Sunlenca Remains Active Against Drug-Resistant HIV

After two years on lenacapavir, people with advanced immune suppression experienced substantial gains in CD4 T cells.

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Sunlenca (lenacapavir), the first HIV capsid inhibitor, remains effective at two years for highly treatment-experienced people with multidrug-resistant virus, according to the latest results from the CAPELLA trial presented at IDWeek 2023 and the European AIDS Conference (EACS 2023).

“With an additional year of follow-up from the previous analysis, CAPELLA participants continued to experience high and sustained rates of virologic suppression” with “clinically meaningful” increases in CD4 counts, the researchers concluded.

Sunlenca, from Gilead Sciences, was approved in December 2022 for heavily treatment-experienced people with multidrug-resistant HIV who are unable to maintain viral suppression on their current antiretroviral regimen. Sunlenca disrupts HIV’s capsid, the cone-shaped shell that surrounds the viral genetic material and essential enzymes. Because it works differently from existing antiretrovirals, it remains active against HIV that has developed resistance to other medications. Thanks to its long half-life in the body, it can be administered just once every six months.

The Phase II/III CAPELLA trial (NCT04150068) evaluated Sunlenca for treatment-experienced people whose virus had developed resistance to several older antiretrovirals. This group includes long-term survivors who used less effective medications early in the epidemic, some of whom rely on complex regimens that still are not fully suppressive.

The study enrolled people who were currently on antiretroviral therapy but unable to maintain an undetectable viral load. Most (75%) were men, and the median age at study entry was 52 years; 40% were white, 38% were Black and 21% were Asian. They had been living with HIV for 24 years, on average, and almost half had viral resistance to all four major antiretroviral drug classes. Nearly two thirds had advanced immune suppression with a CD4 count below 200.

An initial cohort of 36 participants were randomly assigned to add either Sunlenca or placebo pills to their failing regimen for 14 days, after which everyone was offered Sunlenca injections every six months plus an optimized background regimen. Another 36 people in a nonrandomized cohort

received Sunlenca plus an optimized background regimen from the outset, starting with an oral lead-in prior to injections.

At last year's Conference on Retroviruses and Opportunistic Infections, researchers reported that 83% of participants in the randomized cohort had an undetectable viral load (below 50 copies) at 52 weeks. But response rates differed according to the number of active drugs in a person's background regimen. Among those with two or more active agents, 94% reached a viral load below 50, compared with 79% of those with just one active drug and 67% of those with none. Findings presented at last year's HIV Drug Therapy meeting in Glasgow showed that Sunlenca worked well regardless of sex, age, race/ethnicity, baseline viral load or baseline CD4 count.

At IDWeek, Onyema Ogbuagu, MD, of Yale School of Medicine, presented further follow-up data at two years. Additional data on lenacapavir resistance and injection site reactions were presented at EACS 2023.

After reporting safety and efficacy data for the first year, the study protocol was amended to allow for longer follow-up. Five people stopped Sunlenca during the first year (three lost to follow-up, one at the investigator's discretion and one death). One participant who completed the initial part of the study elected not to continue in the extension.

At 104 weeks, 62% of participants achieved viral suppression, 17% had a viral load above 50 copies and 21% were missing data. When looking only at people who remained in the study with complete data, the viral suppression rate was 82%.

Fourteen participants had emergent resistance to Sunlenca, including five who developed resistance during the second year. All of them had either no fully active drugs or inadequate adherence to their background regimen. The main capsid resistance mutations were M66I, Q67H, K70N/H and N74D. Seven people were able to regain viral suppression despite resistance while continuing on Sunlenca, including five who did not change their background regimen.

Researchers previously reported that CD4 counts rose by an average of 83 cells at 52 weeks in the randomized cohort. In the full study population, the mean gain was 122 cells at 104 weeks. This meant that the proportion of participants with a CD4 count below 200 decreased from 64% at baseline to 29%.

Treatment was generally safe and well tolerated with no drug-related serious adverse events. The most common treatment-emergent systemic adverse events were diarrhea and nausea (19% each). Six people (8%) experienced severe side effects. Some participants experienced injection site reactions such as redness, pain, swelling, nodules or induration (hardness). These were mostly mild to moderate.

At EACS, Antonella Castagna, of San Raffaele Hospital in Milan, presented a combined analysis of injection site reactions among 175 participants who received one or more doses of lenacapavir in either CAPELLA or the CALIBRATE trial, which is testing Sunlenca as first-line treatment. Pain,

redness and swelling generally resolved within days, but in some cases nodules and induration lasted for weeks or months. Five people stopped lenacapavir due to injection site reactions, with only one doing so after the first year of follow-up.

“With longer follow-up, lenacapavir combined with an optimized background regimen continued to result in high and sustained rates of virologic suppression though week 104 in heavily treatment-experienced people with HIV, with a clinically relevant increase in CD4 count from baseline to week 104,” the authors of the IDWeek analysis concluded. “These data further support the use of lenacapavir” for heavily treatment-experienced people with multidrug-resistant HIV.

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