Dettaglio abstract

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Title: Prevalence, characteristics and outcome of Heavily treated experienced (HTE) HIV-infected patients: data from the Italian ICONA Cohort

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Abstract
Background: New regimens are becoming available for heavily treated patients with reduced therapy option. Thus, it becomes important to determine the prevalence and characteristics of this population in the present cART scenario of very potent and safe drugs. We aim to analyse the prevalence as well as the virological and clinical outcomes of heavily treated experienced (HTE) patients who could be eligible for fostemsavir (FTV).
Methods: We included all participants of the Icona cohort with ≥1 clinical visit in 2009-2019. HTE were defined according to the antiretroviral and viro-immunological history (Def1) in participants with unsuppressed or stable HIV-RNA (Def2) who could be eligible for FTV (Fig1A). Prevalence of HTE has been calculated overall and stratified by year and gender. Among HTE, Kaplan-Meier method was used to estimate the cumulative probability of virological failure >200 copies/mL (VF) and of a clinical endpoint including AIDS, severe non-AIDS events (SNAEs by NADC-START definition) and death.
Results: A total of 200/ 13,285 (1.5%) patients were defined as HTE (Fig 1B). Of these, 85 participants satisfied the definition of HTE eligible for FTV (Fig1C). At the last clinical visit, 11/85 (12.9%) had unsuppressed HIV-RNA and 74 were virologically stable but compromised. Main patients' characteristics at baseline, by HTE status are shown in Table 1. Overall, the prevalence of HTE was 0.64% (95%CI 0.51-0.69), and, looking at the different calendar years, it declined from 1.15% (0.82-1.56) in 2009 to 0.68% (0.52-0.87) in 2019. A higher prevalence has been identified in females vs. males (OR=2.82; 95%CI 1.85-4.37).
43/85 of HTE subjects (50.6%) experienced a VF over follow-up; the estimated risk of VF was 43.8% (95% CI 32.9-54.7) by 3-years. The composite endpoint of clinical progression or death was experienced by 23 (27.0%) HTE patients (8 AIDS, 13 SNEAs and 2 deaths), with a cumulative probability of 33.4% (20.6-46.2) by 10-years.
Conclusions: In the era of effective and safe cART regimens, few patients (0.64% of our cohort) satisfy the definition of HTE eligible for FTV therapy. Actually, the prevalence of HTE is declining over calendar year. Although a minority, this population is at high risk of virological failure and clinical progression and new effective therapeutic options are needed.

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Fig1. Definitions of HTE (Def1) and of THE FTC eligible (Def2)

Def1) A composite of 2 or more of the below will define those HTE adults living with HIV-1 infection:

1A) Current regimen indicative of HTE : Regimen includes ≥3 drugs, including one or more of the following: DTG BID or DRV BID or T20; ETV + DTG BID or MVC or boosted DRV BID or T20

1B) At least 3 core ARV classes prior to current regimen and last drug regimen included ≥3 drugs

1C) Individuals who had at least 4 anchor agent switches at any previous time with the 4th or subsequent regimen including one of the following: DTG BID or DRV BID or T20; ETV + DTG BID or MVC or boosted DRV BID or T20; ≥2 core agents + any other ARV;

1D) Virologic failure prior to class switch: subjects with history of ≥3 virologic failure followed by a treatment switch (within 90 days)

Def2) THE adults defined by Def1 that are eligible for HTE if are:

2A) unstable unsuppressed

- confirmed virological failure (HIV RNA levels of ≥200 copies/mL, at ≥2 consecutive determinations ≤6 months apart) OR

2B) stable but compromised

- persistent low-level viremia (HIV RNA levels of ≥50, <200 copies/mL, at ≥2 consecutive determinations ≤6 months apart); or
- persistent low CD4 counts (<200 cells/mmc, at ≥2 consecutive determinations ≤6 months); and/or <15% improvement in CD4, following initiation of a new ARV treatment; or
- ≥4 switches in ARV treatment with significant DDI, comorbidities or safety/ tolerability/ toxicity challenges on current ARV treatment.

Fig2.[A] Venn diagram of the 4 used definition for HTE. Subjects falling within at least 2 of the definitions are in bold (n=200); [b] Flowchart of the 85 HTE eligible for FTV

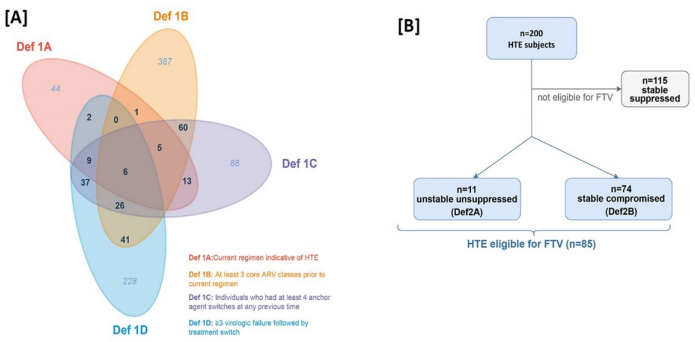

Table 1 – Characteristics of patients according to eligibility for FTV

Characteristics	HTE eligible for FTV (N=85)	Non-HTE / non eligible for FTV (N=13200)	p-value*	Total
Gender, Female, n(%)	37 (43.5%)	2817 (21.3%)	<.001	2854 (21.5%)
Mode of HIV Transmission, n(%)				
PWIDU	29 (34.1%)	1374 (10.4%)	<.001	1403 (10.6%)
MSM	20 (23.5%)	5806 (44.0%)		5826 (43.9%)
Heterosexual contacts	33 (38.8%)	5231 (39.6%)		5264 (39.6%)
Other/Unknown	3 (3.5%)	789 (6.0%)		792 (6.0%)
Nationality, Not Italian, n(%)	6 (7.1%)	2684 (20.3%)	0.002	2690 (20.2%)
Hepatitis B/C coinfection[&], n(%)				
No	47 (55.3%)	9287 (70.4%)	<.001	9334 (70.3%)
Yes	35 (41.2%)	1801 (13.6%)		1836 (13.8%)
Not tested	3 (3.5%)	2112 (16.0%)		2115 (15.9%)
Calendar year of HTE, median (IQR)	2010 (2009, 2015)	.	.	2010 (2009, 2015)
Age, years, median (IQR)	44 (38, 48)	37 (28, 45)	<.001	37 (28, 45)
CD4 count, cells/mmc, median (IQR)	432 (260, 528)	540 (382, 735)	<.001	534 (381, 731)
CD4 count nadir, cells/mmc, median (IQR)	194 (67, 307)	324 (162, 504)	<.001	323 (160, 503)
CD8 count, cells/mmc, median (IQR)	881 (628, 1215)	887 (645, 1207)	0.788	886 (644, 1208)
HIV-RNA, log10 copies/mL, median (IQR)	1.70 (1.70, 3.78)	1.70 (1.69, 3.11)	0.053	1.70 (1.69, 3.13)
Time from HIV diagnosis[&], months, median (IQR)	257 (169, 328)	76 (33, 139)	<.001	77 (33, 140)
**Chi-square or Kruskal-Wallis test as appropriate*				
All variables measured at baseline (2009) apart when noted (2019)[&]				