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Oral Communications

From naive to highly treated subjects. Efficacy of cART

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Title: **Variables related to becoming Heavily Treated Experienced (HTE) patients in a large Italian cohort**

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Abstract body
Background: We aim to analyse of the prevalence over time, immunological virological and clinical outcome of heavily treated experienced (HTE) patients in the Icona cohort.
Methods: We included all participants of Icona for with ≥1 clinical visit in 2008-2018. Four definitions of HTE were used. The date of HTE was defined at time in which one of the following events occured first: D1=to have used ≥4 anchor drugs (including the current one), having experienced virological failures (VF) to ≥2 drugs belonging to ≥3 classes; D2= to have used ≥3 anchor drugs of different classes (including the current one); D3=currently using either dolutegravir (DTG) bid or boosted Darunavir (b-DRV) bid or maraviroc (MVC) not as first line regimens; D4= to have previously experienced >5 therapy switches. A participant was defined as HTE if satisfied ≥1 definition. Patients' characteristics in Jan 2018 (index date) were compared in the HTE and non-HTE subjects by chi2 and Wilcoxon rank test. The prevalence of HTE over 2008-2018 was calculated by each separate definition and using the composite definition. The Kaplan-Meier method was used to estimate the incidence (with 95% CI) of VF>200 copies/mL and of a composite clinical endpoint including AIDS, non-AIDS defining conditions (NADC-START trial definition) and death. A multivariable Cox regression model was used to identify factors associated with faster progression to AIDS/NADC/death among the HTE population.
Results: A total of 1,243 out of 12,301 patients (10.1%) were defined as HTE in 2008-2018. This proportion is composed by the prevalence cumulated by 2008 (including all cases observed in 1997-2008) and by HTE incidence over the following years. The overall proportions were 0.2% for D1, 0.1% for D2, 0.7% for D3 and 6.5% for D4. Figure 1 shows the overlap of the different definitions for the aggregate 2008-2018 proportion. Compared to non-HTE, HTE pts were older (p=<.001), more frequently females (p=<.001), less frequently MSM (p=<.001), less frequently Italian (p=<.001), with lower CD4 nadir (p=<.001) and higher HIV RNA (p=<.001). A total of 28 HTE pts developed AIDS, 68 NADC and 6 died. The probability of various endpoints by 3, 5 and 8 years from HTE are shown in Table 1. Age was the only factor independently associated with the risk of faster progression to AIDS/NADC/death (Table 2).
Conclusions: Using a composite definition including a wide range of criteria signalling high previous treatment exposure, around 10% of HIV-positive subjects seen for care in Italy currently show potentials for having limited drug options even recently. HTE cumulated prevalence was high at 10% in 2008 but

remained stable below 2% over the following years up to 2018. 13% of HTE people progressed to severe clinical outcomes by 8 years from entering the HTE group. It has still to be estimated how many of these patients are likely to necessitate new therapeutic options to further reduce their risk of morbidity and mortality.

Fig 1 – Venn diagram of the four used HTE definitions among 1243 HTE patients

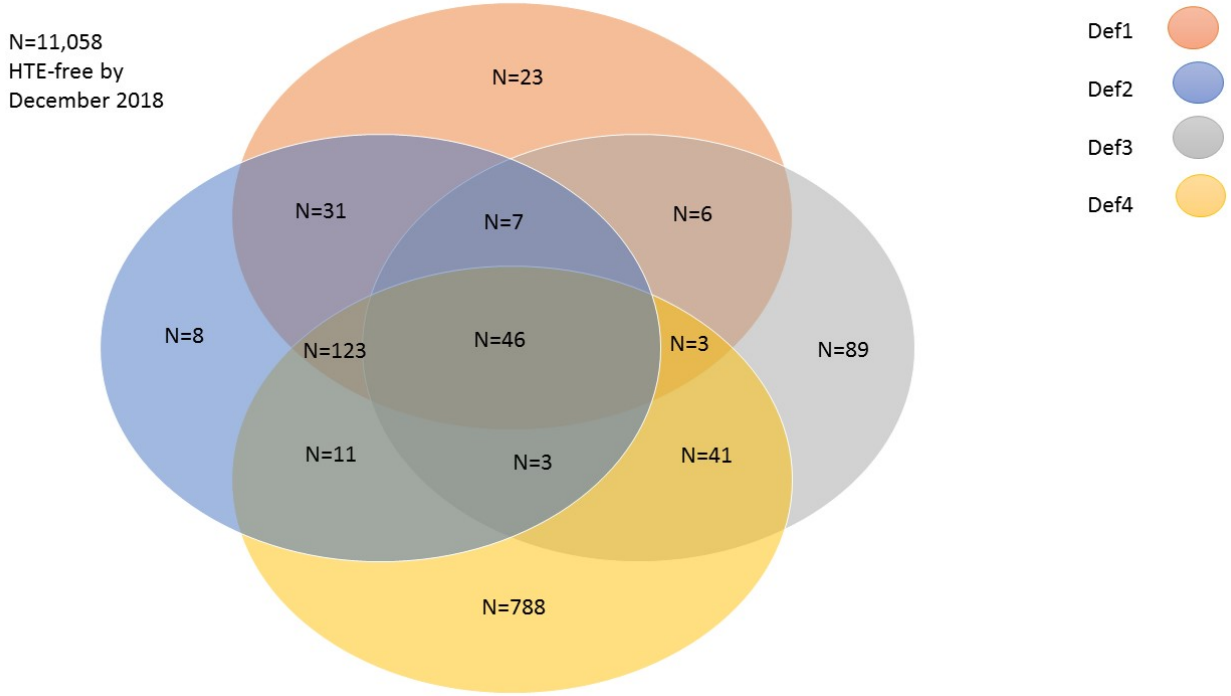

Table 1 –KM estimates of various endpoints at specific times from entering the HTE group

ENDPOINTS	3-year		5-year		8-year	
VF>200	13	2.3 (1.1, 3.6)	16	3.3 (1.6, 5.0)	19	5.0 (2.5, 7.4)
AIDS	9	1.5 (0.5, 2.4)	21	3.8 (2.2, 5.4)	24	4.7 (2.8, 6.6)
NADC	17	2.8 (1.5, 4.1)	38	6.8 (4.7, 8.9)	47	9.0 (6.5, 11.5)
DEATH	1	0.2 (0.0, 0.5)	2	0.4 (0.0, 1.0)	4	0.9 (0.0, 1.8)
COMPOSITE (AIDS, NADC OR DEATH)	24	3.9 (2.4, 5.5)	58	10.4 (7.9, 13.0)	68	12.8 (10.0, 15.7)

Table 2- Factors associated to faster clinical progression among HTE patients by univariate and multivariate Cox regression analysis

	Unadjusted and adjusted relative hazards of AIDS/NADC/death			
	Unadjusted RH (95% CI)	**p-value**	**Adjusted* RH (95% CI)**	**p-value**
Gender				
Male	1.00		1.00	
Female	1.11 (0.73, 1.69)	0.638	1.60 (0.93, 2.73)	0.087
Age				
per 10 years older	1.26 (1.03, 1.55)	0.026	1.33 (1.06, 1.67)	0.013
Mode of HIV transmission				
PWID	1.00		1.00	
MSM	0.85 (0.48, 1.51)	0.581	0.89 (0.38, 2.07)	0.788
Heterosex	0.75 (0.46, 1.23)	0.251	0.65 (0.31, 1.36)	0.250
Other	1.40 (0.63, 3.12)	0.411	1.09 (0.39, 3.07)	0.874
Calendar year of entering HTE				
per more recent	0.96 (0.86, 1.06)	0.413	0.98 (0.85, 1.13)	0.802
Nationality				
Italian	1.00		1.00	
Foreign	1.75 (0.71, 4.34)	0.223	1.69 (0.60, 4.80)	0.320
Anchor drug class				
INSTI	1.00		1.00	
NNRTI	2.60 (0.54, 12.60)	0.235	2.85 (0.57, 14.21)	0.202
PI/r	2.22 (0.52, 9.48)	0.284	2.07 (0.47, 9.14)	0.338
Other	2.46 (0.59, 10.17)	0.215	2.19 (0.49, 9.75)	0.304
BMI				
<18.5	1.00		1.00	
18.5-25	1.42 (0.57, 3.55)	0.453	1.43 (0.56, 3.64)	0.452
25+	1.35 (0.51, 3.60)	0.545	1.45 (0.52, 4.03)	0.479
CD4 count at HTE				
per 100 cells/mm3 higer	0.94 (0.87, 1.01)	0.072	0.96 (0.88, 1.04)	0.334
HIV-RNA at HTE				
per log10 copies/mL higer	1.11 (0.97, 1.27)	0.132	1.06 (0.89, 1.25)	0.533
HCVAb				
Negative	1.00		1.00	
Positive	1.13 (0.73, 1.75)	0.572	0.93 (0.47, 1.82)	0.828
Not tested	1.53 (0.60, 3.88)	0.368	1.07 (0.31, 3.69)	0.919