Measuring the impact of early 3BNC117 intervention at ART initiation on the productive reservoir in a cohort of diverse viral subtypes: results from the VIP-SPOT assay in the eCLEAR trial

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A patent application on the VIP-SPOT assay has been filed (US patent 22/30875).
Fine-tuning “shock-and-kill” therapeutic strategies

Understanding the establishment of the viral reservoir is key to designing effective HIV cure strategies.
The eCLEAR Trial: study design

- Shock & kill intervention at the time of ART initiation

- Gunst et al, Nat Med, Oct 2022. doi.org/10.1038/s41591-022-02023-7

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The eCLEAR Trial: main results

- 3BNC117 treatment (with or without RMD) **enhanced plasma HIV-1 RNA decay** rates.
- 3BNC117 treatment accelerated **clearance of active infected cells** in the first 10 days of ART.
- After 1 year, early 3BNC117+RMD was associated with enhanced HIV-1 Gag-specific CD8+ T cell immunity.
- These effects of 3BNC117 were most pronounced in individuals whose pre-ART plasma HIV-1 envelope sequences were antibody sensitive.

*Gunst. et al, Nat Med, Oct 2022. doi.org/10.1038/s41591-022-02023-7*
Measuring the impact on the viral reservoir

- Which is our target population in a shock-and-kill intervention?
Measuring the impact on the viral reservoir

- Which is our target population in a shock-and-kill intervention?
- Quantify the frequency of peripheral CD4+ T cells able to reactivate and produce viral proteins (Gag).
Evaluating the in vivo clearance of HIV-1 infected cells by VIP-SPOT

- Frequency of cells able to reactivate and produce viral protein is 1000-fold lower than total HIV DNA.
- Most proviruses (even intact) are not able to reactivate productively.
- Correlation between VIP-SPOT assay and other virological parameters at baseline.

Results 1: Frequency of HIV antigen producing cells at baseline
Only half of the individuals (49%) had HIV-1 subtype B infection while the rest of the participants had a broad range of other HIV-1 subtypes and recombinant forms.

No differences in the frequency of detection of HIV-Ag producing cells were observed between B and non-B HIV-1 subtypes.
Only half of the individuals (49%) had HIV-1 subtype B infection while the rest of the participants had a broad range of other HIV-1 subtypes and recombinant forms.

No differences in the frequency of detection of HIV-Ag producing cells were observed between B and non-B HIV-1 subtypes.
After 1 year on treatment, the frequency of HIV antigen producing cells decreased significantly in all study groups.
Results 3: Longitudinal changes throughout the study period

✓ After 1 year on treatment, the frequency of HIV antigen producing cells decreased significantly in all study groups.

✓ A trend towards greater undetectability was observed in participants receiving 3BNC117, especially in individuals whose pre-ART plasma viruses were sensitive to the antibody.

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KEY QUESTION:
How to evaluate the effectiveness of the shock-and kill interventions aimed at impacting the viral reservoir.

KEY FINDINGS:
- The novel **VIP-SPOT assay** is useful to evaluate the impact of shock-and-kill strategies on the productive reservoir **regardless of HIV-1 subtype**.
- The results evidenced the **clearance of CD4+ cells capable of producing HIV-1 protein** upon ART initiation.

NEXT STEPS:
More work is needed to define the dynamics of this fraction of the reservoir to understand how it is established and whether it might be used as a biomarker of effectiveness of these kind of interventions.
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