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Comparing effectiveness and tolerability of emtricitabine/tenofovir alafenamide (F/TAF) with emtricitabine/tenofovir disoproxil fumarate (F/TDF) in HIV-1 infected adult patients in routine clinical practice: a cross cohort analysis

Poster PE2/30

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Background

- Single tablet regimens containing tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) have been shown to be highly efficacious and well tolerated in HIV-1 infected patients in both randomized controlled trials[1-6] and observational studies[7-10].
- Compared to F/TDF-based regimens F/TAF provides approximately 90% lower circulating levels of tenofovir leading to an improved tolerability and renal/bone safety profile, while maintaining effective suppression of viral replication.[1-6]

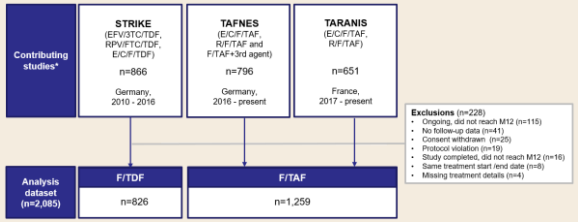
Objective

- To compare F/TDF- and F/TAF-based regimens in routine clinical care
- Outcomes
  - Effectiveness: viral load <50 copies/mL at month 12 (M12)
  - Persistence: % patients remaining on study drug until M12
  - Safety: % patients experiencing drug related adverse events (DRAEs)
  - Adherence: >80%, i.e. <6 missing doses in the last 30 days at M12 using the Visual Analog Scale (VAS) Adherence Questionnaire[11]
  - Physical and mental health status at baseline (M0) and M12 using the Short Form Health Survey (SF-36) questionnaire[12]

Methods

- Multicenter, non-interventional, cross cohort analysis of 3 Gilead sponsored studies (STRIKE, TAFNES, TARANIS) in HIV-1 infected patients (>18 years).
- Patient-level data were pooled.
- Missing data were managed by multiple imputation.[13]
- Propensity scoring using an inverse probability treatment weighted (IPTW) approach was applied to maximize homogeneity and minimize confounding between treatment groups at baseline.[14,15]
- M12 outcomes were evaluated in both antiretroviral treatment (ART)-experienced (TE) and ART-naïve (TN) patients.
- Multivariate analysis was used to measure effectiveness, persistence, adherence (Logistic regression), safety (Poisson regression) and physical and mental health status (repeated measurement ANCOVA) adjusted for confounding factors (HIV RNA, CD4 cell count, alanine aminotransferase (ALT)) at M12. Odds Ratios (OR) and Incidence Rate Ratios (IRR) presented are based on backward selection modelling.
- Sensitivity analyses were carried out in the complete case analysis (CCA), i.e. analyses of data records without missing values in the model variables used.

Figure 1: Patient inclusion



Results

Table 1. Baseline characteristics

	TN		TE	
	F/TDF	F/TAF	F/TDF	F/TAF
Overall, n	280	357	546	902
Sex (male), n (%)	251 (89.6)	334 (93.6)	487 (89.2)	750 (83.1)
Age (years), median (IQR)	38 (30 - 44)	36 (30 - 47)	41 (34 - 48)	50 (40 - 56)
≥50 years	24 (8.6)	52 (14.6)	103 (18.9)	441 (48.9)
Country				
Germany, n (%)	280 (100.0)	286 (80.1)	546 (100.0)	458 (50.8)
France, n (%)	-	71 (19.9)	-	444 (49.2)
CD4, median, IQR	361 (266 - 457)	449 (255 - 614)	516 (360 - 696)	652 (470 - 844)
CD4 <200 cells/mm³, n (%)	28 (10.0)	62 (17.4)	35 (6.4)	40 (4.4)
CD4 Nadir, median (IQR)	338 (255 - 414)	421 (260 - 582)	291 (178 - 450)	295 (163 - 453)
HIV RNA (log_{10}), median (IQR)	4.5 (4.1 – 4.9)	4.5 (3.9 – 5.1)	1.7 (1.7 – 1.7)	1.3 (1.3 – 1.6)
HIV RNA >100,000 copies/mL, n (%)	45 (16.1)	102 (28.6)	13 (2.4)	3 (0.3)
CDC stage C, n (%)	11 (3.9)	29 (8.1)	94 (17.2)	163 (18.1)
Late Presenters (LPs)				
LP_{200}, n (%)	39 (13.9)	71 (19.9)	-	-
LP_{350}, n (%)	153 (54.6)	136 (38.1)	-	-

LP_{200}: CD4 <200/mm³ and/or CDC Stage C1, C2 or C3; LP_{350}: CD4 <350/mm³ and/or CDC Stage C2 or C3

Treatment effectiveness, persistence and safety (Fig. 2a-c)

- Virologic suppression was high with both F/TDF and F/TAF (>90% patients with HIV-1 RNA <50 cp/mL).
- F/TAF regimens compared to F/TDF regimens were associated with higher persistence (p=0.041).
- Fewer patients receiving F/TAF regimens had reported >1 DRAEs compared to patients on F/TAF regimens (p<0.001).
- Inclusion of neither TN/TE status nor LP status showed significance in multivariate models.
- Complete case analyses showed similar results (data not shown).

Self reported treatment adherence (Fig. 2d)

- VAS response rates at M12 were 61.7% and 54.8% for patients on F/TDF and F/TAF respectively. Patients on both regimens were highly adherent to treatment irrespective of treatment history (TN/TE or LP).

Self reported physical & mental health (Fig. 3a-b)

- SF-36 response rates at M0 and M12 were 62.2% and 36.0% for F/TDF and 95.3% and 70.5% for F/TAF patients. No significant differences were observed between the 2 treatment arms in physical and mental health scores (Fig 3a and Fig. 3b).

Figure 3a: Physical Health Score at baseline and M12

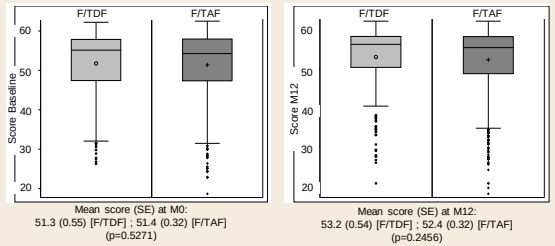


Figure 3b: Mental Health Score at baseline and M12

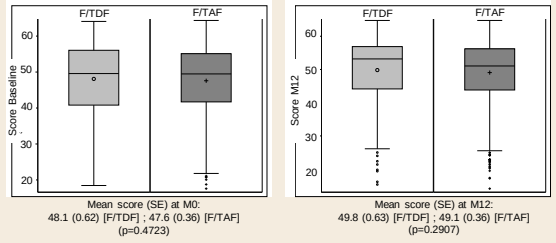
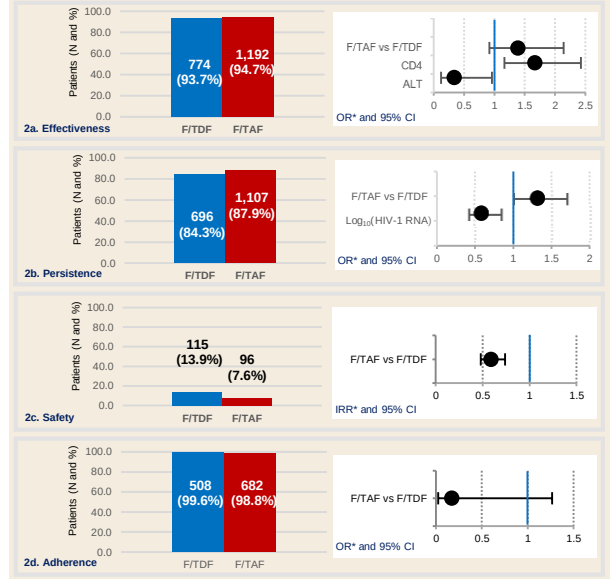


Figure 2: Effectiveness, persistence, safety and adherence at M12



*ORs (—●—), IRRs and 95%-CI (——) are shown for all variables that showed a significant effect in the respective multivariate models (backward selection). Treatment (F/TAF vs F/TDF is shown independent of significance. Blue line indicates odds of no effect. No differences were observed for TN/TE status or LPs.

Conclusions

- Consistent with randomized controlled trials, pooled data from these observational cohorts support the effectiveness, safety and tolerability of F/TAF-based regimens in routine clinical practice in both TN and TE patients.
  - HIV RNA outcomes were similar between the two treatment arms
  - Fewer adverse events were seen in F/TAF patients.
- Higher persistence was observed in F/TAF patients vs F/TDF through 12 months including LP patients.

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