Poster # 421

Statin or ACE/ARB Effects on Neurocognitive Function of HIV-Infected Adults

KM Erlandson[1], D Kitch[2], CW Wester[3], R Kalayjian[4], ET Overton[5], J Castillo-Mancilla[1], SL Koletar[6], C Benson[7], K Robertson[8], J Lok[2].

[1]University of Colorado, Aurora, CO, USA; [2]Harvard TH Chan School of Public Health, Boston, MA, USA; [3]Vanderbilt University, Nashville, TN, USA; [4]MetroHealth, Cleveland, OH, USA; [5]University of Alabama, Birmingham, AL; USA; [6]Ohio State University Medical Center, Columbus, OH, USA; [7]University of California-San Diego, San Diego, CA, USA; [8]University of North Carolina, Chapel Hill, NC, USA.

Background

- Due to anti-inflammatory and anti-oxidant effects, we hypothesized that statins and angiotensin converting enzyme-inhibitors (ACE) or angiotensin-II receptor blockers (ARB) would protect neurocognitive function (NCF) among HIV+ adults on ART.

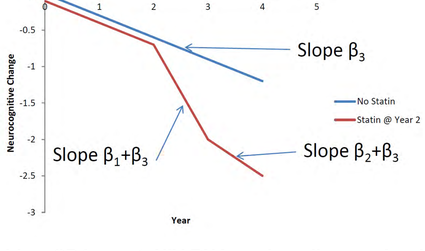
Methods

Study Participants

- Eligible participants from the ACTG ALLRT longitudinal cohort study were:
  - not on a statin or ACE/ARB within 30 days of first neurologic assessment (baseline)
  - had assessments by NPZ-3 (average of Trail making [Trails] A and B, and digit symbol test [DST] z-scores, adjusted for race, language, education, age) from ≥2 measurements, collected every 48 weeks.
- Participants with known impaired NCF, current/prior CNS opportunistic infections, or major psychiatric illness were excluded.
- Baseline diabetes also was excluded from ACE/ARB models (n=124).

Statistical Methods

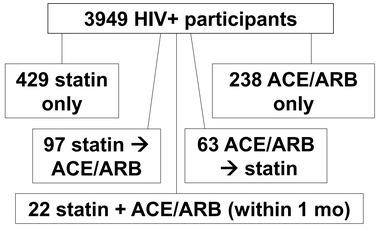
- Marginal structural models estimated the causal effect of statin or ACE/ARB initiation on NCF change among participants that were alive; initial constant slope was assumed during the first year of treatment and a second constant slope thereafter (figure).



- Demographics, CD4 count, HIV RNA, and cardiovascular risk factors were included as confounders of treatment and NCF change. ACE/ARB was included as a confounder in statin initiation models and statins as a confounder in ACE/ARB initiation models.

Results

Statin and/or ACE/ARB Initiation



Characteristics at Initial NPZ-3

	N=3949
Age >60 years	2%
40-60	45%
<40	53%
Female	18%
White	56%
Spanish-speaking	14%
Education	
< high school	14%
HS + some college	58%
Bachelor +/- post	28%
Current smoker	38%
CVD and/or diabetes	4%
HTN	19%
LDL <100 mg/dL	48%
100-160	44%
>160	8%
BMI >30 kg/m^2	16%
25-30	35%
<25	49%
CD4 T-cell >500 cells/μL	28%
200-500	51%
< 200	21%
HIV RNA <400 copies/mL	73%
eGFR (mean, SD)	104 (19.3)

Overall, small increases in the mean adjusted NPZ-3 and component scores:

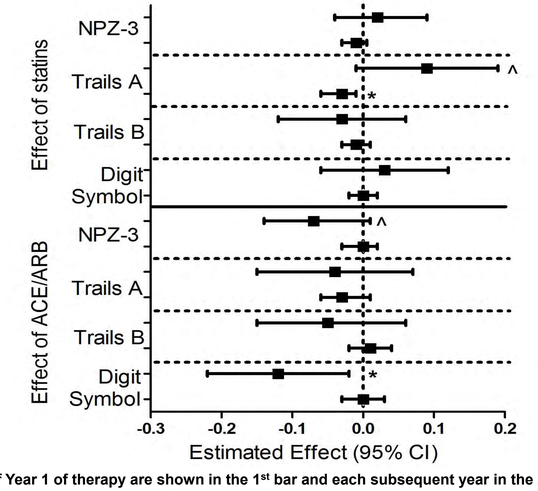
	Statin Model Mean (95% CI) SD/year	ACE/ARB Model Mean (95% CI) SD/year
NPZ-3	0.061 (0.057, 0.065)	0.064 (0.060, 0.068)
Trails A	0.083 (0.077, 0.089)	0.086 (0.080, 0.091)
Trails B	0.071 (0.065, 0.077)	0.073 (0.068, 0.078)
DST	0.030 (0.024, 0.036)	0.036 (0.031, 0.041)

Effect Size of Statin or ACE/ARB on NPZ-3 Score, by Marginal Structural Modeling

	Mean (95% CI) SD/year	P-value
Statin Causal Effect on NPZ-3 Score		
Drug effect in year 1	0.025 (-0.043, 0.093)	0.47
Drug effect after year 1	-0.012 (-0.029, 0.005)	0.16
Years since baseline	0.061 (0.057, 0.065)	<0.001
Statin Causal Effect on NPZ-3, Censored at ACE/ARB Initiation		
Drug effect in year 1	-0.029 (-0.102, 0.045)	0.45
Drug effect after year 1	-0.008 (-0.27, 0.011)	0.38
Years from baseline	0.063 (0.059, 0.068)	<0.001
ACE/ARB Causal Effect on NPZ-3		
Drug effect in year 1	-0.068 (-0.14, .008)	0.078
Drug effect after year 1	-0.005 (-0.027, 0.017)	0.65
Years from baseline	0.064 (0.060, 0.068)	<0.001
ACE/ARB Causal Effect on NPZ-3, Censored at Statin Initiation		
Drug effect in year 1	-0.111 (-0.211, -0.012)	0.028
Drug effect after year 1	0.007 (-0.029, 0.043)	0.71
Years from baseline	0.064 (0.059, 0.068)	<0.001

Models adjusted for baseline age, sex, race, language, education level, smoking status, dyslipidemia, cardiovascular disease or diabetes, CD4 count, HIV-1 virologic suppression, BMI, eGFR, hypertension.

Effect of Statin or ACE/ARB on Neurocognitive Function within Year 1 and Each Subsequent Year of Therapy



Effects of Year 1 of therapy are shown in the 1st bar and each subsequent year in the 2nd bar for each neurocognitive test. Effect size units are reported as the standard deviation of the respective test. * p-value <0.05; ^ p-value 0.05-0.10

- Statin therapy was associated with a positive effect in Trails A during year 1 and a negative effect in each subsequent year.
- ACE/ARB had a negative effect on NPZ-3 scores and Digit Symbol Substitution during year 1 but not in subsequent years or on other neurologic function tests.

Conclusions

- Statins and ACE/ARB were not associated with overall sustained beneficial or harmful neurocognitive effects in HIV-infected adults.
- After censoring for statin initiation, a significantly negative effect of ACE/ARB therapy on NPZ-3 scores was seen within the first year, but not subsequent years.
- Time had a greater effect on NCF than statin initiation.
- The site of drug action (macro vs microvascular) or unmeasured confounders could account for the findings.