Introduction

- Pegylated IFN-α2a (1) and 2b (2.3) maintain viral suppression during and ART interruption (ATI) in approximately 50% of participants.
- A combination of broadly HIV-1-neutralizing monoclonal antibodies (bNAb) 3BC117 and 10-1074 maintains suppression during and ATI in approximately 80% chronically infected individuals (4, 5).
- In the BEAT-2 study (NCT03588715), we evaluated the effectiveness of peg-IFN-α2b in combination with 3BC117 and 10-1074 (Arm 1) or the antibody combination alone (Arm 2) in suppressing HIV replication during and after ATI.
- Primary end-points were safety and frequency of viral control at 12 weeks after end of 26 weeks of immunotherapy (combination of bNAb plus peg-IFN-α2b).

Methods

- Participants: 14 individuals assigned to arm 1 (BEAT-2 study), Arm 2 was discontinued because of COVID.
- Participating centers: University of Pennsylvania and Jonathan Louis clinic/Philadelphia FIGHT, Philadelphia, PA.
- Main entry criteria:
  - HIV VL < 50 copies/ml on ART
  - CD4 count > 450/μL
  - Sensitivity of HIV reservoir to bNAb using the Monogram DNA assay (IC90 > 2.0 μM (3BC117) and <1.5 μM (10-1074)).
- Treatment (see Study Design):
  - Peg-IFN-α2b: 30 weekly doses (1 μg/kg sc, Pegtron, Merck, Inc.) in steps 2 and 3.
  - bNAb 3BC117 and 10-1074: 7 doses (30 mg/kg VV) in step 3.
  - First 26 weeks of ATI on immunotherapy (step 3; combination of bNAb plus peg-IFN-α2b).
- Primary endpoint: resumption of ART at week 38 of ATI (12 weeks after discontinuation of immunotherapy).
- Criteria for resuming ART were confirmed return of HIV-1 viremia greater than 1,500 copies for 6 consecutive weeks OR a confirmed CD4+ T-cell count <300 cells/μL (or CD4 % decrease greater than 50%).
- Statistical analysis. Protocol defined viral failure (retreatment criteria) was compared to that observed in non-NNRTI historical controls from prior ACTG studies (n=61) using the Mantel-Cox Log-rank test.

Study design

- 14 participants enrolled in arm 1 of the BEAT-2 study.
- All participants met bNAb sensitivity criteria and received pegylated IFN and the combination bNAb.

Results

Table 1. Participant characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Total (n)</th>
<th>Females (%)</th>
<th>Black/Other (%)</th>
<th>Baseline CD4 count (median [IQR])</th>
<th>Age (mean [range])</th>
<th>Integrate-based ART regimen (n [%])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14</td>
<td>2 (14%)</td>
<td>11 (79%)</td>
<td>869 (739 – 1079)</td>
<td>50 [21 – 66]</td>
<td>11 (79%)</td>
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HIV Reservoirs

- No detectable change from baseline at end of step 3 by IPDA (n=10, data not shown).

Virological control during ATI (Step 4) (primary endpoint)

- 4/10 did not meet restart criteria: 40% (95% CI 9.92-65.11%)

Virological control while on bNAb + IFN (Step3)

- During Immunotherapy (step 2/3): Proportion with confirmed HIV-1 RNA < 200 copies/ml: 12/14 (86% (95% CI 57-98%)
- See poster 352, CROI 22.

bNAb Resistance

- All participants on ART had sensitive HIV reservoir at baseline to both α2b and 3BNC117.
- 4/10 observed viral rebound during step 3 (at week X and Y).
- NIH criteria and no reportable SUSAR events were observed.

Safety

- 3 participants experienced infusion reactions during the administration of 3BC117 (chills), during step 2 with undetectable HIV-1 RNA (at w5 and w10).
- 2 participants experimented viral rebound during step 3 (at week X and Y).
- 2/10 (20%) maintained viral suppression after all treatments on ART.
- All participants upon rebound.

Conclusions

- Passive administration of a combination of bNAb plus peg-IFN-α2b in subjects with baseline sensitivity is safe and tolerable, and maintains viral suppression for 26 weeks in the absence of traditional ART in 86% participants.
- 4/10 (40%) of the participants did not meet restart criteria during ATI (all treatment discontinued).
- 2/10 (20%) maintained viral suppression after all treatment is discontinued.
- Viral resistance is detected in most of the participants upon rebound.
- The treatment with bNAb plus IFN is not associated with changes in reservoir size.

References


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