EFFICACY AND SAFETY OF LONG-ACTING CABOTEGRAVIR + RILPIVIRINE IN PARTICIPANTS WITH HIV/HCV CO-INFECTION: ATLAS-2M 48-WEEK RESULTS

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833

Introduction

- Cabotegravir (CAB) and rilpivirine (RPV) are approved as the first complete long-acting (LA) injectable regimen recommended by treatment guidelines for the maintenance of virologic suppression in people living with HIV-1[1-3]
- In the phase IIIb ATLAS-2M study, CAB + RPV LA dosed every 8 weeks (Q8W) demonstrated non-inferiority compared with dosing every 4 weeks (Q4W) for maintenance of virologic suppression at Weeks 48 and 96[4-5]
- HCV co-infection occurs in ~6% of people with HIV-1 due to shared modes of transmission[6]
- Here we report efficacy, safety, and pharmacokinetics of CAB + RPV LA in participants with HIV/HCV co-infection through 48 weeks in ATLAS-2M

Methods

- ATLAS-2M is a phase IIIb, randomized, multicenter, parallel-group, open-label, noninferiority study of CAB + RPV LA dosed Q8W vs Q4W in virologically suppressed adults with HIV-1 infection (NCT03299049)
- Virologically suppressed participants receiving CAB + RPV LA Q4W or oral standard-of-care antiretroviral therapy who transitioned from the phase III ATLAS study (NCT02951052) or newly recruited oral standard-of-care antiretroviral therapy participants were randomized 1:1 to receive CAB + RPV LA Q8W or Q4W
- The presence of HCV RNA at baseline was identified by polymerase chain reaction
  - Participants with asymptomatic chronic HCV infection and liver enzymes meeting entry criteria were included if they were not anticipated to require HCV treatment within 52 weeks
    - HCV infection was assessed at baseline in ATLAS and ATLAS-2M by presence of anti-HCV antibodies; for this analysis, only HIV-1 positive individuals with detectable HCV RNA were considered as having HIV/HCV co-infection
  - Individuals could receive HCV treatment after Week 52 with approval from the medical monitor
- Week 48 assessments included proportion of participants with HIV-1 RNA ≥50 and <50 c/mL (Snapshot algorithm), general and hepatic safety, pharmacokinetics, and treatment satisfaction questionnaires

Results

- HIV/HCV co-infection was present in 10 (1%) of 1045 participants in ATLAS-2M, 60% of whom were female at birth (Table 1)

Table 1. Baseline Characteristics

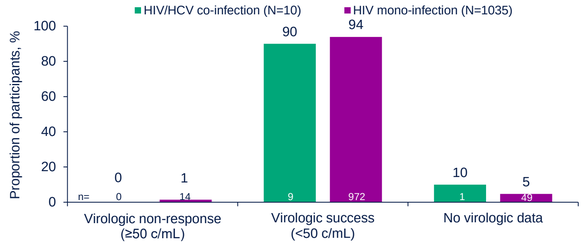
Parameter	HIV/HCV co-infection (N=10)[a]	HIV mono-infection (N=1035)
Age, median (range), y	38 (31-59)	42 (19-83)
≥50, n (%)	3 (30)	279 (27)
Female at birth, n (%)	6 (60)	274 (26)
Race, n (%)		
White	10 (100)	753 (73)
Black or African American	0	191 (18)
Other	0	91 (9)
Body mass index, median (range), kg/m^2	23 (19-30)	26 (17-78)
CD4+ cell count, median (IQR), cells/mm^3	577 (455-708)	662 (508-849)
<350, n (%)	1 (10)	61 (6)
Prior CAB + RPV exposure, n (%)	4 (40)	387 (39)

IQR, interquartile range. [a]Participants received CAB + RPV LA Q8W (n=5) or Q4W (n=5).

Virologic Outcomes

- At Week 48, 90% (9/10) of participants with HIV/HCV co-infection and 94% (972/1035) with HIV mono-infection had HIV-1 RNA <50 c/mL (adjusted difference, 4.1; 95% CI, −14.5-22.6; Figure 1)
- No participants with HIV/HCV co-infection had HIV-1 RNA ≥50 c/mL compared with 1% (14/1035) with HIV mono-infection
- 1 (10%) participant with HIV/HCV co-infection who discontinued for reasons other than adverse events (AEs) had no virologic data at Week 48
  - 5% (49/1035) of participants with HIV mono-infection had no virologic data because of discontinuations due to AE or death (n=22) or other reasons (n=27)
- No participants with HIV/HCV co-infection had confirmed virologic failure through Week 48 compared with 1% (n=10) with HIV mono-infection

Figure 1. Virologic Snapshot Outcomes at Week 48



Safety and Tolerability

- Excluding injection site reactions (ISRs), 4 (40%) participants with HIV/HCV co-infection reported 10 AEs, none of which were serious or led to study withdrawal (Table 2)
- Injection site pain was the most common AE, reported in 50% (5/10) of participants with HIV/HCV co-infection and 70% (729/1035) with HIV mono-infection
  - Other AEs in the HIV/HCV co-infection group were reported in 1 participant each

Table 2. Summary of AEs, Excluding ISRs

Outcome, n (%)	HIV/HCV co-infection (N=10)	HIV mono-infection (N=1035)
Any AE	4 (40)	826 (80)
Drug-related AE	1 (10)[a]	230 (22)
Grade ≥3 AE	0	55 (5)
Drug related	0	9 (<1)
SAE	0	41 (4)
Drug related	0	3 (<1)
Fatal SAE	0	1 (<1)[b]
Drug related	0	0
AE leading to withdrawal	0	18 (2)

AE, adverse event; SAE, serious adverse event. [a]1 participant reported drug-related AEs of influenza-like illness (2 events; both resolved) and asthenia (1 event; remains ongoing). [b]Sepsis (not drug related).

- In participants with HIV/HCV co-infection, ISRs were reported in 38 of 232 total injections, all of which were grade 1 (97%) or 2 (3%), and none led to withdrawal (Table 3)

Table 3. Event-Level ISR Summary

Outcome	HIV/HCV co-infection (N=10)	HIV mono-infection (N=1035)
Total injections, n	232	23,949
ISR event, n[a]	38	5621
Pain, n (%)[b]	33 (14)	4548 (19)
Nodule, n (%)[b]	1 (<1)	316 (1)
Grade 3 ISR, n (%)[b,c]	0	91 (<1)
ISR duration, median (IQR), d	2 (1-3)	3 (2-5)
ISRs leading to withdrawal, n (%)[b]	0	25 (<1)

IQR, interquartile range; ISR, injection site reaction. [a]ISRs reported in ≥1% of total injections in either group. [b]Percentages calculated from total injections. [c]No grade 4 or 5 ISRs were reported.

- Through Week 48, no hepatic abnormalities of alanine aminotransferase (ALT) levels ≥3 × the upper limit of normal (ULN), hepatocellular injury, or liver stopping events were reported in participants with HIV/HCV co-infection, and few were reported in those with HIV mono-infection (Table 4)

Table 4. Hepatic Safety

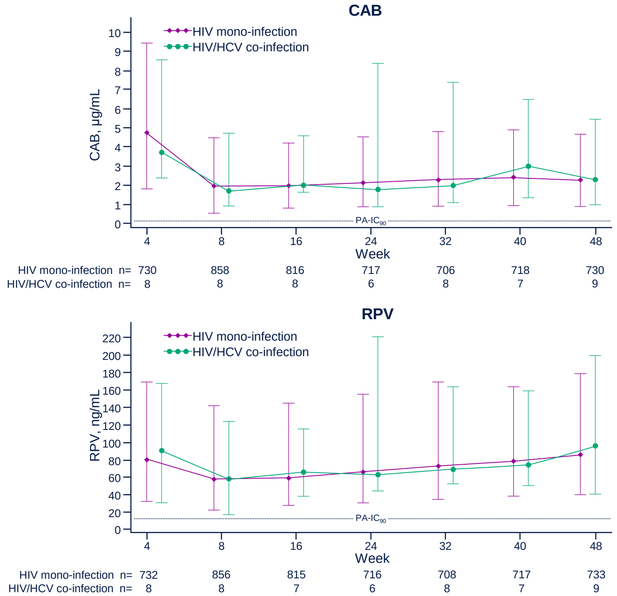
Liver abnormality, n (%)	HIV/HCV co-infection (N=10)	HIV mono-infection (N=1031)
ALT ≥3 × ULN	0	18 (2)
ALT ≥3 × ULN, BIL ≥2 × ULN, and ALP <2 × ULN	0	3 (<1)
Hepatocellular injury[a]	0	15 (1)
Hepatocellular injury and BIL ≥2 × ULN	0	3 (<1)
Liver stopping event	0	4 (<1)[b]
Acute hepatitis B virus infection	0	2[c]
Acute hepatitis E virus infection	0	1[d]
Acute HCV infection	0	1[e]

ALP, alkaline phosphatase; ALT, alanine aminotransferase; BIL, bilirubin; ULN, upper limit of normal.
[a]Defined as ([ALT/ALT ULN]/[ALP/ALP ULN]) ≥5 and ALT ≥3 × ULN. ALT and ALP must be measured on the same day. [b]All liver stopping events occurred after treatment started. [c]Both participants withdrew from the study. [d]Participant continued CAB + RPV LA dosing. [e]Participant continued CAB + RPV LA dosing; event not resolved.

Pharmacokinetics

- Plasma CAB and RPV concentrations were similar between participants with HIV/HCV co-infection and HIV mono-infection (Figure 2)
- >95% of participants in each group had median plasma CAB and RPV concentrations above protein-adjusted 90% inhibitory concentration values through Week 48

Figure 2. Median (5th, 95th Percentile) Plasma CAB and RPV Concentrations

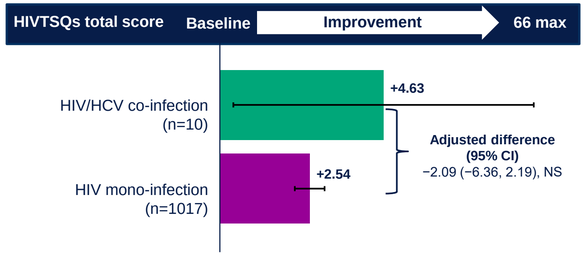


PA-IC$_{90}$, protein-adjusted 90% maximal inhibitory concentration. Due to the balance of dosing regimens in each group, results for Q8W and Q4W dosing are combined. Of participants with HIV/HCV co-infection and available PK data at Weeks 4, 8, and 32, 3 received CAB + RPV LA Q8W (none with prior CAB + RPV exposure) and 5 received CAB + RPV LA Q4W (3 with prior CAB + RPV exposure in ATLAS); PK data at Week 48 includes an additional Q8W participant with prior CAB + RPV exposure in ATLAS.

Participant Satisfaction

- Participants with HIV/HCV co-infection and HIV mono-infection reported improvement from baseline in treatment satisfaction at Week 48, with slightly larger but not statistically significant improvement reported among participants with HIV/HCV co-infection (Figure 3)

Figure 3. Adjusted Mean (95% CI) Change From Baseline in HIVTSQs Total Score at Week 48



Adjusted for baseline score, sex at birth (female, male), age (<50, ≥50 years), and race (White, non-White).

Conclusions

- In this small cohort of participants with HIV/HCV co-infection, CAB + RPV LA was similarly effective and well tolerated through 48 weeks of treatment compared with participants with HIV mono-infection
- Through 48 weeks, no hepatic abnormalities of ALT levels ≥3 × ULN, hepatocellular injury, or liver stopping events were reported among participants with HIV/HCV co-infection
- Plasma CAB and RPV concentrations were similar between participants with HIV/HCV co-infection and HIV mono-infection throughout Week 48
- Treatment satisfaction improved among participants with HIV/HCV co-infection and HIV mono-infection
- These results support the therapeutic potential of CAB + RPV LA for treatment of individuals with HIV-1 and HCV co-infection

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