ABSTRACT

At present, there is still no cure for HIV. Drug combinations have, however, shown success in keeping HIV under control by decreasing viral load while increasing CD4 count. This research project focuses on describing and discussing major drugs used for HIV combination treatment in terms of the mechanism of action for each drug and what drives the combined successful therapeutic effect in reducing viral load and increasing CD4 count. Specifically, research will focus on the following three drugs: Bictegravir, Emtricitabine, and Tenofovir alafenamide. All three play a role in reducing HIV viral load.

BACKGROUND

Human Immunodeficiency Virus Type 1 (HIV-1) is the causative agent of one of the most devastating infectious diseases we have today, called Acquired Immune Deficiency Syndrome (AIDS). HIV infection leads to low levels of CD4+ T-cells by finding white blood cells, called CD4 cells. HIV gets inside the CD4 cell and makes copies of itself, whilst killing the CD4 cell and the new HIV continue the cycle. When CD4+ T cell numbers are below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to infections, leading to the development of AIDS. The management of HIV/AIDS includes the use of antiretroviral drugs. Bictegravir can help increase the number of CD4 T-cells found in the blood which is vital for people with HIV, due to their already compromised immune systems.

SIGNALING PATHWAY

The three combined drugs that make up Bictegravir are; Bictegravir, Emtricitabine, and Tenofovir alafenamide. All three play a role in reducing HIV viral load. Bictegravir contained in Biktarvy is an integrase strand transfer inhibitor (INSTI). The goal of a viral enzyme is to insert itself into the viral genome of the host cell. Bictegravir prevents the replication of the HIV-1 virus by blocking HIV-1 integrase, the enzyme required for replication of HIV virus. It also blocks the formation and propagation of HIV-1 provirus; which is the genome of the host cell containing the genetic material of HIV. Emtricitabine is a synthetic Nucleoside reverse transcriptase inhibitors (NRTI) that blocks the mechanism of HIV-1 reverse transcriptase. It is present in the form of 5’-triphosphate. It integrates itself into the developing viral DNA, which results in chain termination. Tenofovir alafenamide is a second form of nucleoside reverse transcriptase inhibitors (NRTI) present in Biktarvy. It inhibits HIV-1 replication by being integrated with the viral DNA resulting in DNA chain-termination.

METHODS & RESULTS

The methods that were to study if Bictegravir has a high efficacy in reducing HIV viral load and increasing CD4+ cell count were mainly clinical trials. I looked at multiple trials conducted throughout the last four years. FDA approval for Biktarvy was based on data obtained from four ongoing Phase III clinical studies. Biktarvy was tested in adults with no antiretroviral treatment history (Trial 1489) as well as in virologically suppressed adults in another two studies, which switched to Bictegravir (Trial 1490). The results were published in 2019. After 48 weeks, only 1% of patients from Trial 1489, had HIV-1 RNA ≥ 50 copies/mL. In Trials 1489 and 1490, the mean increase from baseline in CD4+ count at Week 48 was 233 and 229 cells per mm³ in the Biktarvy and ABC/DTG/3TC groups, respectively, and 201 and 188 cells per mm³ in the Biktarvy+DTG+ FTC/TAF groups, respectively. The mean change from baseline in CD4+ count at Week 48 was 25 cells per mm³ in patients who switched to Biktarvy and 0 cells per mm³ in patients who stayed on their baseline regimen.

SUMMARY & FUTURE PROSPECTS

In majority of the world, HIV has become a chronic condition where progression to AIDS is very rare. HIV latency, and the resulting reservoir of CD4+ T cells, dendritic cells, as well as macrophages, is the main barrier to eradication of the virus. Biktarvy has successfully been able to prevent transmission through sexual contact. This is because, when an HIV-positive person has a consistently undetectable viral load (<50 copies/ml) due to antiretroviral treatment, they cannot pass the virus to anyone else, and have practically untraceable amounts of HIV in their body. Additionally, during the Bictegravir clinical trials, zero adults new to treatment developed drug resistance to Bictegravir through three years. It is important to note that Bictegravir does not promise to "cure" HIV and completely eradicate it from the body. There are still traces of the virus found mainly in the gut lining and tissue that are almost impossible to kill. However, with further advancements it may be possible to eliminate HIV completely.

REFERENCES


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