Poster # 424LB

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Neurocognitive Safety After 96-Weeks on ATV/r + 3TC: Results of the Randomized SALT Trial

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BACKGROUND

- Due to their low CNS penetrance, there are concerns about the capacity of non-conventional PI-based ART (monotherapy and dual therapies) to preserve neurocognitive (NC) performance (NP).
- There is no evidence regarding the capacity of ATV/r plus 3TC to preserve neurocognitive function in HIV-suppressed patients switching therapy from conventional triple therapy to ATV/r plus 3TC dual therapy.

STUDY DESIGN

The SALT neurocognitive sub-study was designed to compare NC change in aviremic patients randomized to switch to ATV/r + 3TC (dual therapy) or ATV/r + 2NRTI (triple therapy) after 48 and 96 weeks of follow up.

NEUROCOGNITIVE EVALUATION

NEUROCOGNITIVE BATTERY

1. **Working memory:** Trail Making Test – Part A.
2. **Executive Functioning:** Trail Making Test – Part B.
3. **Speed of Information Processing:** WAIS-III Digit Symbol task
4. **Visual & Motor Skills:** Grooved Pegboard Test (dominant and non-dominant hand).

Global Deficit Score: This quantitative neurocognitive score was calculated from T-scores obtained in each of the 5 neurocognitive task assessed (1).

Neurocognitive impairment: Defined as a neurocognitive performance of ≤ -1 SD in ≥ 2 of the 5 neurocognitive task assessed (2).

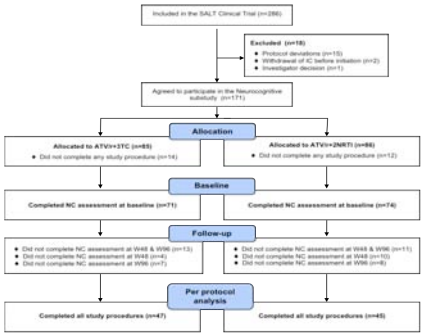
(1) Carey C et al. J Clin Neuropsychol 2004; 18:234-249.
(2) Antinori A et al. Neurology 2007; 69:1789–1799

CONCLUSIONS

- Dual therapy with ATV/r + 3TC did not impact over GDS change after 96 weeks of follow-up, compared to ATV/r + 2 NRTI.
- Neurocognitive stability was observed after 96 weeks in the majority of patients in both treatment groups.
- Neurocognitive impairment incidence rates were similar despite HIV suppression was maintained with ATV/r + 3TC or 2 NRTI.

STUDY FLOW CHART

Baseline characteristic of patients that agreed and refused participation in the neurocognitive sub-study were similar except for patients who refused had longer time since HIV diagnosis, ART initiation and HIV undetectability.



METHODS

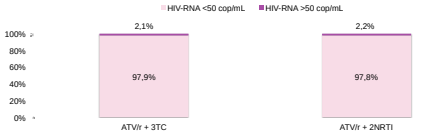
- Patients enrolled in the SALT study who agreed to participate in the NC sub-study were neurocognitively assessed at baseline and weeks 48 & 96.
- Neurocognitive evaluation (five neurocognitive tasks) was performed following recommended AAN 2007 – Frascati diagnostic criteria.
- Change in NC was estimated and compared between therapy arms using a Global Deficit Score (GDS) variation from baseline (BL) to weeks 48 and to week 96.
- Neurocognitive impairment was defined by a GDS value ≥0.5 at baseline, week 48 and week 96 for both therapy arms.
- Neurocognitive distribution at week 96 compared to baseline was also analyzed and reported. Four categories were defined:1) NP impairment both at BL and week 96. 2) NP normal both at BL and week 96. 3) NP improvement from BL to week 96. And 4) NP decline from BL to week 96.
- A crude and adjusted (by potential confounders) estimation of dual therapy effect on GDS change, compared to triple therapy, was performed by ANCOVA were a linear regression was fitted over GDS at week 96 adjusting by GDS at BL and week 48. As a sensitivity analysis, we fitted a linear regression directly over the values of GDS change (CHANGE).
- Selected potential confounders: Age, gender, ethnicity, years on ART, years since HIV detection, years of HIV indetectability , CD4 count (current and nadir), years of education, AIDS, presence of medical, neurological or psychiatric comorbidities, co-infection with hepatitis C, previous use of boosted atazanavir and atherogenic index.
- Variables with a significant p value <0.2 in bivariate analysis were retained in the model.

BASELINE CHARACTERISTICS

		ATV/r + 3TC N = 47	ATV/r + 2 NRTI N = 45	p
Gender: Female. N (%)		12 (25.5)	8 (17.8)	0.452
Age. Mean (SD)		42 (10.1)	42 (7.7)	0.939
Native Spanish. N (%)		37 (78.7)	36 (80)	0.494
Years of education. Mean (SD)		13.3 (5.2)	13.9 (5.2)	0.558
Known duration of HIV detection. Median (IQR)		6.5 (3.2 – 10)	6.1 (3.4 – 10.7)	0.941
Years of ART prior to study entry. Median (IQR)		3.2 (2.2 – 4.9)	3.9 (1.8 – 5.9)	0.734
Years of HIV suppression prior study entry. Mean (SD)		3.1 (2.9)	3 (2.7)	0.92
CD4 (cells/mm3). Median (IQR)	Nadir	218 (70 – 309)	184 (105 – 300)	0.950
	At baseline	633 (440 – 796)	581 (405 – 802)	0.714
Hepatitis C antibody positive. N (%)		6 (12.8)	7 (15.6)	0.771
Aterogenic index (TC/HDL). Median (IQR)		3.9 (3.4 – 4.6)	3.9 (3.4 – 4.6)	0.906
Presence of neurological comorbidities. N (%)		2 (4.3)	5 (11.1)	0.262
Presence of psychiatric comorbidities. N (%)		23 (48.9)	25 (55.6)	0.539
Presence of cardiovascular comorbidities. N (%)		26 (55.3)	22 (48.9)	0.677
Switched to ART including. N (%)	NNRTI	16 (34)	15 (33.3)	0.999
	Protease Inhibitor	28 (59.6)	28 (62.2)	0.833

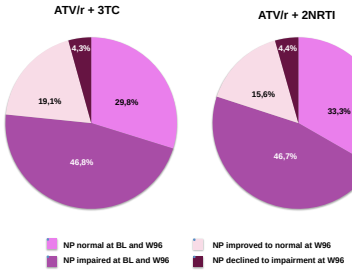
ANTIVIRAL EFFICACY

Per protocol TLOVR efficacy analysis results for patients enrolled in the SALT neurocognitive sub-study at week 96.

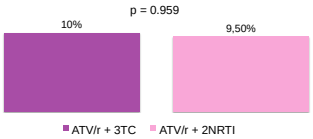


NEUROCOGNITIVE IMPAIRMENT

- Neurocognitive impairment distribution at week 96 by groups



- Incidence of neurocognitive impairment at week 96



CHANGES IN NEUROCOGNITIVE PERFORMANCE BY GDS

Similar GDS evolution was observed in patients receiving dual therapy (ATV/r + 3TC) or triple therapy (ATV/r + 2NRTI).



EFFECT OF DUAL THERAPY (ATV/r + 3TC) OVER GDS AT WEEK 96

Dual therapy was not associated with a worse neurocognitive change

		ATV/r + 3TC N = 47	ATV/r + 2 NRTI N = 45	p
GDS Mean (95% Confidence interval)	Baseline	1.2 (0.9 to 1.5)	1.1 (0.8 to 1.5)	0.802
	Week 48	0.9 (0.6 to 1.1)	1.0 (0.6 to 1.3)	0.844
	Week 96	0.9 (0.6 to 1.1)	0.9 (0.6 to 1.1)	0.987
Crude mean change in GDS from baseline to Week 96 (95%Confidence interval)		-0.29 (-0.44 to -0.13)	-0.24 (-0.40 to -0.08)	0.691
Crude† effect of Dual Therapy over change in GDS (95% Confidence Interval)		0.01 (-0.18 to 0.21)	Reference	0.903
Adjusted†† effect of Dual Therapy over change in GDS (95% Confidence Interval)		0.01 (-0.18 to 0.21)	Reference	0.903

†Regression over global deficit score (GDS) at follow-up visit, adjusted only by GDS at baseline and W48.
†† Additionally adjusted by significant confounders: **NONE**

DISTRIBUTION BY NEUROCOGNITIVE TASKS

Similar performance changes were observed in all the neurocognitive tasks

