

# The 4th International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention

22–25 July 2007, Sydney, Australia

Poster Number

**WEPEB041**

## Virologic Response and Tolerability by Sex and Race in Subjects Receiving Fosamprenavir/ritonavir (FPV/r) BID and Lopinavir/ritonavir (LPV/r) BID, each in Combination with Abacavir/Lamivudine QD (the KLEAN Study)

E DeJesus<sup>1</sup>, J Gathe<sup>2</sup>, C Katlama<sup>3</sup>, P McLeroth<sup>4</sup>, L Yau<sup>5</sup>, L Patel<sup>5</sup>, P Wannamaker<sup>5</sup>

<sup>1</sup>Orlando Immunology Center, Orlando, FL, USA; <sup>2</sup>Therapeutic Concepts, PA, Houston, TX, USA;  
<sup>3</sup>APHP-Groupe Hospitalier Pitie-Salpetriere, Paris, France, <sup>4</sup>Chase Brexton Health Services, Baltimore, MD, USA,  
<sup>5</sup>GlaxoSmithKline, Research Triangle Park, NC, USA

### Abstract

**Objectives:** KLEAN, an open-label, randomized, international study demonstrated the non-inferiority of FPV/r to LPV/r in ART-naïve subjects. Sex and race have been noted to account for differential response to some ARV combinations; we analyzed KLEAN to investigate these subgroups.

**Methods:** The primary endpoint was virologic response at Week 48 (%with HIV-1 RNA <400 c/mL by TLOVR). Race was self-identified.

**Results:**

**Median Baseline (BL) HIV-1 RNA ( $\log_{10}$  c/mL) and CD4+ Count (cells/mm<sup>3</sup>) and Proportion of Subjects with HIV-1 RNA <400 c/mL at Week 48, ITT(E), TLOVR**

	FPV/r			LPV/r		
	BL HIV-1 RNA	BL CD4+ Count	<400 c/mL at Wk 48, % (n/N)	BL HIV-1 RNA	BL CD4+ Count	<400 c/mL at Wk 48, % (n/N)
All Subjects	5.08	188	73 (315/434)	5.06	194	71 (317/444)
Male	5.13	191	75 (254/338)	5.12	191	73 (253/348)
Female	4.93	177	64 (61/96)	4.83	212	67 (64/96)
White/Caucasian	5.15	208	77 (202/264)	5.09	217	74 (183/247)
Black	4.94	144	62 (77/125)	4.98	162	67 (97/145)

Fewer administrative failures (lost to follow-up, consent withdrawn, etc.) were observed in whites (FPV/r: 20%; LPV/r: 20%) and males (FPV/r: 20%; LPV/r: 21%) compared to blacks (FPV/r: 26%; LPV/r: 23%) and females (FPV/r: 28%; LPV/r: 24%). Tolerability (drug-related Grade 2-4 adverse events [AEs]) was similar for both males and females, respectively (FPV/r: 38%, 35%; LPV/r: 33%, 36%); however, blacks reported fewer AEs (FPV/r: 27%; LPV/r: 28%) compared to whites (FPV/r: 44%; LPV/r: 35%).

**Conclusions:** Blacks had generally lower BL CD4+ counts compared to the overall population. Lower response rates were noted in females and blacks which are not fully explained by administrative failures and which appear to be independent of treatment group.

## Introduction

- Differences in response to antiretroviral therapy (ART) may exist among sex- and racial sub-groups.<sup>1</sup>
- KLEAN, an open-label, randomized, international study demonstrated the non-inferiority of fosamprenavir/ritonavir (FPV/r) to lopinavir/ritonavir (LPV/r), each in combination with abacavir/lamivudine (ABC/3TC) fixed-dose combination (FDC) in ART-naïve subjects.<sup>2</sup>
- We investigated response and safety by sex and racial sub-groups in the KLEAN study.

## Methods

- A total of 878 subjects were included in the intent-to-treat exposed [ITT(E)] population from sites across the US, Europe, and Canada.
- The primary endpoint was the proportion of subjects with HIV-1 RNA <400 copies/mL (c/mL) at Week 48 by Time to Loss of Virologic Response (TLOVR) analysis. Race was self-identified. Safety was evaluated by adverse event (AE) reports.
- The TLOVR outcomes and the response rates at Week 48 (<400 c/mL) were summarized for all subjects in the ITT(E) population, as well as, by sex (female or male) and by race (white or black).
- Treatment-related grades 2 to 4 clinical adverse events were presented for all subjects in the safety population and also by sex and by race.
- No formal statistical comparisons were performed in this sub-group analysis.

## Results

This analysis reports results for white and black subjects only as the number of subjects in other racial sub-groups were small.

**Table 1. Baseline Demographics; ITT(E) Population**

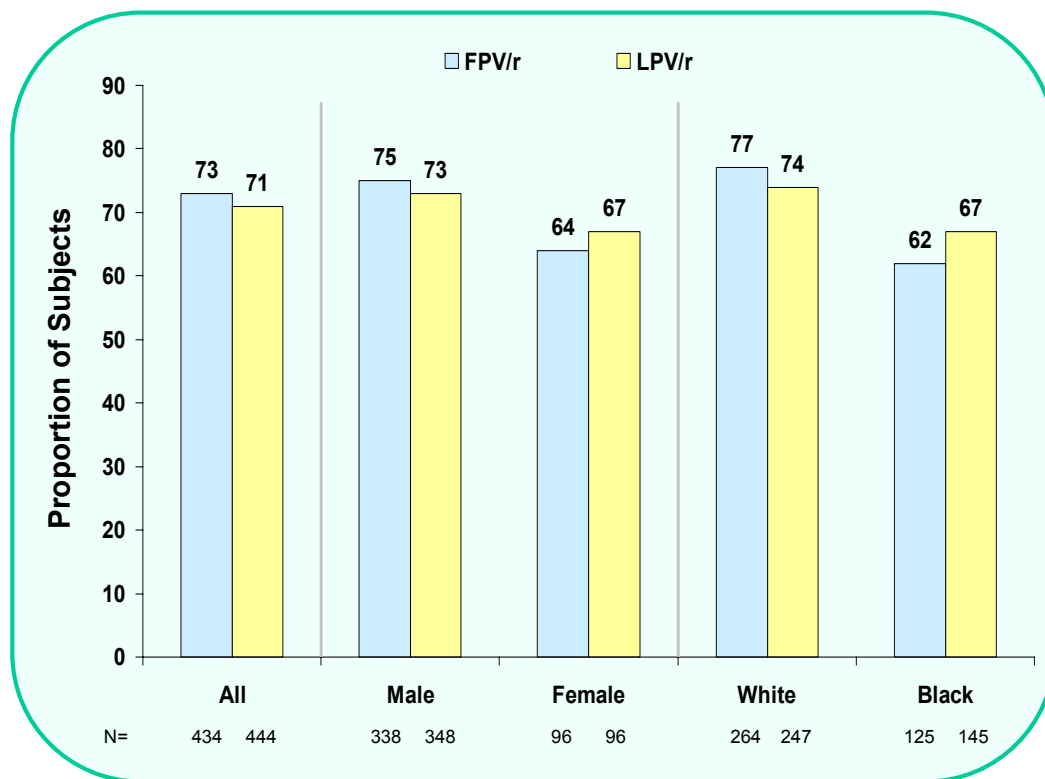
<b>Parameter</b>	<b>FPV/r BID N=434</b>	<b>LPV/r BID N=444</b>
Age, (y), median	38	37
Sex; n (%)		
Male	338 (78%)	348 (78%)
Female	96 (22%)	96 (22%)
Race; n (%)		
White	264 (61%)	247 (56%)
Black	125 (29%)	145 (33%)
Other	45 (10%)	52 (12%)
CDC Class C; n (%)	42 (10%)	53 (12%)

**Table 2. Median Baseline (BL) Viral Load and CD4+ Count; ITT(E) Population**

	FPV/r		LPV/r	
	BL HIV-1 RNA	BL CD4+	BL HIV-1 RNA	BL CD4+
All Subjects	5.08	188	5.06	194
Male	5.13	191	5.12	191
Female	4.93	177	4.83	212
White	5.15	208	5.09	217
Black	4.94	144	4.98	162

Females and blacks had lower baseline viral loads compared to the overall population and other sub-groups. CD4+ counts were generally lower at baseline in black subjects as well.

**Figure 1. Proportion of Subjects with HIV-1 RNA <400 c/mL at Week 48; ITT(E) Population, TLOVR Analysis**



**Table 3. Study Outcomes at Week 48; ITT(E) Population, TLOVR Analysis**

	All Subjects		Male		Female		White		Black	
	FPV/r N=434	LPV/r N=444	FPV/r N=338	LPV/r n=348	FPV/r n=96	LPV/r n=96	FPV/r n=264	LPV/r n=247	FPV/r n=125	LPV/r n=145
<b>Responder</b>	73%	71%	75%	73%	64%	67%	77%	74%	62%	67%
<b>Non-Responder</b>										
Virologic Failure	6%	7%	5%	6%	8%	9%	3%	6%	13%	10%
Administrative Failures including AEs*	21%	22%	20%	21%	28%	24%	20%	20%	26%	23%

\*Includes: lost to follow-up, subject decision, protocol violation, non-compliance, death, pregnancy, no data available, insufficient viral load response, other, and AEs.

The proportion of subjects with an HIV-1 RNA <400 c/mL at Week 48 (primary endpoint) appeared to be lower in female and black subjects compared to the overall population and other sub-groups (*Figure 1*). The difference in females was driven by the increased number of administrative failures due to lost to follow-up, subject decision, protocol violation, etc. but not AEs while the treatment difference in blacks was the result of an increased number of virologic failures (TLOVR analysis) (*Table 3*).

**Table 4. Drug-Related Grade 2-4 Adverse Events (AEs); Safety Population**

	All Subjects		Male		Female		White		Black	
	FPV/r N=436	LPV/r N=443	FPV/r n=339	LPV/r n=347	FPV/r n=97	LPV/r n=96	FPV/r n=265	LPV/r n=246	FPV/r n=126	LPV/r n=145
Any Event	38%	34%	38%	33%	35%	36%	44%	35%	27%	28%
Diarrhea	13%	11%	13%	11%	11%	14%	17%	12%	6%	8%
Nausea	6%	5%	5%	4%	12%	11%	6%	5%	6%	4%
Drug Hypersensitivity	6%	4%	6%	3%	7%	5%	9%	6%	2%	<1%
Vomiting	2%	2%	1%	<1%	3%	6%	2%	2%	3%	2%
Fatigue	2%	1%	1%	1%	5%	1%	2%	1%	2%	2%

The most frequently reported drug-related Grade 2-4 AEs (≥5% in either treatment arm) were diarrhea, nausea, drug hypersensitivity, vomiting, and fatigue. Black subjects generally reported fewer drug-related Grade 2-4 AEs compared to whites and other sub-groups and the difference was primarily the result of a lower incidence of diarrhea and drug hypersensitivity in blacks.

## Discussion

- Although the number of new cases of HIV and AIDS is increasing in women and minorities, these sub-groups are often under-represented in clinical trials.<sup>3</sup>
- In this analysis, females appeared to have more administrative failures due to lost to follow-up, subject decision, and protocol violation leading to a reduced response rate by the TLOVR algorithm.
- Black subjects experienced slightly higher rates of virologic failure in both treatment arms (13% and 10%) compared to the overall virologic failure rates of 6% and 7% for the FPV/r and LPV/r treatment arms, respectively.
- Overall, no apparent differences in tolerability were noted with the exception of black subjects reporting fewer drug-related Grade 2-4 AEs compared to the overall population and other sub-groups. The lower incidence of diarrhea and drug hypersensitivity in black subjects appeared to be responsible for the reporting difference.

## Conclusion

- **Females and blacks had lower baseline HIV-1 RNA values compared to the overall population and other sub-groups. Black subjects also had generally lower baseline CD4+ counts.**
- **In this study, administrative failure was more common among women and virologic failure was more common among black subjects.**
- **Black subjects reported fewer drug-related Grade 2-4 AEs compared to the overall population and other sub-groups.**

## Acknowledgements

The authors would like to extend their thanks to the subjects who participated in this trial and to the study investigators, study coordinators, and the GSK team for their invaluable contributions

## References

1. Tashima K, Kumar P, Rodriguez-French A et al. Gender and race subgroup analyses in 4 large, randomized clinical trials comparing abacavir (ABC) to protease inhibitors (PI) or zidovudine (ZDV) in ART-naïve subjects. 8<sup>th</sup> International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 2006 September 24-26; San Francisco, CA, USA.
2. Eron, J, Yeni P, Gathe J, et al. The KLEAN study of fosamprenavir-ritonavir versus lopinavir-ritonavir, each in combination with abacavir-lamivudine, for initial treatment of HIV infection over 48 weeks: a randomised non-inferiority trial. *Lancet* 2006;368:476-82.
3. UNAIDS/WHO. AIDS Epidemic Update, December 2006.