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Title: Is time from HIV diagnosis to ART initiation predictive of virological outcome and of retention in care?

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Abstract body

Background: Aim of this study is to evaluate the likelihood of early ART initiation in Icona, and whether early ART start is associated to a better virological response and retention in care.

Methods: Patients from Icona cohort with first HIV diagnosis between January 2016 (universal ART initiation recommendation) and December 2017 are divided in 6 groups according to the time from first HIV pos test to ART initiation: ≤ 7 days (G1); 8-14 days (G2); 15-30 days (G3); 31-120 days (G4); 121-365 days (G5) and > 365 days or no start (G6). Primary HIV infections and AIDS presenters are excluded. Time from HIV diagnosis to first visit at ID center (THIVID) has been calculated.

End points: Prevalence of early start (≤ 7 days from diagnosis); virological suppression at 12 weeks from ART start (12wVS); time to virological failure (VF: confirmed HIV-RNA > 50 copies/ml > 6 months from ART start); being in care and with virological suppression (HIV-RNA < 50 copies/ml) 1 year from ART start (cascade of care).

Statistics: logistic regression for predictors of being G1 and 12wVS; Kaplan-Meier curves and Cox model for time to VF and predictors. Follow-up accrued from the date of ART start to the date of VF or at last HIV-RNA (VL). Cascade of care is performed according to the 6 groups of ART start.

Results: A total of 1329 patients included: 85 (6.4%) belonging to G1, 116 (8.7%) to G2, 267 (20.1%) to G3, 639 (48.1%) to G4, 112 (8.4%) to G5 and 110 (8.3%) to G6. Differences in baseline demographic and clinical characteristics are shown in Table 1.

Independent predictors of early start are HIV RNA $> 100,000$ copies/ml, CD4 < 350 cells/mm³, and shorter THIVID (Table 2).

Time to start ART is not associated with 12wVS; other predictors (calendar year, HIV-RNA, CD4 and ART-regimen) are shown in table 3.

The probability of VF by 1-year is 5.7% (1.9-16.5) in G1, 6.1% (2.6-14.0) in G2 and 3.3% (1.5-7.1) in G3, 3.1% (1.8-5.3) in G4 and 4.8% (1.5-14.0) in G5 (log rank=0.37) with no differences according to time of ART start by multivariate Cox model (table 4).

Figure 1 shows the cascade of care according to groups. 91% of patients on ART at 1-year show undetectable VL (89% of G1, 85% of G2, 94% of G3, 90% of G4, 94% of G5; p=0.12). Considering all the patients with HIV diagnosis, 69% of patients are in care with VS 1-year after starting ART (58 -72% G1,

86 -74% G2, 211-79% G3, 481-76% G4, 77-69% G5; p=0.15) with no differences between groups.

Conclusions: Even if 83% of patients diagnosed in 2016-17 started ART within 4 months, only 6% started within 7 days and 65% started ART after 30 days from HIV diagnosis. Advanced HIV disease and shorter time from HIV diagnosis to the first visit are the main predictors of early start. Virological success is obtained in >90% of patients by 1 year from starting ART; in the Italian healthcare setting, timing of starting ART does not associate with differences neither in rate of virological response or shape of the cascade of care distribution.

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Table 1: Main characteristics of the study population at enrolment

	G1: 0-7 d	G2: 8-14 d	G3:15-30 d	G4: 31-120 d	G5: 120-365 d	G6: not started 365d	p value	Total
	N=85	N=116	N=267	N=639	N=112	N=110		N=1329
Year Diagnosis, n (%)							0.252	
2016	45 (52.9)	62 (53.5)	130 (48.7)	325 (50.9)	69 (61.6)	62 (56.4)		693 (52.1)
2017	40 (47.1)	54 (46.6)	137 (51.3)	314 (49.1)	43 (38.4)	48 (43.6)		636 (47.9)
Age at enrolment, median (IQR)	38 (32-48)	42 (32-51)	39 (31-50)	37 (29-46)	35 (28-44)	35 (27-44)	<.001	37 (29-47)
Gender, Female, n (%)	14 (16.5)	27 (23.3)	45 (16.9)	101 (15.8)	13 (11.6)	28 (25.5)	0.039	228 (17.2)
Nationality, Italian , n (%)	65 (76.5)	89 (76.7)	200 (74.9)	462 (72.3)	85 (75.9)	67 (60.9)	0.061	968 (72.8)
Mode of HIV Transmission, n (%)							0.008	
Hetero	28 (32.9)	53 (45.7)	98 (36.7)	211 (33)	30 (26.8)	43 (39.1)		463 (34.8)
IDU	1 (1.2)	2 (1.7)	5 (1.9)	24 (3.8)	6 (5.4)	5 (4.6)		43 (3.2)
MSM	45 (52.9)	55 (47.4)	144 (53.9)	372 (58.2)	73 (65.2)	59 (53.6)		748 (56.3)
Other/Unknown	11 (12.9)	6 (5.2)	20 (7.5)	32 (5)	3 (2.7)	3 (2.7)		75 (5.6)
CD4 cells/mm³ median (IQR)	200 (50-360)	235 (77-385)	300 (150-502)	393 (264-558)	578 (345-740)	563 (416-792)	<.001	378 (225-579)
CD4 <200, n (%)	40 (49.4)	50 (44.3)	82 (31.1)	108 (17)	10 (8.9)	8 (7.5)	<.001	298 (22.7)
CD4 200-349, n (%)	20 (24.7)	26 (23)	70 (26.5)	147 (23.1)	19 (17)	10 (9.4)		292 (22.2)
CD 350-499, n (%)	13 (16.1)	15 (13.3)	45 (17.1)	175 (27.5)	19 (17)	23 (21.5)		290 (22.1)
CD4>=500, n (%)	8 (9.9)	22 (19.5)	67 (25.4)	207 (32.5)	64 (57.1)	66 (61.7)		434 (33.0)
HIVRNA, log₁₀ copies/ml, median (IQR)	5.1 (4.7-5.7)	5.2 (4.6-5.7)	4.8 (4.3-5.5)	4.6 (4.1-5.1)	4.4 (3.5-4.8)	4.3 (3.7-4.8)	<.001	4.7 (4.1-5.3)
HIVRNA >5 log, n (%)	51 (63)	69 (59.5)	111 (42.4)	199 (31.2)	18 (16.1)	19 (17.9)		467 (35.5)
HCVAb pos, n (%)	3 (3.5)	7 (6.0)	12 (4.5)	33 (5.2)	9 (8.0)	5 (4.6)	0.172	69 (5.2)
HBsAg pos, n (%)	5 (5.9)	7 (6.0)	12 (4.5)	25 (3.9)	4 (3.6)	3 (2.7)	0.315	56 (4.2)
First line cART, n (%)							<.001	
2NRTIs+bPI	16 (19.1)	34 (29.6)	45 (17.1)	68 (10.8)	5 (4.5)	4 (13.8)		172 (13.9)
2NRTIs+INSTI	66 (78.6)	73 (63.5)	161 (61.0)	437 (69.3)	74 (66.1)	18 (62.1)		829 (67.1)
2NRTIs+NNRTI	1 (1.2)	5 (4.4)	49 (18.6)	111 (17.6)	24 (21.4)	7 (24.1)		197 (16.0)
Other (dual,4 drugs)	1 (1.2)	3 (2.6)	9 (3.4)	15 (2.4)	9 (8.0)	0 (0.0)		37 (3.0)
NRTI Backbone, n (%)							<.001	
3TC/ABC	8 (9.8)	17 (15.0)	44 (17.2)	207 (33.6)	29 (27.9)	9 (31.0)		314 (26.1)
FTC/TDF or FTC/TAF	74 (90.2)	96 (85.0)	212 (82.8)	410 (66.5)	75 (72.1)	20 (69.0)		887 (73.9)
Italian Zone, n (%)							<.001	
Central	46 (54.1)	51 (44.0)	155 (58.1)	259 (40.5)	40 (35.7)	49 (44.6)		600 (45.2)
Northern	27 (31.8)	40 (34.5)	83 (31.1)	291 (45.5)	48 (42.9)	40 (36.4)		529 (39.8)
Souther	12 (14.1)	25 (21.6)	29 (10.9)	89 (13.9)	24 (21.4)	2 (19.1)		200 (15.1)
Days from diagnosis to first ID contact, median (IQR)	0 (0-3)	4 (0-8)	7 (0-12)	16 (06-30)	40 (11-113)	12 (03-42)	<.001	11 (01-24)

Table 2. Predictors of early ART start (within 7 days from HIV diagnosis)

	OR	95%CI		p	AOR	95%CI		p
Age per 10yrs increase	1.15	0.96	1.38	0.133	0.87	0.67	1.14	0.314
Gender, M (vs F)	1.05	0.58	1.90	0.863	0.77	0.32	1.86	0.569
Nationality, ITA (vs non ITA)	1.23	0.73	2.06	0.437	1.19	0.59	2.39	0.632
Mode of HIV Transmission								
Hetero	1.00							
IDU	0.37	0.05	2.79	0.334	0.45	0.05	4.06	0.476
MSM	0.99	0.61	1.62	0.982	1.04	0.50	2.19	0.917
Other	2.67	1.27	5.63	0.010	1.32	0.47	3.71	0.593
HBV HCV co-infection	0.98	0.44	2.19	0.957	1.06	0.43	2.59	0.902
Year Diagnosis per 1 yr increase	0.97	0.62	1.50	0.879	0.79	0.45	1.39	0.418
HIV-RNA								
<100k	1.00				1.00			
>=100k	3.34	2.10	5.33	<.001	2.01	1.09	3.71	0.025
CD4								
<200	8.26	3.80	17.91	<.001	4.54	1.77	11.68	0.002
200-350	3.92	1.70	9.01	0.001	2.90	1.14	7.38	0.026
350-499	2.50	1.02	6.11	0.045	1.74	0.63	4.81	0.284
>500	1.00				1.00			
Italian Zone								
Central	1.30	0.67	2.51	0.432	0.97	0.42	2.22	0.947
Northern	0.84	0.42	1.70	0.632	1.25	0.52	3.02	0.615
Southern/Islands	1.00				1.00			
Days from diagnosis to first ID contact								
per 1 day increase	0.82	0.78	0.87	<.001	0.83	0.78	0.88	<.001

Table 3. Predictors of VS at 12 weeks from start logistic regression

	OR	95%CI		p	AOR	95%CI		p
Time to ART start								
0-7days	1.00				1.00			
8-14 days	1.16	0.54	2.49	0.703	1.10	0.40	2.99	0.856
15-30 days	1.26	0.67	2.40	0.473	1.07	0.45	2.57	0.874
30-120 days	1.47	0.82	2.63	0.198	0.73	0.32	1.64	0.442
120-365 days	2.04	0.97	4.26	0.059	0.71	0.25	2.01	0.524
Age, 10yrs increase	0.87	0.76	0.98	0.027	0.90	0.75	1.08	0.273
Gender, M	0.78	0.52	1.16	0.216	0.59	0.31	1.11	0.100
Italian	1.05	0.74	1.47	0.794	1.16	0.72	1.85	0.551
Mode of HIV Transmission								
Heterosexual	1.00				1.00			
IDU	0.67	0.30	1.48	0.321	0.75	0.23	2.37	0.620
MSM	1.04	0.75	1.44	0.818	0.83	0.49	1.40	0.476
Other	0.69	0.36	1.30	0.251	0.55	0.21	1.41	0.212
HCV								
Pos	1.09	0.56	2.10	0.800	0.84	0.32	2.20	0.715
HBV								
Pos	1.09	0.56	2.10	0.800	1.36	0.58	3.17	0.477
Anno cART, 1yr increase	2.06	1.59	2.67	<.001	1.68	1.20	2.35	0.002
HIV-RNA, cps/mL								
<100k	1.00				1.00			
>=100k	0.26	0.19	0.36	<.001	0.16	0.10	0.26	<.001
CD4, cells/mm³								
<200	0.36	0.24	0.54	<.001	0.47	0.26	0.87	0.015
200-350	0.42	0.27	0.63	<.001	0.41	0.24	0.72	0.002
350-499	0.61	0.40	0.93	0.021	0.70	0.41	1.19	0.190
>500	1.00				1.00			
ART regimen								
2NRTIs+DTG	1.00				1.00			
2NRTIs+Other INSTI	0.73	0.50	1.07	0.108	1.02	0.56	1.84	0.953
2NRTIs+bPI	0.11	0.06	0.20	<.001	0.09	0.04	0.21	<.001
2NRTIs+NNRTI	0.36	0.23	0.55	<.001	0.19	0.09	0.37	<.001
Other	1.04	0.42	2.62	0.927	0.67	0.04	11.39	0.784
Backbone								
ABC/3TC	1.00							
FTC/TAF or FTC/TDF	0.47	0.33	0.68	<.001	0.66	0.36	1.21	0.174
Italian Zone								
Central	0.66	0.38	1.14	0.140	1.21	0.56	2.58	0.631
Northern	0.94	0.54	1.63	0.827	1.43	0.66	3.09	0.363
Southern/Islands	1.00				1.00			

Table 4. Predictors of VF by fitting a Cox regression model

	HR	95%CI		p	AHR	95%CI		p
Time to ART start								
0-7days	1.00				1.00			
8-14 days	1.76	0.47	6.63	0.404	1.34	0.33	5.41	0.680
15-30 days	0.69	0.18	2.67	0.590	0.76	0.19	3.07	0.705
30-120 days	0.87	0.26	2.94	0.826	1.54	0.43	5.52	0.506
120-365 days	1.24	0.28	5.57	0.776	2.93	0.59	14.53	0.189
Age 10yrs increase	1.02	0.78	1.33	0.881	0.83	0.61	1.13	0.246
Gender, M	0.81	0.37	1.74	0.586	0.90	0.36	2.28	0.827
Italian	0.81	0.41	1.61	0.547	1.11	0.50	2.46	0.796
Mode of HIV Transmission								
Heterosexual	1.00				1.00			
IDU	0.59	0.08	4.40	0.605	0.56	0.07	4.36	0.582
MSM	0.57	0.30	1.09	0.090	0.74	0.33	1.65	0.459
Other	1.27	0.43	3.72	0.669	1.77	0.57	5.56	0.326
Anno cART (1yr increase)								
2017	1.77	0.93	3.39	0.084	2.32	1.18	4.57	0.015
2018	.				.			
HIV-RNA								
<100k	1.00				1.00			
>=100k	4.29	2.15	8.53	<.001	3.64	1.60	8.29	0.002
CD4								
<200	9.44	2.83	31.55	<.001	6.78	1.84	24.99	0.004
200-350	4.06	1.10	14.99	0.036	3.37	0.89	12.80	0.074
350-499	3.54	0.94	13.33	0.062	2.94	0.77	11.25	0.115
>500	1.00				1.00			
Regime								
2NRTIs+INSTI	1.00				1.00			
2NRTIs+bPI	2.42	1.21	4.84	0.013	2.32	1.12	4.82	0.024
2NRTIs+NNRTI	0.73	0.25	2.11	0.565	1.90	0.58	6.23	0.292
Other	1.87	0.44	7.92	0.395	1.93	0.43	8.60	0.389
Italian Zone								
Central	1.05	0.40	2.75	0.914	1.64	0.59	4.58	0.342
Northern	0.65	0.23	1.85	0.422	0.89	0.30	2.68	0.839
Southern/Islands	1.00				1.00			

Figure1: Cascade of HIV care according to time to ART start groups (% of patients with HIV diagnosis)

