Starting ART Early After HIV Acquisition Reduces Long-Term Non-AIDS Defining Malignancy Risk

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Background

- In people with HIV incidence of Non-AIDS-Defining Malignancies (NADM) is increased[1,2], particularly that of infection-related NADM[3,4,5].
- Starting ART at higher CD4-cell counts is associated with a reduced malignancy risk (i.e. including AIDS-defining malignancies)[6,7,8].
- **Aim of our study was to assess if starting ART within 12 months of HIV acquisition reduces the risk of NADM.**

Methods

Study population

- ATHENA cohort participants starting ART between 2000-2022 at age ≥ 18 years, excluding those with a prior NADM
- **Early start of ART was defined as starting ART within 12 months of a documented negative HIV test result or a documented primary HIV infection;** all others were considered as starting ART "late"

Statistical analysis

- We used Cox regression models to estimate **hazard ratios for starting ART early vs. starting ART "late".**
- Baseline was defined as start of ART.
- Models were adjusted for: sex and HIV transmission category, region of origin and nadir CD4-count (fixed at baseline); and age, CD4-count (lagged by 3 months), CD4/8 ratio, smoking status, alcohol use, calendar time, and time spent with HIV RNA > 200 copies/ml while on ART (time-updated).

References

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Starting ART within 12 months of acquiring HIV compared to starting ART later, persistently reduces the risk of Non-AIDS-Defining Malignancy, independent of CD4-cell count

Results

- We identified 23,891 eligible participants, 2,028 (8.5%) of whom started ART early. 81.3% were male, baseline median age 39.0 years and baseline median CD4 370/mm^3. Median follow-up was 110 months: 67 months for those starting ART early, 115 months for those starting "late".

Incidence rates

	"Early ART" start (n = 2,028)			"Late ART" start (n = 21,863)		
	Number	Person Years of Follow-Up	Incidence rate per 1000 PYFU [95% CI]	Number	Person Years of Follow-Up	Incidence rate per 1000 PYFU [95% CI]
NADM	26	12,020	2.2 [1.5-3,2]	1,152	219,138	5.3 [5.0-5.6]
Infection-related NADM	8	12,082	0.7 [0.3-1.3]	375	221,865	1.7 [1.5-1.9]
Infection-unrelated NADM	18	12,046	1.5 [0.9-2.4]	814	220,808	3.7 [3.4-3.9]

Infection-related-NADM: oropharyngeal, laryngeal, anal, penile, vaginal and vulvar cancer, stomach cancer, hepatocellular carcinoma, Hodgkin Lymphoma and non-AIDS defining Non-Hodgkin Lymphoma subtypes

Baseline characteristics

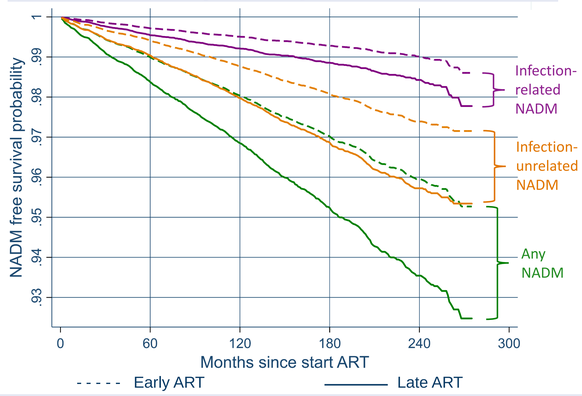
	Early start (N=2,028)	"Late" start (N=21,863)
Age	34.7 (27.9-44.5)	39.3 (31.8-47.5)
Sex & transmission category		
MSM	1,788 (88.2%)	12,654 (57.9%)
Other men	127 (6.3%)	4,866 (22.3%)
Women	113 (5.6%)	4,343 (19.9%)
Region of origin		
Western	1,598 (78.8%)	14,289 (65.4%)
Sub-Saharan Africa	79 (3.9%)	3,217 (14.7%)
Latin America and the Caribbean	259 (12.8%)	3,011 (13.8%)
South-East Asia	49 (2.4%)	852 (3.9%)
Other/Unknown	43 (2.1%)	494 (2.3%)
Nadir CD4 count	430 (280-590)	230 (100-360)
Prior AIDS	53 (2.6%)	3,291 (15.1%)
Smoking status		
Never	791 (39.0%)	8,717 (39.9%)
Current	632 (31.2%)	7,117 (32.6%)
Past	196 (9.7%)	2,918 (13.3%)
Unknown	409 (20.2%)	3,111 (14.2%)
Alcohol use		
Never	216 (10.7%)	3,953 (18.1%)
Ever, not problematic	1,573 (77.6%)	14,377 (65.8%)
Ever, problematic	186 (9.2%)	2,114 (9.7%)
Unknown	53 (2.6%)	1,419 (6.5%)
Time period of starting ART		
2000-2010	310 (15.3%)	10,273 (47.0%)
2011-2015	675 (33.3%)	6,296 (28.8%)
2016-2022	1,043 (51.4%)	5,294 (24.2%)
Months since HIV diagnosis	1.0 (0.5-2.0)	5.4 (1.1-33.0)

Data are presented as median (IQR) for continuous measures, and n (%) for categorical measures

Hazard ratios "Early ART" starters vs. "Late ART" starters

	Unadjusted model, HR [95%CI]	Adjusted model, HR [95%CI]
Any NADM	0.46 [0.31-0.68]	**0.62 [0.42-0.92]**
Infection-related NADM	0.40 [0.20-0.81]	0.63 [0.30-1.32]
Infection-unrelated NADM	0.48 [0.30-0.77]	**0.61 [0.38-0.96]**

Benefit of "early ART" persists over time



Conclusions

Strengths & Limitations

- The ATHENA cohort is one of the few cohorts which collects data on prior negative HIV test results
- In 58% of participants time of HIV acquisition could not be determined and these were considered having started ART "late". A proportion may in fact have started ART "early". If so, this would have resulted in an underestimation of the benefit of starting ART early after HIV acquisition

Conclusions & recommendations

- ART start within 12 months of acquiring HIV resulted in a persistent significantly reduced hazard for NADM overall and infection-unrelated NADM, with a similar trend for infection-related NADM.
- Our results reinforce the importance of early HIV diagnosis and treatment
- Other HIV cohorts should invest in collecting data on prior negative HIV test results as larger studies will be required to definitively assess the impact on infection-related NADM as well as individual NADM types

ATHENA Cohort

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