IMPACT OF SAME-DAY ART INITIATION ON VIRAL SUPPRESSION AND ENGAGEMENT IN A UNIVERSAL CARE SYSTEM

1109

Valentina Mazzotta[1], Alessandro Tavelli[2.3], Giulia Micheli[1], Adriana Cervo[4], Laura Comi[5], Barbara Menzaghi6, Stefano Rusconi[7], Miriam Lichtner[8], Antonella Castagna[9], Enrico Girardi[10], Cristina Mussini[4,11], Antonella d'Arminio Monforte[2], Andrea Antinori[1], Alessandro Cozzi-Lepri[12]

[1] Clinical Infectious Diseases Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy; [2] Icona Foundation, Milan, Italy; [3] National PhD Programme in One Health approaches to infectious diseases and life science research, University of Pavia, Pavia, Italy; [4] Department of Infectious Diseases, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy; [5] Infectious Disease Unit, ASST Papa Giovanni XXIII, Bergamo, Italy; [6] Unit of Infectious Diseases, ASST Della Valle Olona-Busto Arsizio, Varese, Italy; [7] Infectious Diseases Unit, Legnano Hospital ASST Ovest Milanese, Department of Biomedical and Clinical Sciences, University of Milan, Legnano, Italy; [8] Infectious Disease Unit, Sant'Andrea Hospital of Rome, Department of NESMOS, Sapienza University of Rome, Rome, Italy; [9] Infectious Diseases Unit, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy; [10] Scientific Direction, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy; [11] University of Modena and Reggio Emilia, Italy; [12] Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, United Kingdom

Italian Cohort Naive Antiretrovirals I.C.O.N.A. Conceived by Professor Mauro Moroni Fondazione Icona

Our target-trial emulation shows that same-day ART is feasible and non-inferior to starting within 50 days for viral suppression, without clear benefit or harm for retention in care

BACKGROUND

Same-day (SD) antiretroviral therapy (ART) initiation is promoted to accelerate viral suppression and reduce early disengagement from care. Evidence supporting SD still reveals a discrepancy between randomized and observational studies and primarily comes from low- and middle-income countries (LMICs) and U.S. safety-net programs. Whether SD confers benefit in high-income settings with universal, free-of-charge HIV care remains uncertain.

The objective of the study was to emulate a randomised study comparing the strategies of ART initiation at the same day of the first assessment visit (SD) vs. standard of care (SOC) for the endpoints of viral suppression and retention in care

METHODS

Target trial emulation (TTE) comparing SD ART initiation (on the day of first HIV-care contact) with ART started 1–50 days after (SOC) in Italy.

Eligible were non-hospitalised adults, no AIDS presenters, enrolled in the ICONA Foundation cohort between 2018 and 2024.

Cloning, plus censoring and weighting, were used to account for immortal time and confounding bias.

Propensity score models to control for confounding induced by artificial censoring included age, gender identity, ethnicity, mode of transmission, geographical region of ICONA site, CD4 count, HIV-RNA, and time since HIV diagnosis.

Outcomes were time to sustained (2 consecutive) VL ≤200 copies/mL and single VL ≤50 copies/mL. The risk of loss to care by 1 year from enrolment was evaluated in a sub-cohort enrolled before July 2023.

A 4% non-inferiority margin (SD vs SOC) was prespecified per FDA HIV-1 ART guidance (Nov 2015).

Kaplan–Meier estimates, and risk differences (RD) were calculated with and without accounting for bias and 95% CI using bootstrapping.

RESULTS

We included 3,144 persons with HIV PWH, 415 SD, and 2,729 SOC: 17% females, median age 39 (IQR:30,49), 80% Caucasian. Gender identity was cis male in 82%, cis female in 16% and transgender/non-binary in <2%. Median time from HIV diagnosis to the first care visit was 5 (1-14) days for SD and 7 (0-18) days for controls. The SOC group started ART on average 11 days (5-19) after the first contact. (Table 1).

Table 1. Main characteristics of the study population in the original cohort

Characteristics at baseline(BL)$	Same day ART	ART initiation over [1-50] days	p-value*	Total
	N= 415	N= 2729		N= 3144
Age, years			0.246	
Median (IQR)	38 (30, 49)	39 (31, 49)		39 (30, 49)
Sex at birth, n(%)			0.120	
Female	82 (19.8%)	455 (16.7%)		537 (17.1%)
Mode of HIV Transmission, n(%)			0.625	
PWID	14 (3.4%)	129 (4.7%)		143 (4.5%)
MSM	212 (51.1%)	1344 (49.2%)		1556 (49.5%)
Heterosexual	156 (37.6%)	1044 (38.3%)		1200 (38.2%)
Other/Unknown	33 (8.0%)	212 (7.8%)		245 (7.8%)
Nationality, n(%)			0.011	
Italian	318 (76.6%)	1925 (70.5%)		2243 (71.3%)
Location of Icona site, n(%)			0.001	
North	217 (52.3%)	1312 (48.1%)		1529 (48.6%)
Center	144 (34.7%)	1172 (42.9%)		1316 (41.9%)
South	54 (13.0%)	245 (9.0%)		299 (9.5%)
CD4 count, cells/mmc			0.017	
Median (IQR)	387 (208, 567)	353 (187, 535)		355 (190, 541)
HIV-RNA, log10 copies/mL			0.333	
Median (IQR)	5.0 (4.3, 5.6)	4.9 (4.3, 5.5)		4.9 (4.3, 5.5)
Time from HIV diagnosis to enrolment, days			0.205	
Median (IQR)	5 (1, 14)	7 (0, 18)		7 (0, 17)
Time from enrolment to ART start, days				
Median (IQR)	0.0 (0.0, 0.0)	11.0 (5.0, 19.0)		8.0 (3.0, 18.0)
Year of enrolment			0.034	
Median (IQR)	2021 (2019, 2023)	2021 (2019, 2022)		2021 (2019, 2022)
Follow-up, days				
Median (IQR)	73.0 (31.0, 182.0)	79.0 (43.0, 168.0)		79.0 (42.0, 170.0)
Gender identity, n(%)			0.009	
Cisgender	393 (94.7%)	2461 (90.2%)		2854 (90.8%)
Transgender	9 (2.2%)	81 (3.0%)		90 (2.9%)
Non binary/unknown	13 (3.1%)	187 (6.9%)		200 (6.4%)
Ethnicity, n(%)			0.883	
Black	49 (11.8%)	335 (12.3%)		384 (12.2%)
Asian/Ispanic	25 (6.0%)	191 (7.0%)		216 (6.9%)
Caucasian	338 (81.4%)	2184 (80.0%)		2522 (80.2%)
Other/unknown	3 (0.7%)	19 (0.7%)		22 (0.7%)

*Chi-square and Mann-Whitney test as appropriate

Table 2. Results using 100 bootstrap samples for the three outcomes

Original cohort

KM estimates	1-year probability of sustained VL<=200 copies/mL (%)	95% CI	1-year probability of single VL<=50 copies/mL (%)	95% CI	1-year probability of loss to care[4]	95% CI
Same day ART	91.39	90.38, 92.57	91.10	90.51, 92.59	9.43	4.42, 15.51
ART over 1-50 days	90.91	88.51, 93.63	89.45	89.17, 94.09	8.45	5.16, 14.94
Difference[1]	0.48	-3.00, 4.87	1.65	-3.51, 5.64	0.98	-2.23, 1.78

Emulated cohort (cloned and weighted)

Weighted[&] KM estimates	1-year probability of sustained VL<=200 copies/mL (%)	95% CI	1-year probability of single VL<=50 copies/mL (%)	95% CI	1-year probability of loss to care[3]	95% CI
Same day ART	91.46	90.91, 92.58	91.06	90.92, 92.58	9.44	4.34, 91.54
ART over 1-50 days	92.03	90.37, 94.15	91.30	90.69, 94.56	6.78	4.84, 9.99
Difference[2]	-0.58	-3.60, 3.15	-0.24	-3.60, 3.15	2.67	-1.27, 6.34

*The 95% CI were calculated using 100 bootstrap replicates. [1]These differences are prone to both confounding and immortal-time biases. [2]These differences account for all types of biases, under the assumptions detailed in methods. [3]Last clinical visit within 1 year of ART initiation and no other visit in the following year. [&]Weighted for age, gender identity, ethnicity, mode of transmission, geographical region of Icona site, CD4 count, HIV-RNA and time since HIV diagnosis

In both the original and the emulated cohorts, we found no evidence for an advantage of SD over SOC in virological outcomes. Among 2,664 participants with accurate retention in care data, the 1-year risk of loss to care showed a slight advantage for SOC, albeit with considerable uncertainty around the RD (Table 2).

CONCLUSIONS

The comparable results between same-day and SOC strategies in this TTE model suggest that, in a high-income country with a universal, publicly funded care system, the same-day approach was feasible and does not adversely affect virological outcomes after ART initiation.

Potential benefits in specific populations at the earlier stages of the HIV cascade in settings not conditioning on ART start warrant further evaluation.

PLAIN LANGUAGE SUMMARY

Starting HIV treatment on the same day as the first visit worked as well as starting within 50 days in controlling HIV and for retention in care at 1 year, but results were uncertain.

ACKNOWLEDGMENTS: ICONA Foundation study group

Author Contact Information: Valentina Mazzotta, MD, PhD e-mail: valentina.mazzotta@inmi.it