



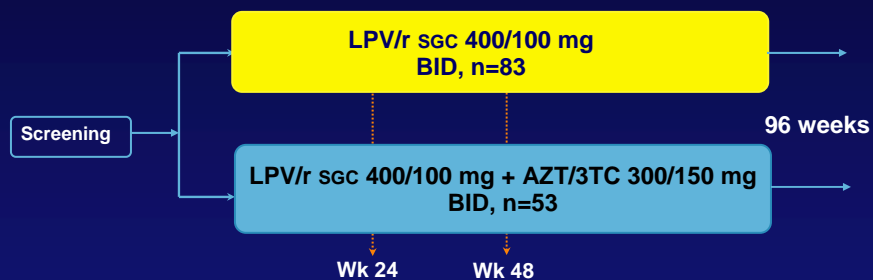
## Prognostic Factors of Virological Success in Antiretroviral-naïve Patients Receiving LPV Monotherapy in the MONARK trial.

Flandre P, Delaugerre C, Ghosn J, Chaix ML, Horban A, Girard PM, Gladysz A, Cohen Codar I, Ngo Van P, Taburet AM, Rouzioux C, Delfraissy JF

## MONARK Study Design and Primary Endpoint

### Main Entry criteria

- Antiretroviral naïve
- HIV-1 RNA <100,000 c/mL
- CD4 > 100 cells/mm<sup>3</sup>



### Primary Endpoint

- Proportion of subjects with HIV-1 RNA < 400 copies/mL at Week 24 **AND** < 50 copies/mL at Week 48 → **Virologic Response**

Delfraissy JF *et al.*, *AIDS* in press

## Background: Main results

<b>ITT: Discontinuation and intensification = failure</b>	<b>LPV/r</b>	<b>ZDV/3TC/LPV/r</b>	<b>P-value</b>
Subjects randomized	<b>83</b>	<b>53</b>	
(1) HIV-1 RNA < 400 c/mL at W24	<b>65/83 [78%]</b>	<b>41/53 [77%]</b>	<b>1.00</b>
(2) HIV-1 RNA < 50 c/mL at W48	<b>56/83 [67%]</b>	<b>40/53 [75%]</b>	<b>0.34</b>
<b>Primary endpoint: (1) <u>and</u> (2)</b>	<b>53/83 [64%]</b>	<b>40/53 [75%]</b>	<b>0.19</b>

<b>On Treatment: available VL</b>	<b>LPV/r</b>	<b>ZDV/3TC/LPV/r</b>	<b>P-value</b>
Subjects randomized	<b>83</b>	<b>53</b>	
(1) HIV-1 RNA < 400 c/mL at W24	<b>65/73 [89%]</b>	<b>41/42 [98%]</b>	<b>0.15</b>
(2) HIV-1 RNA < 50 c/mL at W48	<b>56/67 [84%]</b>	<b>40/41 [98%]</b>	<b>0.03</b>
<b>(1) <u>and</u> (2)</b>	<b>53/66 [80%]</b>	<b>40/41 [98%]</b>	<b>0.02</b>

Delfraissy JF *et al.*, *AIDS* in press

## Background: Main results

- N=83 patients in LPV/r arm
  - 13 discontinuations
  - 3 patients intensified with AZT/3TC
  - 1 patient with missing VL at week 24
- → N=66 patients included in the present OT analysis
  - 53 (80%) responders
  - 13 (20%) non-responders

<b>On Treatment, available VL</b>	<b>LPV/r</b>	<b>ZDV/3TC/LPV/r</b>	<b>P-value</b>
Subjects randomized	<b>83</b>	<b>53</b>	
(1) HIV-1 RNA < 400 c/mL at W24	<b>65/73 [89%]</b>	<b>41/42 [98%]</b>	<b>0.15</b>
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<b>(1) <u>and</u> (2)</b>	<b>53/66 [80%]</b>	<b>40/41 [98%]</b>	<b>0.02</b>

## Objective and Methods

### Objective

- To determine predictive factors of virologic response in patients randomized in the LPV/r monotherapy arm

### Methods

- 'On treatment' analysis on patients with available VL
- Logistic regression model (univariate and multivariate)

## Variables investigated

- Demographic variables
  - Gender and Age
- Baseline characteristics
  - HIV-1 RNA ( $\log_{10}$  copies/mL)
  - CD4 cell count
  - HIV-1 DNA ( $\log_{10}$  copies/mL)
- HIV-1 subtype
- Early virologic response
  - HIV-1 RNA decrease at W1, W2 and W4
  - HIV-1 RNA levels at W1, W2 and W4 (<400 or <50 copies/mL)
- LPV trough concentration at W4, W24 and W48
- Compliance evaluation (W4, W8, W12, W16, W20, W24, W32, W40 and W48)

## Results: Baseline Characteristics

- Gender

	Male	Female
Responders	<b>40 (83%)</b>	<b>13 (72%)</b>
Non responders	8 (17%)	5 (28%)

- HIV-1 subtype

- B subtype n=46 (70%)
- Non-B subtypes n=20 (30%)

- A n=1
- CRF01 n=1
- CRF02 n=12 (18%)
- CRF03 n=1
- CRF06 n=2
- F n=1
- G n=2

	B subtype	CRF02	Other
Responders	<b>40 (87%)</b>	<b>8 (67%)</b>	<b>5 (63%)</b>
Non responders	6 (13%)	4 (33%)	3 (37%)

Flandre P. *et al.*, 11<sup>th</sup> EACS, Madrid, 2007, #PS1/2

MONARK

## Results: Baseline Variables and Early Response

Baseline variables (median)	Responders	Non responders
Age (years)	38	36
<b>HIV-1 RNA (log copies/mL)</b>	<b>4.38 [4.1-4.7]</b>	<b>4.54 [4.4-4.9]</b>
HIV-1 DNA (log copies/millions CD4)*	4.2	4.5
CD4 cells count	235	223
HIV-1 RNA reduction (log <sub>10</sub> copies/mL)		
<b>Week 1</b>	<b>1.07</b>	<b>0.54</b>
Week 2	1.7	1.7
Week 4	1.99	1.96
Proportion of patients with HIV-1 RNA < 400 c/mL at :		
<b>Week 1</b>	<b>8 (16%)</b>	<b>0 (0%)</b>
<b>Week 2</b>	<b>25 (49%)</b>	<b>2 (15%)</b>
<b>Week 4</b>	<b>37 (70%)</b>	<b>4 (31%)</b>

\* Missing data for HIV-1 DNA : N=50 instead of n=66

## Results: LPV Trough Concentrations and Adherence

Median (IQR)	LPV trough concentration (ng/mL)		
	Week 4	Week 24	Week 48
<b>Responders</b>	6,466 (4,406-9,164)	4,518 (3041-7340)	5,149 (2,958-7,541)
<b>Non responders</b>	5,258 (4,295-7,183)	3,499 (2,509-6,700)	4,215 (2,890-5,718)

- Patients had at least one **undetectable** (<75 ng/mL) LPV concentration
  - Responders 2/53 (4%) vs. Non responders 1/13 (8%)
- Patients who **declared having missed** one dose or more in at least 2 evaluations of compliance
  - Responders 10/53 (19%) vs. Non responders 4/13 (31%)

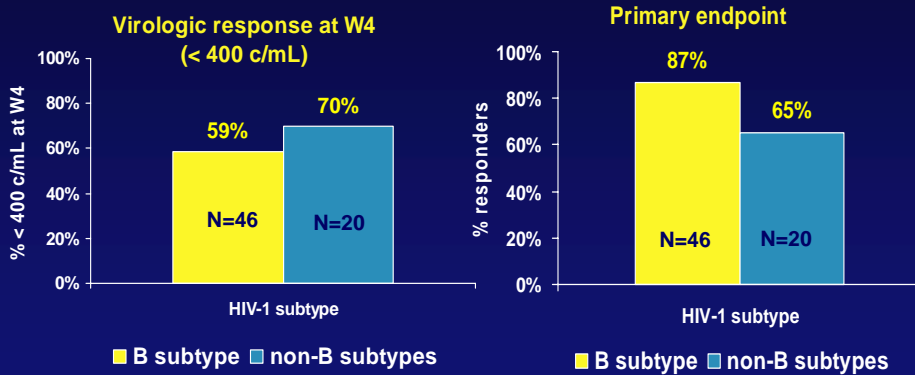
## Results (4): Univariate Logistic Regression

Variable	Unadjusted OR [95%CI]	p-value
Baseline HIV-1 RNA	0.163 [0.02-0.83]	0.03
VL reduction W1	0.285 [0.07-1.14]	0.077
VL < 400 c/mL W2	5.29 [1.26-36.3]	0.02
VL < 400 c/mL W4	5.20 [1.47-21.5]	0.01
Subtype (B vs non-B)	3.59 [1.02-3.62]	0.05

## Results (4): Logistic Regression Final Model

Variable	Unadjusted OR [95%CI]	p-value	Adjusted OR [95%CI]	p-value
Baseline HIV-1 RNA	0.163 [0.02-0.83]	0.03		
VL reduction W1	0.285 [0.07-1.14]	0.077		
VL < 400 c/mL W2	5.29 [1.26-36.3]	0.02		
<b>VL &lt; 400 c/mL W4</b>	5.20 [1.47-21.5]	0.01	<b>7.59 [1.65-34.8]</b>	<b>0.01</b>
<b>Subtype (B vs non-B)</b>	3.59 [1.02-3.62]	0.05	<b>6.36 [1.4-28.9]</b>	<b>0.01</b>

## HIV Subtype and Virologic Response

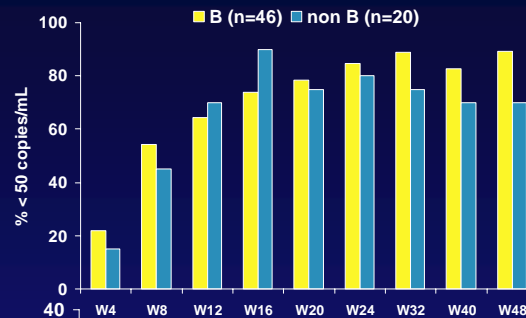


## Differences Between B and Non B Subtypes

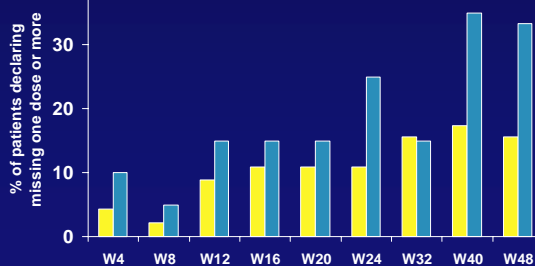
	B subtype N=46	Non B subtypes N=20	p-value
Age (median)	40 years	31 years	0.016
HIV-1 RNA median reduction W4	1.91 log	2.24 log	0.019
Gender (% Female)	17.4%	50%	0.014
% of patients who declared having missed one dose or more in at least 2 evaluations	13%	40%	0.022

## Virologic Response and HIV-1 Subtype

HIV-1 Subtype and % <50 copies/mL



HIV-1 Subtype and reported compliance



## Conclusion

- Naïve patients under LPV/r monotherapy (N=66)
- Early virologic response (<400 copies/mL at W4) and HIV-1 subtype (B vs. non B) were independently predictive to response in these patients
- ITT analysis showed similar results (baseline HIV-1 RNA and HIV subtype)
- Identification of predictive factors to a LPV monotherapy regimen may help to determine which are most likely to benefit from such a strategy

## Discussion

- Effect of HIV-1 subtype?
  - A similar or better early virologic response (Week 4 and Week 16) was observed in non-B subtypes and poorer response thereafter
  - Multiple potential confounding factors need to be considered:
    - Compliance to the regimen
    - Difference in demographic variables
  - True effect ?



## Acknowledgements

- Patients
- 36 Investigators (France, Germany, Italy, Poland, Spain)
  - **France**
    - Pr. Jean-François Delfraissy
    - Pr. François Boué
    - Pr. Pierre Dellamonica
    - Pr. Hervé Gallais
    - Pr. Pierre-Marie Girard
    - Dr. Alain Lafeuillade
    - Pr. Philippe Morlat
    - Pr. Jean-Luc Pellegrin
    - Pr. François Raffi
    - Pr. Jacques Reynes
    - Dr. Olivier Patey
    - Dr. Jacques Gilquin
  - **France**
    - Francisco Vidal
    - Dr. Pascale Leclercq
    - Dr. Caroline Lascoux
    - Pr. Thierry May
    - Pr. Elisabeth Rouveix
    - Dr. Alain Devidas
    - Dr. Marie-Aude Khuong
    - Pr. Jean-Albert Gastaut
    - Pr. Yves Levy
    - Dr. Marc-Antoine Valantin
  - **Germany**
    - Dr. Jäger
    - Dr. Schurmann
    - Dr. Oette
    - Dr. Arastéh
  - **Italy**
    - Pr. Adriano Lazzarin
    - Pr. Mauro Moroni
    - Pr. Giovanni Di Perri
    - Pr. Giampiero Carosi
    - Pr. Vincenzo Vullo
  - **Poland**
    - Pr. Andrzej Gladyzs
    - Pr. Andrzej Horban
  - **Spain**
    - Pere Domingo
    - Bonaventura Clotet
    - Josep Ma Llibre
    - Francisco Vidal
- MONARK study team
- Abbott France and US
- DSMB