CLINICAL AND LABORATORY OUTCOMES OF HEPATITIS C TREATMENT IN AN ACUTE HIV COHORT

Ferron F. Ocampo[1], Carlo Sacdalan[1], Suteeraporn Pinyakorn[2,3], Misti Paudel[2,3], Donn Colby[2], Nathornsorn Poltubtim[1], Somchai Sriplienchan[1], Robert Paul[4], Nittaya Phanuphak[1], Denise Hsu[2,3], Serena Spudich[5], Phillip Chan[5] for the RV254/SEARCH 010 Study Team

[1]SEARCH, Institute of HIV Research and Innovation, Bangkok, Thailand [2]U.S. Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD, USA [3]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD, USA [4]University of Missouri, St. Louis, St. Louis, MO, USA [5]Department of Neurology, Yale University, New Haven, CT, USA

BACKGROUND

- HIV & Hepatitis C (HCV) co-infection is associated with impaired immune recovery and cognitive impairment
- The introduction of direct-acting antivirals (DAA) has dramatically changed the management of HCV due to its efficacy and favorable safety profile
- We compared the laboratory, clinical, and neuropsychiatric parameters before and after DAA therapy and HCV eradication in PWH on stable antiretroviral therapy (ART)

METHODS

Participants

- RV254/SEARCH010 participants who initiated ART immediately during acute HIV infection (AHI)

Selection Criteria

- Participants on at least 24 weeks of ART between May 2009 and July 2022
- Laboratory-confirmed Hepatitis C
- Completed DAA therapy with sustained virologic response (SVR)

Examined Parameters

Laboratory & Clinical	Mood	Cognitive
CBC AST, ALT Lipid profile HCV screening CD4+, CD8+ T-cell counts HIV RNA Neurological examination	Distress thermometer (DT) (range 0-10) Patient Health Questionnaire-9[1] (PHQ-9) (range 0-27)	**Fine motor speed and dexterity** Grooved Pegboard test (GPB) **Psychomotor speed** Color Trails 1 (CT1) Trails Making A (TMA) **Executive functioning** Color Trails 2 (CT2) **NPZ4:** average of z-score for each test

[1]Patient Health Questionnaire (PHQ-9) is a 9-item survey that evaluated the somatic/affective aspects of depression

Study Design

RV254 Enrolment
Initiation of ART during AHI

→

HCV seroconversion after ≥24 wks of ART
May 2009 – Jul 2022
n=79

→

Completed DAA therapy & achieved SVR
n=50

Statistical Analysis

- Wilcoxon signed-rank test or McNemar's test were used to compare parameters before and after DAA therapy and HCV eradication
- Analyses were performed using StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC

In a group of PWH on stable ART, we observed **increased CD4/CD8 ratio & improved cognitive performance** after direct-acting antivirals with HCV eradication

RESULTS

100% males, median age: **30 years** (IQR: 26-35)
AHI to HCV seroconversion: **192 wks** (IQR: 96-312)
HCV seroconversion to DAA initiation: **58 wks** (IQR: 27-70)

33 (66%) diagnosed with STIs within 6 months of HCV seroconversion
31 (62%) denied any past IV drug use

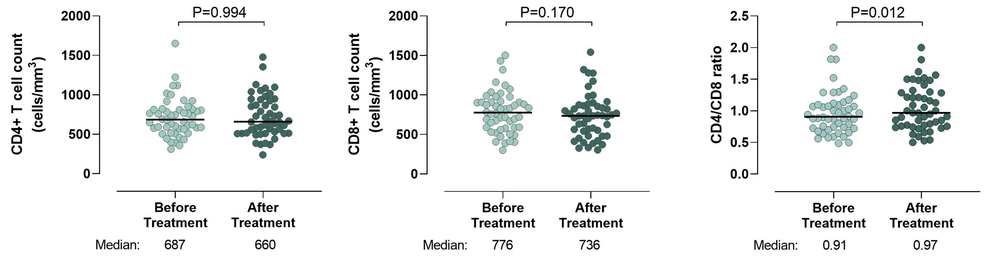

Figure 1 Immunologic parameters before and after DAA treatment and SVR achievement

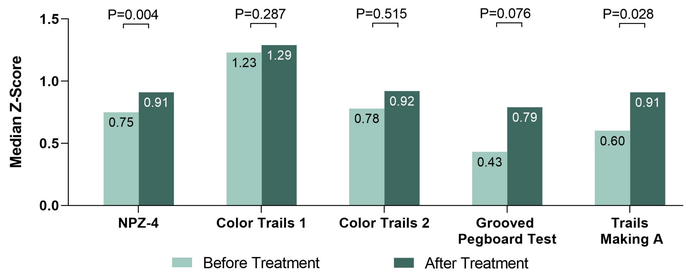

Figure 2 Cognitive test z-scores before and after DAA treatment and SVR achievement

Table 1 Laboratory and clinical outcomes of participants who achieved SVR after DAA treatment

Parameters	Before Treatment[1]	After Treatment[2]	p-value
Biochemistry and hematologic			
ALT, U/L	98.5 (49, 179)	18.5 (13, 26)	**<0.001**
AST[3], U/L	56 (36, 100)	20 (16, 25)	**<0.001**
Plasma HCV RNA, log_{10} cps/mL	6.35 (5.33, 6.91)	ALL undetectable < 1.08	**<0.001**
Total white blood cell count, 10^9/L	5.99 (4.86, 6.94)	5.8 (4.92, 6.88)	0.964
Platelet count, 10^9/L	269 (246, 298)	277 (246, 304)	0.567
Hemoglobin, g/dL	15.1 (14.3, 15.5)	14.85 (13.7, 15.6)	0.153
Total cholesterol, mg/dL	183.5 (159, 210)	200.5 (174, 225)	**<0.001**
Low density lipoprotein (LDL), mg/dL	112.5 (94, 138)	135.5 (111, 160)	**<0.001**
Triglycerides, mg/dL	87 (72, 119)	111.5 (82, 161)	**0.003**
Mood			
PHQ-9 (range 0-27)	6 (2, 8)	4 (2, 8)	0.723
Distress Thermometer (range 0-10)	1.7 (1, 4.2)	2.7 (1.1, 5)	**0.045**
Peripheral neuropathy, n(%)	2 (4%)	1 (2%)	1.00

[1]Median of 103 days (IQR 61.25, 201) before treatment [2]Median of 190 days (IQR 142.5, 267.25) after treatment [3]N=34 participants with pre- and post-treatment AST measurements

SUMMARY OF FINDINGS

After treatment with DAA and achieving SVR:

- **Levels of liver transaminases (AST & ALT) declined** (p<0.001)
- **Total cholesterol, low-density lipoprotein (LDL-C), and triglycerides increased** (p<0.01)
- **CD4/CD8 ratio increased** (0.91 vs. 0.97, p=0.012) but CD4+ and CD8+ T cell counts did not significantly change
- Stress scores measured by DT increased (1.7 vs. 2.7, p=0.045)
- PHQ-9 scores, frequency of moderate and moderate-to-severe depression as well as frequency of peripheral neuropathy remained unchanged
- **NPZ-4** (p=0.004) and **z-Trails Making A** (p=0.028) improved significantly
- In contrast to RV254 participants with HIV monoinfection, **HIV/HCV coinfected participants showed absence of improvement in CD4/CD8 ratio and neuropsychiatric parameters before HCV seroconversion until DAA initiation** over a period of 87 weeks (IQR 64,113)

CONCLUSIONS

- Among PWH on stable ART with HCV co-infection, treatment with direct-acting antivirals (DAA) with sustained virologic response is associated with an increase in CD4/CD8 ratio and improved cognitive test performance
- Early HCV detection and treatment may improve treatment outcomes in PWH on stable ART

ACKNOWLEDGMENTS

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 and, in part, by the Division of AIDS, National Institute of Allergy and Infectious Diseases, National Institute of Health (DAIDS, NIAID, NIH) (grant AAI20052001). Antiretroviral therapy for RV254/SEARCH 010 participants was supported by the Thai Government Pharmaceutical Organization, Gilead Sciences, Merck and ViiV Healthcare. This study was supported by NIH grants focused on neurological and cognitive outcomes in RV254/SEARCH010 including R01 MH113560 and by additional funds contributed by the National Institute of Mental Health.

DISCLAIMER

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army, the Department of Defense, the National Institutes of Health, the Department of Health and Human Services, or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. The investigators have adhered to the policies for protection of human subjects as prescribed in AR-70-25