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Letter to the Editor

Breaking barriers in HIV treatment: the game-changing impact of lenacapavir

Sir,

HIV is a lentivirus that selectively targets and infects CD4 cells, which are integral to the immune system. Through viral integration and replication, infected cells are gradually destroyed, leading to a weakened immune system and an increased susceptibility to illnesses. The HIV epidemic has resulted in approximately 40.1 million deaths and 84.2 million infections to date, with 38.4 million individuals living with HIV as of the end of 2021. The estimated global prevalence of HIV in adults aged 15 to 49 is 0.7%.[1]

Antiretroviral drugs, which fall into seven main categories, are utilized for HIV treatment. A combination of drugs is typically prescribed to combat the virus through different mechanisms and decrease the likelihood of resistance development. Three drugs from two categories are usually recommended, with some options containing three drugs in one pill taken daily. Additionally, a monthly injection of two medications has been approved by the FDA for HIV treatment.[1]

Lenacapavir is a pioneering, multi-stage, selective inhibitor of HIV capsid protein that has recently received FDA approval. Its intended use, in combination with other antiretroviral drugs (ARVs), is for the treatment of heavily treatment-experienced adults with multi-drug resistant HIV-1 infection who are failing their current ARV regimen due to resistance, intolerance, or safety concerns.[2]

Lenacapavir disrupts several stages of the HIV life cycle through its binding to two adjacent subunits of the HIV capsid protein. This interaction is crucial for various phases of viral replication, including capsid-mediated nuclear transport of preintegration complexes, virion production, and the formation of the proper capsid core. The presence of lenacapavir results in the production of viruses with distorted capsids that are capable of entering new target cells but are unable to replicate.[3]

The CAPELLA study is a phase 2/3 global trial evaluating the antiviral effect of lenacapavir, given every six months as a subcutaneous injection, in heavily treated individuals with multi-drug resistant HIV-1 infection. The trial enrolled 72 patients aged 12 or older who had failed drug therapy for at least 8 weeks and had resistance to at least two antiretroviral medications from three of the four primary categories. The study had two cohorts, with cohort 1 receiving oral lenacapavir or placebo during a functional monotherapy period, and cohort 2 receiving open-label oral lenacapavir followed by subcutaneous lenacapavir with optimized background therapy. Lenacapavir demonstrated significant efficacy in both cohorts, leading to a high rate of virologic suppression and a clinically meaningful increase in CD4+ count. One patient died, and 3 discontinued lenacapavir during the trial, with median follow-up durations of 438 days in cohort 1 and 254 days in cohort 2 for the safety analysis. Overall, the results of the trial suggest that lenacapavir is effective in treating multidrug-resistant HIV-1 infection. At week 26, the mean change in viral load was -2.54 log10 copies per milliliter, which is associated with reduced risk of disease progression and death.[4]

Gilead Sciences Inc has recently obtained FDA approval for Sunlenca (lenacapavir).[5] This medication is currently available for use in the United States and offers a less frequent dosing regimen than existing treatment options. Despite the effectiveness of current HIV therapies, some patients may develop resistance to multiple treatments, which can limit their options for viral suppression. Lenacapavir is a promising new option for patients with complex treatment histories and limited therapy choices. Its therapeutic potency, combined with its various dosing frequencies and routes of administration, makes it a versatile and potentially preferred long-acting agent.

Sunlenca carries several warnings regarding its potential adverse reactions, including injection site reactions, persistent nodules, immune reconstitution syndrome, and residual drug amounts that may result in drug interactions and an increased risk of viral resistance if doses are missed or treatment is not maintained.[6] However, Lenacapavir has demonstrated favorable clinical outcomes as functional monotherapy and in combination with optimized background therapy, resulting in significant reductions in viral load, high rates of virologic suppression, and clinically meaningful increases in the CD4+ count.

Despite limitations such as small sample size and limited follow-up duration, further research is ongoing to evaluate the drug's long-term efficacy, given the urgent need for additional therapeutic options for patients with multidrug-resistant HIV-1 infection.

Additionally, lenacapavir is currently being tested in clinical trials for previously untreated patients with HIV-1, indicating its potential to provide benefits to a wider population.

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