Immune activation and HIV-DNA after 96-week of ATV/r monotherapy: a MODAt substudy

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BACKGROUND

In this substudy we investigated the impact of simplification ATV/r monotherapy (mATV/r) as compared to ATV/r+2N(t)RTIs (tATV/r) on immune activation/inflammation and HIV-DNA content over 96-week.

METHODS

MODAt (NCT01511809) is a multicentric, randomized, open-label, non-inferiority trial. Patients on ATV/r 300/100mg+2 N(t)RTIs since≥48 weeks, virologically suppressed since≥24 weeks, randomized to mATV/r or to maintain tATV/r. The Immune-MODAT sub-study included subjects treated for 96 weeks with tATV/r or mATV/r (with no re-intensification during follow-up) and with available samples at 3 timepoints: baseline (T0), w48 and w96. Analyses performed: HLA-DR/CD38/CD57/CD28/PD-1/CD95 on CD4/8 (Flow Cytometry), sCD14, IL-6 (ELISA), HIV-DNA (Real-Time PCR).

Fisher exact test, Wilcoxon rank-sum test for tATV/r vs mATV/r. Wilcoxon signed rank test for differences between timepoints.

RESULTS

The analysis included 40 pts with valid data at least at two timepoints [18 and 22 pts in mATV/r and tATV/r respectively]. No differences between arms either for demographic, clinical and HIV-related characteristics or activation/inflammation markers at T0.

HIV-DNA significantly decreased by w48 (p=.014) in pts on mATV/r but the reduction was not confirmed at w96. HIV-DNA at w96 (p=.013) was lower in tATV/r [change from T0: p=.054] than mATV/r (Table 1).

In Table 1 trend of the major immune activation and inflammation markers over 96 weeks: no differences between the two arms were observed at any timepoint for all markers.

In pts with mATV/r, we found a significant reduction from T0 in HLA-DR+CD38+ CD4 T-cells and a mild increase in IL-6 at w48 not confirmed at w96; senescent CD57+, apoptotic CD95+ CD4 also increased by w96.

In tATV/r, CD57+ CD4 significantly increased over w96 while CD57- CD4, IL-6 and sCD14 slightly decreased.

Fifteen pts (9 in mATV/r 6 in tATV/r) had other concomitant STDs at the examined timepoints that might at least partially explain the increase of inflammation markers: when excluding them, no differences in T-cell phenotype and inflammation markers in both mATV/r and tATV/r were observed.

CONCLUSIONS

In subjects successfully treated with ATV/r monotherapy for 96 weeks control of immune activation/inflammation appeared to be efficient. A minimal HIV-DNA reduction was observed in ATV/r triple therapy compared to ATV/r monotherapy.

Table 1. HIV-DNA content, T-cell phenotypes and pro-inflammatory markers in HIV+pts on ATV/r-triple therapy or ATV/r-monotherapy

	Arm	Baseline	Week 48	p BL vs W48	Week 96	p BL vs W96
HIV-DNA cp/10*6cells	mATV/r	55 (9 , 175)	18 (9 , 54)	**0,014**	25 (9 , 68)	ns
	tATV/r	16 (9 , 61)	10 (9 , 23)	ns	9 (9 , 16)	**0,054**
HLA-DR+CD38+4, %	mATV/r	8.42 (2.52 , 13.11)	1.54 (0.80 , 7.32)	**0,021**	6.38 (3.97 , 7.88)	ns
	tATV/r	2.89 (0.79 , 10.58)	1.73 (1.26 , 7.49)	ns	5.17 (3.49 , 7.51)	ns
CD57+/CD4, %	mATV/r	4.12 (2.86, 8.32)	5.82 (3.33, 11.81)	ns	6.95 (5.20,11.80)	**0,035**
	tATV/r	4.07 (2.53, 9.28)	6.53 (2.86, 8.77)	ns	6.47 (2.98, 17,48)	**0,012**
CD95+/CD4, %	mATV/r	52.43 (40.68 , 62.73)	54.93 (39.85 , 61.81)	ns	64.02 (48.25 , 75.76)	**0,003**
	tATV/r	53.01 (37.05 , 68.59)	58.27 (49.10 , 80.69)	ns	60.84 (49.17 , 74.86)	ns
SCD14 (ug/ml)	mATV/r	4.00 (2.82 , 5.44)	3.90 (2.88 , 4.94)	ns	2.93 (2.32 , 3.53)	ns
	tATV/r	4.03 (3.32 , 5.65)	3.99 (2.81 , 4.89)	ns	2.51 (1.97 , 2.77)	**0,0001**
IL6 (pg/ml)	mATV/r	1.52 (1.36 , 2.07)	2.09 (1.81 , 3.18)	**0,03**	1.60 (0.86 , 2.64)	ns
	tATV/r	1.92 (1.45 , 2.31)	1.76 (1.44 , 3.98)	ns	1.13 (0.76 , 2.18)	**0,018**

NOTE: Data are presented as median (Interquartile Range); mATV/r monotherapy with atazanavir; tATVr: triple therapy with atazanavir; ns: not significant, p>0,05