BEAT2 PRIMARY TRIAL OUTCOMES: PEG-IFN-A2B + 3BNC117 & 10-1074 IN CHRONIC HIV INFECTION

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BEAT-HIV

#431

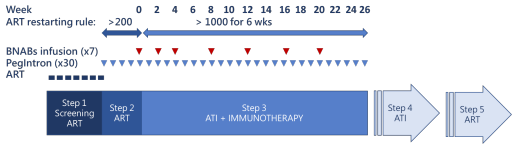
Introduction

- 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 (BNABs) 3BNC117 and 10-1074 maintains suppression during and ATI in approximately 80% n chronically infected individuals (4, 5).
- In the BEAT-2 study (NCT03588715), we evaluated the effectiveness of peg-IFN-α2b in combination with 3BNC117 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 bNaBs plus peg-IFN-α2b)

Methods

- **Participants**: 14 individuals assigned to arm 1 of (BEAT-2 study). Arm 2 was discontinued because of COVID
- **Participating centers**: University of PA and Jonathan Lax clinic/Philadelphia FIGHT, Philadelphia, PA
- **Main entry criteria**:
  - HIV VL < 50 copies/ml) on ART
  - CD4 count > 450/µl)
  - Sensitivity of HIV reservoir to bNabs using the Monogram DNA assay (IC90 < 2.0 µg/mL (3BNC117) and <1.5 µg/mL (10-1074)).
- **Treatment** (see Study Design):
  - Peg-IFN-α2b: 30 weekly doses (1 µg/kg sc, Pegintron, Merck, Inc.) in steps 2 and 3
  - bNabs 3BNC117: and 10-1074: 7 doses (30 mg/kg IV) in step 3
  - First 26 weeks of ATI on immunotherapy (step 3; (combination of bNaBs plus peg-IFN-α2b)
  - Primary end-point: resumption of ART at week 38 of ATI (12 weeks after discontinuation off immunotherapy).
  - Criteria for resuming ART were: confirmed return of HIV-1 viremia greater than 1,000 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

Baseline characteristics	
Total (n)	14
Females (n [%])	2 [14%]
Black/Other (n [%])	11 [79%]
Baseline CD4 count (median [IQR])	869 [739 – 1079]
Age (mean [range])	50 [31 – 60]
Integrase-based ART regimen (n [%])	11 [79%]

Safety

- 3 participants experienced infusion reactions during the administration of 3BNC117 (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)
- No treatment-related grade 3 or higher AEs and no reportable SUSAR events were observed.

Virological control while on bNabs + IFN (Step3)

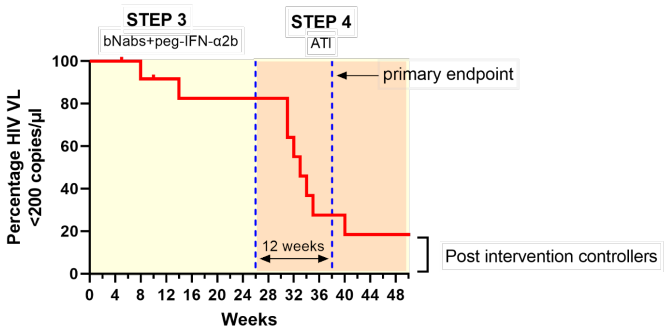
- During Immunotherapy (step 2/3): Proportion with confirmed HIV-1 RNA < 200 copies/ml : 12/14 86% (95% CI 57-98%) (See poster 352, CROI '22)

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%)**



Did not meet re-start criteria at week 38 (week 12 of no intervention)		Exact 95% CI
All participants*	4/12 = 33.33%	(9.92 - 65.11)
All participants entering Step 4	4/10 = 40%	(12.16, 73.76)
Virological rebound > 200 c/ml		
All participants	2/12 = 16.67%	(2.09, 48.41)
All participants entering Step 4	2/10 = 20%	(2.52, 55.61)

bNAb Resistance

- All participants on ART had sensitive HIV reservoir at baseline to both bNAbs
- Resistance developed in 8 of 12 persons that rebounded (8 to 10-1074 and 4 to 3BNC117)
- After re-suppression resistance was detected in 5 participants in PBMCs (3 in 10-1074 and 2 to 3BNC117)

Conclusions

- Passive administration of a combination of bNAbs 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 bNabs plus IFN is not associated with changes in reservoir size.

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