Injection site pain and cabotegravir/rilpivirine plasma concentration in people with HIV

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Injection Site Reactions (ISRs)

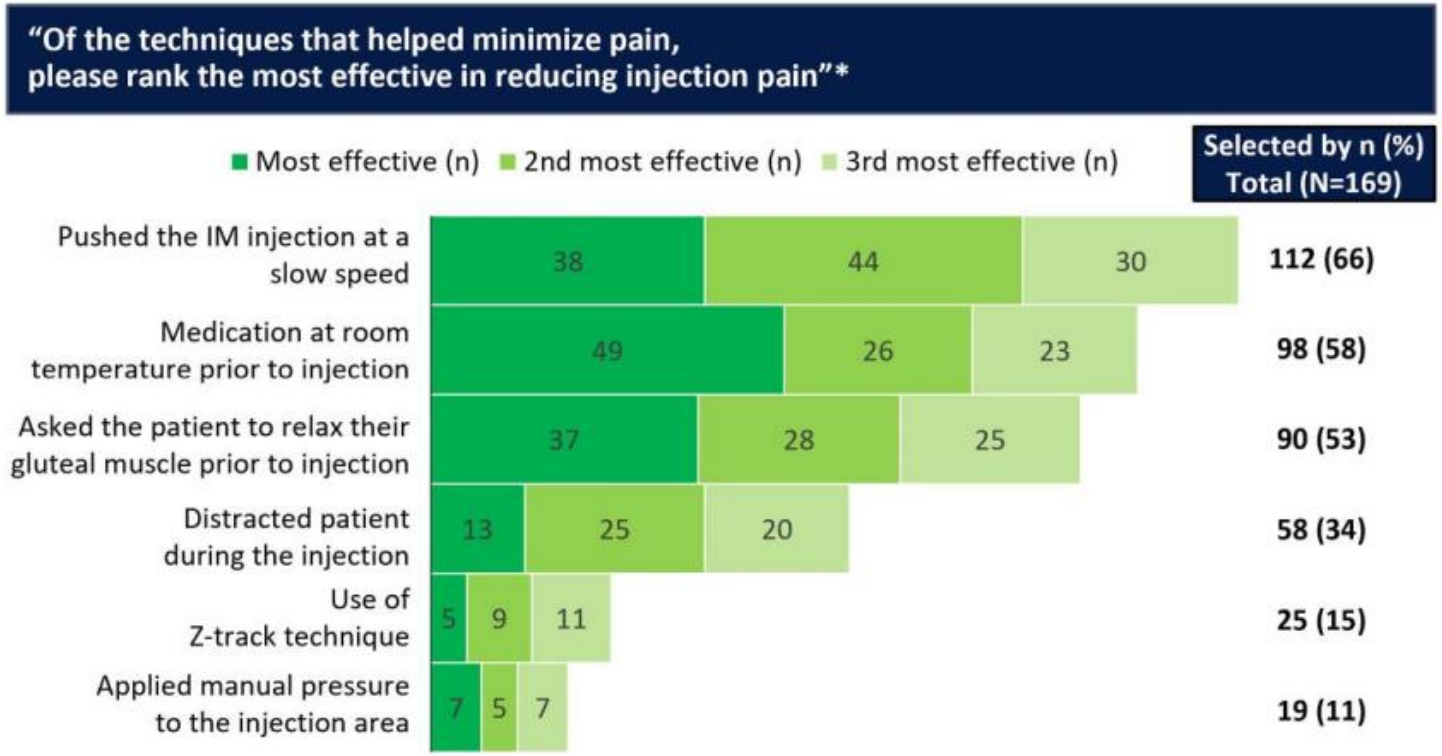
Pooled ISR characteristics and outcomes for participants receiving CAB + RPV LA through week 96 of the FLAIR and ATLAS-2M studies

Parameter	CAB + RPV LA Dosing Regimen			Drug[a]	
	CAB + RPV LA Q8W (n = 327)	CAB + RPV LA Q4W (n = 610)	Total (n = 937)	CAB (n = 937)	RPV (n = 937)
No. (%) of participants receiving ≥1 injection	321 (98)	599 (98)	920 (98)	920 (98)	920 (98)
No. of injections	7954	26 985	34 939	17 468	17 471
No. of ISR events (event-level)[b]	2345	6108	8453	3836	4606
Pain, No. (% of injections)	1904 (24)	5035 (19)	6939 (20)	3142 (18)	3789 (22)
Nodule, No. (% of injections)[c]	107 (1)	355 (1)	462 (1)	213 (1)	249 (1)
Induration, No. (% of injections)	61 (<1)	208 (<1)	269 (<1)	130 (<1)	139 (<1)
Discomfort, No. (% of injections)	113 (1)	107 (<1)	220 (<1)	112 (<1)	107 (<1)
Swelling, No. (% of injections)	56 (<1)	85 (<1)	141 (<1)	65 (<1)	76 (<1)
Grade, No. (%)					
Grade 1	1843 (79)	5157 (84)	7000 (83)	3112 (81)	3880 (84)
Grade 2	468 (20)	889 (15)	1357 (16)	678 (18)	676 (15)
Grade 3[d]	34 (1)	62 (1)	96 (1)	46 (1)	50 (1)
Participants withdrawing due to injection-related reasons, No. (% of participants with ≥1 injection)[e]	5 (2)	15 (3)	20 (2)	7 (<1)[f]	9 (<1)[f]

Teichner P et al. Open Forum Infectious Diseases. 2024.

Health Care Provider Administration

Survey results from healthcare providers (HCPs) giving injections in the ATLAS, FLAIR, and ATLAS-2M studies



Parameter	Total (n = 181)	North America[a] (n = 61)	Europe[b] (n = 71)	Outside of the US, Canada, and Europe[c] (n = 49)
Role of HCP				
Medical doctor	44 (24)	4 (7)	10 (14)	30 (61)
Licensed nurse	99 (55)	32 (52)	57 (80)	10 (20)
NP/prescribing nurse	14 (8)	4 (7)	3 (4)	7 (14)
Physician assistant	2 (1)	2 (3)	0	0
Medical assistant[d]	9 (5)	9 (15)	0	0
Pharmacist	1 (<1)	1 (2)	0	0
Other	12 (7)	9 (15)	1 (1)	2 (4)
No. of years administering gluteal injections				
0–5	76 (42)	30 (49)	20 (28)	26 (53)
6–10	22 (12)	8 (13)	8 (11)	6 (12)
11–20	29 (16)	13 (21)	12 (17)	4 (8)
>20	54 (30)	10 (16)	31 (44)	13 (27)
No. of participants the HCP injected with CAB + RPV LA				
≤10	103 (57)	30 (49)	42 (59)	31 (63)
11–25	52 (29)	23 (38)	17 (24)	12 (24)
26–50	8 (4)	4 (7)	3 (4)	1 (2)
>50	18 (10)	4 (7)	9 (13)	5 (10)
No. of injections of CAB and RPV administered by the HCP[e]				
6–19	20 (11)	6 (10)	5 (7)	9 (18)
20–49	23 (13)	6 (10)	12 (17)	5 (10)
50–99	36 (20)	12 (20)	16 (23)	8 (16)
≥100	102 (56)	37 (61)	38 (54)	27 (55)

Teichner P et al. Open Forum Infectious Diseases. 2024.

ISRs in SCohoLART study (NCT05663580)

- Mostly common at first injection, less frequent over time
- Median duration of 3 days
- Generally mild to moderate, with pain and discomfort, hardened mass or lump, possible redness, itching, swelling or warmth
- Therapy discontinuation in 15 PWH (28.8%)

Muccini C. et al. Open Forum Infectious Diseases. 2024.

Background and research question

- Among PWH on antiretroviral therapy (ART) with long acting (LA) cabotegravir (CAB) and rilpivirine (RPV), ISRs are frequent and typically transient, mild to moderate in severity, and decreasing in frequency over time, with **pain** being the most frequent symptom

- Aim of the study → evaluating the **correlation** between pain as ISR and plasma drug concentrations among PWH on LA ART with CAB/RPV

Methods

- Prospective, observational, cohort study among PWH receiving LA ART with CAB and RPV and presenting stable undetectable viremia, at the Infectious Diseases Department of San Raffaele Scientific Institute, Milan, Italy, between July 2022 and July 2024

- **150** individuals selected and divided in two groups based on presence (100) or absence (50) of pain defined as visual analogue scale **(VAS)>7**, VAS>3 with associated **systemic symptoms/fever**, or duration **>7 days**

- Plasma concentrations of CAB and RPV after 1 year of LA ART assessed using Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

Statistical analyses

- **Mann-Whitney test and Spearman correlation coefficient** for numerical variables used to define the correlation between CAB/RPV plasma concentration and pain/no pain group

- **Mann-Whitney test and Chi-squared test** for categorical variables used to evaluate differences between the two groups and other numerical/categorical predictors

Results

- Overall, 133 male (88.7%), with a median age of 51 years (interquartile range, IQR 40;58)
- **CAB** median concentration 1101 ng/ml (IQR 758;1652) in pain group and 1161 ng/ml (IQR 898;1733) in no-pain, respectively
- **RPV** median concentration 67 ng/ml (IQR 55;92) in pain group and 68 ng/ml (IQR 54;85) in no-pain, respectively
- **No significant differences** in both CAB and RPV concentrations between pain/no-pain group (Spearman's rank correlation coefficient**>0.3**)

Individuals' characteristics at baseline and correlation with pain

	All (N=150) median [q1;q3]	PAIN (N=50) median [q1;q3]	no-PAIN (N=100) median [q1;q3]	p_value
Time from HIV diagnosis (years)	15.02 [9.50;22.36]	19.14 [10.76;23.65]	13.29 [9.26;20.18]	0.113
Duration of ART (years)	12.71 [9.04;18.85]	15.73 [9.78;22.08]	11.67 [8.84;17.56]	0.047
HIV RNA (copies/ml)	0.90 [0.90;19.00]	0.90 [0.90;19.00]	0.90 [0.90;19.00]	0.332
CD4 (cell/mm^3)	836.00 [644.00;1036.00]	802.00 [607.00;1041.00]	839.00 [662.50;1014.00]	0.554
CD4 (%)	36.50 [31.30;43.30]	34.35 [28.80;41.10]	37.600 [32.85;43.60]	0.104
ALT (mg/dl)	24.00 [20.00;32.00]	24.50 [19.00;32.00]	24.000 [20.00;31.50]	0.995
AST (mg/dl)	25.00 [21.00;30.00]	25.00 [20.00;31.00]	25.000 [21.00;29.50]	0.892
LDL (mg/dl)	114.00 [94.00;137.25]	117.00 [94.00;147.00]	114.00 [94.25;132.00]	0.418
Crea (mg/dl)	1.00 [0.87;1.12]	0.97 [0.83;1.09]	1.02 [0.91;1.14]	0.088
Glucose (mg/dl)	89.000 [81.00;95.00]	92.000 [81.00;99.00]	87.50 [81.50;94.00]	0.179
BMI	24.53 [22.53;26.46]	24.68 [21.75;26.64]	24.49 [22.86;26.26]	0.728

(Mann-Whitney test)

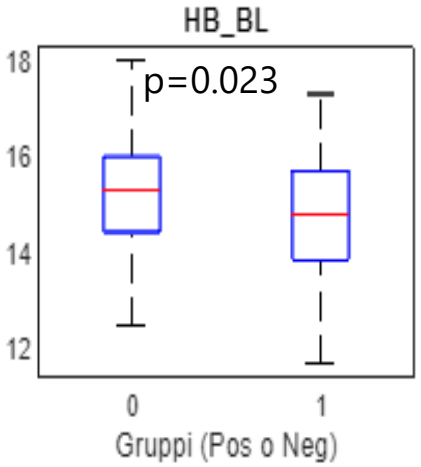
Individuals' characteristics at baseline and correlation with CAB/RPV concentration

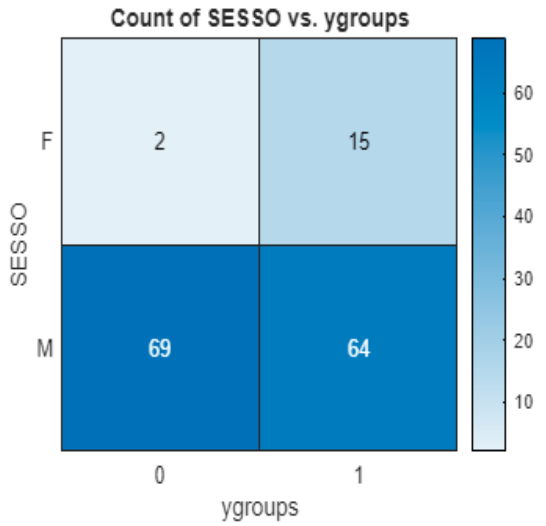
	N	CAB		RPV	
		median [Q1;Q3]	p_value	median [Q1;Q3]	p_value
GROUP					
PAIN	50	1100.500 [758.000;1652.000]	0.574	66.500 [55.000;92.000]	0.582
NO-PAIN	100	1161.500 [897.500;1732.500]		68.000 [54.000;84.500]	
SEX					
FEMALE	17	2080.000 [1394.750;2810.000]	<0.001	83.000 [53.000;116.500]	0.084
MALE	133	1083.000 [785.750;1544.250]		67.000 [55.000;85.250]	

(Chi-squared test)

Panel 1. CAB plasma concentration

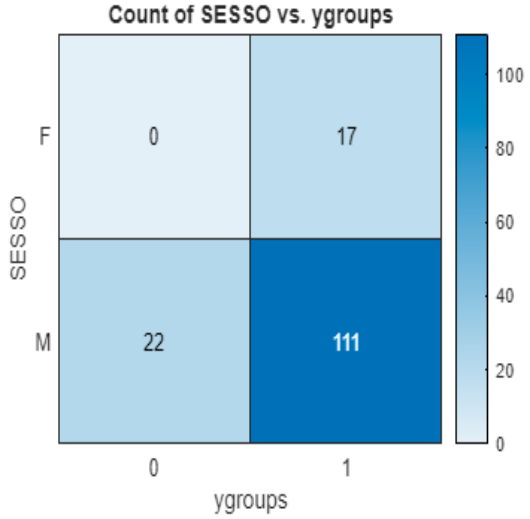
Significant correlations between CAB concentration and numerical/categorical variables (I) and between CAB concentration under/over the treshold of 664 ng/ml (4xPAIC$_{90}$) and categorical variables (II)



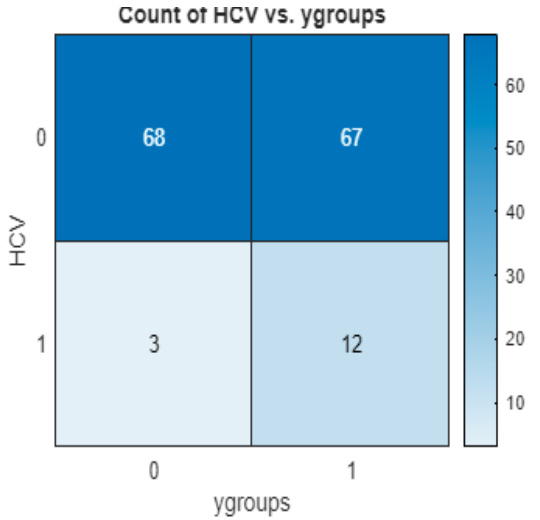


(I)

p=0.002



p=0.070

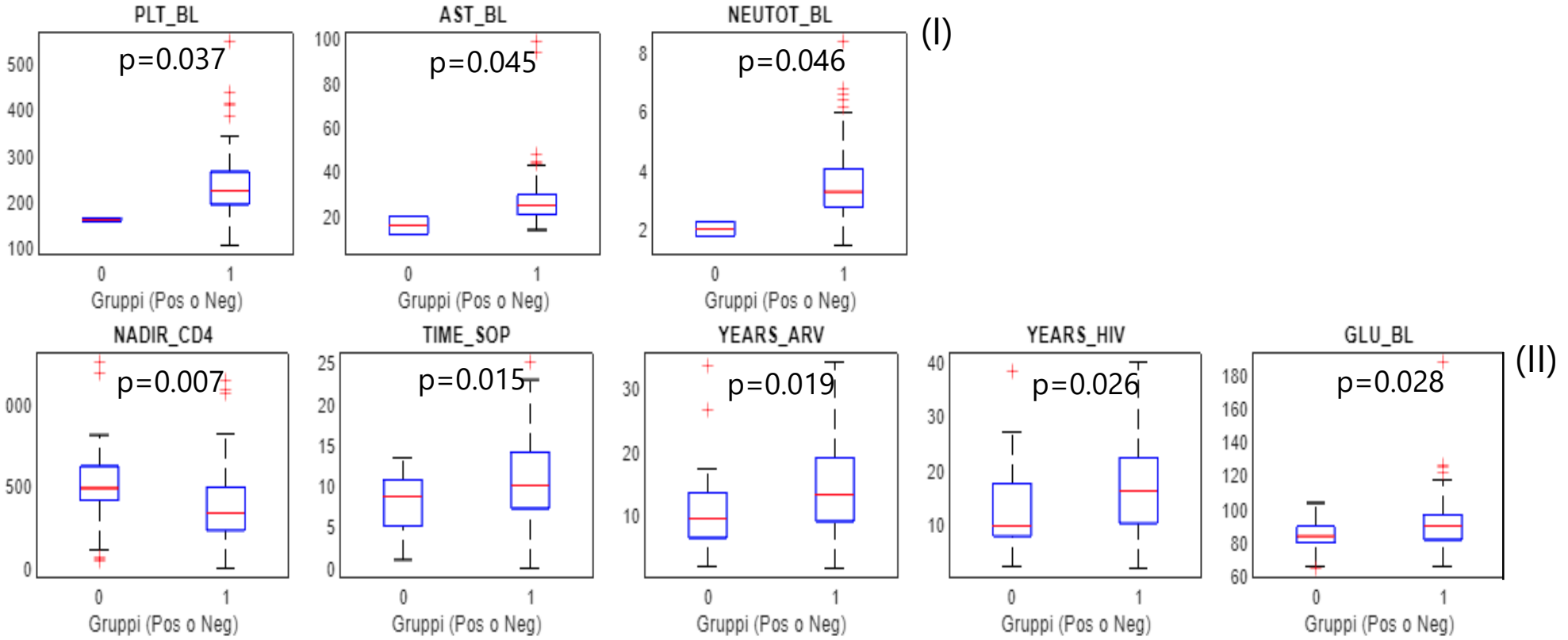


(II)

p=0.025

Panel 2. RPV plasma concentration

Significant correlations between RPV concentration and numerical variables (I) and between RPV concentration under/over the treshold of 50 ng/ml (4xPAIC$_{90}$) and numerical variables (II)



Conclusions

- In our cohort, **no significant correlation** was identified **between both CAB and RPV concentrations and pain** as injection site reaction among PWH on LA ART

- Remarkably, **female** gender represented a correlated factor with higher CAB concentration levels

- Additionally, **duration on ART** in years was significantly correlated to pain

Thanks for your attention!

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