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Prevalence of metabolic syndrome among PLWH assuming NVP containing regimen and INSTI based dual therapy

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Background

- Nevirapine (NVP) is a first-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) no longer recommend as first line therapy for people living with HIV (PLWH). NVP toxicity is mainly represented by hepatotoxicity and skin reactions, which may occur during the first 18 weeks of therapy. Despite this, NVP shows an acceptable long-term safety profile.
- Current EACS guidelines state that in case of ongoing therapy with a regimen that is no longer a preferred option treatment modification is not mandatory, unless to eliminate or improve adverse events, avoid drug-drug interaction, regimen fortification, simplification or cost reduction.
- While increasing the genetic barrier may be a good reason for switching from a NVP containing regimen, removing NVP in order to reduce long term toxicity may be more challenging.
- In fact, NVP shows a favorable lipid profile, increasing HDL and apolipoprotein A1, and shows no central nervous systems side effects. Moreover, NVP is considered relatively safe during pregnancy and lactation and thanks to the availability of generic formulation, NVP is relatively inexpensive.
- Cardiovascular disease and metabolic diseases are among most relevant issues for PLWH. According to meta-analysis, the prevalence of metabolic syndrome (MS) in PLWH is 27.9%. Integrase Strand Transfer Inhibitor (INSTI) based dual therapies have been proposed as a switch strategy to reduce long-term toxicity. However, it is unknown whether those regimens show an advantage over NVP containing regimens in term of metabolic toxicity.

Methods and methods

- We performed a cross-sectional study comparing the prevalence of MS among PLWH on NVP containing regimens and on INSTI single tablet regimens dual therapy.
- All PLWH aged 18 or over and receiving a NVP containing regimen, DTG/3TC or DTG/RPV attending our clinic were eligible for the study. Data were collected from the last available routine visit performed up to December 2023.
- MS was defined according to the 2005 diagnostic criteria of the National Cholesterol Education Program Adult Treatment Panel III.
- The primary outcome was the prevalence of MS. Non-superior prevalence threshold of MS in the NVP group was set at +10% of prevalence of MS for INSTI.

Figure 1 - Prevalence of metabolic syndrome

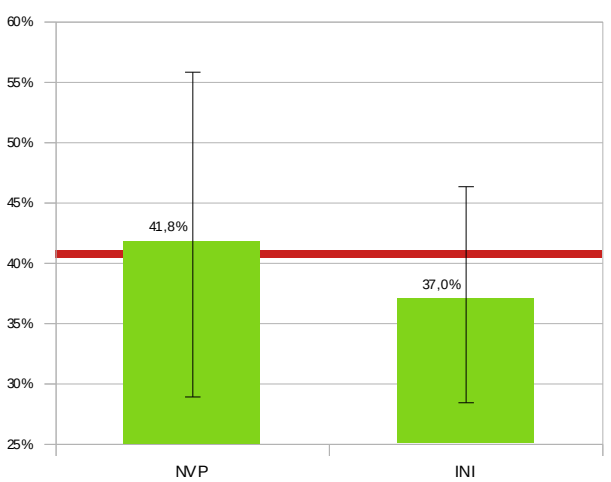


Table 1 - Study population

	overall (n= 198)		NVP (n=62)		INSTI (n=136)		
	median or %	IQR or n	median or %	IQR or n	median or %	IQR or n	p-value
Ethnicity							0,2897
Africa	15,7	(31)	22,6	(14)	12,6	(17)	
Asia	0,5	(1)	1,6	(1)	0	(0)	
Europe	79,7	(157)	72,6	(45)	83,0	(112)	
South America	4,1	(8)	3,2	(2)	4,4	(6)	
Age (years)	55	(47-61)	57	(52-61)	54	(45-61)	0,0730
Gender (male)	72,7	(144)	58,1	(36)	79,4	(108)	0,0018
Route of transmission							0,0009
Heterosexual	48	(95)	69,4	(43)	38,2	(52)	
MSM	36,4	(72)	21,0	(13)	43,4	(59)	
IDU	15,2	(30)	9,7	(6)	17,6	(24)	
MTCT	0,5	(1)	0	(0)	0,7	(1)	
Time of therapy (years)	13	(6-20)	17,5	(13-23)	11	(5-16,75)	<,0001
Current ARV							
NVP+TAF/FC	23,7	(47)	75,8	(47)	-		
DTG/3TC	55,6	(110)	-		80,9	(110)	
DTG/RPV	13,1	(26)	-		19,1	(26)	
NVP +ABC/3TC	7,6	(15)	24,2	(15)	-		
Smokers							0,1391
Ex	8,3	(13)	14,9	(7)	5,5	(6)	
Never	52,2	(82)	46,8	(22)	54,5	(60)	
Current	39,5	(62)	38,3	(18)	40,0	(44)	
Height (cm)	173	(168-178)	170	(165-178)	173	(169-178)	0,0962
Weight (kg)	77	(67-89)	77	(65-88)	78	(69,75-89,25)	0,4779
BMI	27	(23-29)	27	(22,5-29)	26	(23-29)	0,7325
Waist circumference (cm)	94	(84-102,5)	92,5	(84-104)	94	(84-102)	0,6869
PAS (mmHg)	132	(119-145)	137	(120-152)	130	(118-142)	0,0535
PAD (mmHg)	72	(63-81)	72	(64-81)	71	(63-80)	0,6945
CD4 (cell/ml)	726	(559-1024)	747	(591-952)	723	(553-1018)	0,9970
HIVRNA<50 cp/ml	96,4	(190)	96,7	(59)	96,3	(131)	0,8891
HIVRNA<200 cp/ml	99,0	(195)	98,4	(60)	99,3	(135)	0,5584
CD4/CD8 ratio	0,82	(0,57-1,23)	0,88	(0,67-1,29)	0,81	(0,56-1,19)	0,1863
Creatinine (mg/dl)	0,95	(0,84-1,13)	0,86	(0,77-0,96)	1	(0,88-1,15)	
Triglycerides (mg/dl)	113	(79-162)	112	(83-137)	113	(79-163)	0,6811
Total cholesterol (mg/dl)	182	(158-207)	204	(165-226)	176	(152-197)	0,0004
HDL (mg/dl)	50	(41-62)	59	(51-77)	46	(37-54)	<,0001
LDL (mg/dl)	107	(85-129)	107	(89-142)	103	(82-125)	0,1095
ALT (U/l)	22	(18-34)	22	(19-29)	23	(18-35)	0,1874
Glucose (mg/dl)	91	(84-99)	92	(84-99)	91	(84-100)	0,9664
Diabetes mellitus	11,7	(23)	11,3	(7)	11,9	(16)	0,9093
Statins	33,9	(79)	45,2	(28)	37,5	(51)	0,3073
Hypertension	66,1	(127)	73,8	(45)	62,6	(82)	0,1276
Antihypertensive therapy	33,8	(67)	41,9	(26)	30,1	(41)	0,1040
Diabetes medications	9,1	(18)	9,7	(6)	8,8	(12)	0,8463
Abdominal obesity	35,5	(65)	43,1	(25)	32,0	(40)	0,1442
Metabolic syndrome	38,5	(67)	41,8	(23)	37,0	(44)	0,6578

- Characteristics across group were compared using chi-square or Wilcoxon rank-sum test as appropriate. Multivariate logistic regression was performed to assess factors associated with MS.

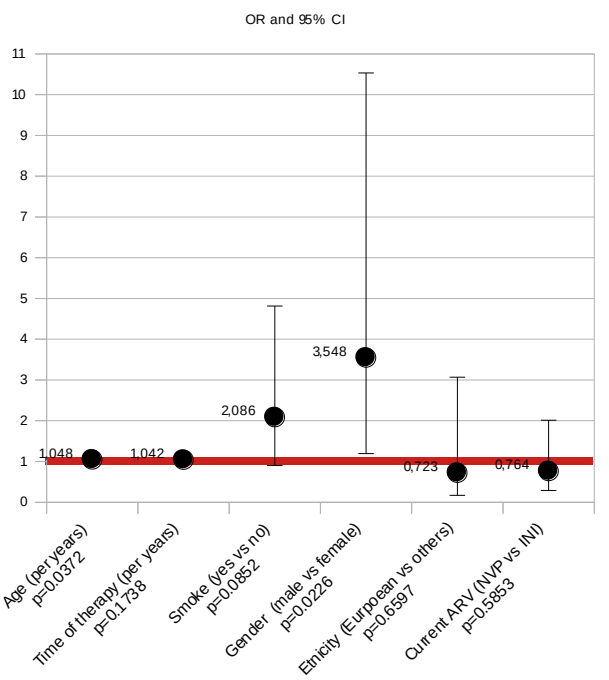
Results

- We enrolled 198 subjects, 62 in the NVP group and 136 in the INSTI group.
- Characteristic across group were similar, except gender, time of therapy and route of transmission. Notably in the NVP group were enrolled more women (41,9% vs 20,6%; p=0,0018) and subject with a longer time of therapy (median 17,5 years vs 11, p<0,0001). Study population characteristics are detailed in table 1.
- Overall prevalence of MS was 38,5% (n=67). The prevalence of MS in the NVP group was 41,8% (95%CI 28,9-55,9; n=23) and 37,0% (95%CI 28,4-46,4; n=44) the INSTI group, thus not meeting the criteria for non-superiority threshold of +10% (figure1).
- Interestingly, levels of total and HDL cholesterol were higher in the NVP group (median 204 vs 176 p=0.0004 and 59 vs 46 mg/dl p<0,0001 respectively), while LDL did not differ across groups.
- At multivariate analysis only age (OR 1,048 per years, 95%CI 1,003-1,096) and male gender (OR 3,548, 95%CI 1,195-10,532) were significantly associated with MS, while NVP regimen (OR 0,76, 95%CI 0,29-2,01), time of therapy (OR per years 1,04, 95%CI 0,98- 1,11), smoke (OR 2,07, 95%CI 0,90-0,82) and ethnicity (OR for European 0,723, 95%CI 0,17-3,07) were not significantly associated with MS (figure2).

Conclusions

- Despite not being able to demonstrate a non-superior incidence of MS in the NVP group due to small sample size, our study showed a significant correlation of age and sex, but not of therapy, with MS. NVP was associated with higher HDL and total cholesterol, but not higher LDL levels.

Figure 2 - Multivariate analysis, factor associated with metabolic sindrome



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