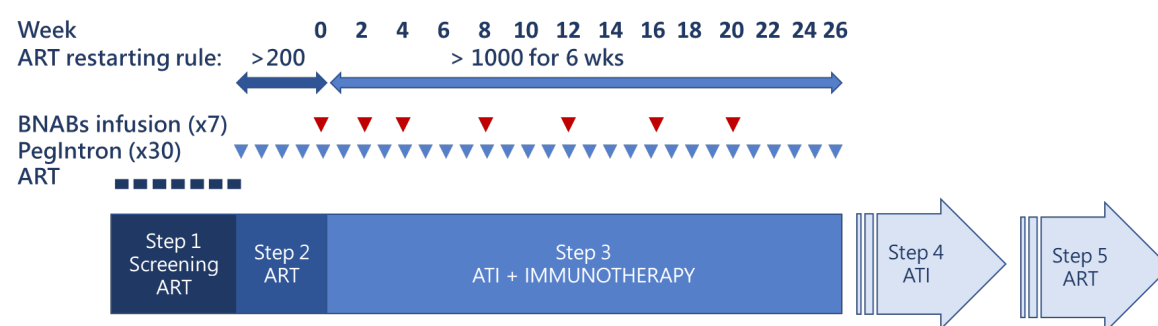


## Introduction

- We have previously reported similar efficacy of pegylated IFN- $\alpha$ 2a (1) and 2b (2,3) in supporting viral suppression in the course of ART interruption (ATI).
- A combination of broadly HIV-1-neutralizing monoclonal antibodies (BNABs) 3BNC117 and 10-1074 have also been shown to safely and effectively suppress HIV replication in viremic individual or during an analytical ART interruption (ATI) in chronically infected individuals (4, 5).
- In the BEAT-2 study we sought to evaluate the effectiveness of peg-IFN- $\alpha$ 2b in combination with 3BNC117 and 10-1074 or the antibody combination alone in suppressing HIV replication during ATI.

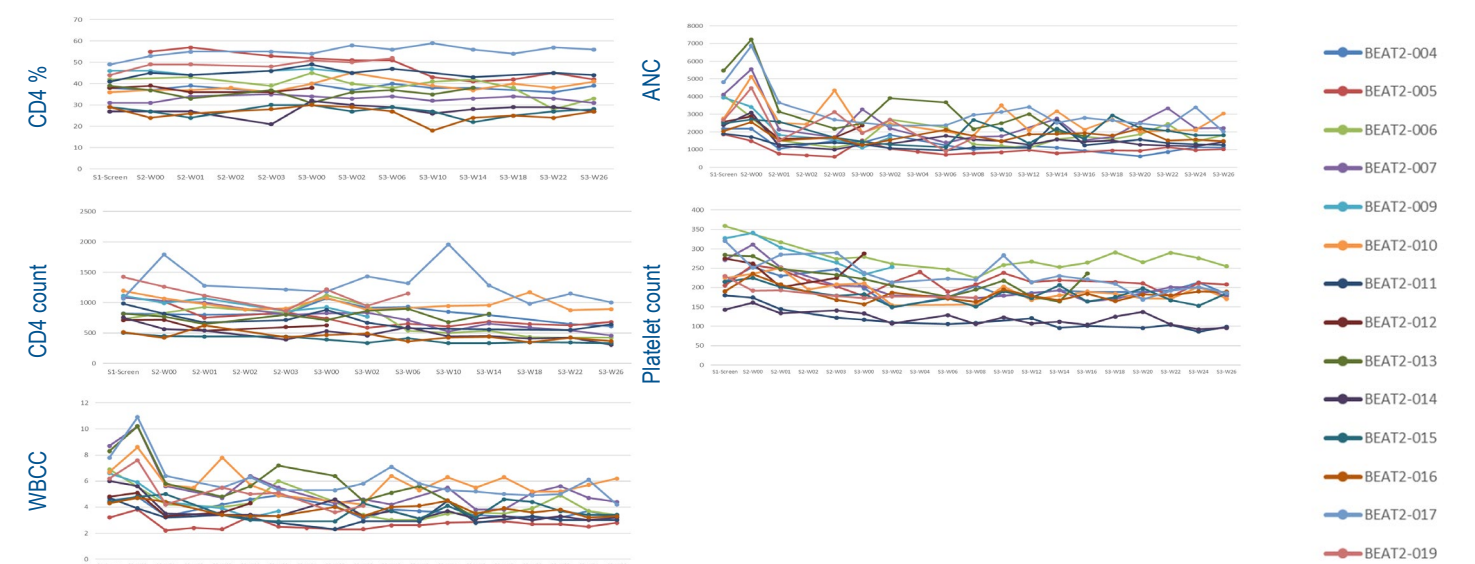
## 1. Study design



- 14 participants enrolled in group 1 of the BEAT-2 study (NCT03588715) were assessed.
- All participants received pegylated IFN and the combination bNAB

## 2. Safety

- Key indicators (CD4 count and %, ANC, WBCC, platelet count) were assessed at each clinical visit to monitor the safety of the treatment.
- 3 participants experienced infusion reactions during the administration of 3BNC117 (chills), 2 of them withdrew consent due to infusion chills during the intervention with undetectable HIV-1 RNA (at w5 and w10). The infusion reactions responded to a combination of diphenhydramine and low dose meperidine.
- No treatment-related grade 3 or higher AEs and no reportable SUSAR events were observed.



| Adverse event grade | N (%)                 |
|---------------------|-----------------------|
| 0                   | 5 (3.9%)              |
| 1                   | 79 (61.7%)            |
| 2                   | 42 (32.8%)            |
| 3                   | 2 (1.6%) <sup>a</sup> |
| 4/5                 | 0 (0.0%)              |
| Total               | 128                   |

## 4. Conclusions

- Passive administration of a combination of bNABs plus peg-IFN- $\alpha$ 2b in subjects with susceptible virus is safe and tolerable, and maintains viral suppression for 26 weeks in the absence of traditional ART in most participants.
- In our hands, baseline sensitivity testing identified participants that maintained suppression but did not predict viral rebound.
- We are currently evaluating the effects of this treatment on the HIV reservoir, as well as pharmacokinetics, immunological and virological parameters.
- These data provide the rationale for future HIV cure-related strategies utilizing BNABs and interferon-alpha2b.

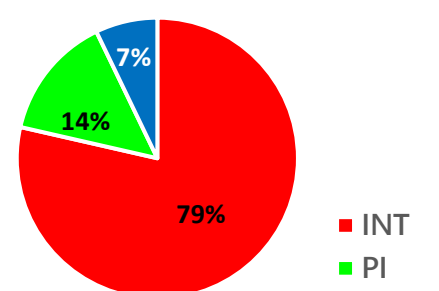
## Methods

- Participants:** 14 individuals assigned to arm 1 of NCT03588715 (BEAT-2 study, IND Number: 141578 )
- Participating clinics:** University of PA (Penn Presbyterian Medical Center and Perelman Center for Advanced Medicine) and Jonathan Lax clinic/Philadelphia FIGHT, Philadelphia, PA (IRB of record: University of PA)
- Main entry criteria:** receiving suppressive (HIV VL < 50 copies/ml) ART; CD4 count > 450/ $\mu$ l; sensitivity to Broadly HIV-1 Neutralizing Antibodies (BNABs) 3BNC117 and 10-1074 using the Monogram DNA assay (IC90 < 2.0  $\mu$ g/mL (3BNC117) and <1.5  $\mu$ g/mL (10-1074)).

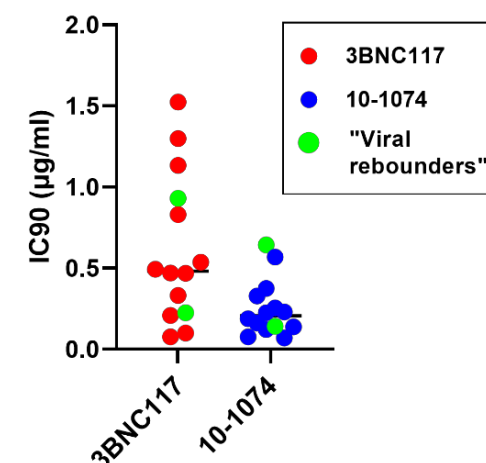
## 2. Participant characteristics

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

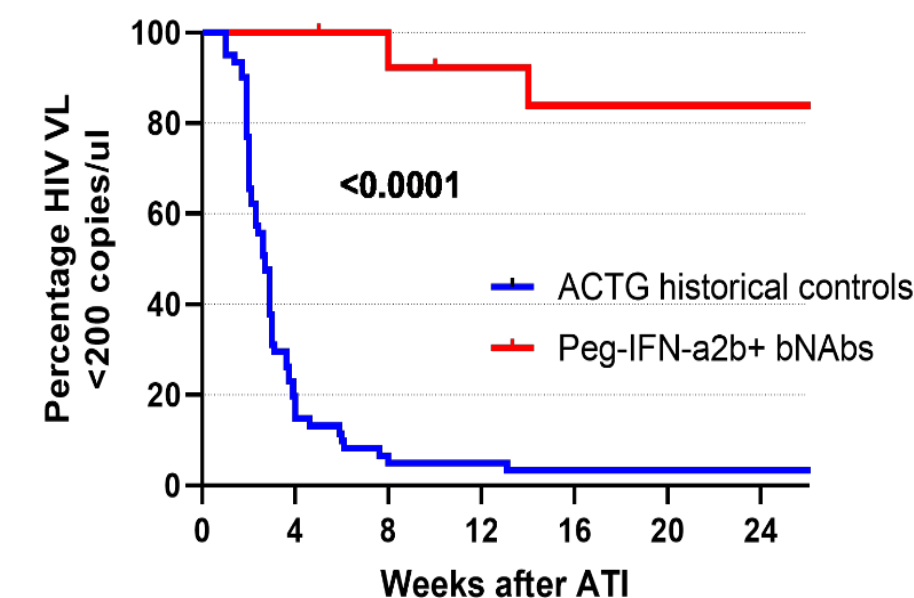
### ART regimens



### Baseline sensitivity to 3BNC117 and 10-1074 BNABs



## 3. Proportion of participants with confirmed HIV-1 RNA <200 copies/ml



- Two of 12 (17%) participants completing treatment had viral rebound (w8 and w14) during immunotherapy, with 10/14 completing 26 weeks of step 3.
- A greater proportion of BEAT-2 participants maintained viral suppression during the ATI compared to non-NNRTI-treated chronically infected historical controls from prior ACTG studies (n=61) (Log-rank Mantel-Cox test p<0.0001; HR (logrank) 16.7 95% CI 9.9-27-9)

## References

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Acknowledgements: Funded by BEAT-HIV UM1 AI26620, The Jacobs Fund of the Philadelphia Foundation, and Wistar Institute.

- Statistical analysis.** Protocol defined viral failure (VL  $\geq$  200 copies/ml) was compared to that observed in non-NNRTI historical controls from prior ACTG studies (n=61) using the Mantel-Cox Log-rank test