Real-world clinical outcomes of patients switched from complex multi-tablet regimens to TAF-based single-tablet regimens plus a boosted protease inhibitor

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Poster PE2/26

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17th EUROPEAN AIDS CONFERENCE
November 6 – 9, 2019
Basel, Switzerland

BACKGROUND:

- Complex, multi-tablet regimens (MTRs) are often used to achieve virologic suppression in HIV-1 infected, treatment-experienced patients with antiretroviral (ARV) resistance[1]
- However, MTRs are associated with increased adverse events and non-adherence which may ultimately lead to virologic failure and increased drug resistance[2]
- Current treatment guidelines recommend regimen simplification whenever possible, however simplification is often challenging in patients with a history of ARV resistance
- The strategy of combining newer single tablet regimens (STRs) plus a boosted protease inhibitor (PI) is a promising treatment option for MTR-treated patients seeking simplification; however real-world data is needed to validate this therapeutic strategy

METHODS:

- Retrospective, observational cohort study to describe the efficacy, safety and tolerability of switching treatment-experienced patients on complex MTRs to tenofovir-alafenamide (TAF)-based STRs plus a boosted PI
- Eligible patients included HIV-1 infected patients seen at the Orlando Immunology Center between 8/2012-12/2017 who were switched from BID regimens ***or*** regimens containing ≥ 3 pills daily to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) plus darunavir (DRV) or rilpivirine/emtricitabine/tenofovir alafenamide (RPV/F/TAF) plus DRV boosted with norvir or cobicistat
- Eligible patients had baseline HIV-1 RNA<200 copies/mL and at least two HIV-1 RNA measurements after switch
- Demographics, lab values and clinical parameters were extracted from the charts of all eligible patients through Week 48 of treatment with the TAF-based STR plus boosted PI
- The primary endpoint of the study was the proportion of patients with plasma HIV-1 RNA<50 copies/mL at Week 48
- Secondary endpoints included change in CD4$^+$ cell counts, adherence, safety and tolerability during treatment with the TAF-based STR plus boosted PI

RESULTS:

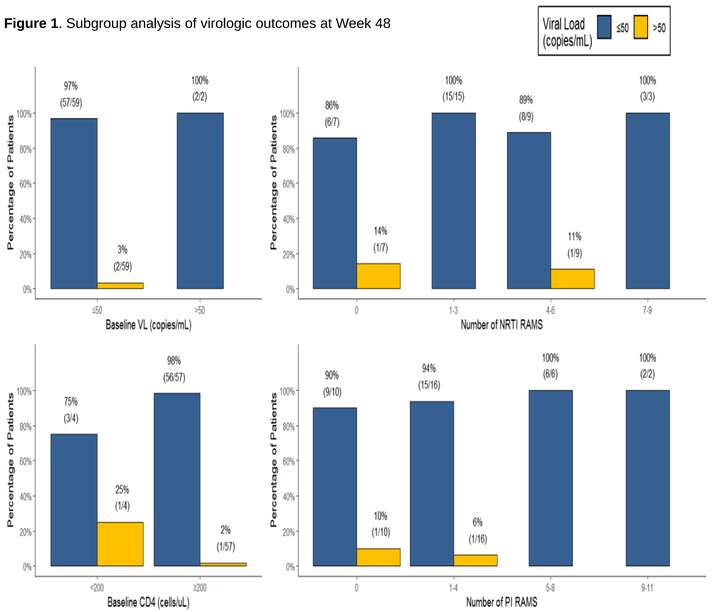
Table 1. Baseline demographic and clinical characteristics

Characteristic	N=61
Median Age (range)	53 (27; 70)
Sex	
Male, n (%)	47 (77)
Female, n (%)	14 (23)
Race/Ethnicity	
Caucasian, n (%)	20 (33)
Black, n (%)	15 (24)
Hispanic, n (%)	14 (23)
Other, n (%)	12 (20)
Median BMI (range)	26.7 (18.9; 45.4)
Median Baseline CD4$^+$ cell count, cells/mm^3 (range)	510 (87; 1798)
Prior ARV Experience	
>2 NRTIs, n (%)	45 (74)
≥1 NNRTI, n (%)	39 (64)
0 PIs, n (%)	5 (8)
1 PI, n (%)	20 (33)
≥2 PIs, n (%)	36 (59)
1 INSTI, n (%)	50 (82)
>1 INSTI, n (%)	6 (10)
Median Number of ARV regimens prior to switch (range)	4 (1; 10)
Complex MTR prior to switch	
BID regimen, n (%)	49 (80)
Median number of pills daily (range)	5 (3; 9)
Reasons for switch	
Simplification, n (%)	53 (87)
Side effects, n (%)	4 (6.5)
None documented, n (%)	4 (6.5)
Baseline genotypic resistance	
Overall Group, n	61
Pattern of NRTI RAMs	
M184V/I alone, n (%)	3 (5)
M184V/I+ 1 NRTI RAM, n (%)	3 (5)
M184V/I + > 1 NRTI RAM, n (%)	11 (18)
Number of RAMS	
NRTI RAMs, median (range)	2 (0; 9)
NNRTI RAMs, median (range)	1 (0; 5)
PI RAMs, median (range)	2 (0; 11)
INSTI RAMs, median (range)	0 (0; 6)

Abbreviations. BMI, body mass index; ARV, antiretroviral; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor; MTR, multi-tablet regimen; BID, twice-daily; RAM, resistance associated mutation

56 patients (92%) were switched to E/C/F/TAF+ DRV and 5 (8%) were switched to RPV/F/TAF plus boosted DRV

Figure 1. Subgroup analysis of virologic outcomes at Week 48

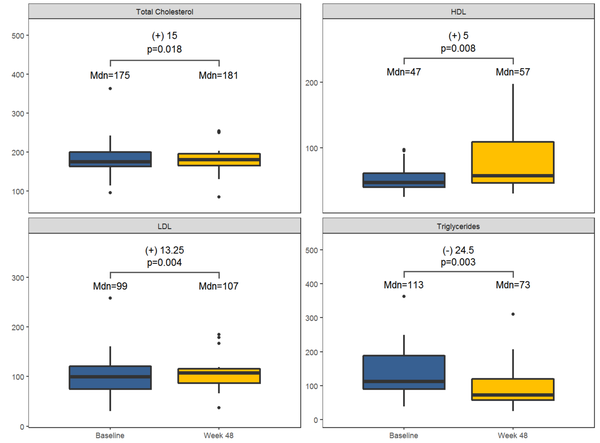


Two patients treated with E/C/F/TAF plus DRV experienced confirmed virologic rebound (HIV-1 RNA>50 copies/mL) during the study period, both patients reported suboptimal adherence. There was no evidence of treatment-emergent resistance in either case

RESULTS cont'd:

There was no significant change in median CD4$^+$ count from Baseline to Week 48 (+14 cells/mm^3, 95% confidence interval (CI): [-50.5; 78.3])

Figure 2. Changes in lipid parameters through Week 48



There were significant changes in all lipid parameters from baseline to Week 48. Median total cholesterol increased by 15 mg/dL, 95% CI: [2.5; 28.5], median HDL increased by 5 mg/dL, 95% CI: [2.5; 42.5], median LDL increased by 13.25 mg/dL, 95% CI: [8; 30], and median triglycerides decreased by 24.5 mg/dL, 95% CI: [-89.5; -13.0]

Table 2. Safety and Tolerability

Characteristic	Frequency, n (%)
Adverse Events (AEs), n (%)	3 (5)[a]
Discontinuations, n (%)	4 (7)[b]
Grade 1-2 lab abnormalities, n (%)	38 (62)[c]
Grade 3-4 lab abnormalities	8 (13)[d]

[a] 3 patients experienced Grade 2 AEs, all were felt to be treatment-related. These included weight gain (1), tinnitus (1) and nausea/vomiting (1)
[b] 3 patients discontinued due to AEs (weight gain, tinnitus and nausea/vomiting), 1 patient discontinued due to provider decision to change regimen
[c] Grade 1-2 lab abnormalities included LDL elevations (17), elevations in glucose (17), elevations in triglycerides (13), elevations in LFTs (11), and elevations in creatinine (3)
[d] Grade 3-4 lab abnormalities included elevations in triglycerides (5), elevations in glucose (3), and elevations in LDL (1)

CONCLUSIONS:

- In this small "real-world" cohort of MTR-treated patients, switching to a TAF-based STR plus boosted PI maintained virologic control and was well-tolerated
- There were no cases of treatment-emergent HIV-1 resistance mutations in patients who experienced virologic failure
- This data supports use of this switch strategy for regimen simplification in patients treated with complex MTRs who may have underlying ARV resistance

References
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This work was supported by a research grant from Gilead Sciences, IN-US-292-5356 (PI: Rolle)