Safety and Efficacy of TDF/FTC/RPV and TDF/FTC/EFV Subgroup-analyses from the SALIF Study

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Introduction

- In the randomized, phase 3b, open-label SALIF study (Switching At Low HIV-1 RNA Into Fixed Dose Combinations) adult patients from five African countries and Thailand who were on 1st line NNRTI-based ART with a viral load <50 copies/mL were randomized (1:1) to switch to an open-label single table regimen (STR) of Tenofovir DF/Emtricitabine/ Rilpivirine (TDF/FTC/RPV; 300/200/25 mg qd) or TDF/FTC/Efavirenz (TDF/FTC/EFV; 300/200/600 mg qd) for 48 weeks (Figure 1)
- The overall analysis demonstrated non-inferiority in maintaining virologic suppression defined as HIV-1 RNA <400 copies/ml (FDA Snapshot, intent-to-treat) (93.9% vs. 96.2%; 95% CI (-6.4%, 1.8%)).[1] Results were similar for the secondary endpoint of maintaining virologic suppression <50 copies/mL
- To provide further insights regarding the utility of switching strategies a subgroup analysis was performed

Methods

- Response rates (HIV-1 RNA <400 copies/mL) and safety and tolerability at week 48 were analysed for the following subgroups: sex, age, women of childbearing potential (WOCBP), region, and NNRTI at switch

Results

Baseline Characteristics

- Median age was similar across the subgroups sex, region, and NNRTI at switch
- The proportion of women in the African sites was 73% vs. 38% in Thailand

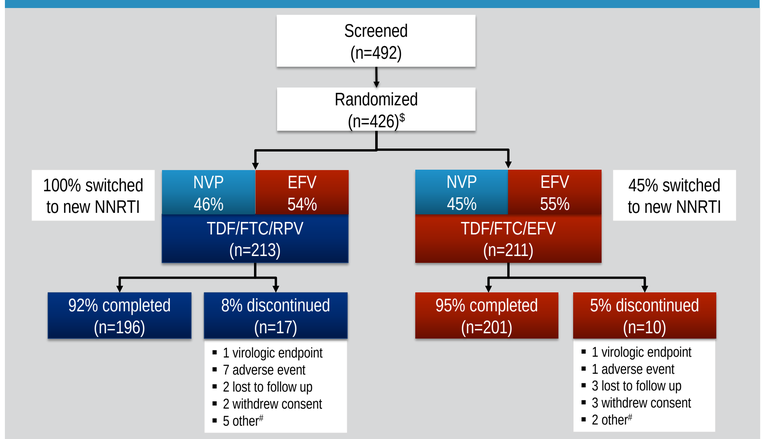
Efficacy

- Efficacy (HIV-1 RNA <400 (Figure 2) and <50 copies/mL) of TDF/FTC/RPV vs. TDF/FTC/EFV was similar across the subgroups sex, age, WOCBP and region
- In patients already receiving EFV at screening, efficacy was 98.3% in the TDF/FTC/EFV arm and 93.0% in the TDF/FTC/RPV arm. For patients switching from NVP-based ART the efficacy was 93.7% in the TDF/FTC/EFV arm and 94.9% in the TDF/FTC/RPV arm

Safety and Tolerability

- Most patients experienced at least one AE, any grade, any cause with similar proportions when analysed by subgroups (Figure 3)
- The proportion of patients experiencing AEs grade 3-4 at least possibly related to the study medication was 6.1% on TDF/FTC/RPV and 1.9% on TDF/FTC/EFV with similar proportions per treatment arm when analysed by subgroups
- Seven patients (3 African women, 4 Thai men) discontinued TDF/FTC/RPV early due to AEs versus one male Thai patient who discontinued TDF/FTC/EFV early due to AEs
- The observed differences in number of AEs may be explained by the switch study design. While 55% of patients randomized to the TDF/FTC/EFV arm remained on EFV, all patients in the TDF/FTC/RPV arm switched their NNRTI to RPV.
- There was no formal statistical testing of safety parameters in the study

Figure 1. Study Disposition



$ Two patients were randomized but not treated
# One site was closed for administrative reasons; 5 patients did not consent to continue at another site (4 RPV arm versus 1 EFV arm)

Table 1. Baseline Demographics (ITT)

		TDF/FTC/RPV (n=213)	TDF/FTC/EFV (n=211)	All Subjects (n=424)
Female, n (%)		137 (64.3%)	134 (63.5%)	271 (63.9%)
	WOCBP, n/N (%)	98/137 (71.5%)	97/134 (72.4%)	195/271 (72.0%)
Age, years	Median (min – max)	41.0 (21 – 64)	41.0 (18 – 65)	41.0 (18 – 65)
	<50 years	186 (87.3%)	182 (86.3%)	368 (86.8%)
	≥50 years	27 (12.7%)	29 (13.7%)	56 (13.2%)
Race	Black, n (%)	157 (73.7%)	152 (72.0%)	309 (72.9%)
	Asian, n (%)	51 (23.9%)	58 (27.5%)	109 (25.7%)
	Other, n (%)	5 (2.3%)	1 (0.5%)	6 (1.4%)
Region	Africa, n (%)	162 (76.1%)	153 (72.5%)	315 (74.3%)
	Thailand, n (%)	51 (23.9%)	58 (27.5%)	109 (25.7%)
NNRTI at Switch	EFV, n (%)	115 (54.0%)	116 (55.0%)	231 (54.5%)
	NVP, n (%)	98 (46.0%)	95 (45.0%)	193 (45.5%)

Figure 2. Efficacy (HIV-1 RNA <400 copies/mL per FDA Snapshot – ITT) at Week 48 per Subgroup

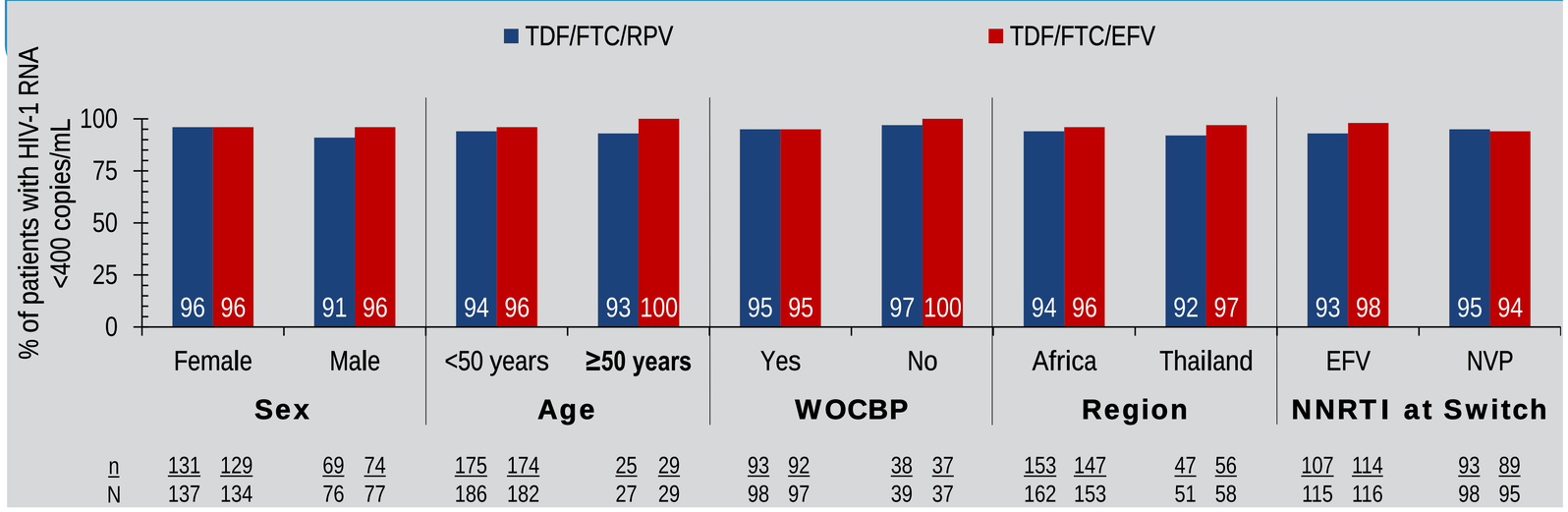
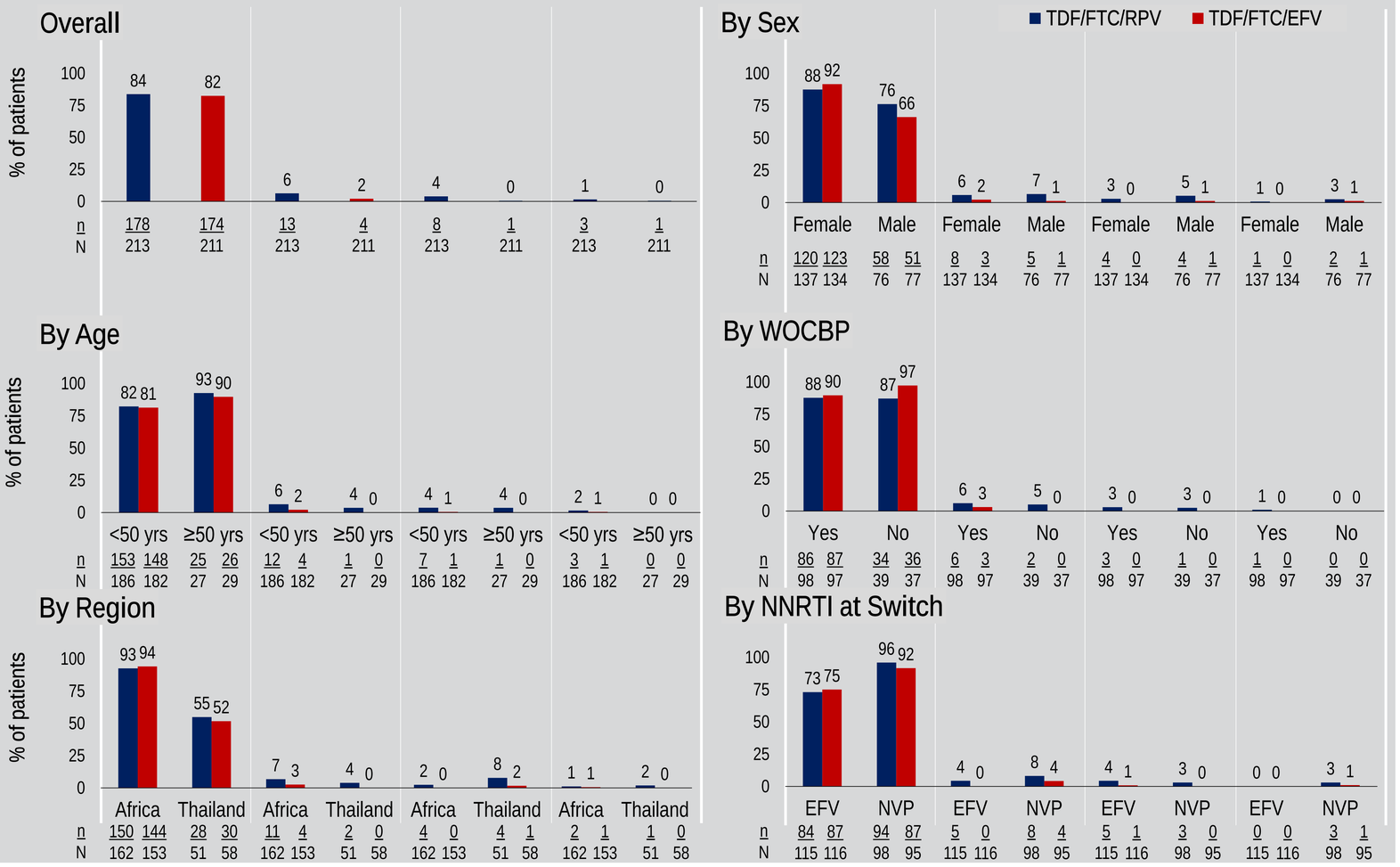


Figure 3. Safety Evaluation per Subgroup (ITT)

* At least possibly related to study medication.

≥1 AE any grade, any cause	Grade 3-4*	Discontinuation*	SAE*



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References

[1] P Munderi et al. AIDS 2016, Durban. THAB0104

Conclusions

- The STR of TDF/FTC/RPV compared to the STR of TDF/FTC/EFV is an effective, well-tolerated once-daily treatment option for virologically suppressed first-line patients on EFV- or NVP-based therapies.
- No clinically relevant differences in efficacy between TDF/FTC/RPV and TDF/FTC/EFV were observed across sex, age, region, childbearing potential, or NNRTI at switch.
- Adverse events after switching were mostly low-grade.