IMPACT OF INTEGRASE STRAND TRANSFER INHIBITORS ON COGNITION IN THE HAILO COHORT

Jane A O'Halloran[1], Charles W Goss[1], Mansi Agarwal[1], Sarah Cooley[1], Kunling Wu[2], Rachel Presti[1], Beau Ances[1], Katherine Tassiopoulos[2], Kristine M Erlandson[3]

[1]Washington University School of Medicine, St Louis, Missouri, USA ; [2]Harvard T. H. Chan School of Public Health, Boston, Massachusetts, USA; [3]University of Colorado Denver, Aurora, Colorado, USA

400

BACKGROUND

- Understanding the impact of antiretroviral therapy (ART) on neuropsychological (NP) outcomes, particularly cognition, in aging people with HIV (PWH) is important.
- Integrase Strand Transfer Inhibitors (INSTIs) have previously been associated with poorer cognitive outcomes[1,2].

METHODS

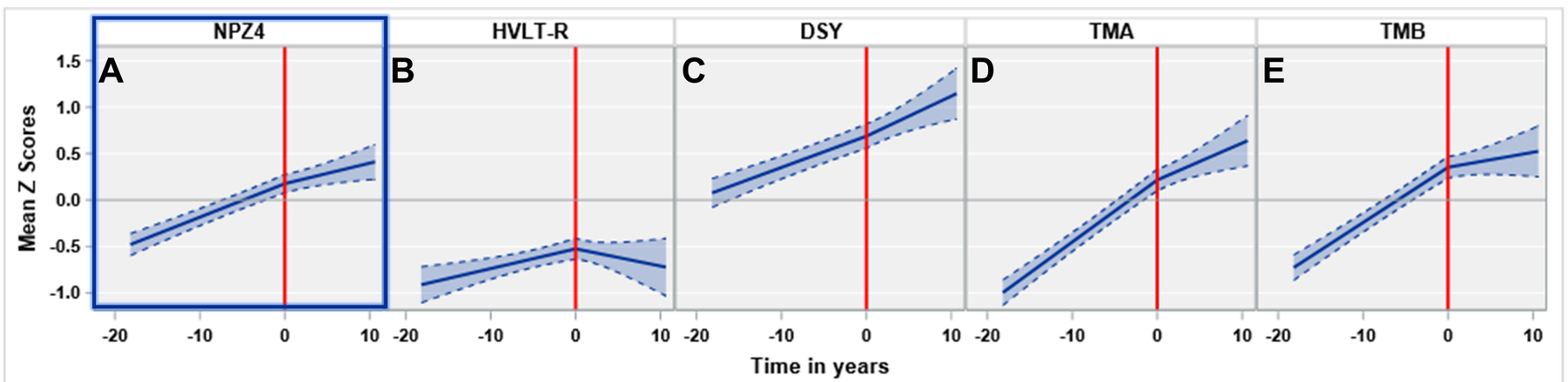
- We used data from ACTG's observational cohort study A5322 (HAILO), and identified PWH who had 1) switched to an INSTI 2) had at least two NP assessments prior to and one after switch, 3) and maintained viral suppression throughout the follow up period on INSTI.
- Prior to HAILO enrollment, participants were followed in ACTG A5001 (ALLRT) cohort and this data was included. NP performance was assessed by NPZ4 (z-scores [normed raw scores] averaged for Trail making A [TMA] and B [TMB], Digit Symbol [DSY] and Hopkins Verbal Learning Test [HVLT-R]).
- Scores were adjusted for sex, race, age, education and learning effects. Changes in cognitive outcomes from the pre-switch (initial NP tests to INSTI switch) and post-switch (INSTI switch to end of follow up) periods were estimated using piecewise linear mixed models.

Overall neuropsychological outcomes improved over time on ART although, not to a clinically significant level.
Switch to INSTI did not influence overall trend towards improvement but may have affected specific domains.

RESULTS

Data from 395 PWH, including 5,824 NP assessments were included. Mean age at switch was 54 years, 81% were male sex (gender not collected). 51% were White non-Hispanic, 29% Black non-Hispanic, and 20% Hispanic.

Figure 1. Neuropsychological assessment trajectories pre- and post-switch to INSTIs



Time 0 (indicated by the red line) represents switch to INSTI. TMA, Trail making A; TMB, Trail making B, DSY, Digit Symbol; HVLT-R, Hopkins Verbal Learning Test

RESULTS continued

- Average observation time was 9 years pre- and 3 years post-switch.
- NPZ4 scores significantly increased during the pre- (0.036/year [95% CI 0.03 to 0.043] $p<0.001$) and post-switch (0.022/year [95% CI 0.006 to 0.039] $p=0.01$) periods, but there was no significant difference in slopes between the time periods (-0.014/year [95% CI -0.033 to 0.005] $p=0.147$) (Figure 1, panel A).
- Each NP component test increased pre-switch (all $p<0.01$) (panel B-E). Post-switch, DSY and TMA continued to increase (all $p<0.01$) (panel C and D), but there were no differences in the rate of change pre-switch compared to post-switch (all $p>0.05$).
- Although the HVLT-R rate of change in the post-switch period was not different from zero ($p=0.22$) there was a significant change in the slope ($p=0.03$) indicating the slope was attenuated in post-switch compared to the pre-switch period (panel B).

CONCLUSIONS

- In this cohort, after adjusting for learning effets, NP assessment scores increased over time, which is not usually seen in aging cohorts. However, the overall mean change in NPZ4 was less than half a standard deviation and not clinically significant. HVLT-R, an assessment of learning/memory, did have a small, but statistically significant decrease post switch to INSTI.
- Further research is required to determine if the domain specific changes identified are clinically relevant, but overall, INSTIs did not have a clear or consistent detrimental effect on NP outcomes.

ACKNOWLEDGEMENTS

The authors would like to thank the participants of A5322 HAILO and the study site staff.

REFERENCES

1. AIDS. 2019 Jul 15; 33(9): 1477–1483.
2. J Acquir Immune Defic Syndr. 2021 Apr 15;86(5):593-599

CONTACT INFORMATION

Janeaohalloran@wustl.edu

ACTG AIDS CLINICAL TRIALS GROUP

The A5322 (HAILO) Study