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ViiV Healthcare
Cabotegravir + Rilpivirine as Long-Acting Maintenance Therapy: LATTE-2 Week 32 Results
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Disclosures

- Dr. David A. Margolis is an employee of ViiV Healthcare

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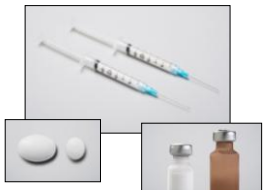
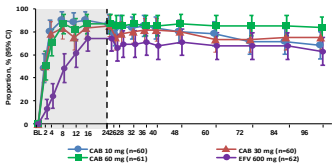
Background

- CAB is an HIV-1 integrase inhibitor
  - Oral 30 mg tablet (t½, ~40 hours)
  - LA nanosuspension 200 mg/mL (t½, ~20-40 days)
- RPV is an HIV-1 NNRTI
  - Oral 25 mg tablet (t½, ~50 hours)
  - LA nanosuspension 300 mg/mL (t½, ~30-90 days)
- Oral 2-drug CAB + RPV proof of efficacy through Week 96 in LATTE-1





Margolis et al. *Lancet Infect Dis.* 2015;15:1145-1155.

BL, baseline; CAB, cabotegravir; CI, confidence interval; EFV, efavirenz; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine; $t_{1/2}$, half-life.

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LATTE-2 Objectives

Establish proof of principle for the first ever LA HIV treatment regimen

Primary Objective

- Evaluate the safety and efficacy of CAB LA + RPV LA as maintenance therapy, and
- Select a dosing schedule of CAB LA + RPV LA for progression into phase III studies

Key Secondary Objectives

- Characterize LA pharmacokinetics
- Evaluate the tolerability and acceptability of injectable dosing

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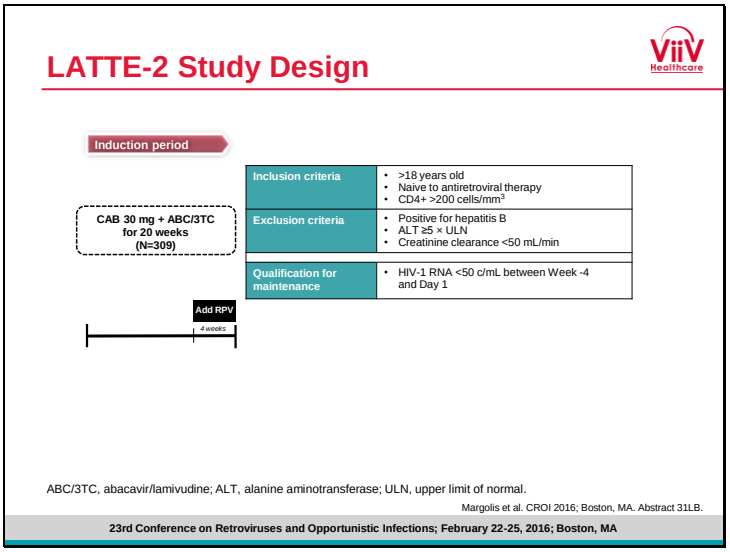
LATTE-2 Study Design
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Induction period
CAB 30 mg + ABC/3TC for 20 weeks (N=309)
Add RPV
4 weeks
Inclusion criteria
>18 years old
Naive to antiretroviral therapy
CD4+ >200 cells/mm3
Exclusion criteria
Positive for hepatitis B
ALT ≥5 × ULN
Creatinine clearance <50 mL/min
Qualification for maintenance
HIV-1 RNA <50 c/mL between Week -4 and Day 1
ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; ULN, upper limit of normal.
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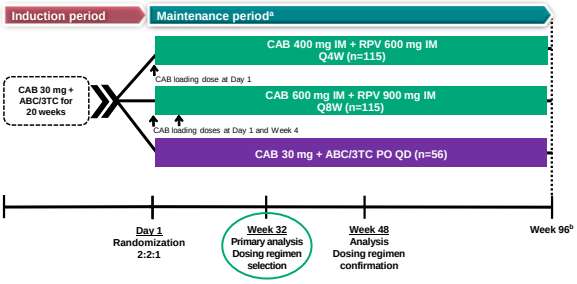
LATTE-2 Study Design



ABC/3TC, abacavir/lamivudine; IM, intramuscular; PO, orally; Q4W, every 4 weeks; Q8W, every 8 weeks; QD, once daily. [a]Subjects who withdrew after at least 1 IM dose entered the long-term follow-up period. [b]Subjects can elect to enter LA Extension Phase beyond Week 96.

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Baseline Characteristics: ITT-ME Population

	Q8W IM (n=115)	Q4W IM (n=115)	Oral CAB (n=56)	Total (N=286)
Median age, years	35.0	36.0	35.0	35.0
Female, n (%)	8 (7)	6 (5)	10 (18)	24 (8)
African American/African heritage, n (%)	17 (15)	12 (10)	15 (27)	44 (15)
CDC class C, n (%)	1 (<1)	2 (2)	0	3 (1)
Median HIV-1 RNA, log_{10} c/mL	4.419	4.455	4.289	4.393
≥100,000, n (%)	16 (14)	28 (24)	7 (12)	51 (18)
Median CD4+, cells/mm^3	449.0	499.0	517.5	489.0

CDC, Centers for Disease Control and Prevention; ITT-ME, intent-to-treat maintenance exposed.

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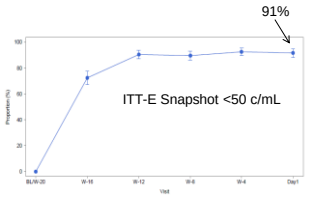
Day 1 Induction Outcomes (ITT-E)

Day 1 Snapshot outcome	Oral CAB (N=309)
Virologic success	282 (91%)
Virologic non-response	14 (5%)
Data in window not <50 c/mL	9 (3%)
Discontinued for lack of efficacy	2 (<1%)
Discontinued for other reason while not <50 c/mL	3 (<1%)
No virologic data in window	13 (4%)
Discontinued due to AE or death	6 (2%)
Discontinued for other reasons	7 (2%)



Day 1 drug-related AEs	Oral CAB (N=309)
Preferred term ≥3%	
Nausea	27 (9%)
Dyspepsia	9 (3%)
Headache	9 (3%)
Fatigue	8 (3%)

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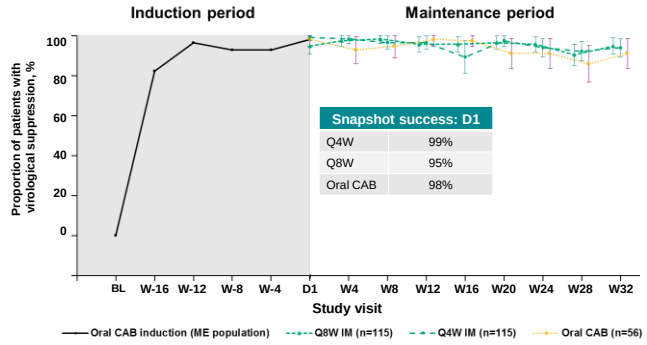
LATTE-2 Week 32 Results: HIV-1 RNA <50 c/mL by Snapshot (ITT-ME)



Snapshot success: D1	
Q4W	99%
Q8W	95%
Oral CAB	98%

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LATTE-2 Week 32 Primary Endpoint: HIV-1 RNA <50 c/mL by Snapshot (ITT-ME)

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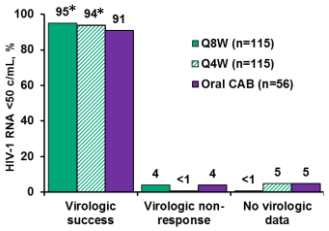
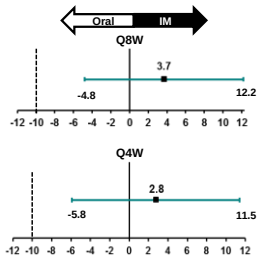
Virologic outcomes



Treatment differences (95% CI)



Both Q8W and Q4W comparable to oral CAB at Week 32

*Met pre-specified threshold for concluding IM regimen is comparable to oral regimen (Bayesian posterior probability >90% that true IM response rate is no worse than -10% compared with the oral regimen).

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Snapshot Outcomes: HIV-1 RNA <50 c/mL at Week 32 (ITT-ME)

Week 32 outcome	Q8W IM (n=115)	Q4W IM (n=115)	Oral CAB (n=56)
Virologic success	**109 (95%)**	**108 (94%)**	**51 (91%)**
Virologic non-response	**5 (4%)**	**1 (<1%)**	**2 (4%)**
Data in window not <50 c/mL[a]	3 (3%)	1 (<1%)	1 (2%)
Discontinued for lack of efficacy	1 (<1%)	0	1 (2%)
Discontinued for other reason while not <50 c/mL	1 (<1%)	0	0
No virologic data in window	**1 (<1%)**	**6 (5%)**	**3 (5%)**
Discontinued due to adverse event or death[b]	0	4 (3%)	1 (2%)
Discontinued for other reasons[c]	1 (<1%)	2 (2%)	2 (4%)

[a]Week 32 HIV-1 RNA Q8W: 53 c/mL, 70 c/mL, 91 c/mL; Q4W: 70 c/mL; oral CAB: 243 c/mL. All 5 are still in the study. [b]Q4W: hepatitis C, rash, depression, and psychosis; oral CAB: hepatitis C. [c]Q8W: ISR; Q4W: pregnancy and prohibited medication; oral CAB: lost to follow-up, relocation.

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Protocol-Defined Virologic Failure (PDVF): Genotype

- No INI, NNRTI, or NRTI mutations were detected through Induction or Maintenance

Maintenance period	Q8W IM (n=115)	Q4W IM (n=115)	Oral CAB (n=56)
Subjects with PDVF[a]	1[b] (1%)	0	1 (2%)
INI-r mutations	0	0	0
NRTI-r mutations	0	0	0
NNRTI-r mutations	0	0	0

[a]One additional PDVF occurred during oral Induction Period due to oral medication non-adherence. [b]PDVF at Week 4; no detectable RPV at Week 4 and Week 8, suggesting maladministration.

PDVF: <1.0 $\log_{10}$ c/mL decrease in plasma HIV-1 RNA by Week 4, OR confirmed HIV-1 RNA ≥200 c/mL after prior suppression to <200 c/mL, OR >0.5 $\log_{10}$ c/mL increase from nadir HIV-1 RNA value ≥200 c/mL.

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Adverse Events and Labs—Maintenance Period

ITT-ME population, n (%)	Q8W IM (n=115)	Q4W IM (n=115)	Oral CAB (n=56)	IM subtotal (N=230)
Drug-related AEs, excluding ISRs (≥3%)				
Pyrexia	3 (3)	5 (4)	0	8 (3)
Fatigue	2 (2)	4 (3)	1 (2)	6 (3)
Influenza-like illness	3 (3)	2 (2)	0	5 (2)
Grade 3 and 4 AEs, excluding ISRs	10 (9)	12 (10)	1 (2)	22 (10)
Drug-related Grade 3/4 AEs[a], excluding ISRs	3 (3)	4 (3)	0	7 (3)
Serious AEs[b]	7 (6)	6 (5)	3 (5)	13 (6)
AEs leading to withdrawal[c]	2 (2)	6 (5)	1 (2)	8 (3)
Grade 3 and 4 labs[d]	17 (15)	20 (17)	8 (14)	37 (16)

[a]Q8W: influenza-like illness, chills and pain, and lipase; Q4W: influenza-like illness, rash, depression, and psychosis. [b]None drug related; one death (epilepsy) evaluated as not likely related to study drug. [c]Q8W: ISR × 2; Q4W: Churg Strauss vasculitis, hepatitis C, depression, epilepsy, psychosis, and rash; oral CAB: hepatitis C. dMaintenance emergent. AE, adverse event; ISR, injection-site reaction.

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Adverse Events and Labs—Maintenance Period

	Q8W IM (n=115)	Q4W IM (n=115)	IM subtotal (N=230)
Number of injections	1623	2663	4286
Number of ISRs (events/injection)	1054 (0.65)	1228 (0.46)	2282 (0.53)
Grades			
Grade 1	839 (80%)	1021 (83%)	1860 (82%)
Grade 2	202 (19%)	197 (16%)	399 (17%)
Grade 3	12 (1%)	10 (<1%)	22 (<1%)
Grade 4	0	0	0
Duration, days			
≤7	943 (89%)	1121 (91%)	2064 (90%)
Median	3.0	3.0	3.0

- Most common ISR events overall were pain (67%), swelling (7%), and nodules (6%)
- Number of subjects reporting ISRs decreased over time, from 86% (Day 1) to 33% (Week 32)[a]
- 2/230 subjects (1%) withdrew as a result of injection reactions (Q8W)

[a]Represents percent of subjects with a Week 32 visit (n=220).

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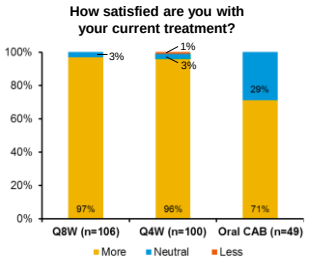
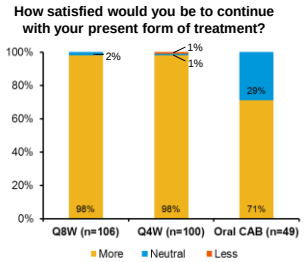
Patient-Reported Outcomes at Week 32: Maintenance Treatment Compared With Oral Induction Treatment[a]





Note: based on observed case dataset of subjects who completed Week 32 questionnaires.
[a]HIV Treatment Satisfaction Questionnaire change version (HIVTSQc).

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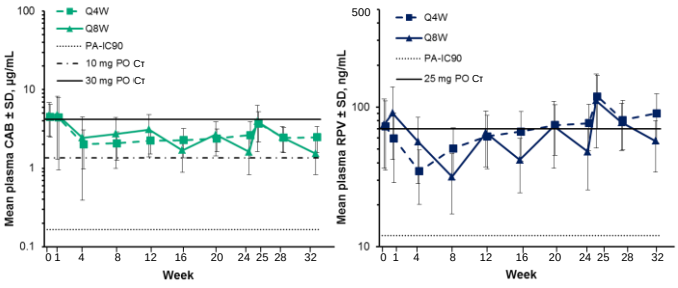
Pharmacokinetics



Cτ, trough concentration; PA-IC90, protein binding–adjusted 90% inhibitory concentration; SD, standard deviation.

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Conclusions

- LATTE-2 results successfully demonstrate the potential to maintain HIV-1 viral load <50 c/mL with LA IM CAB + RPV, dosed once Q4W or Q8W
- Two subjects met PDVF criteria
  - Q8W (n=1), oral CAB (n=1); both without evidence of resistance at failure
- Injection tolerability
  - Majority of ISRs were Grade 1 to 2 pain, with a median duration of 3 days
  - Few subjects had an ISR that led to discontinuation, with high overall reported satisfaction
- Regimen selection criteria
  - Neither Q4W IM or Q8W IM dosing was ruled out on the basis of pre-specified criteria
  - Upcoming Week 48 analysis will contribute to final dose selection for phase III studies

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Thank You

- We thank everyone who has contributed to the success of this study, including
  - All study participants and their families
  - The LATTE-2 clinical investigators and their staff in Spain, Germany, France, Canada, and the United States
  - The ViiV Healthcare, GSK, Parexel, and Janssen study team members