P129

Effectiveness and persistence of F/TAF-containing regimens (E/C/F/TAF, R/F/TAF or F/TAF+3rd agent) in late and very late presenters – Final 24-month results from the German TAFNES cohort study

Nils Postel[1], Heiko Jessen[2], Ramona Pauli[3], Heribert Hillenbrand[4], Thomas Heuchel[5], Ansgar Rieke[6], Heribert Knechten[7], Claudia Emmerich[8], Sandra Schreiber[8], Frank Mack[8], Richard Haubrich[9], Hans-Jürgen Stellbrink[10]

[1]prinzmed private practice Munich Germany; [2]Praxis Jessen[2] + Kollegen, Berlin Germany; [3]Gemeinschaftspraxis Becker/Pauli Munich Germany; [4]MVZ Praxis City Ost Berlin Germany; [5]Praxis Heuchel Chemnitz Germany; [6]Gemeinschaftspraxis Koblenz-Mayen Kemperhof Koblenz Germany; [7]PZB Aachen Germany; [8]Gilead Sciences Munich Germany; [9]Gilead Sciences Foster City USA; [10]ICH Study Center Hamburg Germany

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Tel: (650) 522-6009
Fax: (650) 522-5260

Background

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+3rd 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-naive 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+3rd 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

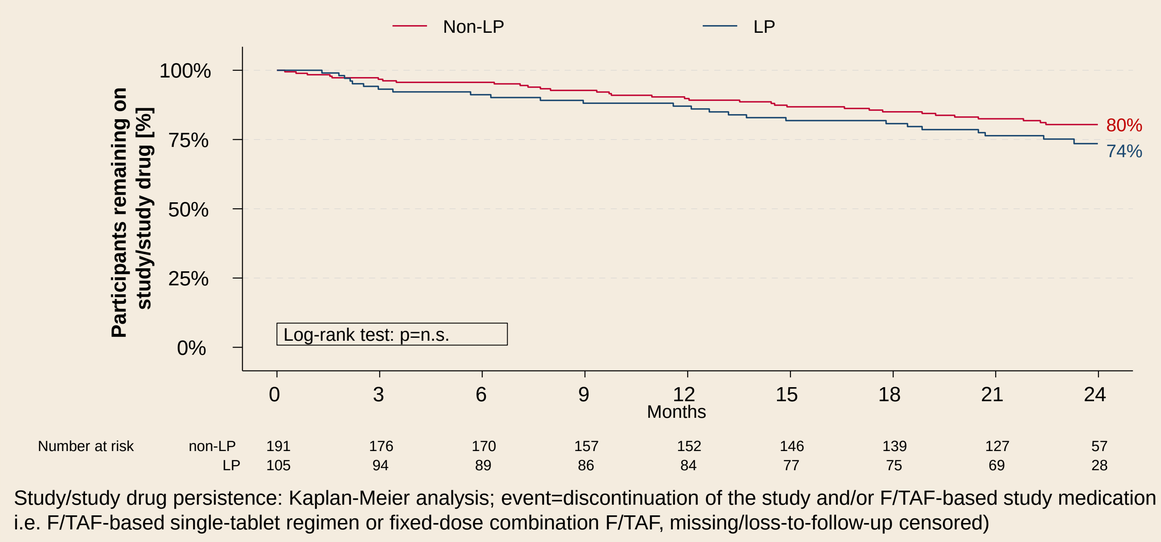
Subgroup		ADRs per patient	Disc.*	Regimen
LP	-	Dyspepsia, malaise and pruritus	No/No/Yes	E/C/F/TAF
	-	Flatulence	No	E/C/F/TAF
	-	Migraine and sleep disorder	Yes/Yes	E/C/F/TAF
LP-AD (Subgroup of LP)	-	Erectile dysfunction	Yes	E/C/F/TAF
	-	Diarrhoea	Yes	F/TAF + DTG
	-	Headache and general feeling of illness**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

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 (Figure1).

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



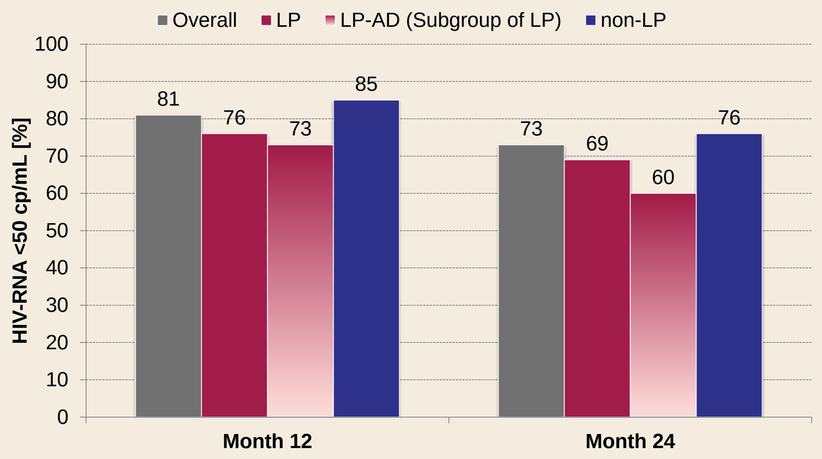
Study/study drug persistence: Kaplan-Meier analysis; event=discontinuation of the study and/or F/TAF-based study medication i.e. F/TAF-based single-tablet regimen or fixed-dose combination F/TAF, missing/loss-to-follow-up censored)

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 <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).

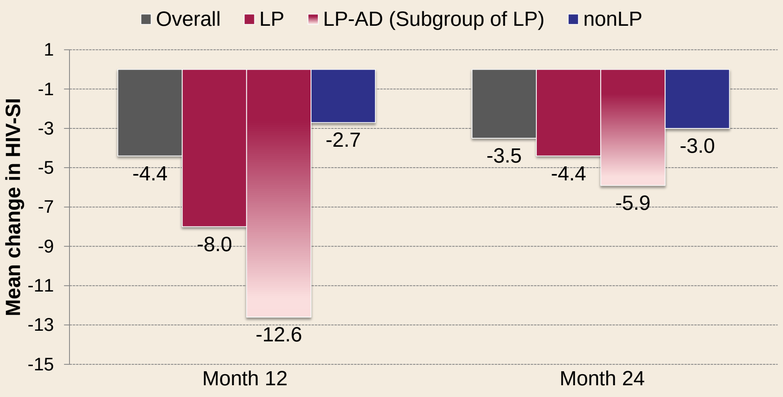
Table 4. HRQL: Baseline (BL) and M24 outcomes, changes from BL[1]

			Overall	LP	LP-AD (Subgroup of LP	non-LP
SF-36 score	mental component[2], mean (+/-SD)	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]
	physical component[2], mean (+/-SD)	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]
HIV-SI[3]	mean (+/-SD)	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]

[1]Calculations based on patients who completed both questionnaires (at BL and M24); SD, standard deviation; [2]norm based scoring, higher scores indicate higher HRQL, [3]range 0-80, higher scores indicate more bothering symptoms

Figure 3. HIV-SI: Change in symptom distress

HIV-SI (20 items), range 0-80, higher summary scores indicate more bothering symptoms, a decrease in HIV-SI indicates an improvement; see Table 4 for total scores at baseline and M24.



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 non-late 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.

Acknowledgments

- Design, study conduct and financial support were provided by Gilead Sciences.
- Statistical analysis and support in medical writing were provided by MUC Research, Munich, Germany.
- We extend our thanks to all participating patients and investigators of the TAFNES cohort:
  Bellmunt Zschaepe A. Dortmund; Brockmeyer N. Bochum; Christensen S. Muenster; Cordes C. Berlin; Esser S. Essen; Heiken H. Hannover; Heuchel T. Chemnitz; Jaeger H. Munich; Jessen H. Berlin; Khaykin P. Frankfurt am Main; Koeppe S. Berlin; Mauss S. Duesseldorf; Meurer A. Munich; Moll A. Berlin; Mueller A. Frankfurt; Mueller M. Stuttgart; Obst W. Magdeburg; Pauli R. Munich; Postel N. /Anzboeck M. Munich; Qurishi N. Cologne; Rausch M. Berlin; Rieke A. Koblenz; Schaffert A. Stuttgart; Schattenberg J. Mainz; Schleenvoigt B. Jena; Spinner C. Munich; Stephan C. Frankfurt; Stoehr A. Hamburg; Usadel S. Freiburg; Waizmann M. Leipzig.