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Long-Term Durability of Rilpivirine + Darunavir/cobicistat Dual Regimen in Antiretroviral-Experienced People Living with HIV (RilDaco study)

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Study Background

Two-drug oral regimens based on a high genetic barrier agent (i.e. dolutegravir or boosted protease inhibitor) is used in both naïve and switch strategies. Rilpivirine (RPV) plus darunavir-cobicistat (DRV-c) may be useful in people living with HIV (PLWH) when the integrase inhibitor class is contraindicated for intolerance, toxicity or resistance issues. We here report on the durability of this combination assessed by treatment failure (TF) over time.

Methods

This is a retrospective, observational, single-centre study in virologically suppressed PLWH switched to RPV + DRV-c for any reasons. Data were collected from the electronic database of the HIV centre which prospectively includes the information, laboratory markers, clinical decisions and drug prescriptions.

The primary composite endpoint was TF defined as any reason of discontinuation, including virological failure (VF) (i.e. HIV RNA > 50 copies/mL or any values followed by a switch).

Survival analysis with Kaplan-Meier estimator was used to assess the probability of treatment failure over time.

Multiple logistic regression was used to estimate the probability of TF at 1 year following the initiation of RPV + DRV-c.

Results 1: Baseline characteristics

Table 1. Baseline characteristics of subjects switching to RPV+ DRV-c

Number of subjects	**97**
age, years, median (IQR)	57 (50-63)
gender, male, n (%)	78 (80)
Ethnicity, n (%)	
Caucasian	92 (95)
risk factor for HIV acquisition, n (%)	
MSM	37 (38)
heterosexual	40 (41)
intravenous drug use	17 (17)
other, unknown	3 (3)
comorbidities, n (%)	
none	35 (36)
1-2	55 (57)
3-5	7 (7)
AIDS, n (%)	14 (15)
nadir CD4+T cell count, median (IQR)	260 (125-350)
treatment lines, n. (%)	
< 3	31 (32)
3-5	44 (45)
>5	22 (23)
primary resistance mutations*, n. (54 tested)	
NRTI	5 (9%)
NNRTI	3 (6%)
PI	0
INSTI	0
last ARV regimen, n (%)	
2NRTI+ INI	8 (8)
2NRTI+ NNRTI**	79 (81)
2NRTI+ PI	10 (10)
CD4+T cell count at study entry, patients N. (%)	
median (IQR) cells/mmc	732 (597-1010)
200-500	13 (13)
> 500	84 (87)
baseline HIV RNA, n (%)	
<50 copies/mL	96 (99)
50 -100 copies/mL	1
HBV serology, n. (%)	
HBsAg +	0
HBsAb +	58 (81)
HBcAb +	16 (36)

Numbers are median (percentage), if not otherwise specified.
*according to the Stanford HIVdb mutation list https://hivdb.stanford.edu/
** rilpivirine: 45, efavirenz: 27, nevirapine: 7

Results 2

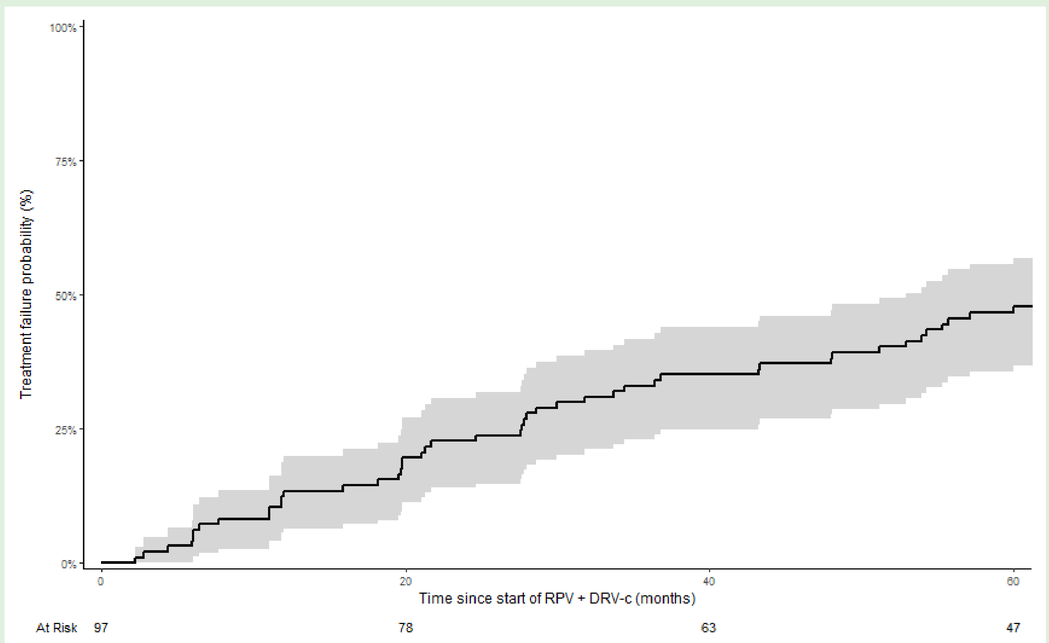
A total of 97 individuals were included. Median follow-up was 69 (IQR: 66-73) months since RPV+DRV-c initiation.

The probability of treatment failure was 2%, 13%, 23%, 33%, 38% and 48% after 6, 12, 24, 36, 48 and 60 months of treatment, respectively (figure1).

Table 2 shows the reasons for therapy discontinuations.

At multiple logistic regression with age, sex and baseline CD4 count as predictors for TF at 1 year (*no more than three predictors could be included based on the number of events*), no association was found with any of the aforementioned predictors (p>0.05 for all).

Figure 1. Kaplan-Meier curve for treatment failure over time



Results 3

Table 2. Reasons of treatment discontinuation

Number of subjects: 54/97 (55%)	
virological failure	1 (single blip, 95 copies)
dyslipidemia	20 (37%)
drug interaction	10 (19%)
simplification	9 (17%)
side effects	5 (9%)
patient's choice	3 (5%)
other	2 (4%)
lost to follow- up	1 (2%)
unknown	3 (5%)

Table 3: median values of triglicerydes (TGs) and total cholesterol according to months on treatment. A total of 35/97 (36%) subjects were on statins and 7/97 (7%) on anti-TGs medications

	T0 months	T12 months	T24 months	T36 months	T48 months	T60 months	T72 months
Triglicerydes median (IQR)	122 96-191	153 108-213	151 114-216	164 108-230	178 117-247	148 116-180	150 100-205
Total cholesterol median (IQR)	191 173-215	211 185-238	212 183-240	204 188-240	203 181-232	199 190-236	205 188-223
Patients at risk	94	94	75	63	61	53	35

Conclusions

RPV+DRV-c is an effective and durable combination in switch strategy. Most reasons of discontinuations were other than VF (mainly metabolic issues or drug-interactions), confirming its virological efficacy for those not eligible to INSTI-based options.

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