	VL>50	1*	3.2%	0	0
	VL<50	30	96.8%	31	100%
	Total	31	100%	31	100%

*Negative in the resistance study.

CONCLUSION

LPV/r-MT is as safe and effective as LPV/r-T for controlling both HCV and HIV infection in HIV/HCV-coinfected patients receiving PegRB. LPV/r-MT might therefore be an option for coinfected patients who require nucleoside analog–free ART to treat HIV.