Using Climate-HIV to Describe Non-Antiretroviral Use and Potential DDIs for People Living With HIV Within a UK Cohort

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Introduction

- A large HIV cohort study suggested that ≥1 in 4 patients receiving antiretrovirals (ARVs) have a potential drug–drug interaction (DDI) with concomitant therapy, and this proportion is set to rise with increasing age and multimorbidity[1]
- Healthcare professionals (HCPs) caring for people living with HIV (PLHIV) must be aware of the potential for DDIs with ARVs, especially in aging populations

Objective

- To describe the use of non-ARVs among PLHIV on ARV treatment and highlight the risk of DDIs

Methods

- PLHIV aged ≥18 years with an ARV record current in Feb 2018 attending one of 4 UK HIV units using Climate-HIV, an electronic patient record system managed by the clinicians supporting the care of PLHIV, were included in this cross-sectional analysis
  - Data regarding demographics, ARV regimen, comorbidities, and current comedications were collected and analyzed
- DDI were analyzed as observed or potential
  - Observed DDIs were current comedications and assessed against current ARVs. There were analysed for incidence (i.e. how many patient were subject to that DDI) and severity (as per Liverpool category)
  - Potential DDIs, were extrapolated non-ARVs recommended in the treatment guidelines for National Institute for Health and Care Excellence (NICE) based on observed comorbidities against categorized ARVs[3].
- DDIs were categorized in accordance with the University of Liverpool HIV drug interaction checker[2]
  - DDIs categorized as red meant “do not coadminister”; amber, “potential interaction” (ie, managed by dose adjustment or monitoring); yellow, “potential weak interaction”; and green, “no interaction expected”
- Stepwise logistic regression was used to estimate the odds of a patient having a red/amber interaction, DTG + 2 nucleoside reverse transcriptase inhibitors was used as the reference category for the other ARV regimens

Results

- Patient characteristics are shown in Table 1

Table 1. Patient Characteristics

Parameter	Overall cohort (N=4630)
Male, n (%)	2609 (56)
Race/Ethnicity, n (%)	
African heritage	2064 (45)
White	1582 (34)
Black Caribbean/Other	446 (10)
Asian	155 (3)
Mixed/Unknown	383 (8)
Age, median (IQR), y	47 (39-54)
Age ≥50 y at baseline, n (%)	1898 (41)
Time since HIV-1 diagnosis, median (IQR), y	11.0 (5.7-15.7)
Proportion of patients with ≥1 non-ARV medication, n (%)	2992 (64.6)
Proportion of patients with ≥1 non-HIV comorbidity, n (%)	1838 (39.7)
Most common (>5%) ARV regimens, n (%)	
EFV/TDF/FTC	811 (17.5)
DTG/ABC/3TC	644 (13.9)
RPV/TDF/FTC	308 (6.7)
DRV/c/TDF/FTC	295 (6.4)
DRV/r/TDF/FTC	244 (5.3)
EFV/ABC/3TC	238 (5.1)

ARV, antiviral; IQR, interquartile range.

- 3010 (65%) patients were taking ≥1 non-ARV medications, and 787 (17%) patients were taking ≥5 non-ARV medications
  - 508 (26.8%) patients aged ≥50 years were taking ≥5 non-ARV medications, whereas 262 (9.6%) patients aged <50 years were taking ≥5 non-ARV medications (*P*<0.0001)
- Notable disparities between drugs prescribed for patients aged ≥50 years and those aged <50 years included atorvastatin (18.6% vs 2.6%, respectively), amlodipine (12.1% vs 3.5%), and ramipril (10.5% vs 2.4%; Table 2)

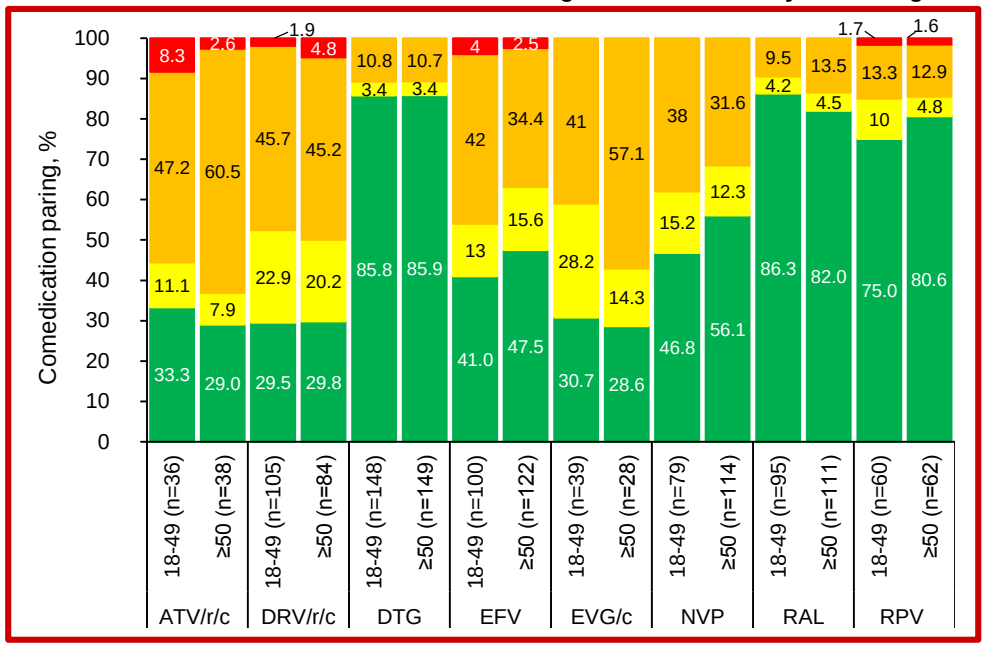
Table 2. Most Commonly (>5%) Reported Non-Antiretroviral Concomitant Medications

Non-antiretroviral drug, n (%)	Age <50 y (n=2732)	Age ≥50 y (n=1898)	Overall cohort (N=4630)
Cholecalciferol	668 (24.5)	494 (26.0)	1162 (25.1)
Atorvastatin	72 (2.6)	352 (18.6)	424 (9.2)
Trimethoprim/Sulfamethoxazole	247 (9.0)	171 (9.0)	418 (9.0)
Amlodipine	96 (3.5)	229 (12.1)	325 (7.0)
Salbutamol	151 (5.5)	174 (9.2)	325 (7.0)
Ramipril	66 (2.4)	200 (10.5)	266 (5.8)
Lansoprazole	95 (3.5)	158 (8.3)	253 (5.5)
Paracetamol	84 (3.1)	136 (7.2)	220 (4.8)

Observed categorized DDIs

- There were similar proportions of categorized DDIs observed in patients aged ≥50 vs <50 years treated with DTG-based (14.1% vs 14.2%) and RAL-based regimens (13.7% vs 18.0%; Figure 1)
- Observed amber and yellow DDIs were slightly higher with RAL compared with DTG, as RAL was mainly prescribed with TDF/FTC and DTG was mainly prescribed with ABC/3TC.

Figure 1. Proportion of Categorized Observed Drug–Drug Interactions of the Non-ARV Comedications Taken With ARV Regimens[a] Stratified by Patient Age

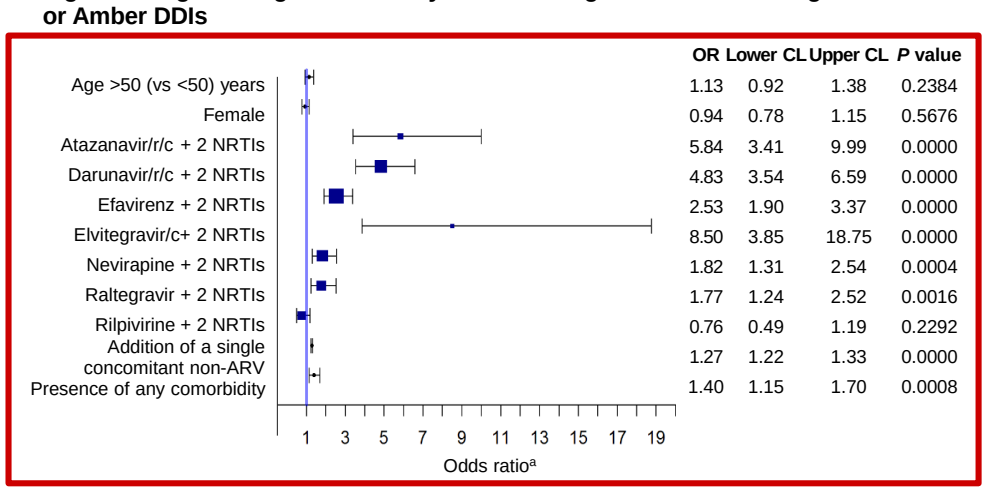


ARV, antiretroviral. [a]All regimens listed are taken with 2 nucleoside reverse transcriptase inhibitors.

Observed incidence of DDIs

- There were 40 red and 1458 amber DDIs observed in this population
- DDI risk was significantly increased in regimens with any ARV (except for RPV) vs DTG, with added use of an concomitant non-ARV or with any comorbidity (Figure 2).
- Age ≥50 years and gender did not present a significant risk in observing an amber or red DDI.

Figure 2. Logistic Regression Analysis Assessing Factors Influencing Risk of a Red or Amber DDIs



ARV, antiretroviral; CL, confidence level; DDI, drug–drug interaction; NRTI, nucleoside reverse transcriptase inhibitor. OR, odds ratio. [a]For ORs associated with ARV regimens, the reference regimen is DTG. The symbol size represents the relative number of patients.

Potential DDIs and Comorbidities

- The most commonly reported comorbidities were hepatitis B virus (HBV) infection (n=290), mental health (n=282), hypertension (n=271), and tuberculosis (TB; n=230)
  - Mean (SD) number of comorbidities were 0.8 (1.0) and 0.4 (0.7) in those aged ≥50 years and <50 years, respectively
- Amongst NICE guideline treatment recommendations of the observed comorbidities, 22%, 20%, and 14% of hepatitis C virus (HCV), HBV, and TB treatments, respectively, would lead to red DDIs in combination with an ARV regimen; HCV (58%), malignancy (50%), and mental health (32%) treatments would be most likely to cause amber DDIs

Conclusions

- Most DDIs were rated as amber (ie, managed by dose adjustment or monitoring)
  - More red or amber DDIs were observed in regimens that included a pharmacokinetic booster (ritonavir or cobicistat) compared with RAL- or DTG-based regimens
- Logistic regression shows that, while age and gender had no effect on the risk of DDIs, the risk of DDIs increased with the presence of a comorbidity, with increasing numbers of concomitant non-ARVs, and with all ARV regimen compared with DTG (expect for rilpivirine based regimens)
- HBV/HCV infections, TB, malignancies, and mental health were comorbidities that led to the highest risk of red/amber DDIs

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