Prescription Patterns of Comedication and Potential for Drug–Drug Interactions With Antiretroviral Therapy (ART) in Human Immunodeficiency Virus (HIV) Patients in a Retrospective Claims Database in Germany: Implications for Adequate HIV Treatment Selection

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Sara Lopes,[1] Ken O'Day,[2] Joris Van Stiphout,[3] Yogesh Punekar,[1] Matthew Radford,[1] Jennifer Scarlet Haas[4]

[1]ViiV Healthcare, London, UK; [2]Xcenda LLC, Palm Harbor, FL, USA; [3]Xcenda Switzerland GmbH, Bern, Switzerland; [4]Xcenda GmbH, Hannover, Germany

Introduction

- As people living with HIV (PLHIV) age, they may experience an increased prevalence of age-related comorbidities, which typically occur earlier in PLHIV than in the general population[1,2]
- Higher prevalence of comorbidities leads to polypharmacy, thus increasing the risk of drug–drug interactions (DDIs) and contraindications (CIs)[3-5]
- Different recommended antiretroviral therapy (ART) regimens have different DDI profiles, potentially impacting the clinical management of PLHIV when treated for several conditions by multiple clinicians

Objective

- Estimate the risk of potential DDIs or CIs in patients prescribed non-ART comedication and ARTs based on real-world prescription patterns

Methods

- This was a retrospective study with a cross-sectional, cohort design using claims from 2016 from the Institut für angewandte Gesundheitsforschung (InGef) database in Germany
  - Adults aged ≥18 years in 2016 being treated with any ART and diagnosed with HIV infection were included
  - Demographics, comorbidities, and prescription patterns of non-ART comedications were analyzed
  - Comorbidities and HIV diagnosis were identified using codes from the *International Classification of Diseases*, *10th Revision*, or an OPS code
  - Non-ART comedications were identified by Anatomical Therapeutic Chemical classification; only medicines reimbursed by the health insurance were included
- Real-world prescription pattern results from the cross-sectional analysis were subsequently populated into a DDI risk-evaluation model based on a well-established DDI database (www.hiv-druginteractions.org, accessed Feb 2018),[6] where the whole cohort was simulated to be treated with each of the ART regimens and evaluated for potential:
  - Weak DDI (additional action/monitoring or dosage adjustment unlikely to be required)
  - DDI (may require close monitoring, alteration of drug dosage or timing of administration)
  - CI (the drugs should not be coadministered)

Results

Population Characteristics

- 2680 patients were identified in the InGef database, predominantly male (86.1%)
- Mean age of PLHIV receiving ART in 2016 was 45.6 years (range, 18-86; Table 1)
- Prescriptions of non-ART medications were common (median of 7 in the overall population); patients aged ≥50 years were prescribed on average 3.2 more non-ART medications per year, and patients taking ART for ≥5 years were prescribed on average 1 more non-ART medication per year when compared with the overall population in the same period (Table 1)
- 30,947 non-ART prescriptions were counted in 2016, nearly half of which were prescribed to patients aged >50 years

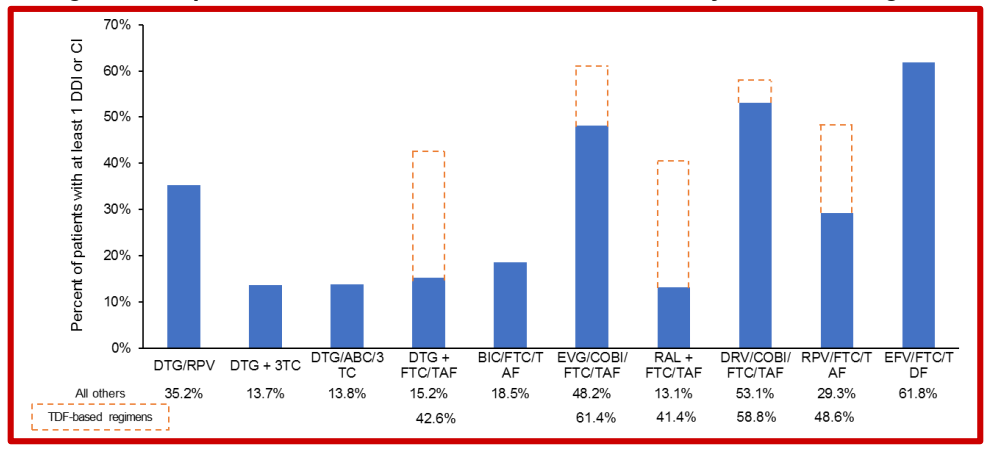
Table 1. Population Characteristics of PLHIV in 2016 From the German InGef Database

Parameter	Overall population (N=2680)	Age ≥50 years (n=910)	≥5 years on ART (n=789)
Male, %	86.1	86.4	84.5
Mean age, years	45.6	57.9	49.5
Age subgroups, n (%), years			
18-34	452 (16.9)	—	42 (5.3)
35-49	1318 (49.2)	—	391 (49.6)
≥50	910 (34.0)	910 (100)	356 (45.1)
Mean number of non-ART medications per patient, n	7.0	10.2	8.0
Total number of non-ART prescriptions, n	30,947	14,484	10,533
3 most commonly prescribed non-ART medications, n (%)[a]	Systemic antibacterials, 2272 (84.8)	Systemic antibacterials, 674 (74.1)	Systemic antibacterials, 565 (71.6)
	Anti-inflammatories, 888 (33.1)	Renin-angiotensin–acting agents, 330 (36.3)	Anti-inflammatories, 279 (35.4)
	Analgesics, 667 (24.9)	Anti-inflammatories, 328 (36.0)	Drugs for acid-related disorders, 209 (26.5)
Prevalence of top 3 comorbidities, n (%)	Acute upper respiratory infections, 873 (32.6)	Hypertensive diseases, 373 (41.0)	Mood disorders, 252 (31.9)
	Anxiety/Other nonpsychotic mental disorders, 826 (30.8)	Metabolic disorders, 367 (40.3)	Metabolic disorders, 250 (31.7)
	Mood disorders, 784 (29.3)	Other dorsopathies, 318 (35.0)	Hypertensive diseases, 237 (30.0)

ART, antiretroviral therapy; PLHIV, people living with HIV. [a]Non-ART medication not limited to those included in www.hiv-druginteractions.org.

- In the overall population, the ART regimens with the lowest proportion of patients with ≥1 DDI or CI were unboosted, integrase strand transfer inhibitor (INSTI) regimens, namely raltegravir (RAL) + emtricitabine (FTC)/tenofovir alafenamide fumarate (TAF), closely followed by dolutegravir (DTG)-based regimens, including DTG + lamivudine (3TC), DTG/abacavir (ABC)/3TC, DTG/FTC/TAF, and bictegravir (BIC)/FTC/TAF (Figure 1)
- Efavirenz (EFV)-based and boosted regimens with cobicistat (COBI) presented the higher proportion of patients who would have had ≥1 DDI or CI, namely elvitegravir/COBI/FTC/TAF or respective tenofovir disoproxil fumarate (TDF) and darunavir/COBI/FTC/TAF or TDF (Figure 1)
- Similar results, but with higher proportion of patients with DDIs/CIs, were obtained for the subgroup of patients aged ≥50 years and receiving >5 years of ART

Figure 1. Proportion of Patients With at Least 1 DDI or CI by Treatment Regimen



ABC, abacavir; CI, contraindication; COBI, cobicistat; DDI, drug–drug interaction; DRV, darunavir; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; 3TC, lamivudine; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate.

- Overall, approximately 1 out of 7 patients could potentially have a DDI or CI when prescribed RAL + FTC/TAF; 1 in 6 patients could potentially have a DDI/CI when prescribed DTG + 3TC, DTG/ABC/3TC, or DTG + FTC/TAF; and approximately 1 in 5 patients could potentially have a DDI/CI when prescribed BIC/FTC/TAF (Table 2)
- Boosted regimens presented the highest potential for DDIs/CIs, accounting for more than 1 event per patient per year (Table 2)

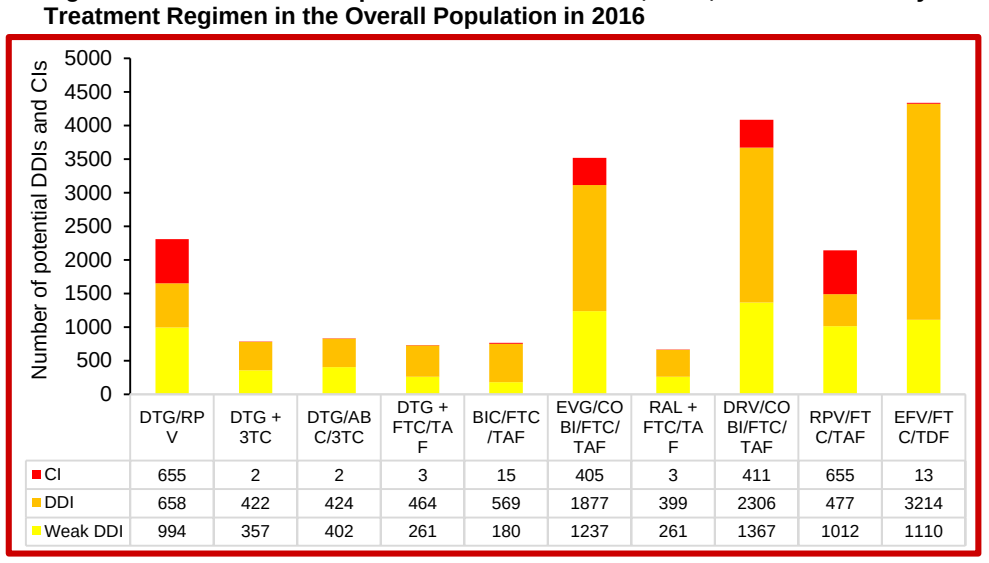
Table 2. Rate Potential DDI or CI/Patient/Year for Each Regimen

Regimen	Risk Rate	Regimen	Risk Rate
DTG/RPV	0.490	RAL + FTC/TAF	0.150
DTG + 3TC	0.158	RAL + FTC/TDF	0.536
DTG/ABC/3TC	0.159	DRV/COBI/FTC/TAF	1.014
DTG + FTC/TAF	0.174	DRV/r + FTC/TDF	1.150
DTG + FTC/TDF	0.560	RPV/FTC/TAF	0.422
BIC/FTC/TAF	0.218	RPV/FTC/TDF	0.758
EVG/COBI/FTC/TAF	0.851	EFV/FTC/TDF	1.204
EVG/COBI/FTC/TDF	1.246		

ABC, abacavir; COBI, cobicistat; DDI, drug–drug interaction; DRV, darunavir; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; 3TC, lamivudine; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; r, ritonavir.

- Overall CIs would be uncommon and more frequent in non-nucleoside reverse transcriptase inhibitor regimens (Figure 2)
- The largest number of potential DDIs was observed with EFV/FTC/TDF and boosted regimens
- Potential weak DDIs represent a significant proportion of interactions for all regimens

Figure 2. Number of Prescriptions With Potential CIs, DDIs, and Weak DDIs by Treatment Regimen in the Overall Population in 2016



ABC, abacavir; BIC, bictegravir; CI, contraindication; COBI, cobicistat; DDI, drug–drug interaction; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; FTC, emtricitabine; 3TC, lamivudine; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate.

Conclusions

- Comedication with potential DDIs/CIs with ARTs is frequently prescribed among PLHIV in Germany
- The potential risks for DDIs and CIs widely vary by ART regimen; the regimens with the lowest potential for DDIs or CIs were unboosted INSTI-based regimens, including RAL + FTC/TAF followed by 3 DTG-based regimens
- As PLHIV age, understanding the DDI profile for each ART regimen and the comorbidities and comedications of the HIV-infected population can help inform treatment decisions

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References: 1. Guaraldi et al. *Clin Infect Dis.* 2011;53:1120-1126. **2.** Schouten et al. IAS 2012; Washington, DC. Abstract B53. **3.** Edelman et al. *Drugs Aging.* 2013;30:613-628. **4.** Katlama et al. *AIDS.* 2017;31:1065-1071. **5.** Tseng et al. *Ann Pharmacother.* 2013;47:1429-1439. **6.** Liverpool Drug Interactions Group. https://www.hiv-druginteractions.org/checker. Accessed Oct 12, 2018.