A New Anti-HIV Drug Rukobia: A Literature Review

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Abstract

About 37 million people are diagnosed with HIV worldwide. Antiretroviral drugs can be implemented to treat and delay effects, however HIV is highly susceptible to mutation, resulting in difficulties with treatment. In HIV patients with multi-drug resistance, an antiretroviral drug with a novel mechanism may be necessary. Rukobia (Fostemsavir), can be beneficial in these types of patients. According to the BRIGHTE study (n=371 [99 non randomized participants]), patients who received rukobia had a notably greater decrease in HIV-1 RNA levels, than those who received the placebo. This research project will examine the role of rukobia in the body in respects to the role of glycoproteins in biological processes, the mechanistic details of the types of immune cells that are protected by rukobia from HIV viral attachment, and how rukobia can be combined with existing anti-HIV drugs to increase treatment efficacy.

Background Information

HIV-1 is a part of the lentivirus family of animal retroviruses. The HIV-1 life cycle can typically be divided into two phases of replication. The early phase consists of attachment of the virion at the surface of the host cell, and incorporation of proviral DNA into the host genome. The late phase begins with budding and maturation facilitate HIV to release into the bloodstream and infect other cells.

The Life Cycle of HIV

The cycle begins with binding and fusion, where HIV attaches to the T-helper cell and releases genetic material into the cell. Reverse transcription occurs; viral RNA are transcribed into DNA. Following this, transcription and translation allow HIV to incorporate its viral genome into the host cell to produce gene expression and productive infection. Assembly, budding and maturation facilitate HIV to release into the bloodstream and infect other cells.

Method

Participants had already undergone at least four of the six antiretroviral medications, which resulted in failure. The first group of 272 patients were assigned in a 3:1 ratio, where they were given either rukobia (600 mg twice daily) or a placebo along with their current failing regimen of medication for 8 days. After day 8, all patients received rukobia. The second group consisted of 99 patients with no approved drug regimen. These patients received rukobia (600 mg twice daily), with the option of partaking in other trials for antiretroviral drugs.

Results

On day 8, the mean decrease in HIV-1 RNA levels was 0.79 log10 copies per milliliter in the group receiving rukobia. The placebo group read 0.17 log10 copies per milliliter. At week 48, a virologic response was detected in 38% of the patients in the nonrandomized group. The mean of the CD4+ t-cell count was 139 cells per cubic millimeter and approximately 64 cells per cubic millimeter. In the randomized group, gp120 substitution was noticed in 43% of patients who underwent virologic failure. After 24 weeks 53% of patients receiving fostemsavir along with other antiretrovirals achieved HIV-RNA suppression, where levels of HIV were low enough to be considered undetectable. After 96 weeks, 60% of patients continued to have HIV-RNA suppression.

Summary & future perspectives

Spike protein gp120 aids in the attachment to CD4 receptors to initiate HIV infection. Due to multidrug resistance, HIV can be extremely difficult to treat. Rukobia is a beneficial option for these types of patients. Regarding future possibilities, the presence of CCR5, a chemokine receptor involved in the entry of HIV-1 and the cellular spread, can be examined. Anti-CC45 immunity was found in patients with HIV-1. Studies have shown that these antibodies have a correlation with HIV-1 disease control. This suggests the possibility that inhibiting CC45 may be an effective way to control the development of HIV-1.

References


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