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Passive transfer of neutralizing monoclonal antibody KD-247 reduces plasma viral load in patients chronically infected with HIV-1 : A Phase-1b clinical study of a humanized monoclonal antibody KD-247 (KD-1002).

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Background: KD-247 is a humanized monoclonal antibody (mAb) with potent neutralizing activity. The epitope recognized by the mAb was mapped to IGPGRA of the V3-tip that covers about a half of subtype B. The objectives of this Phase 1b study were to evaluate the safety and tolerability of 3 infusions of KD-247 over 2 weeks in HIV-1 seropositive individuals, to determine the pharmacokinetic (PK) parameters when administered as above and to assess the effect of KD-247 infusions on plasma HIV-1RNA load and on $CD4^+$ T cell counts.

Methods: A Phase 1, double-blinded, placebo-controlled, dose escalation cohort study of KD-247 in asymptomatic HIV-1 seropositive individuals who did not currently need antiretroviral therapy. Eligible subjects were randomized to 1 of 3 cohorts to receive 3 infusions of 4, 8, or 16 mg/kg of KD-247 or placebo over a 2-week period. A minimum of 6 active-agent subjects and 3 placebo subjects for each dose cohort were to complete 2 weeks of infusions. Dose escalation proceeded only after safety data through Day 18 for all subjects in the lower-dose cohort were reviewed.

Results: A total of 30 subjects were enrolled in the study with 20 receiving KD-247 and 10 subjects receiving placebo. KD-247 was safe and well tolerated and we observed moderate but significant decreases in HIV-RNA in the 8 and 16 mg/kg cohorts of KD-247. We observed two in six cases of 16 mg/kg cohort that achieved >1 log reduction of HIV-RNA and long-term suppression of viral load for one patient despite significant decrease in plasma concentration of the antibodies, suggesting that effects other than neutralization or loss of fitness of the virus with the mutations acquired. Two subjects in the 16 mg/kg cohort had selections and/or mutations in the V3-tip region that suggested neutralization escape. No tropism shifts was observed for these mutants.

Conclusion: Results should be interpreted with caution due to the small sample size. However, these results taken together, suggest that neutralizing mAbs would be a promising candidate of intensification therapy added-on to the current suppressive cART aiming toward functional cure of the disease.