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KEY FACTORS FOR TREATMENT CHANGES WITHIN ONE YEAR AFTER STARTING cART IN THE GERMAN CLINSURV COHORT, BETWEEN 2005-2017

Stecher M.[1,2]*, Schommers P.[1,2]*, Kollan C.[3], Hamacher L.[1], Platten M.[1,2], Lehmann C.[1,2], Dold L.[4,5], Schmidt D.[3], Gunsenheimer-Bartmeyer B. [3], Vehreschild J.J.[1,2], on behalf of the ClinSurv Study Group

[1]University Hospital of Cologne, Cologne, Germany, [2]German Center for Infection Research (DZIF), partner site Bonn-Cologne, Cologne, Germany, [3]University Hospital of Bonn, Bonn, Germany, [4]German Center for Infection Research (DZIF), partner site Bonn-Cologne, Bonn, Germany, [5]Robert-Koch Institute, Berlin, Germany

Background

- Initiation of combined antiretroviral therapy (cART) has markedly increased survival and quality of life in people living with HIV/AIDS (PLWHA) [1;2].
- In 2017, approximately 36.9 million people were living with HIV. Of those, 21.7 million people were accessing cART [3].
- The effectiveness of cART is commonly measured by its ability to durably suppress HIV replication and to affect immune system reconstitution, which in turn result in decreased rates of HIV clinical progression, AIDS-related opportunistic diseases, and death [5].
- With the advent of new treatment options, including fixed-dose combinations and an increasing number of single-tablet combinations, the durability of first-line cART regimes is developing [4].
- These newer therapies have been associated with greater efficacy, tolerability, and convenience [4].

Objective

Assessing predictors of first-line cART treatment changes within the German ClinSurv cohort between 2005 and 2017

Methods

- We used data from the prospective multicenter German Clinical Surveillance of HIV Disease (ClinSurv) cohort of the Robert-Koch-Institute (RKI) [5].
- We included PLWHA, aged ≥18 years of age, who initiated cART as first-line therapy between 2005 and 06/2017.
- Sociodemographic and geographic data were used to characterize our study population (**Table1**).
- Time to event was calculated as the time between initiation of first-line cART and therapy change or stop, using Kaplan Meyer.
- Differences between groups were analyzed and compared using the log rank test. Pairwise log rank comparisons were used to determine differences within each group.
- To counter multiple comparisons, we applied a Bonferroni correction [6].
- A multivariable Cox proportional hazard model was used to assess predictors of treatment change after starting cART.

References:

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- A total of 4,210 (47.9%) stopped or changed their first-line cART between 2005 and 06/2017.
- The most frequently used first-line combinations were nucleoside reverse-transcriptase inhibitor/protease inhibitor/boosted (NRT/PI/boosted) (3,683; 41.9%) and nucleoside and non-nucleoside reverse-transcriptase inhibitor (NRT/NNRTI) (2,951; 33.6%) (Table 1). Changes over time are displayed in Figure 1.

Table 1: Patient characteristics, median time to stop/change cART (months) and baseline characteristics (Kaplan-Meyer method) with overall comparison using log-rank test.

	No of patients, n (%)	Median time (months) to stop/change first-line cART (IQR)	p-value**	HR (95%CI)***	p-value
Total	8,788 (100)				
Age (Median, IQR)	38 (31-46)		0.772		
18-39	4,629 (52.7)	63 (59-68)			
40-69	3,770 (42.9)	60 (56-65)			
≥70	77 (0.9)	49 (26-72)			
Sex			<0.001		
Female	1,748 (19.9)	45 (38-51)		1.21 (1.12-1.31)	<0.001
Male	7,040 (80.1)	66 (62-69)			
Risk group*			<0.001		
MSM	4,470 (50.9)	67 (62-72)			
HTS	1,467 (16.7)	62 (55-69)			
ENDEMIC	1,171 (13.3)	53 (44-62)			
PWID	451 (5.1)	47 (34-61)			
Other/ Unknown	1,229 (14.0)	56 (47-65)			
Baseline CD4+ T cell count (µl) (Median, IQR)	287 (111-369)		<0.001		
<200	3,479 (39.6)	52 (47-57)		0.97 (0.86-1.10)	0.727
200 – 349	2,631 (29.9)	72 (66-78)		0.89 (0.78-1.01)	0.063
350 – 499	1,399 (15.9)	69 (60-78)		0.91 (0.83-1.05)	0.222
≥500	992 (11.3)	61 (51-71)			
Baseline HIV-1 RNA viral load (copies/ml) (Median, IQR)	65,000 (13,903-213,000)		<0.001		
<10,000	1,787 (20.3)	63 (56-69)			
10,000 - 99,999	3,152 (35.9)	70 (65-76)		0.92 (0.83-1.01)	0.065
100,000 - 999,999	2,929 (33.3)	58 (53-64)		0.99 (0.90-1.09)	0.886
≥1mio.	489 (5.6)	29 (23-36)		1.32 (1.14-1.52)	<0.002
Year of ART start			0.198		
2005-2009	3,624 (41.2)	66 (60-71)			
2010-2015	4,584 (52.2)	56 (53-60)		1.26 (1.16-1.35)	<0.001
2016/2017	580 (6.6)	n.a.		1.30 (1.03-1.65)	0.027
First-line regimens			<0.001		
NRTI/PI/boosted	3,682 (41.9)	44 (40-47)			
NRTI/NNRTI	2,951 (33.6)	92 (86-98)			
NRTI/II	1,324 (15.1)	n.a.			
NRTI/II/boosted	352 (4.0)	n.a.			
PI/boosted	87 (1.0)	7 (2-12)			
Others	392 (4.4)	19 (15-23)			
Number of tablets per day			<0.001		
1	1,113 (13)	90 (77-103)			
2-3	4,614 (53.7)	76 (71-82)		1.42 (1.23-1.63)	<0.001
4-9	2,796 (32.5)	42 (38-46)		1.90 (1.63-2.22)	<0.001
10	69 (0.8)	18 (7-29)		2.23 (1.61-3.01)	<0.001
Tablet administration			<0.001		
Once per day	6,063 (69.0)	71 (66-75)			
Twice per day	2,529 (28.8)	40 (35-46)		1.21 (1.12-1.32)	<0.001

*MSM, men who have sex with men; HTS, heterosexual; ENDEMIC, recent immigration from a country with a HIV prevalence; PWID, people with injection drug use. NRTI; nucleoside reverse-transcriptase inhibitor, NNRTI; non-nucleoside reverse-transcriptase inhibitors II; integrase inhibitor, PI; protease inhibitor. ** Log-rank overall comparison (p<0.05).***Cox regression mode, Hazard ratios (HRs) and 95% confidence intervals (CI) associated with treatment stop/change. Cox regression adjusted for gender, age, year of cART initiation, number of tablets per day, tablet administration per day, viral load and CD4+ T cell count at time of cART initiation, risk group, cART regime and country of origin.

Results

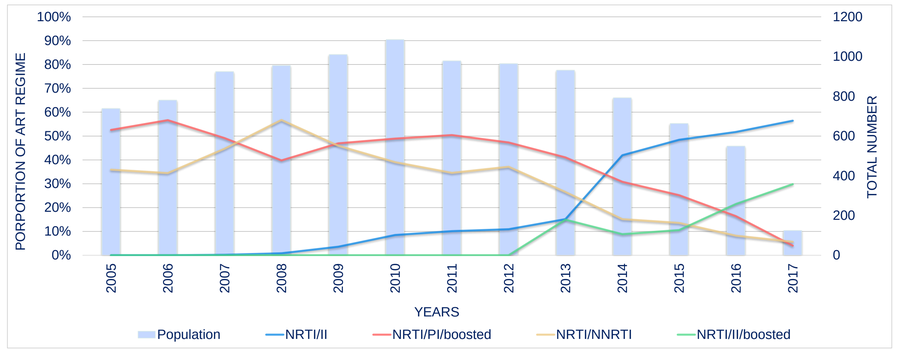

Figure 1. First-line cART regime and total number of patients over time. NRTI; nucleoside reverse-transcriptase inhibitor, NNRTI; non-nucleoside reverse-transcriptase inhibitors, II; integrase inhibitor, PI; protease inhibitor

- Time to event analysis indicated strong prognostic factors regarding the time to stop/ change cART (Table 1). Illustrated by the Kaplan Meyer curve in Figure 2A) by first-line regime and B) by baseline HIV-1 RNA viral load (VL).
- Factors most strongly associated with first-line stop/change in the Cox regression model, were a VL >1Mio. (vs. <10,000 (copies/ml)) and tablet administration twice per day (vs. once per day) (Table 1).
- The HR increased markedly with the amount of daily administered tablets from HR 1.42, 95% CI 1.23-1.63 (2-3 tablets) to HR 2.23, 95% CI 1.61-3.01 (10 tablets) (vs. one tablet).

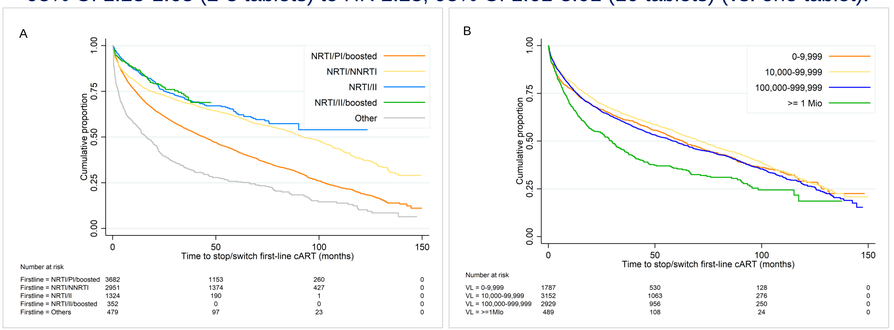

Figure 2: Unadjusted cumulative proportion of stopping first-line cART by A) first-line regime and B) HIV RNA viral load (VL) in copies/(ml) at baseline.

Conclusion

- Our analysis revealed, that the VL at baseline, the number of tablets per day and the amount of daily administered tablets are significantly associated with treatment change.
- Understanding the complex interplay of factors more clearly is essential for clinicians and healthcare decision-makers to be able to achieve the level of adherence required to effectively enhance the first-line cART regime.

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Corresponding Authors:
Melanie Stecher, melanie.stecher@uk-koeln.de
Jörg Janne Vehreschild, joerg.vehreschild@uk-koeln.de