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Research Article

Evaluating the Role of IgG1 Broadly Neutralizing Antibodies as Alternatives to Combination Antiretroviral Therapy in HIV Treatment

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Abstract

Human immunodeficiency virus (HIV) is a sexually transmitted infection which significantly impairs the immune system's ability to mount a defense against pathogens. While there is currently no cure, the conventional therapy is an anti-retroviral combination therapy consisting of zidovudine, lamivudine, and indinavir. Following the emergence of monoclonal antibody therapies, the IgG1 broadly neutralizing antibody (bnAb) asdirected at the HIV type 1 (HIV-1) envelope protein CD4-binding site, VRC01, has been discussed as a potential therapy for HIV. A systematic review was then conducted utilizing a research study of patients which had HIV and were treated with combined antiretroviral compared to one in which the patients were treated with VRC01. Patients who were treated with VRC01 experienced greater reductions in HIV viral load than did those who were treated with the combined antiretroviral therapy. This alludes to the fact that the envelope protein CD4-binding of the HIV virus prior to its entry into the cell is much more heavily implicated in the disease's pathogenesis than its reverse transcription or integration into the host's genome.

While a preliminary evaluation of the two agents seems to suggest that VRC01 is superior to conventional combined antiretroviral therapy, it must be noted that the study which subjected participants to VRC01 had an incredibly small sample size. More studies utilizing greater amounts of participants and over longer courses of time must be conducted to make this determination with more confidence.

Kew Words: human immunodeficiency virus; monoclonal antibodies, zidovudineindinavir: lamivudine: vrc

Introduction

Worldwide, the majority of new HIV-1 infections occur through mu:osal exposures, including sexual transmission as well as perinatally acquired infections. Mucosal fluids contain different classes of immunoglobulins: IgM, IgG, and IgH. Depending on the mucosal fluid, either IgG or IgH predominate (1). In Humans, IgA exists as two isotopes, IgA-1 and IgA-2 (2). This article will seek to evaluate the role of IgG-1 neutralizing antibodies as alternative to combination antiretroviral therapy in HIV treatment.

Methods:

For the study that treated participants with VRC01(3): This was a phase 1 study which was designed to evaluate the safety, pharmacokinetics, and impact on HIV-1 viral reservoir in patients. 27 people with the diagnosis of HIV were utilized as participants for this study (n=27). Participants received two VC01 infusions (1–40 mg/kg IV or 5 mg/kg SC) 28 days apart. The change in viral load was tracked amongst participants and a statistical analysis was subsequently performed. For the study that treated participants with conventional antiretroviral therapy (4): Fifteen patients diagnosed with HIV that had a high viral load or disease progression under their prior antiretroviral therapy were switched to zidovudine/lamivudine/indinavir (Group A, n = 10) or stavudine/lamivudine/indinavir (Group B, n = 5). Serial determinations of viral load and CD4 cells were performed at both 3 and 6 months.

Results:

For the study that treated participants with VRC01(3): VRC01 did not reduce the viral reservoir in ART-treated participants with undetected viremia. In ART-untreated individuals, 75% (6/8) showed decreased plasma viremia (1.1 to 1.8 log10 reduction). Viral load was decreased by 12- to 59-fold in these individuals. Two participants with low viral loads achieved undetectable levels for over 20 days. For the study that treated participants with conventional antiretroviral therapy(4): In Group A the median of the relative increase of CD4 cells was 37% after 3 months and 57% after 6 months (P = 0.002); in Group B the medians of the relative increase of CD4 cells were 145 and 163% (not significant), respectively. The median reduction of the viral load was 0.6 log after 3 months and 0.8 log after 6

months in Group A and 2.5 and 2.4 log after 3 and 6 months in Group B, respectively. After 3 and 6 months 3 of 10 patients in Group A and 3 of 5 patients in Group B had viral load reductions below the detection limit of the assay.

Treatment	Reduction in Viral Load (%)
VRC01	~90%
Conventional	84.2%

Table 1: The above table depicts the reduction in viral load for those participants who were treated with VRC01 compared to those who were treated with conventional antiretroviral therapy.

Conclusion:

Both studies suggest that VRC01 and conventional antiretroviral therapy have significant reductions on HIV viral load. However, those who were treated with VRC01 achieved a greater reduction in viral load than those who were treated with conventional antiretroviral therapy. This correlates to the CD4 receptor's interaction with the HIV gp120 envelope protein being a more vital step in the pathogenesis of HIV compared to the integration of the virus into the host genome or its protease-mediated cleavage of polyproteins. Longitudinal studies conducted throughout longer periods of time need to be done to assess if these effects are longstanding and if there are any potential side effects that might be of concern with these treatments. Studies assessing the comparative efficacies of both treatments given numerous HIV strains must also need to be done. Also studies with larger sample sizes and controlling for more variables is necessary to decrease the likelihood of confounding variables influencing results. Since IgG1 broadly neutralizing antibodies are not the conventional treatment for HIV, further barriers such as insurance coverage may present significant obstacles for patients as well.

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