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EFFICACY AND DURABILITY OF 2-DRUG VS 3-DRUG INSTI-BASED REGIMENS: DATA FROM REAL-LIFE

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BACKGROUND

Despite the increasing support in favour of using 2DR, made possible by the availability of drugs with high genetic barrier[1-2], there are conflicting data on DTG tolerability, in particular regarding high rate of discontinuations of DTG-based regimens due to neuropsychiatric events in some cohorts.[3-4]

The Observational cohort for the study of DOlutegravir in Antiretroviral Combination REgimens (ODOACRE) cohort evaluates the overall efficacy and tolerability of dolutegravir (DTG)-based antiretroviral (ARV) regimens in clinical practice in 11 italian clinical centres.[5]

METHODS

STUDY DESIGN

Retrospective multicentre observational study in 8 italian clinical centres

Inclusion criteria

- *HIV-1 infected treatment-experienced patients*
- *HIV-1 RNA (VL)<50 copies/mL*
- *Switch to InSTI-based 2DR or 3DR*
- *At least one follow-up visit*

Exclusion criteria

- *HBsAg+*
- *Switch for virological failure*

MAJOR OUTCOMES

- Virological Failure (VF): 1 VL>1,000 copies/mL or 2 consecutive VL>50 copies/mL
- Regimen discontinuation due to any reason

Statistical analyses

- Kaplan-Meier curves were used to analyze the estimated probability of VF and discontinuation
- Cox regression analysis was used to analyze predictors of VF and discontinuation

Tab 1. Baseline characteristics of population

	Overall (n=1,666)	2DR (n= 332)	3DR (n=1,334)	P (2DR vs 3DR)
Males, n (%)	1,225 (73.5%)	245 (73.8%)	980 (73.5%)	0.945
Age, median (IQR)	50.8 (43.1-55.8)	52.4 (44.8-57.0)	50.4 (42.8-55.3)	<0.001
Caucasian ethnicity, n (%)	1,420 (85.2%)	293 (88.3%)	1,127 (84.5 %)	0.142
Risk factor, n (%)				0.035
Heterosexual contacts	637 (38.2%)	121 (36.4%)	516 (38.7%)	
MSM/bisexual	647 (38.8%)	150 (45.2%)	497 (37.3%)	
IDU	272 (16.3%)	45 (13.6%)	227 (17.0%)	
Other/Unknown	110 (6.6%)	16 (4.8%)	94 (7.0%)	
HCV coinfection, n (%)	260 (15.6%)	49 (14.8%)	211 (15.8%)	0.673
Years from HIV diagnosis, median (IQR) (on 1,608)	13.9 (7.0-21.7)	15.2 (8.8-21.1)	13.6 (6.9-21.7)	0.144
Years of HAART, median (IQR) (on 1,590)	11.2 (5.1-17.8)	12.4 (6.7-18.4)	10.9 (4.9-17.6)	0.004
Nadir CD4$^+$, cells/µL, median (IQR) (on 1,593)	184 (51-304)	192 (57-295)	180 (51-305)	0.942
Baseline CD4$^+$, cells/µL, median (IQR)	676 (488-896)	680 (520-910)	674 (475-892)	0.193
Zenith HIV-1 RNA $\log_{10}$, cps/mL, median (IQR) (on 1,473)	4.9 (4.4-5.4)	4.9 (4.3-5.3)	4.9 (4.4-5.4)	0.525
CDC C, n (%)	446 (26.8%)	83 (25.0%)	363 (27,2%)	0.446
InSTI in last regimen, n (%) (on 1,624)	318 (19.4%)	70/328 (20.7%)	248/1314 (18.8%)	0.552
InSTI previous used, n (%) (on 1,650)	436 (26.4%)	108/330 (32.7%)	328/1320 (24.8%)	0.011
History of previous VF, n (%) (on 1,573)	492 (31,3%)	123/315 (39.0%)	369/1258 (29.3%)	0.004
Time of virosuppression (months), median, IQR (on 1,484)	4.6 (1.3-9.2)	6.5 (2.2-10.6)	4.2 (1.1-8.9)	<0.001
Time of follow-up (weeks), median (IQR)	100.4 (52.0-150.6)	125.9 (59.3-172.5)	95.1 (50.8-143.8)	0.140

RESULTS

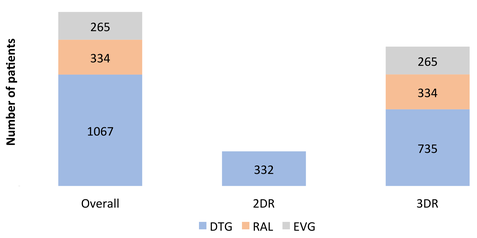


Fig.1 Current ART InSTI-regimens

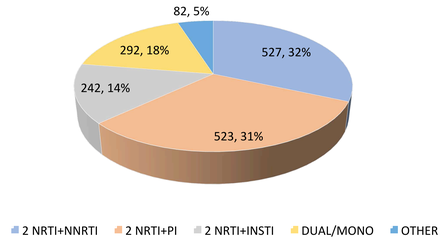


Fig.2 Previous ART regimen

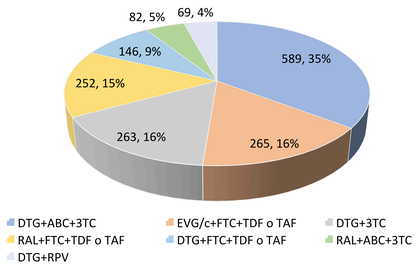


Fig.3 Current ART regimens

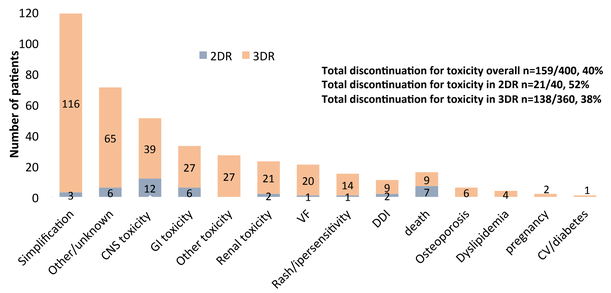
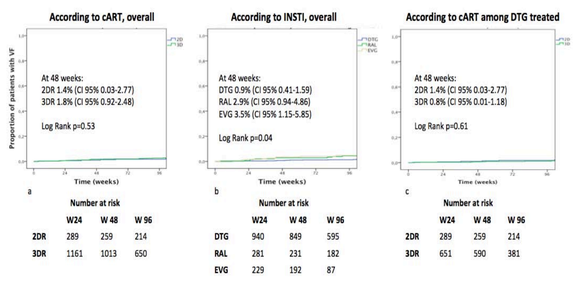
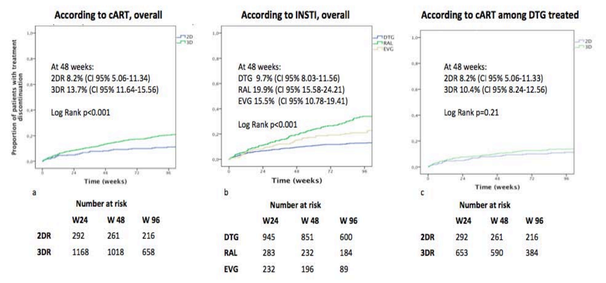


Fig.4 Reasons for InSTI-based regimens discontinuation



✓ Over a median follow-up of 100 weeks (IQR 52-150), 52 (3.1%) VF (1.5 per 100 PYFU)

Fig.5 Estimated probability of virological failure



✓ 400 (24%) patients discontinued InSTI-based regimen (11.3 per 100 PYFU)

Fig.6 Estimated probability of treatment discontinuation for any reason

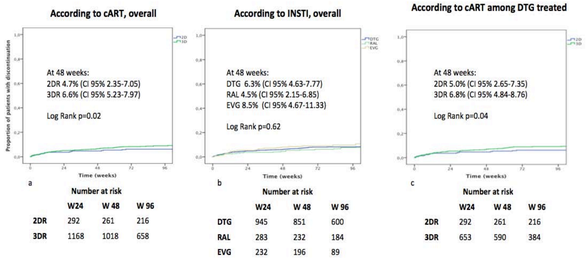


Fig.7 Estimated probability of treatment discontinuation for toxicity

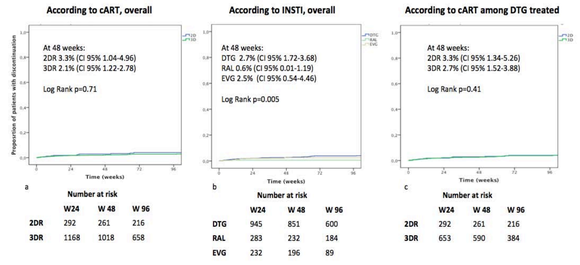


Fig.8 Estimated probability of treatment discontinuation for neurological toxicity

Tab.2 Predictors of VF, overall

	Unadjusted HR (CI 95%)	P value	Adjusted HR (CI 95%)	P value
History of previous virological failure	3.17 (1.82-5.51)	<0.001	2.73 (1.56-4.80)	<0.001
Virosuppression time (per 1 month increase)	0.995 (0.989-1.0)	0.09	0.994 (0.988-1.0)	0.049

Adjusted for simplification as reason for start, zenith VL, regimen (DTG+RPV vs 3DR, DTG+3TC vs 3DR)

Tab. 3 Predictors of InSTI regimens discontinuation, overall

	Unadjusted HR (CI 95%)	P value	Adjusted HR (CI 95%)	P value
Risk factor heterosexuals (ref)				
Risk factor MSM	1.43 (0.88-2.34)	0.150	0.75 (0.58-0.96)	0.022
Risk factor IDU	1.13 (0.69-1.85)	0.630	1.18 (0.85-1.63)	0.322
Risk factor unknown	2.03 (1.22-3.36)	0.006	0.59 (0.33-1.06)	0.076
Simplification as reason for start	0.61 (0.49-0.76)	<0.001	0.53 (0.4-0.69)	<0.001
3DR vs 2DR	2.16 (1.55-2.99)	<0.001	2.09 (1.47-2.98)	<0.001

Adjusted for age, CDC stage C, HCV positivity, time of virosuppression, previous VF, previous InSTI use, nadir CD4 cells count, ethnicity, toxicity as reason for start, zenith VL>100,000 cps/mL

Tab.4 Predictors of regimens discontinuation among DTG treated

	Unadjusted HR (CI 95%)	P value	Adjusted HR (CI 95%)	P value
Risk factor heterosexuals (ref)				
Risk factor MSM	1.34 (0.67-2.69)	0.415	0.59 (0.4-0.89)	0.011
Risk factor IDU	0.92 (0.45-1.88)	0.820	1.05 (0.65-1.71)	0.840
Risk factor unknown	1.58 (0.74-3.39)	0.238	0.71 (0.34-1.49)	0.366
Virosuppression time (per 1 month increase)	0.996 (0.993-0.999)	0.009	0.996 (0.993-0.999)	0.012
Previous InSTI use	1.46 (1.03-2.06)	0.033	1.47 (1.02-2.12)	0.039
Simplification as reason for start	0.75 (0.54-1.04)	0.084	0.54 (0.36-0.83)	0.004

Adjusted for previous VF, toxicity as reason for start, regimen (DTG+RPV vs 3DR, DTG+3TC vs 3DR)

CONCLUSIONS

- ✓ In our real-life setting, both 2DR and 3DR INSTI-based regimens showed high efficacy and durability
- ✓ Regimens including dolutegravir were associated with a lower risk of VF and discontinuation
- ✓ Regimens including raltegravir were associated with a lower risk of discontinuation for neurological toxicity

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