ABSENCE OF CROSS-RESISTANCE TO LENACAPAVIR IN HIV ENTRY INHIBITOR-RESISTANT ISOLATES

Griffiths L[2], Margot N[1], Naik V[1], VanderVeen L[1], Rhee M[1], Callebaut C[1]

[1]Gilead Sciences, Inc., Foster City, CA, [2]Gilead Sciences, Pty Ltd, Melbourne AUS,

Background:
Lenacapavir (LEN) is an inhibitor of HIV-1 capsid function in clinical development. In people with HIV (PWH), LEN (50-750 mg) showed a rapid and strong antiviral effect, with up to 2.3 mean $\log_{10}$ decrease in HIV-1 RNA at day 10. In people with multi-drug-resistant (MDR) HIV, subcutaneous (SC) LEN administered every 6 months in combination with other antiretroviral agents led to high rates of virologic suppression. LEN shows no cross resistance to HIV-1 isolates with resistance to the 4 main classes of ARVs or to maturation inhibitors. Here we have characterized the activity of LEN in HIV-1 isolates with phenotypic resistance to entry inhibitors (EIs).

Methods:
HIV-1 isolates (n=72) from PWH with MDR were tested for phenotypic susceptibility to EIs maraviroc (MVC), fostemsavir (FTR), ibalizumab (IBA), and enfuvirtide(T20) using the PhenoSense Entry assay (Monogram Biosciences). Phenotypic resistance cutoffs for MVC and T20 were based on Monogram's assessment; resistance cutoffs for FTR and IBA were based on published data. The isolates were also tested in the Gag-Pro assay (Monogram).

Results:
Susceptibility data for FTR, IBA, T20, and MVC were obtained. Resistance to MVC was most prevalent (67.2%), followed by FTR, IBA and T20 (31.5%, 29.3%, and 8.6% respectively). Susceptibility data for LEN were obtained for 62 of the 72 isolates, with a mean overall susceptibility to LEN unchanged from wild-type (mean fold change [SD] = 1.0 [0.31], ranging from 0.3 to 1.7). Wild-type susceptibility to LEN was noted for all the isolates regardless of their level of resistance to EIs.

Conclusions:
The gag sequence from EI-resistant isolates did not impact LEN susceptibility, indicating no association between EI resistance and LEN activity. These data, along with prior data, indicate that LEN does not show cross resistance to any of the classes of ARVs in clinical use.

Disclosure of Interest:
Lindsey Griffiths is an employee of Gilead Sciences.

Acknowledgement of Funding:
This study was funded by Gilead Sciences.