Cabenuva: Rates of Virologic Suppression by Baseline Body Mass Index

Summary

- A 48 week pooled analysis of ATLAS, FLAIR and ATLAS-2M which stratified patients by body mass index (BMI, < 30 kg/m² or ≥ 30 kg/m²) showed high and comparable virologic suppression rates between BMI categories.[1]
  - No participant with high BMI as the only baseline factor met confirmed virologic failure (CVF) criterion.
  - Use of 2-inch needles resulted in higher median cabotegravir trough concentrations for participants with BMI ≥30 kg/m².
- A post hoc multivariable analysis (MVA) showed that baseline BMI was one of four factors that was associated with confirmed virologic failure (CVF) through Week 48 in FLAIR, ATLAS, and ATLAS-2M.[2]
  - A post hoc baseline factors analysis (BFA) at 48 weeks showed that there is an increased risk of CVF if 2 or more baseline factors (among RPV RAMs, HIV-1 subtype A6/A1, and BMI ≥30 kg/m²) are present.
  - In an updated analysis (data through Week 124 from FLAIR, Week 96 from ATLAS, and Week 152 from ATLAS-2M) CVF occurred in 0.5% (n=1/216) of participants with BMI ≥30 kg/m² as their only baseline factor.
- Similar rates of virologic suppression (90% and 91%) and virologic nonresponse (1%) were observed when patients were stratified by baseline BMI (< 30 kg/m² and ≥ 30 kg/m²) in the SOLAR trial.[3] Limited data is available on patients with baseline BMI ≥ 40 kg/m².
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SUBGROUP ANALYSIS OF POOLED PHASE 3 DATA

For information on the study design of ATLAS and FLAIR please click here. For information on the study design of ATLAS-2M please click here.

Efficacy, safety, and pharmacokinetics of CAB + RPV LA through Week 48 were evaluated among participants receiving CAB + RPV LA in the ATLAS, FLAIR, and ATLAS-2M studies.[1] Participants were stratified by dosing regimen (Q8W vs. Q4W) and BMI category (lower, < 30 kg/m²; higher, ≥ 30 kg/m²). Of the 1,245 participants randomized to receive CAB + RPV LA, 213 (17%) had a BMI ≥30 kg/m² and 25 (20%) had BMI ≥ 40 kg/m² at baseline.

Across both dosing regimens, 93–94% of participants with BMI < 30 kg/m² and 92% with BMI ≥ 30 kg/m² had HIV-1 RNA < 50 copies/mL. CVF events were uncommon across all three studies (n=13/1245; 5 in the lower BMI group and 8 in the higher BMI group). Among 153 participants with BMI ≥ 30 kg/m² as the only baseline factor, none met CVF criterion.[1]

BMI categories did not affect cabotegravir or rilpivirine trough levels, which remained above PA-IC_{90} targets. Median CAB trough levels tended to be lower in patients with baseline BMI ≥ 30 kg/m²; however, this trend disappeared by Week 48. Higher cabotegravir trough levels were observed in participants in the higher BMI cohort who utilized longer 2-in needles. Longer 2-inch needles are

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recommended for participants with BMI ≥ 30 kg/m² to ensure appropriate administration into gluteal muscle.[1]

Through 48 weeks, adverse events leading to study withdrawal occurred in 2-3% of participants in the low BMI group and < 1% in the high BMI group. Most ISRs were classified as mild to moderate in severity and decreased in incidence over time.[1]

MULTIVARIABLE ANALYSES (MVA)

Week 48

The objective of this post hoc MVA was to provide an understanding of potential factors associated with CVF through Week 48 among patients receiving CAB + RPV LA in ATLAS, FLAIR, and ATLAS-2M.[2,2,2,2,2]A logistic regression model was used to assess the influence of 10 covariables suspected to contribute to virologic outcomes, including baseline BMI ≥30 kg/m².

Results

Patients were included if they were naïve to CAB + RPV LA (n=1039).[2] Patients (n=597) were excluded from the analysis if they were not naïve to CAB + RPV LA (n=391), had not received CAB + RPV LA (n=22), or had missing data (n=184).

Seventeen patients met the criteria for CVF through Week 48.[2,2,2,2,2] Of these, 13 patients were included in the MVA. Four patients were excluded from the analysis.

Baseline BMI was among 4 factors identified that were associated with an increased risk of CVF (the other 3 factors were: RPV resistant associated mutations [RAMs] at baseline, baseline HIV-1 subtype A6/A1, and $\log_2$ of post hoc Week 8 RPV C_{min}).[2] See Table 1. It is important to note that the magnitude of the odds ratio in Table 1 below does not show that there is a causal relationship between certain covariables and CVF; it shows the strength of the association.

Table 1. Strength of Association of BMI and CVF through Week 48[2,2,2,2]

Covariable	Odds Ratio* (95% CI)	*P* value
BMI at baseline	1.13 (1.03 to 1.25)	0.014

*Odds ratios (ORs), 95% penalized profile CIs and penalized likelihood ratio p-values are provided. Covariates with p<0.05 in the final backwards elimination model are presented. CAB and RPV PK parameters were $\log_2$-transformed; therefore, the corresponding ORs are per halving of each variable.

CVF = confirmed virologic failure; RPV = rilpivirine; C_{min} = trough concentration; BMI = body mass index; CAB = cabotegravir

Baseline Factor Analysis

A post hoc baseline factor analysis showed that there is an increased risk of CVF if 2 or more baseline factors (RPV RAMs, HIV-1 subtype A6/A1, and BMI ≥30 kg/m²) are present.[2] BMI as a risk factor by itself did not increase the risk of failure. The rate of CVF among patients no or 1 factor present was <0.5%.

Beyond Week 48

The MVA was updated with data through Week 124 from FLAIR, Week 96 from ATLAS, and Week 152 from ATLAS-2M.[4,4,4,5,5,4,5] The updated analysis confirmed the results of the BFA conducted at Week 48. The presence of a combination of ≥2 baseline factors (pre-existing RPV RAMs, HIV-1 subtype A6/A1, and/or BMI ≥30 kg/m²) increased the risk of failure. CVF occurred in 0.5% (n=1/216) of participants with BMI ≥30 kg/m2 as their only baseline factor.

SOLAR SUBGROUP ANALYSIS

For information on the study design of SOLAR, please click here.

Please see Table 2 for a description of baseline BMI distribution among patients receiving CAB + RPV LA in the SOLAR study.

Table 2. Baseline BMI Distribution Among Participants Receiving CAB + RPV LA in SOLAR[6]

BMI at baseline	
< 30 kg/m^2	79% (354/447)
≥ 30 to 40 kg/m^2	17% (77/447)
≥ 40 to < 50 kg/m^2	3% (14/447)
≥ 50 kg/m^2	1% (2/447)

BMI = body mass index; CAB + RPV LA = long acting cabotegravir + rilpivirine

Efficacy and safety data were analyzed by BMI (< 30 kg/m² and ≥ 30 kg/m²).[3] Of the 447 participants who received CAB +RPV LA (mITT-E), 93 (21%) had a BMI ≥ 30 kg/m² at baseline. At Month 12, 1% of patients in both BMI groups had virologic nonresponse (HIV-1 RNA ≥ 50 copies/mL). Virologic suppression (HIV-1 RNA < 50 copies/mL) was similar between groups (90% and 91%, respectively).

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This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

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