CEREBROSPINAL FLUID MARKERS IN LONG-TERM ATAZANAVIR/RITONAVIR MONOTHERAPY

Francesca Ferretti
Clinical research fellow
Department of Infectious Diseases
San Raffaele Scientific Institute Milan

Disclosures

MODAt study

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Background

Ritonavir boosted protease inhibitors monotherapy (mono PI/r)

- Lower virological efficacy compared to standard treatment
- Prompt reintensification usually sufficient for re-suppression
- Virological failure usually not associated with:
  - Resistance mutations
  - loss of future therapeutic options
- Concerns about efficacy in the CNS compartment

Arribas J et al J Int AIDS Soc.2014, 17(Suppl 3):19788**. Paton N** et al. CROI 2014.
Vernazza, AIDS 2007, 21:1309–1315**. Gutman, AIDS 2010**, 24:2347–2354. **Katlama, C., et al. AIDS 2010 ,** 24(15): 2365-2374

Methods

CSF biomarker pilot substudy of the RCT MODAt

Primary Objective:

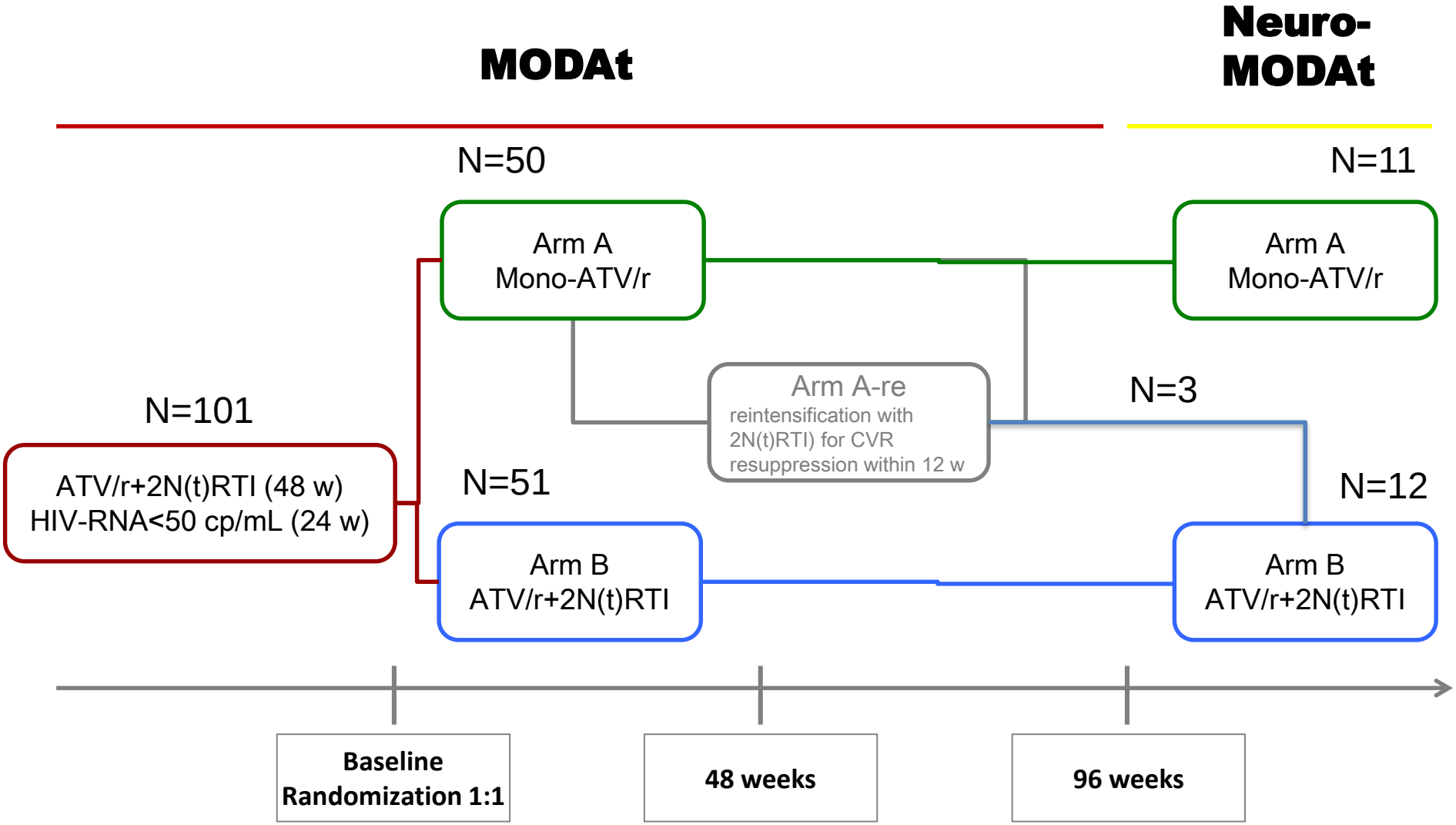
- virological efficacy of ATV/r monotherapy in CSF

Secondary objectives:

- presence of neurological symptoms
- presence of morphological MRI abnormalities
- levels of CSF immune activation biomarkers

Castagna, A. et al. AIDS 2014."Simplification to atazanavir/ritonavir monotherapy for HIV-1 treated individuals on virological suppression:48-week efficacy and safety results." 28(15): 2269-.-2279

Study design



Castagna, A. et al. AIDS 2014."Simplification to atazanavir/ritonavir monotherapy for HIV-1 treated individuals on virological suppression:48-week efficacy and safety results." 28(15): 2269-.-2279

Pts characteristics at randomization

	Arm A (mono-ATV/r) N=11	Arm B (ATV/r + 2N(t)RTIs) N=12	p	All N=23
Age	42 (37-50)	43 (41-47)	0.926	43 (38-47)
Male gender (nr, %)	11 (100%)	11 (92%)	0.999	22 (95%)
Years from HIV diagnosis	6 (4-8)	4.5 (3-6.5)	0.352	5 (4-7)
Nadir CD4+ (cells/μL)	282 (228-363)	347 (315-419)	0.103	334 (268-366)
Nadir CD8+ (cells/ μL)	908 (665-133)	694 (529-912)	9.207	814 (551-1256)
Pre ART HIV-RNA (log10 c/mL)	4.76 (4.05-5.60)	4.88 (4.58-5.32)	0.735	4.86 (4.49-5.43)
Current CD4+ (cells/μL)	641 (464-812)	586 (485-673)	0.644	599 (467-699)
AIDS	0	0	-	0
HCV infection (nr, %)	1 (9%)	3 (25%)	0.590	4 (17%)
Duration of current ART (months)	26.3 (19.5-70.5)	25 (17.9-45)	0.518	25.2 (19.5-54.0)
Duration of HIV-RNA <50 c/mL (months)	20.7 (13.7-65.5)	19.3 (12.1-39.6)	0.518	19.5 (13.7-48.7)

Median (interquartile range IQR) are reported. P values were calculated with Wilcoxon rank sum or Fisher exact test, as appropriate
HIV-RNA determined by Versant k PCR (limit of detection 37 c/mL)

Results

	Arm A (mono-ATV/r) N=11	Arm B (ATV/r + 2N(t)RTIs) N=12	p	All N=23
Study week	123 (109-138)	124 (115-133)	0.758	123 (110-134)
CD4+ (cells/µL)	691 (544-836)	680 (580-813)	0.975	691 (544-836)
Plasma HIV-RNA <50 c/mL	11 (100%)	12 (100%)	-	23 (100%)
CSF HIV-RNA >50 c/mL	1 (9%, 114 c/mL)	0	-	1 (4.3%)
CSF cells (cells/µL)	2 (1-4)	1 (1-2)	0.056	1.5 (1-3)
CSF glucose (mg/dL)	63 (62-68)	61 (59-64)	0.156	63 (60-64)
CSF protein (mg/dL)	36 (27-49)	34 (30-39)	0.669	35 (30-45)
Neurological symptoms	0	0	-	0
MRI microvascular changes	4 (36%)	4 (33%)	0.998	8 (38%)

Median (interquartile range IQR) are reported. P values were calculated with Wilcoxon rank sum or Fisher exact test, as appropriate
HIV-RNA determined by Versant k PCR (limit of detection 37 c/mL)

CSF viral escape case

Characteristics

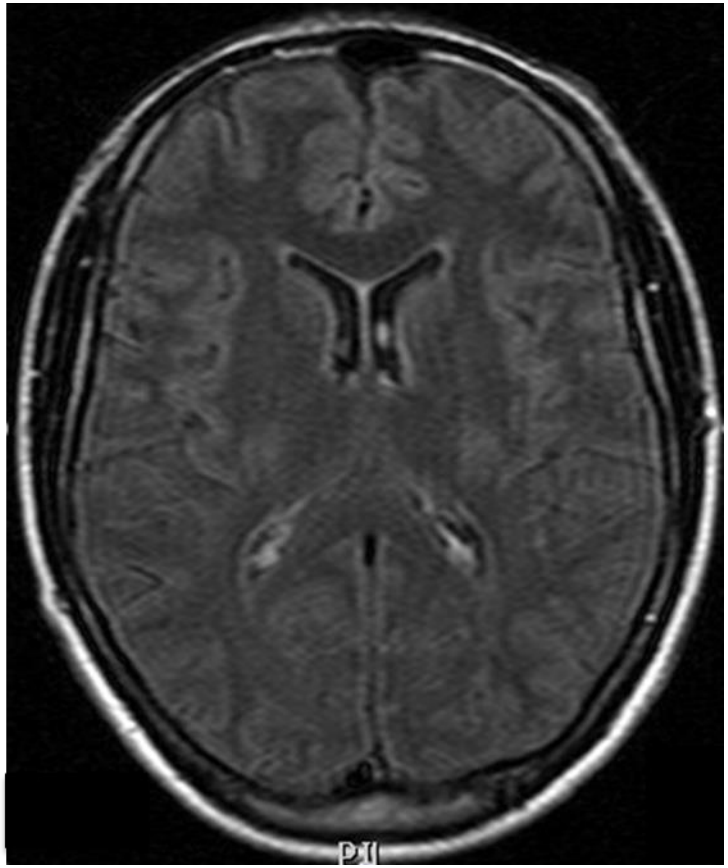
- ATV/r monotherapy for 120 weeks
- 2 non consecutive HIV-RNA blips in plasma (94, 99 c/mL)
- CD4+ nadir: 311 cells/µL
- Neuroasymptomatic
- No MRI abnormalities
- CSF: unremarkable protein and cell levels

Intervention

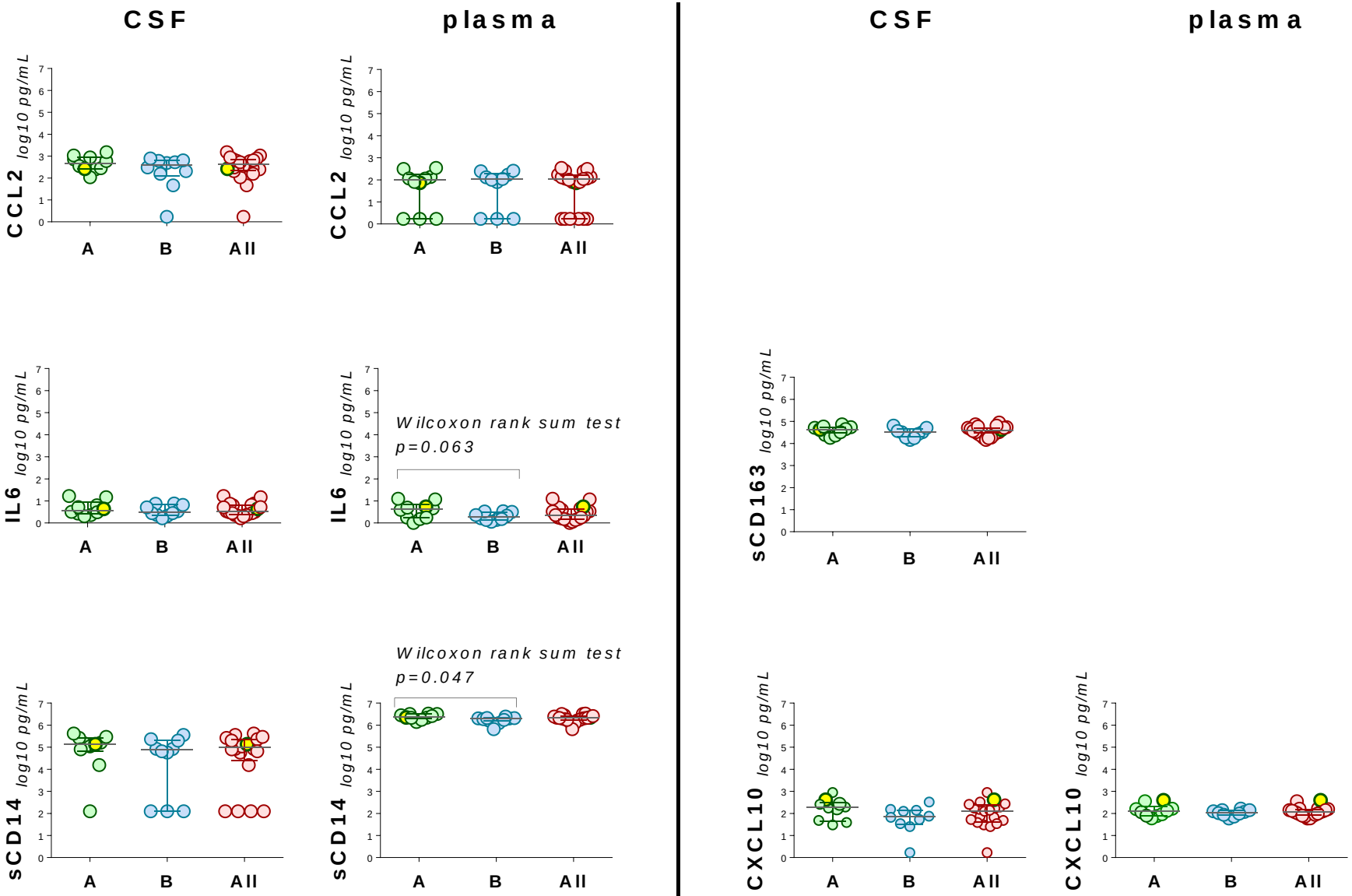
- re-intensification (TDF FTC)

Outcome

- Plasma and CSF HIV-RNA undetectable after 20 w



Biomarkers of immune activation



Conclusions

- Asymptomatic CSF viral escape uncommon in selected pts on ATV/r monotherapy
- Re-intensification sufficient for CSF re-suppression
- CSF biomarkes of immune activation not increased in patients receiving monotherapy compared to patients receiving standard treatment

Aknowledgments

Patients

Alba Bigoloni

Valeria Longo

Laura Galli

Laura Passeri

Simonetta Gerevini

Vincenzo Spagnuolo

Adriano Lazzarin

Paola Cinque

Antonella Castagna

Alan Winston

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