Broadly neutralizing antibody treatment found to reduce viral reservoir in some infants with HIV-1

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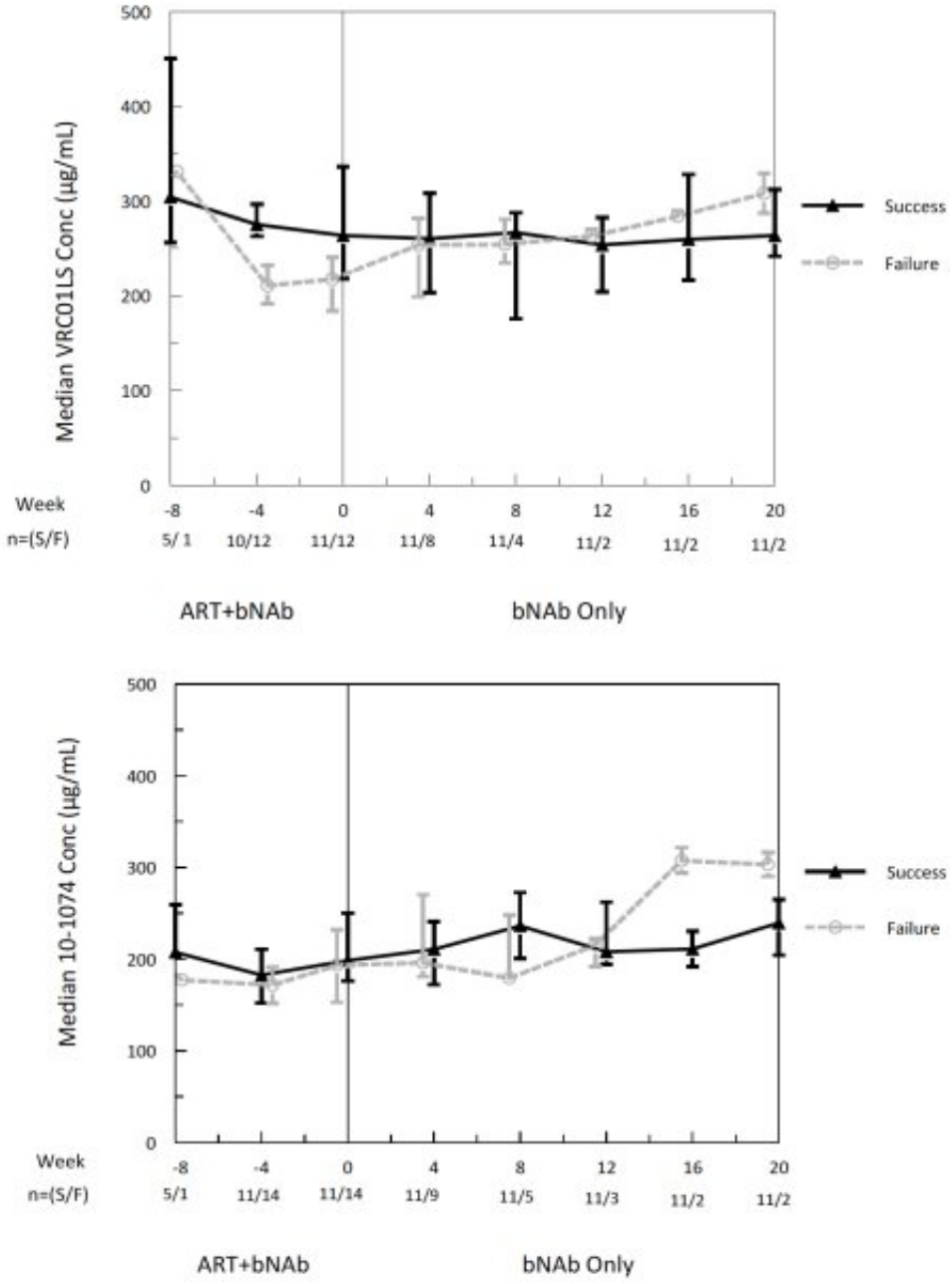

Median trough concentrations of VRC01LS and 10-1074, showing the overlap period with antiretroviral therapy (ART) and the broadly neutralizing antibody (bNAb)- only step. Trough VRC01LS and 10-1074 concentrations during ART/bNAb overlap and in the bNAb-only step are shown. Bars indicate interquartile range (IQR). The immediate 8 weeks prior to the bNAb-only step are included for the six children with longer (32 weeks) ART/bNAb overlap. Conc, concentration; S, success; F, failure. Credit: *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.adh0004

Research led by the Department of Immunology and Infectious Diseases, Harvard T. H. Chan School of Public Health, Boston, has found a potentially better alternative to standard antiretroviral treatment for controlling HIV-1 replication with additional benefits against HIV-1 reservoirs.

In the paper, "Broadly neutralizing antibody treatment maintained HIV suppression in children with favorable reservoir characteristics in Botswana," published in *Science Translational Medicine*, the researchers detail a prospective clinical trial on children in Botswana, Africa, born with HIV-1. A Focus article on the research by Maud Mavigner and Ann Chahroudi was published in the same journal issue.

In the study, two broadly neutralizing antibodies (bNAbs) were given to children who had been on standard antiretroviral treatment since birth and continued treatment for at least 96 weeks.

Both bNAbs were dosed intravenously every four weeks, overlapping with antiretroviral treatment for at least eight weeks and then continued for up to 24 weeks or until HIV-1 RNA rose above 400 copies per milliliter without antiretroviral treatment.

Eleven (44%) children maintained HIV-1 RNA below 400 copies per milliliter through 24 weeks on bNAb-only treatment, and 14 (56%) had detectable viremia above 400 copies per milliliter at a median of 4 weeks and returned to antiretroviral therapy.

HIV-1 is difficult to cure due to reservoirs of the virus that hide in tissue compartments and are established rapidly upon infection, allowing the virus to avoid targeting and continually reinfecting the host. Antiretroviral therapy can target circulating virus load but does not

eliminate the fortified reservoirs.

The authors found that the infants given the bNAbs treatment had more favorable HIV-1 reservoir characteristics. While not cured, it did show that the therapy can neutralize some of the fortified viral load, which then reduces the future reinfection capacity of the virus.

Broadly neutralizing antibodies are an emerging treatment option for people living with HIV-1 with the potential to maintain HIV-1 RNA suppression. One of the benefits of the treatment is that it can be administered monthly instead of the daily use of antiretroviral treatment.

This could improve compliance consistency and reduce long-term toxicity associated with prolonged antiretroviral treatment. The current findings, supporting the depletion of residual viral reservoirs, suggest that bNAbs could become a better option for viral control in some individuals.

Next, researchers need to find out why it only worked well in some individuals and not others. Future studies using more formulations of bNAb combinations with greater breadth and potency are needed.

More information: Roger L. Shapiro et al, Broadly neutralizing antibody treatment maintained HIV suppression in children with favorable reservoir characteristics in Botswana, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.adh0004

Maud Mavigner et al, Broadly neutralizing antibodies: "The next thing" to treat children with HIV?, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.adi0293