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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Software for obtaining the sequencing data was MiSeq Control Software 2.6 2.1. Software for tracking the clinical samples was IRIS by iMedRIS.
Data analysis	- Pharmacokinetics analysis was performed with Phoenix WinNonlin Build 8 (Certara). - Effects of antibody combination on time to viral rebound was compared to previous published data with antibody monotherapy or in the antibody treatment. R (version 3.4.2) with the package coin (version 1.2-2) was used for exact Wilcoxon tests in the presence of ties, as well as flexsurv (version 1.1) and fitdistrplus (version 1.0-9) for parametric survival regression. The weighted log-rank test was implemented in Matlab (version R2018a). Class probabilities were estimated with a lasso logistic regression model (Matlab function lassoglm) using five values for lambda and threefold cross-validation. - Analysis of HIV-1 envelope sequences was performed at two time points during viral suppression and at viral rebound. Nucleotide alignments of intact env sequences were translation-aligned using ClustalW v2.1. Maximum likelihood phylogenetic trees were then generated from these alignments with PhyML v3.1. Multiple alignment of nucleotide sequences guided by amino acid translations of env sequences was performed by TranslatorX (http://translatorx.co.uk/). Latent and rebound sequences were analyzed for the presence of recombination using the 3SEQ recombination algorithm (http://mol.ax/software/3seq/). - Levels of antibody in serum by ELISA were calculated with Softmax Pro, v5.4.5 (Molecular Devices).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The sequences will be available in GenBank upon publication with the accession numbers MH575375-MH576416.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	One of the primary outcomes of the study was the percentage of participants who met ART reinitiation criteria prior to week 8. A one-sided upper confidence interval was constructed for the probability of meeting ART reinitiation criteria using the Clopper-Pearson method. As such, a sample size of 15 HIV-infected individuals would allow the rejection of the null hypothesis (rate = 0.85) with 80% power for an effect size equal or higher than 0.33, if at least 6 out of 15 participants enrolled in Group 2 did not experience viral rebound by week 8 (2 weeks after last mAb infusion). If 10 or more participants experienced viral rebound prior to week 5 [5 weeks after ART interruption and weeks after second 3BNC117 and 10-1074 infusions], additional participants would not undergo ART interruption.
Data exclusions	No data were excluded.
Replication	This study was a clinical trial and the analyses were performed on individual trial participants. Experiments did not include replicates as all participants and data points are unique. All available data is included in the manuscript.
Randomization	The study was single arm.
Blinding	The study was open label.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	The study included the analyses of blood samples collected from enrolled HIV-infected trial participants. These samples were obtained under an IRB approved protocol for the purposes of this study and associated analytical plan, therefore they cannot be shared without appropriate IRB review and future studies would be limited to what was covered under the original informed consent.

Antibodies

Antibodies used

3BNC117 and 10-1074 are investigational anti-HIV-1 neutralizing antibodies manufactured for clinical use. They are being investigated under US FDA INDs 118225 and 123713.

Antibodies for the Ab detection in serum by ELISA included:
- Anti-ID 3BNC117: DHVI Protein Production Facility
  Lot #: 3BNC 29Nov2017
  Dilution: 4 ug/ml coating concentration
  Clone name: anti-ID 1F1-2E3 mAb
- Anti-ID 10-1074: DHVI Protein Production Facility
  Lot #: 3Aug2016
  Dilution: 2 ug/ml coating concentration
  Clone name: anti-ID 3A1-4E11 mAb
- (HRP)-conjugated mouse anti-human IgG kappa-chain-specific antibody (Abcam), Catalog #: ab79115
  Dilution: 1:15,000
  Clone name: SB81a

Validation

3BNC117 and 10-1074 that were administered to the participants were manufactured by Celldex Therapeutics under Good Manufacturing Practice and have been fully characterized in terms of biophysical properties and potency (INDs 118225 and 123713). Both drug products are under long term stability monitoring.
Anti-idiotypic antibodies from the Duke Human Vaccine Institute (DHVI) Protein Production facility have been validated for their use in ELISA against human antibodies.
HRP-mouse monoclonal anti-human IgG kappa-chain-specific antibody has been validated for its use in ELISA and ICC/IF, reactivity against Human Kappa Chain. This product has been referenced in Scheid JF et al. Nature 535:556-60 (2016).

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

MOLT-4/CCR5 cell lines obtained from NIH AIDS Reagent Program, catalog number 4984.
A stable hibridoma cell line from the Duke Protein Production Facility was utilized for the production of anti-idiotypic mAbs for the quantification of Ab levels in serum by ELISA.

Authentication

The cells were analyzed by flow cytometry to determine the levels of CCR5 and CD4 expression.

Mycoplasma contamination

The cell lines were not tested for mycoplasma contamination.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used.

Human research participants

Policy information about studies involving human research participants

Population characteristics

Eligible participants were adults aged 18-65 years, HIV-1-infected, on ART for a minimum of 24 months, with plasma HIV-1 RNA levels of 50 copies/ml for at least 18 months (one viral blip of >50 but <500 copies/ml during this 18-month period was allowed), plasma HIV-1 RNA levels of 20 copies/ml at the screening visit, and a current CD4+ T cell count 500 cells/µl.

Recruitment

Participants were pre-screened for sensitivity of latent proviruses against 3BNC117 and 10-1074 antibodies by bulk PBMC viral outgrowth. Sensitivity was defined as an IC50 <2 µg/ml for both 3BNC117 and 10-1074 against outgrowth virus. Participants harboring sensitive viruses were invited for screening and were enrolled in the study sequentially. Participants were enrolled at two clinical sites at the Rockefeller University (New York, US) and Cologne University Hospital (Germany).