CHARACTERISATION AND OUTCOMES OF DIFFICULT-TO-TREAT PATIENTS IN AN ITALIAN COHORT OF PLWH STARTING MODERN ART REGIMEN

P065

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BACKGROUND

✓ In the last years, almost 30% of PLWH discontinue 1st-line ART (≥1 drug) and 12-20% of PLWH interrupt 2nd-line ART (≥ 1 drug) within 1 year;

✓ Treatment failures to modern ART regimens are of concern, as they might limit future drug options and lead to clinical failure

✓ Real world estimates of rate of multiple failures to modern regimens are lacking and long-term consequences remain unclear.

AIM

Primary objective
To estimate and characterize the proportion of subjects defined as "difficult to treat" in recent years

STUDY DESIGN AND METHODS

Study population: adult HIV+ pts enrolled in **Icona** Foundation Study starting a **modern ART**, defined as:

- 2NRTI (TAF, TDF, ABC, 3TC or FTC) + DRV/b qd or + any INSTI or + DOR or + RPV
- DTG+3TC

Classified as "**difficult to treat**" (DTT) if, after starting ART, experienced ≥1 of the following events:

i) ≥2 VF (VF defined as 2 consecutive viral load, VL>50 copies/mL) with or without subsequent ART change;

ii) ≥2 treatment discontinuations due to toxicity/intolerance/failure on 2 different regimens;

iii) ≥1 VF followed by ART change plus ≥1 treatment discontinuation due to toxicity/intolerance/failure.

Time to fulfill DTT definition at its first occurrence (index date) was estimated using the Kaplan-Meier method.

We then identified PLWH who, after the same time from starting ART, were still free from DTT events. In a subset of these who subsequently initiated a new regimen, we compared the treatment response between DTT (**exposed**) and **matched unexposed** with respect to the following **endpoints**:

➢ VF
➢ discontinuation of ≥1 drug due to intolerance/toxicity/failure;
➢ treatment failure (composite of VL>200 cp/ml or discontinuation of ≥1 drug due to intolerance/toxicity/failure);
➢ clinical failure: AIDS/death, SNAE (serious non-AIDS event)/death.

Statistical analysis:

➢ Chi-square test for categorical and non-parametric Mann-Whitney test for continuous variables;
➢ Weighted and standard unweighted survival analysis by KM curves and Cox regression model were employed, adjusted for age, VL at ART starting, calendar year of ART and nationality.

RESULTS

Among 8,061 PLWH included, **320 (4%)** experienced one of the **DTT**-defining events (75% had 2 discontinuations, 18% had 1 VF + 1 discontinuation, 7% had 2 VF).
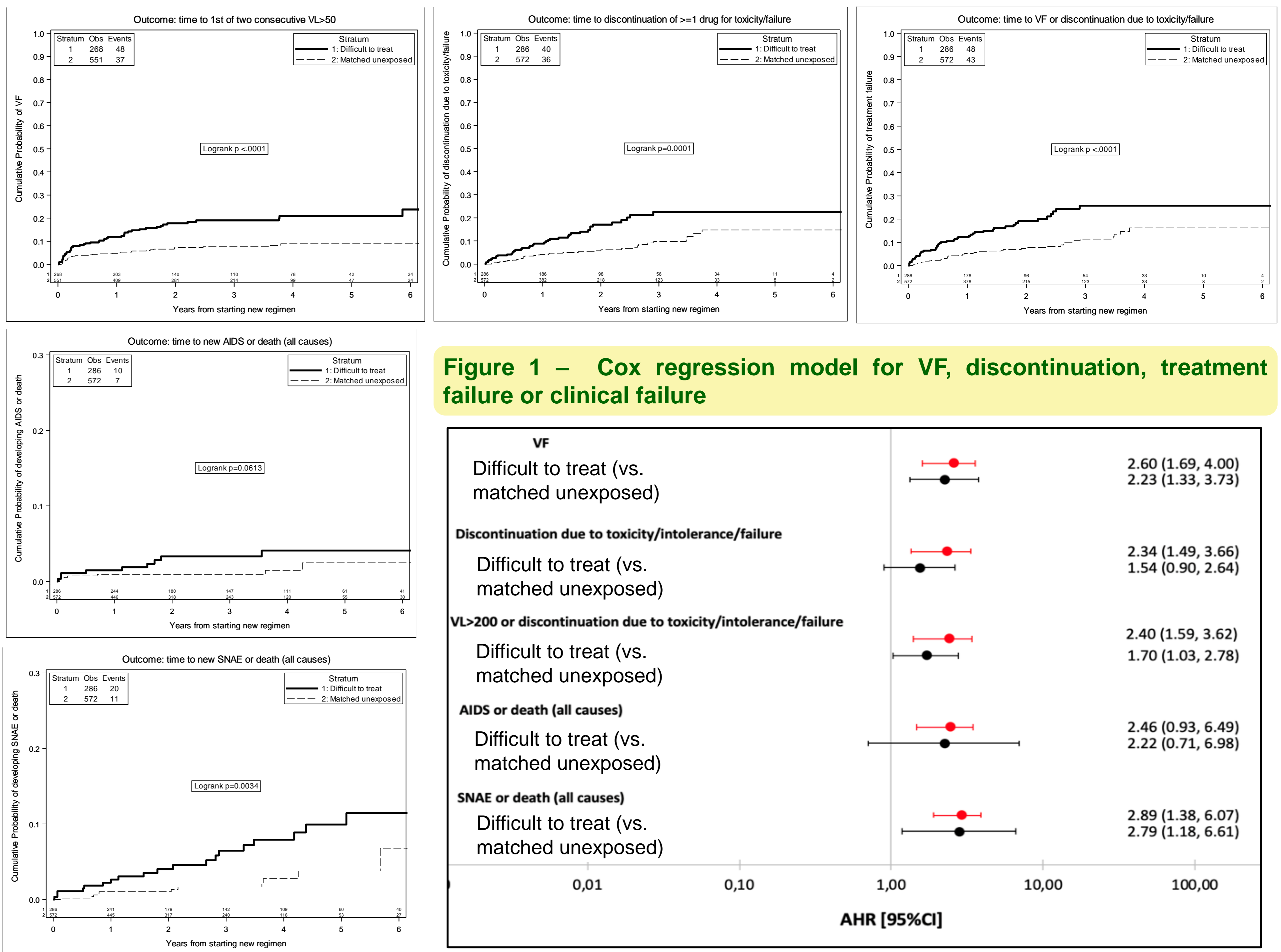
Table 1 – Patients' characteristics

	Difficult to treat (n=320)	Not difficult to treat (n=7741)	P-value	Overall population (n=8061)
Female gender, n (%)	61 (19.1%)	1412 (18.2%)	0.709	1473 (18.3%)
Age, median (IQR)	43 (36, 50)	39 (31, 49)	<.001	40 (31, 49)
Mode of HIV transmission, n(%)				
IVDU	22 (6.9%)	464 (6.1%)		486 (6.1%)
MSM	137 (43.2%)	3774 (49.4%)	0.075	3911 (49.2%)
heterosexual	141 (44.1%)	2895 (37.4%)		3036 (37.7%)
Other/unknown	17 (5.4%)	503 (6.6%)		520 (6.5%)
CDC stage C, n(%)	55 (17.2%)	763 (9.9%)	<0.001	818 (10.1%)
HCV Ab, n(%)				
negative	230 (71.9%)	5774 (74.6%)		6004 (74.5%)
positive	33 (10.3%)	438 (5.7%)	0.002	471 (5.8%)
missing	57 (17.8%)	1529 (19.8%)		1586 (19.7%)
HBsAg, n(%)				
negative	254 (79.4%)	6177 (79.8%)		6431 (79.8%)
positive	1 (0.3%)	13 (0.2%)	0.824	14 (0.2%)
missing	65 (20.3%)	1551 (20.0%)		1616 (20.0%)
Nadir CD4+, cell/mmc, median (IQR)	285 (104, 453)	348 (164, 510)	<0.001	346 (160, 508)
CD4+ at BL, cell/mmc, median (IQR)	305 (105, 473)	355 (167, 534)	<0.001	353 (163, 532)
Viral load, log10 copies/mL, median (IQR)	4.93 (4.34, 5.42)	4.72 (4.11, 5.30)	0.001	4.73 (4.12, 5.31)
Time from HIV diagnosis to date of starting ART, months, median (IQR)	1 (1, 12)	1 (1, 6)	0.186	1 (1, 6)
Calendar year of BL, median (IQR)	2014 (2013, 2016)	2016 (2015, 2018)	<0.001	2016 (2015, 2018)
Not Italian nationality, n (%)	97 (30.3%)	4171 (53.9%)	<.001	4268 (52.9%)
Anchor drug started				
NNRTI	37 (12%)	1469 (19%)	<.001	1506 (19%)
PI	149 (47%)	1568 (20%)		1717 (21%)
INSTI	134 (42%)	4704 (61%)		4838 (60%)

Outcomes of difficult-to-treat patients

Matched analysis performed in 286 DTT and 572 matched-unexposed.

Estimates of becoming difficult-to-treat

✓ Estimated probability of becoming DTT: 6.5% (95% CI 5.8- 7.4%) by 6 years.

✓ PLWH with advanced HIV disease (CD4<200 and/or AIDS) were 2,402 (30%): more frequently females, infected through heterosexual contacts, not Italians, older and had greater viral load than PLWH without advanced HIV disease.

✓ PLWH with advanced HIV disease had higher aHR of becoming DTT (aHR=1.30, 95% CI 0.98-1.74, p=0.072) when compared to PLWH without advanced HIV.

Figure 1 – Cox regression model for VF, discontinuation, treatment failure or clinical failure

	AHR [95%CI]
VF	
Difficult to treat (vs. matched unexposed)	2.60 (1.69, 4.00) / 2.23 (1.33, 3.73)
Discontinuation due to toxicity/intolerance/failure	
Difficult to treat (vs. matched unexposed)	2.34 (1.49, 3.66) / 1.54 (0.90, 2.64)
VL>200 or discontinuation due to toxicity/intolerance/failure	
Difficult to treat (vs. matched unexposed)	2.40 (1.59, 3.62) / 1.70 (1.03, 2.78)
AIDS or death (all causes)	
Difficult to treat (vs. matched unexposed)	2.46 (0.93, 6.49) / 2.22 (0.71, 6.98)
SNAE or death (all causes)	
Difficult to treat (vs. matched unexposed)	2.89 (1.38, 6.07) / 2.79 (1.18, 6.61)

CONCLUSIONS

A total of 6.5% of PLWH who started a modern first-line ART satisfied our arbitrary definition of DTT by 6 years from ART initiation. This appears to be a more vulnerable PLWH population who may experience a higher risk of treatment and clinical failure in the long-term.

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