P046

Outcomes of Unboosting Atazanavir (ATZ) in Regimens with a Tenofovir (TDF) Backbone

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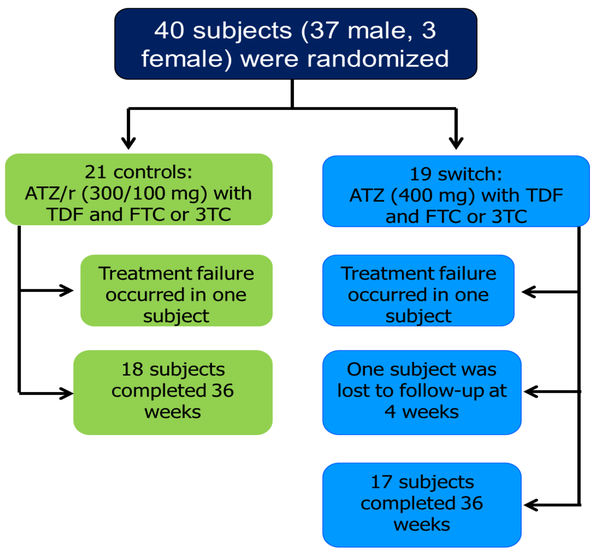
BACKGROUND

- Tenofovir (TDF) lowers plasma levels of atazanavir (ATZ), leading to the current recommendation that ATZ be boosted with ritonavir (RTV) when coadministered with TDF [1].
- Serum lipid levels can be adversely affected by RTV, which may contribute to increased cardiovascular risk [2-4].
- Switching from RTV-boosted to unboosted ATZ has been shown to be safe and effective in the setting of abacavir/3TC backbones [5]; however, this strategy has not been formally studied in the context of TDF-based regimens.
- We conducted a randomized controlled trial to evaluate whether HIV+ patients with virologic control on regimens including ATZ/RTV and TDF can safely be maintained on unboosted ATZ with TDF .

METHODS

Design: 48-week open label randomized controlled trial



Inclusion criteria

- HIV infected adults
- Receiving ATZ /RTV 300mg/ 100mg daily with either TDF/FTC or TDF/3TC, for ≥ 6 months
- Plasma viral load (pVL) ≤40 copies/mL at screening, and <100 copies/mL continuously for ≥6 months prior to screening (based on ≥ 2 previous measurements)
- No evidence of resistance to any NRTIs or PIs on previous genotypic tests

Exclusion criteria

- Pregnancy or breast-feeding
- Concomitant treatment with proton pump inhibitors, rifampin, St John's wort, or garlic supplements

Statistics

- A preliminary analysis was conducted when 35 subjects reached 36 weeks.
- Friedman's nonparametric test was used to for data analysis.
- Treatment failure is defined as either regimen change for any reason, or pVL >200 copies/mL on 2 consecutive measurements > 2 weeks apart

RESULTS

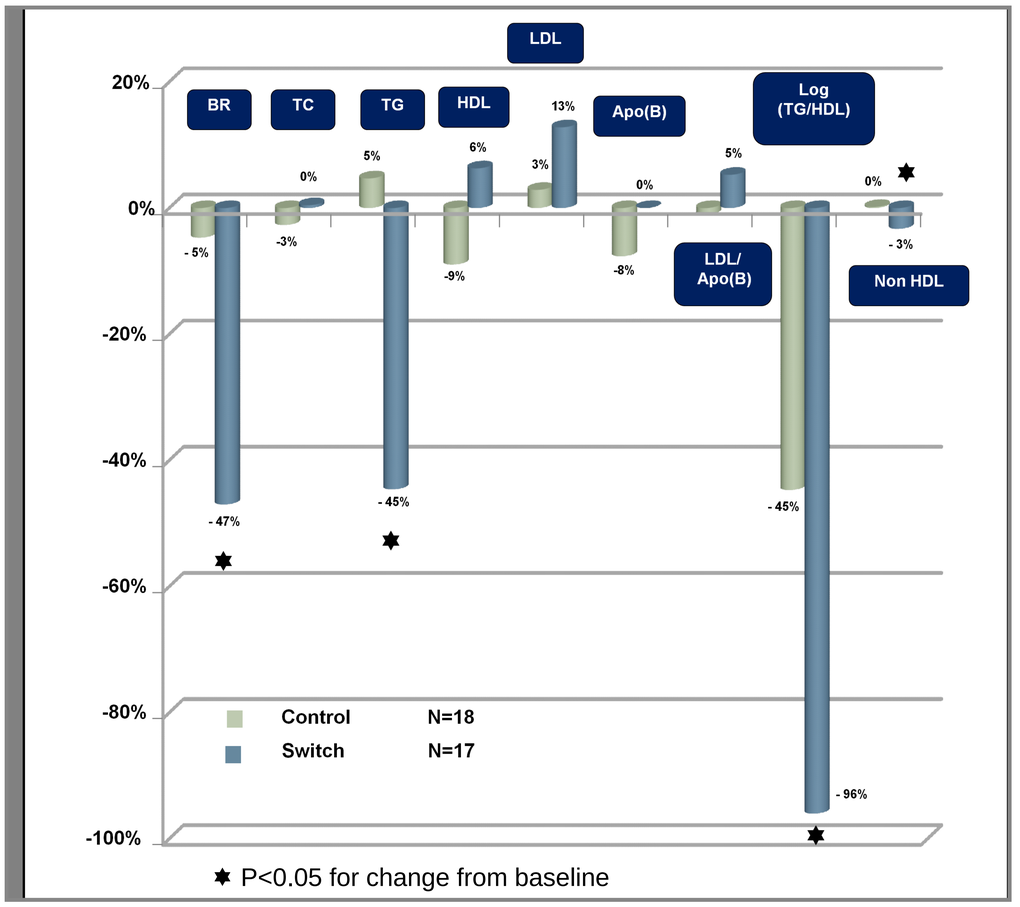
Table 1: Baseline Characteristics*

	Control: Continue ATZ/RTV	Experimental: Switch to unboosted ATZ
N	18	17
Age, years	46 (35.7 - 55.5)	47.5 (41.5 - 52.5)
Emtricitabine (FTC)/Lamivudine (3TC), N	17/1	14/3
Male/female, N	16/2	16/1
Time with pVL <50 copies/mL on current regimen, months	6 (4-60)	5 (2-49)
CD4 count , cells/mm3	615 (417 - 692)	540 (465 - 580)
CD4/CD8 ratio	0.80 (0.55 - 1.16)	0.72 (0.52 - 0.92)
Total Bilirubin (BR), µmol/L	40.5 (34.25 - 52.5)	26 (9.5 - 34)
Creatinine, µmol/L	81 (74.2 - 92.7)	81 (73 - 90.5)
Estimated glomerular filtration rate (eGFR)** , mL/min	85.5 (76 - 96)	89 (78.5 - 1.5)
Urine albumin/creatinine ratio (UACR), mg/mmol	1.2 (0.75 -3.75)	1.0 (0.52 - 2.2)
Serum Phosphate, mmol/L	0.87 (0.78 – 1)	0.97 (0.89 - 1.05)
Total cholesterol (TC) , mmol/L	4.15 (3.8 – 4.7)	4.46 (3.87 - 4.77)
Triglycerides (TG), mmol/L	1.33 (0.93 – 1.54)	1.18 (0.88 - 1.55)
HDL-Cholesterol (HDL-C), mmol/L	1.3 (1.1 – 1.74)	1.35 0.94 - 1.66)
LDL-Cholesterol (LDL-C), mmol/L	2.3 (1.5 – 2.7)	2.6 (2.13 - 3.1)
Apolipoprotein B (ApoB), g/L	0.72 (0.64 – 0.96)	0.86 (0.64 - 0.99)
LDL-C/ApoB, mmol/L [6]	2.8 (2.5 – 3.2)	3.0 (2.7 - 3.2)
Log(TG/HDL-C) [7]	-0.04 (-0.27 – 0.14)	0.01 (-0.19 - 0.15)
Non-HDL-Cholesterol (non-HDL-C), mmol/L	2.7 (2.0 – 3.4)	3.1 (2.5 - 3.7)
C-Reactive Protein, mg/L	1.3 (0.5 – 2.1)	1.1 (0.6- 3.4)

*Data shown as median (interquartile range) unless otherwise indicated
**eGFR calculated by MDRD equation

RESULTS CONTINUED

Figure. 1:
Median Percent Change in Bilirubin and Lipid Parameters from Baseline to week 36



- No significant changes between baseline and 36 weeks were observed in either arm with respect to CD4, creatinine, eGFR, phosphate, UACR, or C-reactive protein.

SUMMARY & CONCLUSIONS

In this preliminary 36-week analysis of subjects randomized to continue ATZ/RTV or switch to unboosted ATZ with a TDF backbone:

- **treatment failure rates were similar in both arms (1 in each arm).**
- **favourable changes in bilirubin and certain lipid parameters were observed in the unboosted ATZ arm.**

REFERENCES

1.Gilead Sciences Inc. Viread Product monograph, November 2012.
2.Carey D, Amin J, et al. *Antimicrob Chemother* 2010; 65: 1878–88.
3. Podzamczer D, Andrade-Villanueva J, et al. *HIV Medicine* 2001; 12: 374-82.
4. Sension M, de Andrade Neto JL, et al. *J Acquir Immune Defic Syndr* 2009;51:153–162.
5. Squires KE, Young B, DeJesus E, et al. *HIV Clinical Trials* 2012; 13(5):233-44.
6. Wagner AM, Jorba O, et al. *Acta Diabetol* 2002; 39(4):215-20.
7. Dobiášová M, Frohlich J, Šedová M, et al. *J Lipid Res* 2011; 52: 566–71 .

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