BIC CNS Study

Study results lay summary

Study title: Brain connectivity and patient reported outcomes in people with HIV (PWH) with symptoms of insomnia switching integrase inhibitor-based ART; a randomised controlled study

This study was done to try to find out if changing anti-HIV therapy could reduce sleeping difficulties in people with HIV who had insomnia. Current anti-HIV therapy (antiretroviral therapy) is very effective in controlling the HIV virus and keeping people well. But much is not known about how taking the drugs affect some parts of the body, such as the nervous system, and what effect different drugs have on how well people sleep. One group of HIV drugs, called "integrase inhibitors" has been linked to more sleep difficulties, particularly a drug called dolutegravir. This study explored whether switching to a different drug from the same group, called bictegravir, might cause less difficulties sleeping.

Study visits took place between August 2021 to May 2023 at two participating sites in London and Brighton. It was sponsored by the University of Sussex and funded by Gilead Sciences (investigator-sponsored research project). Public involvement in the study was by means of an HIV peer mentor who reviewed the participant information sheet, and their suggestions were incorporated.

People with HIV who were taking dolutegravir plus one or two other drugs called NRTIs nucleoside reverse transcriptase inhibitors) as anti-HIV therapy were considered for the study. People who were generally well but had difficulty sleeping (insomnia) were asked to take part. People who had a diagnosed sleep problem, a disease relating to their nervous system, or major depression or psychosis were not able to take part.

The study had aimed to recruit 46 participants however due to delays caused by to the Covid-19 pandemic and changes to clinic appointments in the post-Covid environment, final enrolment was 19 participants. All participants who were enrolled in the study were included in the analyses.

Participants were randomly assigned to one of two groups:

- 12 participants continued their dolutegravir containing anti-HIV therapy of dolutegravir plus one or two other NRTI drugs.

- 7 participants switched their anti-HIV therapy to bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy).

No serious adverse events were reported during the study period.

The participants attended for 6 clinic visits over about a 5-month period. At these visits they had some blood collected and completed some questionnaires about their sleep, any side effects from their anti-HIV therapy, any food cravings, and their quality of life. In addition, participants had 2 imaging visits at which they had a brain MRI scan performed.

From the analysis of the questionnaires, it was found that insomnia symptoms and sleep quality improved more for the participants who switched their anti-HIV therapy to Biktarvy compared to those who stayed on the dolutegravir containing regimen. Participants' perception of their health in

relation to their ability to perform activities of daily living (physical function) also improved for those who switched to Biktarvy. In addition, in a group of participants who reported that they used recreational drugs, the ability to interact with others and fulfil roles in their environment (social functioning) was improved in those who switched to Biktarvy.

From the analysis of the brain scans, brain activity seen in one of the brain networks known as the Default Mode Network improved in those who switched to Biktarvy. No other differences in brain activity were found in the other three brain networks that were examined.

From the analysis of the research blood samples, no significant changes were found.

The results of this study suggest that for people with HIV who have symptoms of insomnia and who are taking anti-HIV therapy that contains dolutegravir, sleep could improve by switching to Biktarvy. However, it should be noted that this was a small study with limited participants enrolled. Therefore, further studies looking at these changes in a larger group of participants and across more diverse populations would be beneficial.

While the study showed some interesting results, no firm conclusions can be made because it was a small, exploratory study. A larger study may be needed to fully understand the effect of switching medications in people with HIV who have insomnia.

Participants wishing to learn more about the study results should speak to their local research clinic.

The study team would like to thank all study participants for their contribution to this research.