A phase 1 trial of the combination of 3BNC117 and 10-1074 in HIV-uninfected adults


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BACKGROUND

• Broadly neutralizing anti-HIV-1 antibodies are currently being developed for the treatment and prevention of HIV infection.
• Effective broadly neutralizing antibody therapy or prophylaxis will likely require a combination of antibodies to increase breadth and potency and prevent the emergence of resistance.
• 3BNC117 is a broadly neutralizing CD4-binding site antibody that has been shown to suppress viremia and delay viral rebound.1,2
• 10-1074 is a broadly neutralizing antibody that targets the V3-glycan and has also been shown to suppress viremia.3
• Participants in each group were randomized 3:1 to Groups 2 and 3 received 3 doses of both antibodies 8 weeks apart at 3 mg/kg and 10 mg/kg, respectively.
• Both antibodies have been well tolerated when administered alone.
• This study was performed to evaluate the combination of these 2 antibodies in HIV-uninfected individuals.

STUDY OBJECTIVES

• To evaluate the safety and tolerability of the combination of 3BNC117 and 10-1074 in HIV-uninfected individuals.
• To evaluate the pharmacokinetics of the combination of 3BNC117 and 10-1074 in HIV-uninfected individuals.

STUDY DESIGN

• Placebo-controlled, double blind, randomized trial consisting of 3 groups of 6 participants. The study design is shown in Figure 1.
• All participants were enrolled at The Rockefeller University, NY, USA.
• Group 1 received a single dose of both antibodies at 10 mg/kg.
• Groups 2 and 3 received 3 doses of both antibodies 8 weeks apart at 3 mg/kg and 10 mg/kg, respectively.
• Participants in each group were randomized 3:1 to receive the study products or placebo, administered by intravenous infusion.
• Enrollment in each group only began following the availability of 28-day safety data from all participants in the prior group.
• Each antibody was administered over 60 minutes. The second antibody was infused following completion of first infusion.
• Main inclusion criteria: age 18 – 65, behavior consistent with low risk of exposure to HIV.
• Main exclusion criteria: HIV infection, chronic hepatitis B or C, STI within 12 months of enrollment, clinically significant acute or chronic medical condition.

RESULTS

• Twenty-four participants were enrolled. Demographic characteristics for the enrolled participants are shown in Table 1.
• All follow up visits have been completed at this time, but the study remains blinded.
• Although the study remains blinded, few adverse events were reported overall. Reactogenicity included 2 instances of headache and 1 of fatigue, all graded as mild, and 1 instance of fever, graded as moderate.
• Additional adverse events considered at least possibly related to the infusions included one instance of elevated bilirubin and a URI.
• Overall, the safety profile of the antibody combination was similar to the safety profile of either antibody administered alone.
• Serum 3BNC117 and 10-1074 levels were measured by anti-idiotype ELISA and compared to results obtained in prior trials of each antibody administered alone (Figures 2 and 3).
• Pharmacokinetic analyses have been performed by non-linear mixed effects modeling for Groups 1 and 2.
• The average half-life of 3BNC117 was 18.4 and 15.6 for Group 1 and 2 respectively. (Table 2)
• The average half-life of 10-1074 was 22.3 and 20.3 for Group 1 and 2 respectively. (Table 3)
• Pharmacokinetic analyses for Group 3 is ongoing.
• Serum neutralizing activity against selected viral strains correlated with measured antibody levels.

CONCLUSIONS

• The broadly neutralizing anti-HIV-1 antibodies 3BNC117 and 10-1074 were well tolerated when administered in combination.
• Preliminary pharmacokinetic analyses demonstrate that the half-life of each antibody administered in combination was similar to the half-lives observed for each antibody administered alone.
• These results support the continued development of combinations of broadly neutralizing antibodies for the treatment and prevention of HIV-1 infection.

REFERENCES


ACKNOWLEDGEMENTS

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• M.C.N. is a Howard Hughes Medical Investigator.

**Table 1. Demographic characteristics of participants**

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