SUSCEPTIBILITY TO 3BNC117 AND 10-1074 IN ART SUPPRESSED CHRONICALLY INFECTED PERSONS

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Introduction

- Broadly neutralizing anti-HIV monoclonal antibodies (bNAbs) may have a role in the prevention and treatment of HIV.
- Preexisting resistance and the rapid development of resistance when used as monotherapy may limit their utility
- The PhenoSense mAb Assay is the only CLIA/CAP compliant screening test available to assess bNAb susceptibility in people with HIV infection.
- As part of the screening process for the BEAT2 trial we evaluated the sensitivity of the HIV reservoir in suppressed participants against two bNAbs: a CD4 binding antibody 3BNC117 and a V1-V2 loop binding antibody 10-1074

Subjects, Materials & Methods

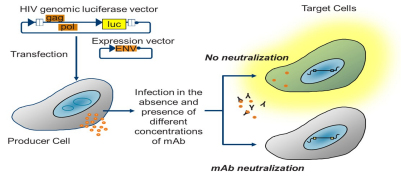
Study participants

- 61 HIV$^+$ individuals were screened.
- All participants were chronically suppressed on ART at <20 HIV-1 copies/ml and had CD4$^+$ T cell count ≥450 cells/mm^3 and nadir CD4$^+$ T cell count >200 cells/mm^3 .

Methods

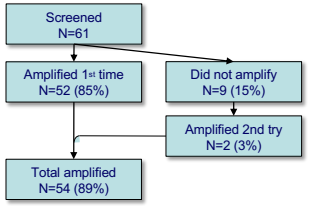
- The PhenoSense Monoclonal Antibody (mAb) Assay (Labcorp-Monogram Biosciences) assess the susceptibility of pseudo-virions bearing plasma or PMBC derived HIV-1 envelope proteins to anti-envelope mAbs.
- Full-length envelope sequences, amplified from PBMC-associated HIV DNA were cloned into an envelope expression vector.
- Pseudo-virions were then tested for neutralization sensitivity to 3BNC117 and 10-1074 bNAbs. The concentration of bNAb required to inhibit virus infectivity by 50%, 80%, 90% and 95% (IC50, IC80, IC90 and IC95, respectively), as well as the maximum percent inhibition (MPI) was assessed.
- Clinical cut-off values for neutralization sensitivity have not been established for the PhenoSense mAb Assay.
- For the BEAT2 study, the following exploratory values were utilized to define mAb sensitivity: IC90 < 2 µg/mL for 3BNC117 and < 1.5 µg/mL for 10-1074 and a maximum percent inhibition (MPI) > 98%.

Figure 1. PhenoSense Monoclonal Antibody (mAb) Assay



Results

Figure 2 Screening subjects and amplification results



- 9 (15%) were not amplifiable on first pass, ere not amplifiable, of those 2 amplified on a 2nd attempt

Table 1. Demographic information (n=61)

Ethnicity	Hispanic	3 (5%)
Race	Caucasian	8 (13%)
	Black	53 (87%)
Gender	Male	52 (85%)
	Female	9 (15%)
Age (median, IQR)		50 (40-57)

- Demographic characteristics were not associated with sensitivity to bNAb.

Figure 3. Distribution of IC90, , cut offs and percentage of isolates with IC90 above the 10-1074 and the 3BNC117 cutoff, and spearman correlation between bNAbs susceptibility

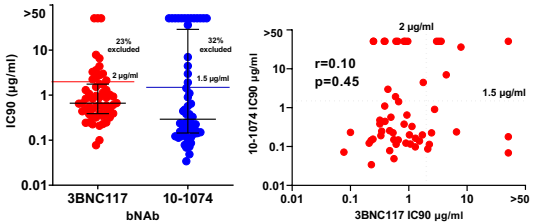
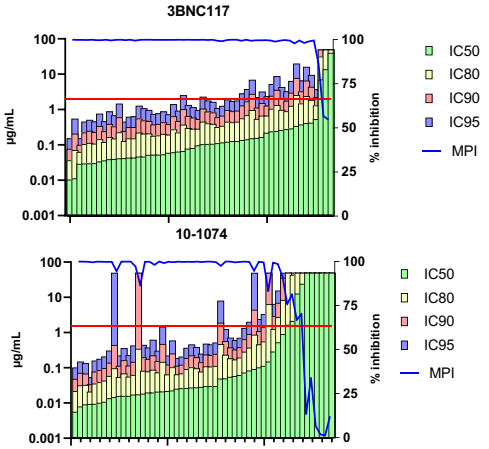


Figure 4. Distribution of IC50, IC80, IC90, IC95 and MPI of all isolates. The MPI values identify 10-1074 resistant isolates.



Conclusions

- 15% can not be amplified initially, reduced to 11% on second try
- Preexisting resistance was common
- Only 50% of the chronically infected, virologically suppressed individuals harbored virus sensitive to both 3BNC117 and 10-1074.
- Sensitivity of the two antibodies were independent of one another
- MPI values identify virus resistant to 101-1074
- Demographic characteristics were no associated with sensitivity to bNAbs.

Interpretation

- Our data can be used in sample size calculations for the rate of screening failure when using combination bNAbs for maintenance and curative strategies.
- As the reservoir of chronically infected individuals is a representation of the circulating and transmissible virus our data suggest that the combination of 2 bNABs will not neutralize infection in approximately 50% of potentially transmissible virus.

Future Direction

Definition and validation of the clinical correlates of bNAb susceptibility thresholds for therapeutic maintenance protocols and curative treatment strategies

References

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Acknowledgements and contact

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