ARV Therapies and Therapeutic Strategies

REPORTING ON CROI 2015

Comprehensive Expert Review and Discussion of Key Presentations

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Cabotegravir and Rilpivirine as 2-Drug Oral Maintenance Therapy: LATTE W96 Results

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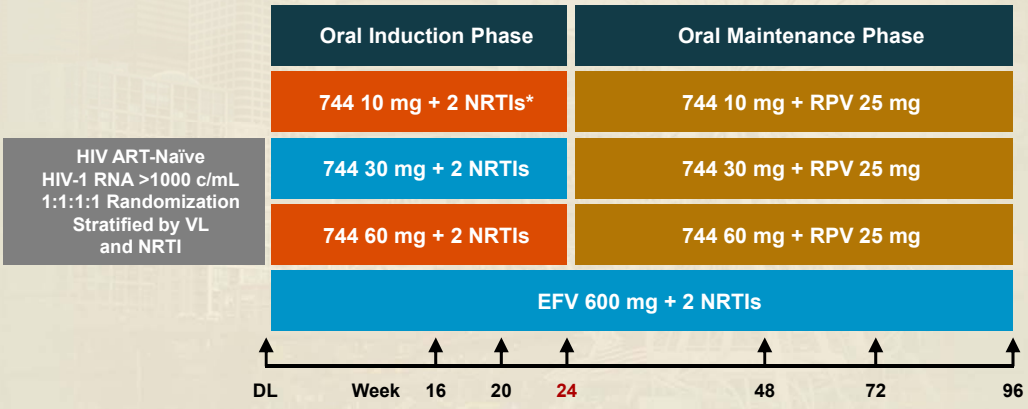
Abstract 554LB

LATTE: Study Design

- **Phase IIb, randomized, multicenter, partially blind, dose-ranging study**
- **Patients on 744 + NRTI: If week 20 VL <50 c/mL – simplify to 744/RPV at week 24**



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LATTE Study: Baseline Characteristics

		744 10 mg n=60	744 30 mg n=60	744 60 mg n=61	EFV 600 mg n=62
Age	Median (y)	32.0	32.5	36.0	32.5
Gender	Male	95%	97%	93%	98%
Race	White	62%	65%	59%	63%
	African American/African	35%	28%	30%	32%
Ethnicity	Hispanic/Latino	15%	27%	23%	19%
Baseline HIV-1 RNA	Median (log_{10} c/mL)	4.281	4.178	4.349	4.343
	>100,000 c/mL	13%	12%	20%	13%
Baseline CD4+	Median (cells/mm^3)	415.0	404.0	420.0	416.5
	<200 cells/mm^3	3%	7%	3%	2%
Hepatitis coinfection	HCV	0	5 (8%)	4 (7%)	1 (2%)
Investigator-selected dual NRTIs at Day 1	TDF/FTC	37 (62%)	37 (62%)	37 (61%)	38 (61%)
	ABC/3TC	23 (38%)	23 (38%)	24 (39%)	24 (39%)

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LATTE Study: Subject Disposition

Subject Disposition – ITT-E

	CAB 10 mg n=60	CAB 30 mg n=60	CAB 60 mg n=61	CAB Total n=181	EFV 600 mg n=62
Subjects Withdrawn Through W96	**14 (23%)**	**12 (20%)**	**9 (15%)**	**35 (19%)**	**21 (34%)**
Adverse Event*	1 (2%)	1 (2%)	4 (7%)	6 (3%)	9 (15%)
Lack of Efficacy	5 (8%)	2 (3%)	2 (3%)	9 (5%)	5 (8%)
Insufficient Viral Load Response†	3 (5%)	0	1 (2%)	4 (2%)	1 (2%)
PDVF	2 (3%)	2 (3%)	1 (2%)	5 (3%)	4 (6%)
Protocol Deviation	2 (3%)	1 (2%)	1 (2%)	4 (2%)	0
Lost to Follow-up	3 (5%)	2 (3%)	1 (2%)	6 (3%)	5 (8%)
Investigator Discretion	0	2 (3%)	0	2 (1%)	1 (2%)
Withdrew Consent	3 (5%)	4 (7%)	1 (2%)	8 (4%)	1 (2%)
Subjects Withdrawn at W24-W96	**6 (10%)**	**5 (8%)**	**3 (5%)**	**14 (8%)**	**5 (8%)**

*Most occurred during the Induction Phase.
†Week 20 HIV-1 RNA values: CAB 10 mg, 51, 107, 189 c/mL; CAB 60 mg, 108 c/mL; EFV 600 mg, 146 c/mL. CAB 10 mg (n=1) and EFV (n=2) met the definition for PDVF (not primary reason for WD).

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LATTE: HIV-1 RNA <50 c/mL

Week 96 Treatment Outcomes

Outcome at Week 96	CAB 10 mg	CAB 30 mg	CAB 60 mg	CAB Total	EFV 600 mg
% <50 c/mL at W96 Snapshot (ITT-E)	**41/60 (68%)**	**45/60 (75%)**	**51/61 (84%)**	**137/181 (76%)**	**39/62 (63%)**
Protocol-defined Virologic Failure	3 (5%)	2 (3%)	1 (2%)	6 (3%)	6 (10%)
Failure – Adverse Event	1 (2%)	1 (2%)	4 (7%)	6 (3%)	9 (15%)
Failure – HIV-1 RNA ≥50 c/mL	5 (8%)	1 (2%)	2 (3%)	8 (4%)	2 (3%)
Failure - Other[+] Reasons while ≥50 c/mL	2 (3%)	2 (3%)	1 (2%)	5 (3%)	3 (5%)
Failure - Other[+] Reasons while <50 c/mL	8 (13%)	9 (15%)	2 (3%)	19 (10%)	3 (5%)
% <50 c/mL at W96 Snapshot (ITT-ME)	**41/52 (79%)**	**45/53 (85%)**	**51/55 (93%)**	**137/160 (86%)**	**39/47 (83%)**
Protocol-defined virologic failure	2 (4%)	1 (2%)	0	3 (2%)	2 (4%)
Failure – Adverse Event	1 (2%)	0	1 (2%)	2 (1%)	2 (4%)
Failure – HIV-1 RNA ≥50 c/mL	4 (8%)	1 (2%)	1 (2%)	6 (4%)	2 (4%)
Failure - Other[+] Reasons while ≥50 c/mL	1 (2%)	1 (2%)	1 (2%)	3 (2%)	0
Failure - Other[+] Reasons while <50 c/mL	3 (6%)	5 (9%)	1 (2%)	9 (6%)	2 (4%)

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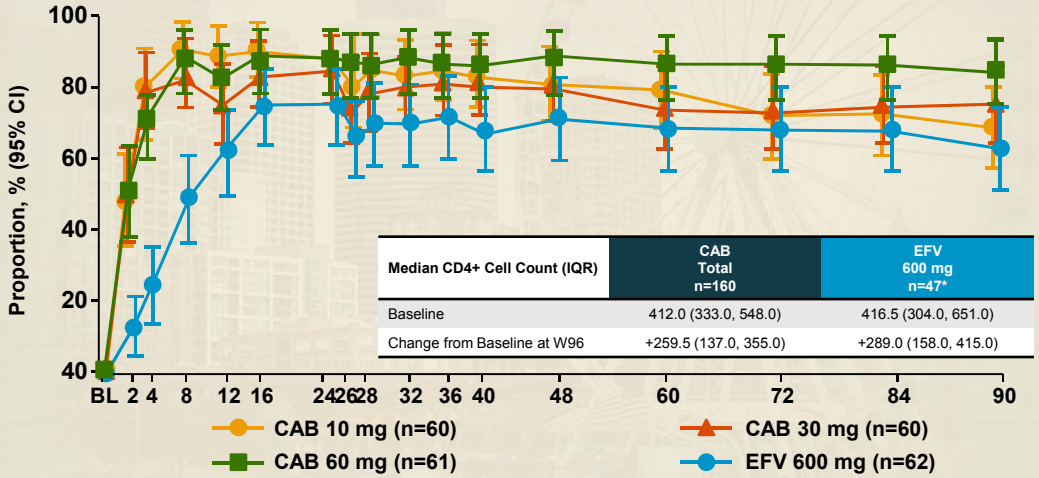
HIV-1 RNA <50 c/mL by "Snapshot" Algorithm at Week 96

Virologic Success: HIV-1 RNA <50 c/mL by FDA Snapshot (ITT-E)



Median CD4+ Cell Count (IQR)	CAB Total n=160	EFV 600 mg n=47*
Baseline	412.0 (333.0, 548.0)	416.5 (304.0, 651.0)
Change from Baseline at W96	+259.5 (137.0, 355.0)	+289.0 (158.0, 415.0)

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LATTE: Adverse Events

	CAB 10 mg n=60	CAB 30 mg n=60	CAB 60 mg n=61	EFV 600 mg n=62
Grade 2-4 Drug-related Events (>3% Any Arm)	**5 (8%)**	**8 (13%)**	**13 (21%)**	**12 (19%)**
Insomnia	1 (2%)	2 (3%)	0	4 (6%)
Depression	0	0	2 (3%)	0
Nausea	0	2 (3%)	3 (5%)	1 (2%)
Fatigue	0	2 (3%)	1 (2%)	1 (2%)
Headache	1 (2%)	1 (2%)	3 (5%)	0
Rash Macular	0	0	0	3 (5%)
% <50 c/mL at W96 Snapshot (ITT-ME)	**1 (2%)**	**2 (3%)**	**3 (5%)**	**2 (3%)**
Serious AEs	**7 (12%)**	**5 (8%)**	**7 (11%)**	**4 (6%)***
Serious AEs (W24+)	**5 (8%)**	**5 (8%)**	**5 (8%)**	**2 (3%)**
AEs Leading to Withdrawal (>1 Subject)	**1 (2%)**	**2 (3%)**	**4 (7%)**	**9 (15%)**
Dizziness	0	0	0	2 (4%)
ALT Increased	0	0	2 (3%)**	0
Grade 1-4 ALT Abnormalities	**8 (13%)**	**12 (20%)**	**17 (28%)**	**13 (21%)**
Select Grade 3-4 Laboratory Abnormalities				
Creatine Phosphokinase (CPK)	7 (12%)	7 (12%)	5 (8%)	9 (15%)
Alanine Aminotransferase (ALT)	0	1 (2%)	2 (3%)**	1 (2%)
Lipase	3 (5%)	2 (3%)	6 (10%)	1 (2%)
Total Bilirubin	0	0	0	0
Total Neutrophils	1 (2%)	1 (2%)	2 (3%)	2 (3%)
Creatinine	0	0	0	0

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