PATIENT-REPORTED OUTCOMES ON LONG-ACTING CABOTEGRAVIR + RILPIVIRINE AS MAINTENANCE THERAPY: FLAIR 96-WEEK RESULTS

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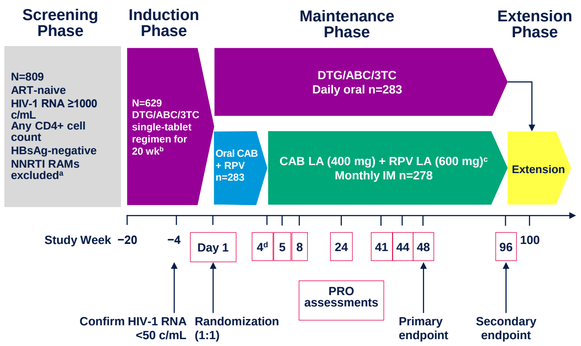
Introduction

- Long-acting (LA) injectable formulations of ART are expected to provide an alternative to current daily oral dosing regimens and may help reduce the daily reminder and unwanted disclosure of HIV status, enhance convenience, reduce dosing frequency, and may facilitate adherence[1-4]
- In phase III FLAIR (ClinicalTrials.gov identifier: NCT02938520), monthly CAB LA + RPV LA was noninferior to continuing oral DTG/ABC/3TC based on the primary endpoint of proportion of participants with HIV-1 RNA ≥50 copies/mL at Weeks 48[5] and 96[6] in virologically suppressed PLHIV
- Here we present patient-reported outcomes (PROs) from FLAIR (Figure 1) up to Week 96 to understand patient preferences and experiences with the LA formulation

Figure 1. FLAIR Study Design and PRO Assessments



[a]NNRTI RAMs but not K103N were exclusionary. [b]DTG + 2 alternative non-ABC NRTIs was permitted if participant was intolerant or *HLA-B*5701*-positive. [c]Participants who withdraw/complete CAB LA + RPV LA enter 52-wk long-term follow-up. [d]Participants received initial loading doses of CAB LA 600 mg + RPV LA 900 mg at Week 4. Beginning at Week 8, participants received CAB LA 400 mg + RPV LA 600 mg injections every 4 wk.

Methods

Baseline Characteristics in the Intention-to-Treat–Exposed Population

- Eligible participants were ART-naive adults with HIV-1 infection
- 566 participants were randomized (median age, 34 years; female, 22%; white, 74%; median body mass index, 24 kg/m^2 [range, 13-47]); baseline and demographic characteristics in the intention-to-treat–exposed population were similar between treatment groups[5]

Study Design

- Literature reviews and qualitative interviews from the LATTE-2 study informed the concepts of interest for the phase III development program; additional literature searches were conducted to identify PRO instruments best able to measure the selected endpoints (Table)

Table. Summary of PRO Measures

PRO	Description	Endpoint
Perception of Injection Questionnaire (PIN)	21 items total produce 4 dimensions: "acceptance of ISRs," "bother from ISRs," "leg movement," "sleep," and 5 individually reported items Modified from a Vaccinees' Perception of Injection (VAPI) questionnaire[a]	Acceptability of injections and ISRs over time from Weeks 5, 41, 48, and 96
Chronic Treatment Acceptance Questionnaire (ACCEPT)	3 items that produce the "general acceptance" score were included, asking participants to weigh the advantages and disadvantages associated with their treatment	Change from Day 1 in general acceptance of HIV treatment at Weeks 8, 24, 48, and 96
HIV Treatment Satisfaction Questionnaire status version (HIVTSQs)	12 items total: produce treatment satisfaction total score (11 items) and 1 stand-alone item on pain/discomfort Adapted from the 10-item HIVTSQ and validated in the LATTE-2 study	Change from Day 1 in treatment satisfaction at Weeks 24, 44, and 96
Short Form 12 Health Survey (SF-12)	12 items produce 2 component scores: the physical component summary (PCS) score and the mental component summary (MCS) score	Change from Day 1 in physical and mental health status at Weeks 24, 48, and 96

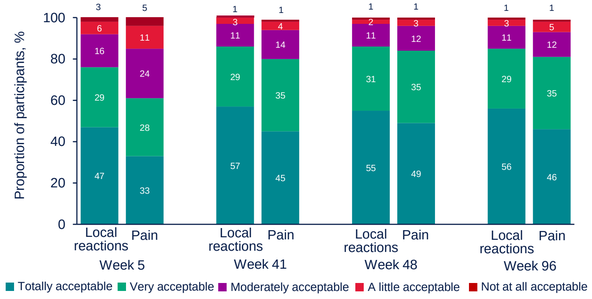
[a]VAPI copyright © Sanofi Pasteur 2009, all rights reserved.[7]

Results

Increased Acceptability of ISRs (Pain and Local Reactions) Over Time

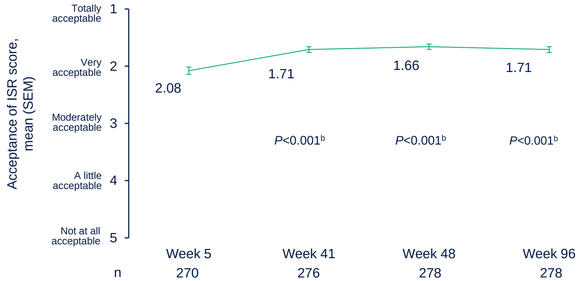
- In participants receiving CAB LA + RPV LA, acceptability of ISRs improved over time from Week 5; mean score for the "acceptance of ISRs" dimension of the PIN (scale, 1-5) significantly decreased (improved) from Week 5 (2.08) to Weeks 41 (1.71), 48 (1.66), and 96 (1.71); *P*<0.001 for all (Figures 2 and 3)
  - 82% and 85% of participants receiving LA therapy rated pain and local reactions, respectively, due to injections as "totally" or "very acceptable" at Week 96 vs 61% and 75%, respectively, of participants at Week 5 (first week following first injection of CAB LA + RPV LA), according to the PIN Questionnaire (Figure 2)
  - Those results are consistent with a reduction in incidence of ISRs reported over time in safety data previously presented[6]

Figure 2. Proportion of Participants' Response Options for Items of "Acceptance of ISRs" by Visit Through 96 Weeks (ITT-E Population)



- To avoid multiplicity, statistical tests of significance were preplanned only for the "acceptance of ISRs" dimension of the PIN
- For the remaining dimensions of the PIN ("bother of ISRs," "leg movement," and "sleep"), consistent results were observed between Weeks 5 and 96 following the trend of the "acceptance of ISRs" dimension

Figure 3. Mean Acceptance Score by Visit Through 96 Weeks (ITT-E Population)[a]

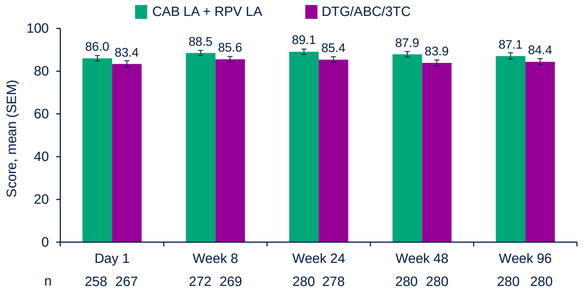


SEM, standard error of mean. [a]Scores for other dimensions were bother of ISRs: Week 5: 1.62, Week 41: 1.48, Week 48: 1.47, Week 96: 1.50; leg movement: Week 5: 2.17, Week 41: 1.58, Week 48: 1.53, Week 96: 1.56; and sleep: Week 5: 2.15, Week 41: 1.57, Week 48: 1.56, Week 96: 1.58. [b]*P* value from Wilcoxon signed rank test for change from value at Week 5 for acceptability of ISRs dimension; last observation (post-Week 5) carried forward analysis.

Similar and High Levels of Acceptance for LA and Daily Oral Therapy

- On Day 1, mean "general acceptance" scores on the ACCEPT Questionnaire, which assessed experience with current treatment prior to randomization, were high and similar for both treatment groups
- A numeric improvement in favor of the CAB LA + RPV LA group was consistently observed for Weeks 8, 24, 48, and 96, with no statistically significant differences, partly due to high initial acceptance rates
  - This finding indicates that CAB LA + RPV LA has at least the same level of acceptance as DTG/ABC/3TC (Figure 4)

Figure 4. General Treatment Acceptance (ACCEPT) Scores by Visit[a]

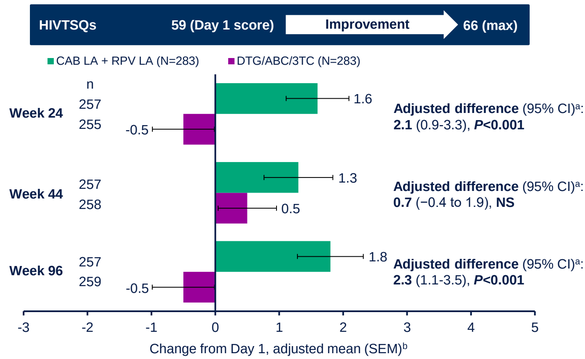


[a]Scores taken from last observation (post-Day 1) carried forward during maintenance phase.

Greater Participant Treatment Satisfaction for LA vs Daily Oral Therapy

- Mean HIVTSQs scores at Day 1, assessing experience with treatment prior to randomization, were high with values of 59.3 and 59.1 out of a maximum of 66 for the CAB LA + RPV LA and DTG/ABC/3TC groups, respectively
- At Week 96, significantly greater improvement from Day 1 in total treatment satisfaction score was observed with CAB LA + RPV LA vs DTG/ABC/3TC (adjusted mean difference [95% CI], 2.3 [1.1-3.5]; *P*<0.001), further increasing from Weeks 24 (2.1 [0.9-3.3]) and 44 (0.7 [−0.4, 1.9]; Figure 5)
  - Key drivers for the difference in HIVTSQs scores between treatment groups were items assessing convenience, flexibility, and satisfaction with LA therapy

Figure 5. Change From Day 1 in HIVTSQs Total Scores From Weeks 24 to 96



NS, not significant; SEM, standard error of mean. [a]*P* value from ANOVA model for adjusted mean change from baseline; last observation (post-Day 1) carried forward. [b]Adjusted for induction baseline score, baseline viral load, sex at birth, age, and race.

No Significant Changes Observed in the SF-12 PCS and MCS

- No significant difference in change from Day 1 in SF-12 PCS or MCS was observed between treatment groups at any visit

Conclusions

- At Week 96, FLAIR participants receiving LA therapy reported greater improvement in treatment satisfaction compared with those continuing daily oral ART
- For most participants receiving CAB LA + RPV LA, acceptability of ISRs after first injection was high and improved over time, consistent with the reduced number of ISRs as adverse events[6]
- Overall, these PRO results support monthly CAB LA + RPV LA as a potential alternative to daily oral ART for adults with HIV-1 infection

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References: 1. Mantsios et al. *Cult Health Sex*. 2020:1-13. **2.** Mantsios et al. *AIDS Behav*. 2020 [Epub ahead of print]. **3.** Kerrigan et al. *PLoS One*. 2018;13:e0190487. **4.** Kerrigan et al. *AIDS Behav*. 2018;22:3540-3549. **5.** Orkin et al. *N Engl J Med*. 2020;382:1124-1135. **6.** Orkin et al. CROI 2020; Boston, MA. Poster 482. **7.** Chevat et al. *Health Qual Life Outcomes*. 2009;7:21.

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