A RANDOMIZED TRIAL OF ADJUNCTIVE TELMISARTAN TO REDUCE CNS INFLAMMATION IN ACUTE HIV

406

Michael J. Peluso[1], Eugene Kroon[2], Phillip Chan[2], Somporn Tipsuk[2], Carlo Sacdalan[2], Andrew Belden[3], Jennifer Chiarella[4], Magnus Gisslen[5], Henrik Zetterberg[5], Robert Gorelick[6], Duanghathai Suttichom[2], Naponon Sailasuta[2], Robert Paul[3], Jintanat Ananworanich[2,7], Serena Spudich[3], for the RV408/SEARCH018 Study Team

INHCC International NeuroHIV Cure Consortium

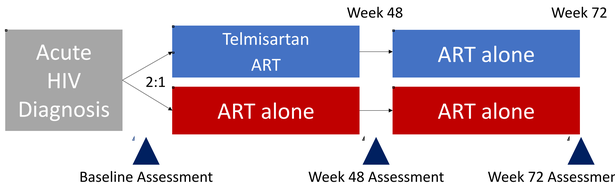
[1]University of California, San Francisco, CA, USA, [2]Thai Red Cross AIDS Research Centre, Bangkok, Thailand, [3]University of Missouri, St. Louis, MO, USA, [4]Yale School of Medicine, New Haven, CT, USA, [5]University of Gothenburg, Gothenburg, Sweden, [6]National Institutes of Health, Bethesda, MD, USA, [7]Military HIV Research Program, Bethesda, MD, USA

BACKGROUND

- Telmisartan is an angiotensin II receptor antagonist that inhibits inflammatory cytokines and macrophage activity.
- We hypothesized that initiation of antiretroviral therapy (ART) with adjunctive telmisartan in acute HIV infection (AHI) might reduce inflammation and immune activation and alter central nervous system (CNS) HIV pathogenesis.

METHODS

- 21 male participants with AHI were randomized 2:1 to initiate treatment with ART +/- telmisartan; after 48 weeks, all individuals received ART alone.



- We measured blood and cerebrospinal fluid (CSF) biomarkers of HIV infection, inflammation, and neuronal injury, brain magnetic resonance spectroscopy (MRS) metabolites, and neuropsychological (NP) performance (16 tests summarized as NPZ Total).
- Nonparametric tests examined differences within individuals and between groups at each time point.

Characteristic	ART+Tel (n=14)	ART Alone (n=7)	P-value
Age (years)	29 (23-40)	28 (24-32)	0.79
Male (n, %)	14 (100%)	7 (100%)	1.0
Sex with men (n, %)	14 (100%)	7 (100%)	1.0
Education	9/14 high school 5/14 college/technical	4/7 high school 3/7 college/technical	0.78
Days of infection	15 (11-20)	21 (16-26)	0.03
Fiebig stage	4/14 Fiebig I-II 10/14 Fiebig III-V	2/7 Fiebig I-II 5/7 III-V	1.0
Plasma HIV RNA (log_{10} copies/mL)	5.9 (5.2-6.4)	5.8 (5.4-6.6)	0.94
CD4+ T cell count (cells/uL)	377 (265-455)	457 (251-666)	0.23
CSF HIV RNA (log_{10} copies/mL)	2.8 (2.2-4.1)	4.4 (2.7-4.7)	0.19

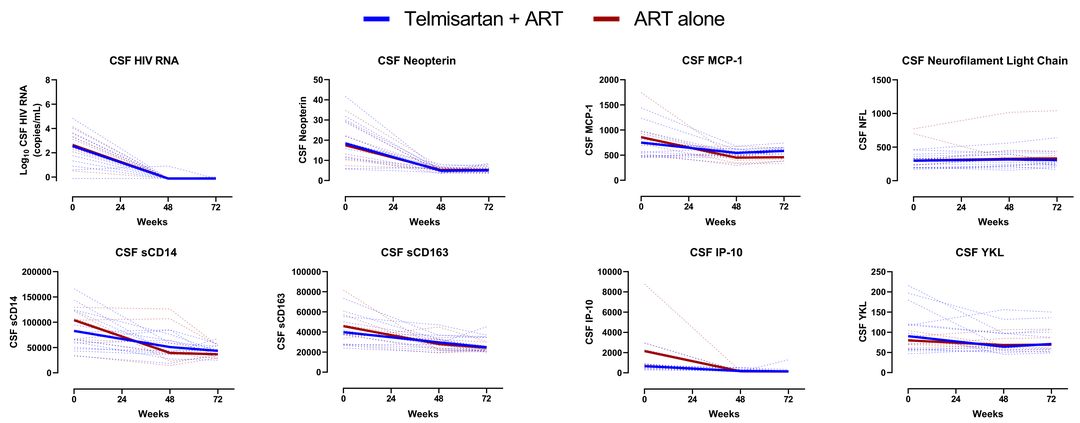
Contact: Michael Peluso, MD: michael.peluso@ucsf.edu

In this pilot study of telmisartan as an adjunct to ART during acute HIV infection, telmisartan did not affect CNS biomarkers of inflammation or injury.

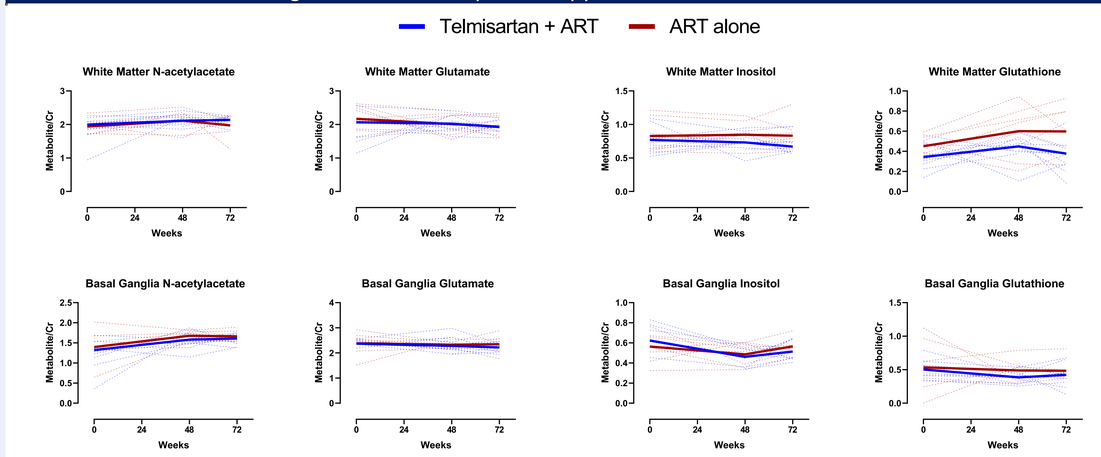
The association with improved neuropsychological testing performance warrants further investigation.

RESULTS

Cerebrospinal Fluid Markers of Viral Replication, Inflammation, and Injury

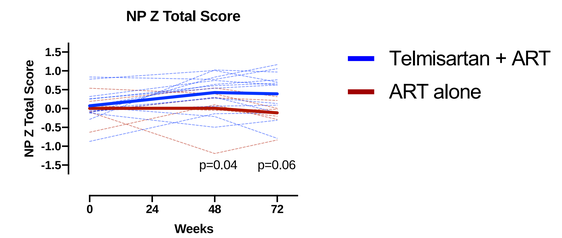


Magnetic Resonance Spectroscopy Markers of Neuroinflammation



RESULTS, CONTINUED

Neuropsychiatric Testing



- In a series of Related Samples Wilcoxon Signed Rank Tests to examine within group and within subject differences in the NPZ Total Score, we found:
  - Telmisartan group showed improvement between week 0 and 48 (p=0.013) and week 0 and 72 (p=0.04).
  - Control group showed no change between week 0 and 48 (p=0.87) and week 0 and 72 (p=0.61).
- An exploratory analysis using repeated measures univariate analysis of variance to determine trends in the data was consistent with this trend but underpowered to detect a difference.

CONCLUSIONS

- Telmisartan did not have a significant impact on neurologic inflammation or injury measured by CSF markers or MRS.
- There was an effect of treatment group on NPZ Total scores, but further work is needed to clarify this trend.
- This study of the impact of an intervention on carefully measured CNS outcomes was feasible in our setting.

ACKNOWLEDGEMENTS & DISCLAIMERS

We would like to thank the study participants who committed so much of their time for this study. The participants were from the RV254/SEARCH 010, which is supported by cooperative agreements (WW81XWH-18-2-0040) between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the U.S. Department of Defense (DOD) and by an intramural grant from the Thai Red Cross AIDS Research Centre. This research was funded, in part, by the U.S. National Institute of Allergy and Infectious Diseases. Antiretroviral therapy for RV254/SEARCH 010 participants was supported by the Thai Government Pharmaceutical Organization, Gilead, Merck and ViiV Healthcare.

Disclaimer: The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of any of the institutions mentioned above, the U.S. Department of the Army or the U.S. Department of Defense, the Henry M. Jackson Foundation for the Advancement of Military Medicine, the National Institutes of Health, the Department of Health and Human Services, or the United States government, nor does mention of trade names, commercial products, or organizations imply endorsement by the Thai Red Cross AIDS Research Centre. The investigators have adhered to the policies for protection of human participants as prescribed in AR-70-25.