P063

Impact of baseline comorbidities on ART persistence and effectiveness in people living with HIV (PLWH) receiving F/TAF-based regimens – Final 24-month results from the German TAFNES cohort study

Stefan Scholten[1], Heribert Hillenbrand[2], Nils Postel[3], Heribert Knechten[4], Ramona Pauli[5], Heiko Jessen[6], Claudia Emmerich[7], Claudia Pehlivan[7], Boris Albuquerque[7], Richard Haubrich[8], Hans-Jürgen Stellbrink[9]

[1]Praxis Hohenstaufenring Köln Germany; [2]MVZ Praxis City Ost Berlin Germany; [3]prinzmed private practice Munich Germany; [4]PZB Aachen Germany; [5]Gemeinschaftspraxis Becker/Pauli Munich Germany; [6]Praxis Jessen[2] + Kollegen, Berlin Germany; [7]Gilead Sciences Munich Germany; [8]Gilead Sciences Foster City USA; [9]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. With an ageing HIV population, comorbidity burden increases and represents a major challenge in the management of HIV care. Here we present 24-month (M24) effectiveness and safety outcomes of the TAFNES cohort (for F/TAF-based ART) stratified by the presence of comorbidities at baseline.

Methods

- M24 evaluation of treatment with F/TAF-based single-tablet regimen with elvitegravir/cobicistat (E/C/F/TAF) or rilpivirine (R/F/TAF) or on F/TAF-based multi-tablet combinations with a 3rd agent (F/TAF+3rd agent).
- Inclusion criteria for the treatment-experienced F/TAF+3rd agent group was age ≥50 years.
- Effectiveness outcomes comprise viral response (HIV-RNA <50 cp/mL; discontinuation=failure, loss-to-follow-up/missing=excluded) and study/study drug persistence (Kaplan-Meier estimates; event=discontinuation, loss to follow-up censored).
- Documentation of comorbidities was based on predefined comorbidity categories and free-text entries for “other comorbidities”.

Results

Study population

714 PLWH were evaluable for analysis, 92% were men and the median age was 45 years. 16% of patients with CDC stage C, 39% were treatment-naïve (TN) and 61% treatment-experienced (TE) (Table 1).
308 patients received E/C/F/TAF, 179 R/F/TAF and 227 F/TAF+3rd agent.

Table 1. Baseline characteristics among baseline comorbidity subgroups

	Overall	Number of baseline comorbidities		
		No	1	≥2
N (%)	714 (100)	358 (50)	165 (23)	191 (27)
Male gender, n (%)	655 (92)	326 (91)	153 (93)	176 (92)
Age, years, median (IQR)	45 (34-54)	40 (32-49)	48 (36-55)	52 (42-58)
TN, n (%)	278 (39)	177 (49)	63 (38)	38 (20)
TE, n (%)	436 (61)	181 (51)	102 (62)	153 (80)
CD4 count, cells/µL, median (IQR)	556 (390-765)	543 (398-756)	553 (384-740)	588 (384-815)
CDC stage C (AIDS), n (%)	112 (16)	52 (15)	23 (14)	37 (19)
TN: HIV-RNA, log cp/mL, median (IQR)	4.5 (4.0-5.2)	4.5 (3.9-5.3	4.5 (4.2-5.0)	4.6 (4.0-5.1)
HIV-1 RNA >100,000 cp/mL , n (%)	86 (31)	58 (33)	16 (26)	12 (32)
TE: HIV-RNA, log cp/mL, median (IQR)	1.3 (1.3-1.6)	1.3 (1.3-1.6)	1.3 (0.0-1.6)	1.3 (1.3-1.6)
HIV-1 RNA <50 cp/mL , n (%)	403 (95)	162 (93)	96 (96)	145 (97)

IQR: interquartile range; TN: treatment-naïve; TE: treatment-experienced

Baseline comorbidities

Comorbidities (documented in 50% of patients) were more common among treatment-experienced (58% vs 36% in TN) and PLWH ≥50 years (70% vs 36% in PLWH <50 years). Distribution across treatment groups is shown in Table 2.

Table 2. Baseline comorbidities among treatment groups

	Overall (N=714)	E/C/F/TAF (N=308)	R/F/TAF (N=179)	F/TAF+ 3rd agent (N=227)
Documented comorbidities, n (%)	356 (50)	115 (37)	99 (55)	142 (63)
TE vs TN, %	58 vs 36	46 vs 29	54 vs 61	78 vs 39
≥ 50 years vs <50 years, %	70 vs 36	70 vs 36	70 vs 49	75 vs 36

TN, treatment-naïve, TE, treatment-experienced

Comorbidities present in ≥5% of patients were hypertension (15%), neuropsychiatric disorders (11%), hyperlipidemia (6%), and cardiovascular diseases (5%). Among “others”, “gastrointestinal disorders” (6%) and “metabolism/nutrition disorders” (10%; including vitamin-D deficiency [8%]) were reported most frequently. Of note, the clinical relevance of documented “other” comorbidities has not been further specified.

Reasons for discontinuation

Overall, 28% (n=198/714) of patients discontinued study drug (E/C/F/TAF, R/F/TAF or F/TAF) and/or the study before M24 visit. Main reasons were treatment simplification (in 3.1%, 4.2% and 6.3% of patients, respectively) and adverse drug reactions (ADRs, in 3.1%, 5.5% and 3.1%). Discontinuation due to virologic failure was reported in 0.8%, 2.4% and 1.0%, respectively (Table 3).

Table 3. Reasons for discontinuation of study drug (E/C/F/TAF, R/F/TAF or F/TAF) and/or study

	Overall (N=714)	Number of baseline comorbidities		
		No (N=358)	1 (N=165)	≥2 (N=191)
Discontinuations by M24, n (%)	198 (28)	90 (25)	52 (32)	56 (29)
Due to – therapy simplification[1]	30 (4.2)	11 (3.1)	7 (4.2)	12 (6.3)
– adverse drug reaction (ADR)[2]	26 (3.6)	11 (3.1)	9 (5.5)	6 (3.1)
– patient wish/withdrawal of consent	23 (3.2)	12 (3.4)	4 (2.4)	7 (3.7)
– investigator’s discretion	13 (1.8)	10 (2.8)	1 (0.6)	2 (1.0)
– drug-drug interaction	9 (1.3)	0 (0.0)	3 (1.8)	6 (3.1)
– virologic failure[3]	9 (1.3)	3 (0.8)	4 (2.4)	2 (1.0)
– death[4]	5 (0.7)	0 (0.0)	3 (1.8)	2 (1.0)
– other/no reason specified	15 (2.1)	5 (1.4)	3 (1.8)	7 (3.7)
– loss to follow-up	68 (9.5)	38 (10.6)	18 (10.9)	12 (6.3)

[1] All F/TAF+3rd agent; [2]incl. 2 patients with SADRs (see Table 4); [3]Two virologic failures documented as ADR (“virological failure” and “blood HIV RNA increased”); [4]sepsis, cardiac arrest, acute hemorrhagic shock caused by esophageal varices bleeding, thrombosis after surgical procedure of dysplasia esophageal and gastric, unknown

Safety

By M24, in 28 patients (3.9%), ADRs were the documented reason for study and/or study drug (E/C/F/TAF, R/F/TAF or F/TAF) discontinuation, including 2 patients with virologic failure as documented ADR and 7 patients without further specification or documented ADR (Tables 3 and 4). Overall, 51 ADRs were reported including 3 serious adverse drug reactions (SADRs) in 5.7% of patients (n=41) (Table 4).

Table 4. Adverse drug reactions (ADRs) reported in the study

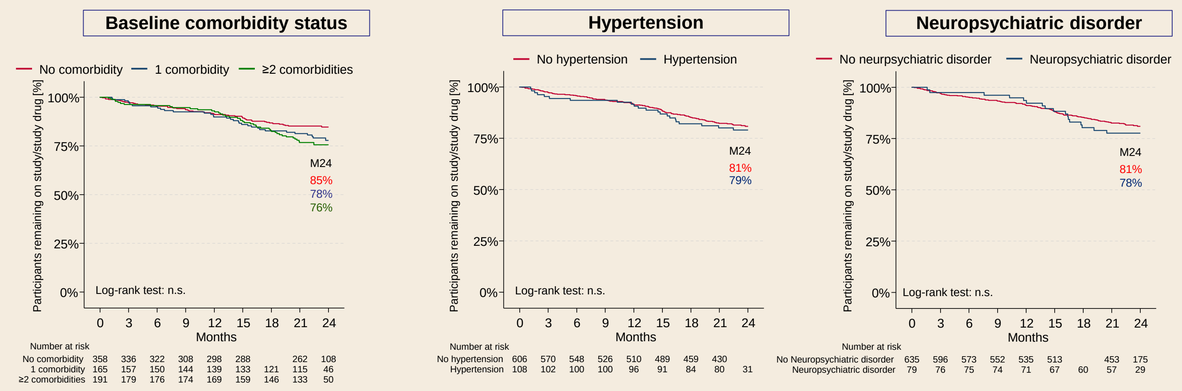
BL status	ADRs per patient	Disc.[1]	ADRs per patient	Disc.[1]
No comorbidity	- Blood HIV RNA increased[2]	Yes	- Headache[3]	Yes
	- Dermatological ADR[3]	Yes	- Headache (SADR), palpitations (SADR)	Yes/Yes
	- Depression	Yes		
	- Depression	Yes	- Insomnia	No
	- Diarrhoea, acne	No/No	- Pain in extremity	Yes
	- Erectile dysfunction[3]	Yes	- Pathological fracture	No
	- Fatigue	Yes	- Pruritus	No
	- Feeling unwell[3]	Yes	- Sleep disorder (SADR)	Yes
	- Flatulence, vertigo, abnormal dreams	No/No/No	- Weight increased	Yes
	- Headache	No	- Virologic failure[2]	Yes
1 comorbidity	- Abdominal pain upper	Yes	- Headache, vertigo, hyperhydrosis	Yes/Yes/Yes
	- Arthralgia	Yes	- Headache, general feeling of illness[3]	Yes/Yes
	- Disturbance in attention, dizziness	Yes/Yes		
	- Dyspepsia, malaise, pruritus	No/No/Yes	- Libido decreased	Yes
	- Fatigue	No	- Loss of libido	No
	- Feeling unwell[3]	Yes	- Nephropathy toxic	Yes
	- Headache, nausea	No/No	- Weight increased	No
≥2 comorbidites	- Constipation	Yes	- Flatulence	No
	- Diarrhoea	Yes	- Nausea	No
	- Diarrhoea	Yes	- Neuropsychiatric ADR[3]	Yes
	- Erectile dysfunction	Yes	- Weight increased	Yes

[1]Disc.: study drug (E/C/F/TAF, R/F/TAF or F/TAF) or study discontinuation due to serious (S)ADR; [2]Virologic failure documented as ADR; [3]Not documented as ADR, but as F/TAF study drug discontinuation reason

Persistence on study/study drug

Overall study/study drug persistence through M24 was 81%. Persistence with 0, 1 or ≥2 baseline comorbidities was 85%, 78% and 76%, respectively (Figure 1).
Through month 24, persistence in patients with hyperlipidemia was 77% (no hyperlipidemia 81%; number at risk at baseline 44 vs 670), persistence in patients with cardiovascular disease was 89% (no cardiovascular disease 81%; number at risk 38 vs 676). Persistence in patients with hypertension and neuropsychiatric disorder is shown in Figure 1.

Figure 1. Time on study/study drug by different baseline comorbidity groups
(Kaplan-Meier analysis)



Study/study drug persistence (Kaplan-Meier estimates censoring loss-to follow-up; event=discontinuation of the study and/or F/TAF-based study medication (E/C/FTAF, R/F/TAF or F/TAF)).

Virologic effectiveness at month 24

Overall virologic effectiveness was 75% (n=452/602): 79% in patients without comorbidities (n=239/301), 73% with one (n=99/136), 69% with ≥2 comorbidities (n=114/165) (see Figure 2 and Table 5). Regarding subgroups with specific comorbidities, rates were 74% (hypertension; n=72/97), 73% (hyperlipidemia; n=30/41), 69% (neuropsychiatric disorders; n=47/68), and 64% (cardiovascular disease; n=23/36).

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

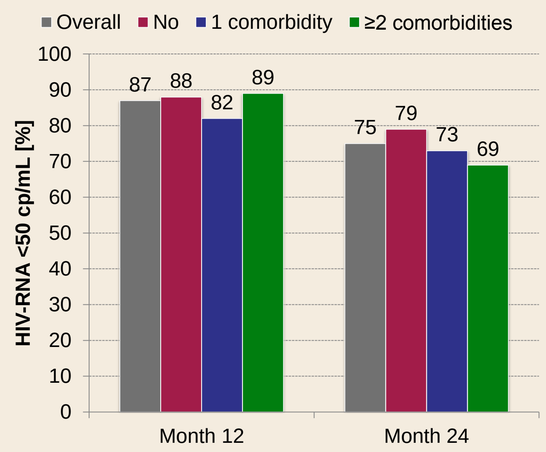


Table 5. Patient disposition and virologic outcomes at M24

	Overall	Number of baseline comorbidities		
		No	1	≥2
Total, N	714	358	165	191
Loss to follow-up, n	68	38	18	12
Missing values, n	44	19	11	14
Effectiveness set, n (%)	602 (84)	301 (84)	136 (82)	165 (86)
HIV-RNA<50, n (%)	452 (75)	239 (79)	99 (73)	114 (69)
HIV-RNA<200, n (%)	15 (2.5)	9 (3.0)	1 (0.7)	5 (3.0)
HIV-RNA≥200, n (%)	5 (0.8)	1 (0.3)	2 (1.5)	2 (1.2)
Disc. due to VF, n (%)	9 (1.4)	3 (1.0)	4 (2.9)	2 (1.2)
Disc. for other reasons[1], n (%)	121 (20)	49 (16)	30 (22)	42 (25)

[1]see Table 3 for details; Disc.: study and/or study drug discontinuation; VF: virologic failure

Conclusions

- Patients included in TAFNES reflect the aging HIV population with accumulating comorbidities.
- Despite different patient and treatment characteristics, persistence on study drug and/or study was similar with respect to the presence of comorbidities with a slight divergence after month 12 attributed to other reasons than virologic failure or ADR.
- Discontinuation rates due to virologic failure or drug-related AEs were low in patients presenting without, with one or with ≥2 comorbidities.

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.