# FEASIBILITY AND VIRAL RESPONSE TO TREATING ACUTE/EARLY HIV IN A MULTINATIONAL STUDY

00492

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## BACKGROUND

- ART initiation during acute or early HIV infection (AEHI) may limit HIV reservoir establishment, enhance reservoir decay, and limit viral genetic diversification, thereby facilitating HIV remission
- Characterizing the virologic and immunologic impact of therapy is a high priority for defining HIV pathogenesis
- Studies of cure/sustained virologic remission may benefit from the establishment of a well-characterized cohort treated during AEHI
- ACTG A5354 was designed to rapidly initiate antiretroviral therapy (ART) in those identified with AEHI in order to address pathogenesis-related questions and establish a cohort of well-characterized participants for future cure research

## METHODS

- Adults with anticipated AEHI were enrolled into a single-arm, open-label clinical trial at 30 sites in the Americas, Africa, and Southeast Asia (**Table 1**)
- Participants initiated ART during AEHI with study-provided EVG/COBI/FTC/TDF (or TAF) or other regimens
- Fiebig stage at ART initiation was retroactively assigned by centralized testing and categorized per protocol as Group 1 (Fiebig I/II), Group 2 (Fiebig III/IV) or Group 3 (Fiebig V)
- Participants were followed longitudinally with visits at weeks 1, 4, 12, 24, 36, 48, 60 and 72 to monitor plasma HIV RNA in real-time
- This analysis summarizes enrollment and virologic response to therapy

**Table 1. Study Population Characteristics, by Study Group**

| | Group 1 (Fiebig I/II) (n=49) | Group 2 (Fiebig III/IV) (n=79) | Group 3 (Fiebig V) (n=60) |
|---|---|---|---|
| **Age**, median years (IQR) | 26 (22-35) | 30 (24-40) | 26 (23-38) |
| **Male** | 92% | 85% | 82% |
| **Cisgender** | 96% | 92% | 100% |
| **Race** | | | |
| Black/African American | 42% | 49% | 70% |
| White | 31% | 50% | 28% |
| Asian | 27% | 1% | 2% |
| **Initial ART Regimen** | | | |
| EVG/COBI/FTC/TAF | 63% | 82% | 83% |
| DTG/3TC/TDF | 37% | 13% | 13% |
| **CD4**, median cells/mm$^3$ (IQR) | 348 (211-493) | 383 (264-538) | 490 (366-652) |
| **HIV RNA**, median $\log_{10}$ cp/mL (IQR) | 6.4 (5.3-7.0) | 6.5 (6.0-7.0) | 5.4 (5.0-6.4) |

Rapid ART initiation was feasible, well-tolerated, and virologically effective in a prospective, multinational study of AEHI: Potential implications for patients and the establishment of cohorts for testing cure strategies.

Shortened time to HIV RNA target not detected after initiation of ART during seronegative phase may reflect virologic benefits associated with early therapy.

**Figure. Proportion (95% CI) of participants with HIV-1 RNA <50 copies/mL (A) and target not detected (B) over time**

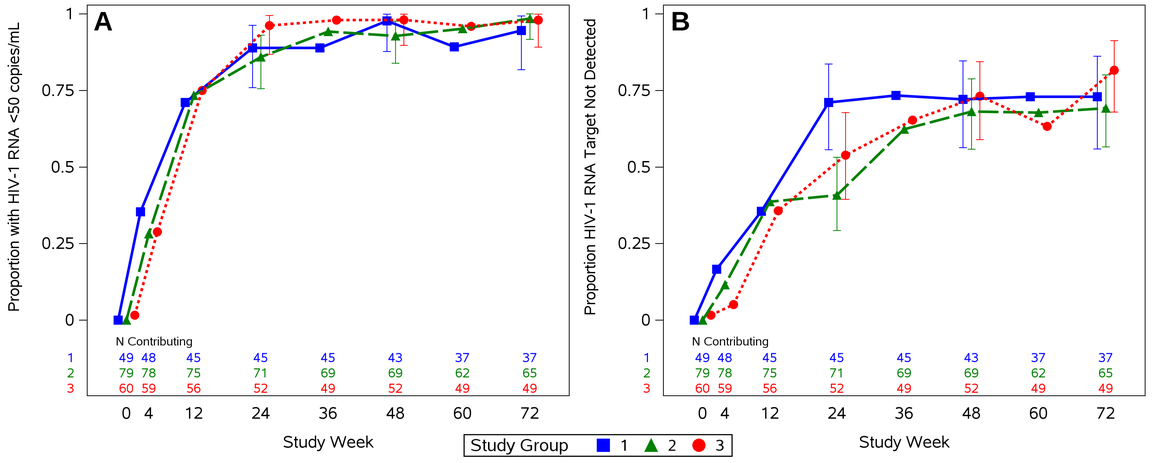


**Table 2. Proportion (95% CI) with HIV-1 RNA <50 copies/mL**

| | Group 1 (Fiebig I-II) | Group 2 (Fiebig III-IV) | Group 3 (Fiebig V) |
|---|---|---|---|
| **Week 24** | 0.89 (0.76, 0.96) | 0.86 (0.76, 0.93) | 0.96 (0.87, 1.00) |
| **Week 48** | 0.98 (0.88, 1.00) | 0.93 (0.84, 0.98) | 0.98 (0.90, 1.00) |
| **Week 72** | 0.95 (0.82, 0.99) | 0.98 (0.92, 1.00) | 0.98 (0.89, 1.00) |

**Table 3. Proportion (95% CI) with HIV-1 RNA TND**

| | Group 1 (Fiebig I-II) | Group 2 (Fiebig III-IV) | Group 3 (Fiebig V) |
|---|---|---|---|
| **Week 24** | 0.71 (0.56, 0.84) | 0.41 (0.29, 0.53) | 0.54 (0.39, 0.68) |
| **Week 48** | 0.72 (0.56, 0.85) | 0.68 (0.56, 0.79) | 0.73 (0.59, 0.84) |
| **Week 72** | 0.73 (0.56, 0.86) | 0.69 (0.57, 0.80) | 0.82 (0.68, 0.91) |

## RESULTS

- From January 2017 to December 2019, 195 participants were enrolled with anticipated Fiebig I-V; 3 were uninfected, 4 were Fiebig VI and 188 initiated ART during AEHI

Among the N=188 AEHI participants (see **Table 1**) :

- 6 Fiebig stage I, 43 stage II, 56 stage III, 23 stage IV, 60 stage V
- 132 (70%) from US and 56 (30%) from ex-US sites
- 72% were screened, enrolled and treated on the same day
- 36% were hospitalized and 28% were asymptomatic
- Premature study discontinuation occurred in 18% of US and 20% of ex-US participants
- Over 72 weeks of follow-up, ART was held or switched in 43 (23%) with confirmed virologic failure in 4 (2%)
- Those remaining in follow-up had high rates of virologic suppression (**Figure; Table 2**)
- Group 1 had a higher proportion of participants with HIV RNA target not detected than Groups 2 and 3 at week 24 (P = 0.005; **Figure; Table 3**)

## CONCLUSIONS

- The identification and rapid initiation of ART during AEHI is feasible across multinational sites
- Although premature study discontinuation occurred in ~19% of participants, those that remained on study maintained high rates of viral suppression.
- The shortened time to HIV RNA target not detected is of unknown clinical relevance but may suggest virologic benefits that would be further characterized by studies of viral reservoir
- Additional results of A5354 are presented in Abstracts 00265, 00367, and 00387

## ADDITIONAL INFORMATION

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