Noninferiority of Immediate ART vs Conventional Start in Advanced HIV: 48-Week Trial Results

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Immediate initiation of antiretroviral therapy (within 48 hours of admission) is as safe and effective as delaying treatment for 7–14 days in people with advanced HIV who are hospitalized with opportunistic infections or neoplastic processes.

1. INTRODUCTION

BACKGROUND:

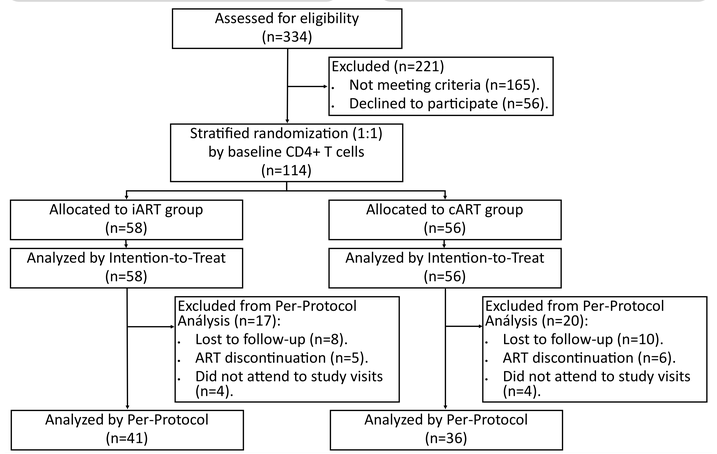
- Optimal ART initiation in advanced HIV disease and opportunistic infections (OI's) or malignancies remains a critical dilema.
- While immediate ART could prevent disease progression, conventional practice defers initiation until OI's control, to mitigate the risk of IRIS.
- Evidence from randomized trials in this specific population is limited.

OBJECTIVE: To determine whether immediate ART (<48hrs) is non-inferior to conventional ART (7-14 days) in achieving virological suppression at 48 weeks without increasing IRIS risk in adults living with advanced HIV and active OI's.

2. METHODS

Inclusion criteria
- Adults with confirmed HIV + active opportunistic infections or malignancies.
- ART naive or >3 months interruption.

Exclusion criteria
- CNS opportunistic infection.
- Pregnancy.
- No OI'S suspicion at admission.



Evaluated outcomes at 7, 14, 30, 90, 180 and 365 days since ART start:

- HIV RNA <50 copies/mL (ITT)	- CD4+/CD8+ change	- Inflammatory markers
- Adverse events	- IRIS incidence	-All cause mortality

Figure 1. Study Design and Participatn Flow: Adults with advanced HIV (CD4 <200 cells/μL) and an active opportunistic infection were randomized 1:1 to initiate InSTI-based ART either within 48 hours (iART, n=58) or at 7–14 days (cART, n=56). Stratification by baseline CD4 (<50 vs. ≥50 cells/μL). Follow-up: 48 weeks with visits at days 7, 14, 30, 90, 180, and 365. Primary outcome: HIV RNA <50 copies/mL at week 48 (ITT). Secondary outcomes included time to suppression, CD4+ recovery, IRIS incidence, and mortality. 105/114 (92%) completed follow-up.

Starting ART immediately in people with advanced HIV and opportunistic infections is not only safe, it's just as effective as waiting. Despite persistent clinical fears, immediate initiation **did not increase IRIS or mortality**, challenging decades of cautionary practice.

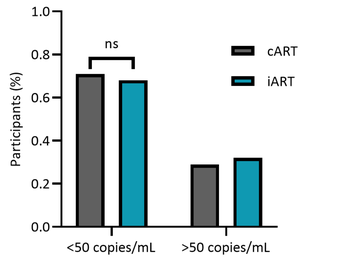
3. RESULTS

Table 1. Characteristics of the study groups

	iART (n =58)	cART (n = 56)	p-value
Age, yr.—median (IQR)	38 (30-48)	35 (28-41)	0.08
Gender—no. (%)	52 (90)	49 (87)	
MSM	6 (10)	7 (13)	0.62
HIV RNA log10copies/ mL—mean (SD)	5.24 (0.7)	5.24 (0.7)	0.65
CD4+ T cells, cells/mcL—median (IQR)	29 (13–68)	35 (17–78)	0.39
CD4+ <50 cells/mcL—no. (%)	36 (62)	35 (63)	0.96
OI's type—no. (%)			
P. jirovecii pneumonia	39 (67)	32 (57)	
Candidiasis	24 (41)	30 (54)	
Chronic diarrea	18 (31)	10 (18)	
Other	35 (60)	32 (57)	0.85

Table1. Characteristis of the Study Groups: Data are median (IQR) or n (%). P-values: Mann-Whitney U, χ^2, or Fisher's exact test. Abbreviations: iART, immediate ART; cART, conventional ART; IQR, interquartile range; MSM, men who have sex with men. *Other OIs: tuberculosis, cryptococcosis, histoplasmosis, herpes viruses, bacterial pneumonia, molluscum, CMV, EBV, HHV-8, syphilis, HPV, other

Virological Suppression at 48 Weeks (ITT Analysis)
Comparison between Immediate and Conventional ART



Risk Ratio for Virological Suppression at Week 48
Comparison between Immediate and Conventional ART

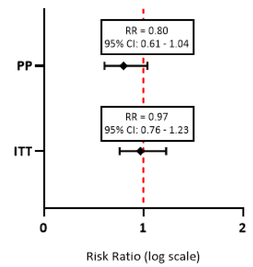


Figure 2. Virological Suppression at Week 48. Proportion with HIV RNA <50 copies/mL: iART 69% vs. cART 71% (p=0.77). Risk ratio: 0.97 (95% CI 0.76–1.23). ITT analysis. Error bars: 95% CI.

Number of participants with virologic suppression by visit
Comparison between immediate antiretroviral therapy (iART) and conventional therapy (cART)

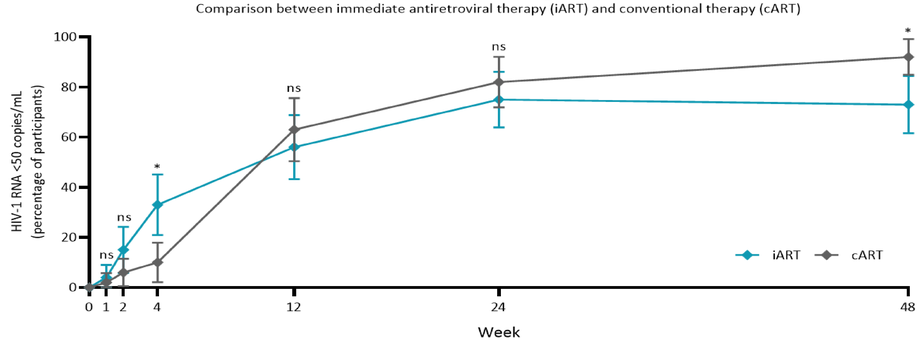


Figure 3. Virological Suppression Over Time. Proportion with HIV RNA <50 copies/mL by visit. Error bars: 95% CI. ITT analysis.

Cumulative Probability of Virological Suppression
HIV RNA <50 copies/mL

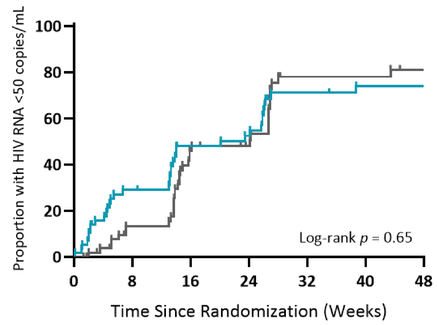


Figure 4. Cumulative probability of Virological Suppression (HIV RNA <50 copies/mL).

Kaplan-Meier curves demonstrate non-inferiority observed in time to achieve virological suppression between participants starting immediate antiretroviral therapy (iART) versus conventional ART (cART) (Log-rank p = 0.66; Hazard Ratio 1.11, 95% CI 0.70–1.71). The number of participants at risk at each time point is shown below the figure.

iART cART

Table 2. Clinical outcomes at week 48

	iART (n =58)	cART (n = 56)	p-value
MedianCD4+ increase (cells/mcL)	184	185	>0.90
IRIS incidence—no. (%)	6 (10)	7 (13)	0.77
All-cause mortality—no.(%)	7 (12)	4 (7)	0.53

Table 2. Clinical outcomes at week 48. Comparison of median CD4 increase, IRIS incidence, and all-cause mortality between iART (n=58) and cART (n=56) groups. Data are presented as median or n (%). P-values were calculated using the Mann-Whitney U test, Chi-square test, or Fisher's exact test as appropriate.

4. Discussion

- Despite initial differences in early visits (Days 30–90), **the overall time to achieve virological suppression was comparable between groups** (Log-rank p=0.66; HR 1.11), suggesting no significant delay with either strategy.
- **No difference was observed in the probability of suppression at 48 weeks by intention-to-treat** (RR 0.97; 95% CI 0.76–1.23), confirming non-inferiority between iART and cART in the real-world setting.
- Among adherent participants, cART showed a higher suppression rate (93% vs. 74%), although this did not reach statistical significance (RR 0.80; 95% CI 0.61–1.04).
- **No significant differences were found in median CD4 increase, IRIS incidence, or all-cause mortality.** The numerically higher mortality in iART (12% vs. 7%) warrants caution and further investigation in larger cohorts.

5. Conclusions

In this study, iART and cART were equally effective in achieving virological suppression by week 48 in the intention-to-treat population, with no significant differences in CD4 gain, IRIS incidence, or all-cause mortality. While iART may offer a faster initial response, cART tended toward higher long-term suppression in the per-protocol analysis, although this did not reach statistical significance. These findings highlight the importance of considering both short-term dynamics and long-term efficacy when selecting ART initiation strategies. Overall, the comparable safety and virological outcomes support the clinical acceptability of both approaches.