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## Background and Aim

- The prospective TAFNES cohort was initiated to provide real world data on the effectiveness and safety of emtricitabine/tenofovir alafenamide (F/TAF)-based regimens in routine clinical care in Germany. Here we present the final 24-month (M24) outcomes in ART-naïve PLWH (people living with HIV) comparing late presenters (LP) with PLWH in earlier disease stages (non-LP).

## Methods

- Inclusion criteria: ART-naïve PLWH initiated on F/TAF-based ART with elvitegravir/cobicistat (E/C/F/TAF) or rilpivirine (R/F/TAF) or on F/TAF+3<sup>rd</sup> agent as multi-tablet regimen. Definition of late presenters:
  - LP: PLWH with a CD4 cell count <350/μL and/or history of AIDS
  - LP-AD (subgroup of LP with advanced HIV disease): PLWH with a CD4 cell count <200/μL and/or history of AIDS
- Outcomes of interest of the M24 evaluation comparing LP and non-LP:
  - Viral response (HIV-RNA <50cp/mL; discontinuation=failure, loss to follow-up/missing =excluded). Differences in viral response were tested for significance applying logistic regression adjusting for gender, age, HIV-RNA level, and treatment group
  - Study/study drug persistence (Kaplan-Meier estimates)
  - Non-serious/serious adverse drug reactions (ADRs/SADRs)
  - Health-related-quality of life (HRQL) using validated questionnaires, namely the SF-36 (norm based scoring, higher scores indicate higher HRQL) and the HIV Symptom Index (HIV-SI; range 0-80, higher scores indicate more bothersome symptoms)

## Results

## Study population

- N=296 ART-naïve PLWH were eligible for M24 analysis at study completion on March 30, 2020, among them were 94% men with a median age of 37 years (Table 1).
- N=105 of patients were LP (35%); including 56 LP-AD (19%) and 191 non-LP (65%).
- N=156 patients received E/C/F/TAF (30% LP), 41 received R/F/TAF (22% LP), and 99 received F/TAF+3<sup>rd</sup> agent (49% LP; including 84 on F/TAF+DTG, 7 on F/TAF+DRV/r and 5 on F/TAF+RAL).

Table 1. Baseline characteristics

	Overall	LP	LP-AD (Subgroup of LP)	non-LP
N (%)	296 (100)	105 (35)	56 (19)	191 (65)
Male gender, n (%)	278 (94)	97 (92)	51 (91)	181 (95)
Age, years, median (IQR)	37 (30-47)	41 (33-48)*	42 (33-49)	34 (28-45)*
CD4 count, cells/μL, median (IQR)	454 (254-614)	205 (102-276)*	106 (50-159)	559 (456-713)*
CDC stage C (AIDS), n (%)	28 (9)	28 (27)*	28 (50)	0 (0)*
HIV-RNA, log cp/mL, median (IQR)	4.5 (4.0-5.2)*	5.0 (4.5-5.6)*	5.1 (4.5-5.7)	4.3 (3.8-4.9)*
HIV-1 RNA >100,000 cp/mL, n (%)	92 (31)	54 (52)*	32 (59)	38 (20)*

IQR, interquartile range; \*p<0.05 for univariate comparison between LP and non-LP

## Study/study drug persistence: Reasons for discontinuation

- Overall, 34% (n=101/296) of patients discontinued study drug (E/C/F/TAF, R/F/TAF or F/TAF) and/or the study before M24 visit, after a median treatment time of 43 weeks with no significant difference between LP and non-LP. Low rates of discontinuation due to ADRs or virologic failure of 6% and 0% in LP (7% and 0% in LP-AD) and 3% and 2% in non-LP. Reasons for study drug and/or study discontinuation are shown in Table 2.

Table 2. Reasons for discontinuation of study drug (E/C/F/TAF, R/F/TAF or F/TAF) and/or study

	Overall	LP	LP-AD (Subgroup of LP)	non-LP
Discontinuations by M24, n (%)	101 (34)	38 (36)	24 (43)	63 (33)
Due to - therapy simplification	13 (4.4)	8 (7.6)	5 (8.9)	5 (2.6)
- ADRs	11 (3.7)	6 (5.7)	4 (7.1)	5 (2.6)
- patient wish/withdrawal of consent	10 (3.4)	3 (2.9)	3 (5.4)	7 (3.7)
- investigator's discretion	8 (2.7)	2 (1.9)	0 (0.0)	6 (3.1)
- drug-drug interaction	4 (1.4)	1 (1.0)	1 (1.8)	3 (1.6)
- virologic failure*	4 (1.4)	0 (0.0)	0 (0.0)	4 (2.1)
- death	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.5)
- other/no reason specified	9 (3.0)	5 (4.8)	3 (5.4)	4 (2.1)
- loss to follow-up	41 (13.9)	13 (12.4)	8 (14.3)	28 (14.7)

\*last HIV-RNA level in these 4 patients: 32, 158, 1000, 49000 (only BL); baseline resistance available for 1 of 4 patients (no RAMS, i.e. no resistance associated mutations); 1 patient with resistance data at VF (only PI resistance)

## Safety

- Incident ADRs are shown in Table 3. By M24, 19 ADRs (in 4.7% of patients [n=14]) were documented, in 1.4% of patients [n=4] discontinuation due to ADR was reported, but without documented ADR. No SADRs were documented.

Table 3. Reported ADRs

Subgroup	ADRs per patient	Disc.*	Regimen
LP	- Dyspepsia, malaise and pruritus - Flatulence - Migraine and sleep disorder	No/No/Yes No Yes/Yes	E/C/F/TAF E/C/F/TAF E/C/F/TAF
LP-AD (Subgroup of LP)	- Erectile dysfunction - Diarrhoea - Headache and general feeling of illness** - Nephropathy toxic	Yes Yes Yes/Yes Yes	E/C/F/TAF F/TAF + DTG F/TAF + DTG F/TAF + DTG
Non-LP	- Diarrhoea - Diarrhoea and acne - Disturbance in attention and dizziness - Fatigue - Headache - Headache** - Loss of libido - Nausea - Pruritus - Feeling unwell** - Feeling unwell**	Yes No/No Yes/Yes No No Yes No No No Yes Yes	E/C/F/TAF E/C/F/TAF E/C/F/TAF E/C/F/TAF E/C/F/TAF E/C/F/TAF E/C/F/TAF E/C/F/TAF F/TAF + DTG F/TAF + DTG

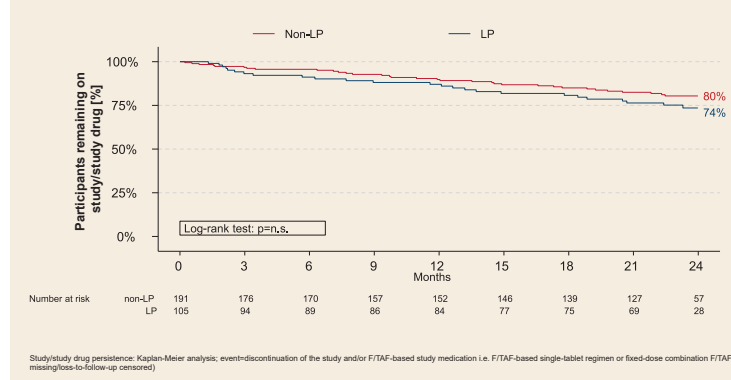
\*Disc. of study drug (E/C/F/TAF, R/F/TAF or F/TAF) due to ADR (no serious ADR); \*\*discontinuation due to ADR, but not documented as ADR

## Results (cont'd)

## Study/study drug persistence: Kaplan-Meier analysis

- Study/study drug persistence through M24 in LP and non-LP was 74% (LP-AD 69%) and 80%, respectively (Figure 1).

Figure 1. Time on study/study drug stratified by late presentation (Kaplan-Meier analysis)

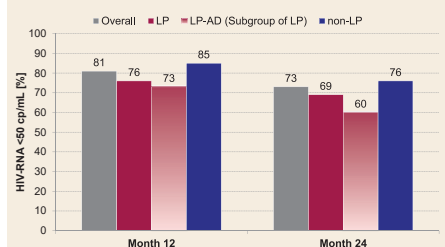


## Virologic effectiveness (Month 24)

- Overall: 73% (n=177/241)
  - <50 cp/mL: n=177
  - ≥50 cp/mL: n=4
  - discontinuation: n=60
- LP 69%\* (n=62/90) [LP-AD 60% (n=28/47)]
- non-LP 76%\* (n=115/151)
- Excluded:
  - loss to follow-up: n=41
  - missing: n=14

\*No significant difference between LP and non-LP in univariate analysis and adjusted for covariables.

Figure 2. HIV-RNA &lt;50 cp/mL (discontinuation = failure; loss to follow-up/missing = excluded)



## Health-related quality of life (HRQL): SF-36 and HIV Symptom Index (HIV-SI)

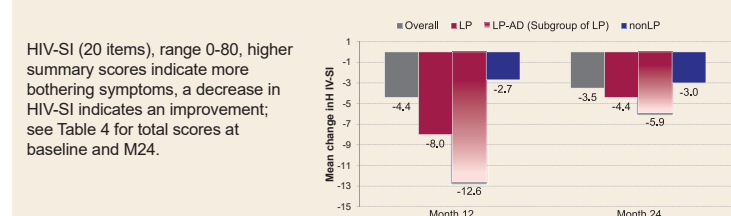
- Changes in HRQL scores reflect improvements within all subgroups for HIV-SI and in LP and LP-AD for SF-36 (Table 4).

Table 4. HRQL: Baseline (BL) and M24 outcomes, changes from BL<sup>1</sup>

	Overall	LP	LP-AD (Subgroup of LP)	non-LP
BL	45.9 (11.2)	43.7 (11.6)	42.8 (10.2)	47.1 (10.8)
M24	49.4 (10.6)	50.3 (8.7)	49.4 (7.7)	48.9 (11.5)
Change	+3.5 (12.3)	+6.6 (12.4)	+6.7 (8.7)	+1.8 (12.0)
[n]	[127]	[43]	[19]	[84]
BL	54.7 (8.0)	52.5 (9.1)	48.0 (8.8)	55.8 (7.2)
M24	56.7 (7.1)	55.9 (6.4)	55.4 (5.7)	57.0 (7.5)
Change	+2.0 (9.1)	+3.4 (8.8)	+7.4 (9.6)	+1.2 (9.2)
[n]	[127]	[43]	[19]	[84]
BL	12.9 (12.3)	15.0 (12.4)	17.8 (12.5)	11.8 (12.1)
M24	9.4 (10.0)	10.7 (10.7)	11.9 (11.0)	8.7 (9.6)
Change	-3.5 (11.0)	-4.4 (11.4)	-5.9 (12.1)	-3.0 (10.9)
[n]	[126]	[44]	[20]	[82]

<sup>1</sup>Calculations based on patients who completed both questionnaires (at BL and M24); SD, standard deviation; \*norm based scoring, higher scores indicate higher HRQL; \*range 0-80, higher scores indicate more bothersome symptoms

Figure 3. HIV-SI: Change in symptom distress



## Conclusions

- In the German TAFNES cohort of patients on F/TAF based regimens, late presenters had a similarly high persistence and virologic response rate as nonlate presenters at month 24. Discontinuation due to virologic failure was rare irrespective of stage of HIV disease (<2%).

- Improvements from baseline in HRQL were observed in late presenters, particularly in those with advanced disease.

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