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# Role of Clinical Pharmacist to Reduce Risk in Patients Involving Antiretroviral Drugs at Abidjan Cohort

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## Abstract

**Introduction:** The rapid increase in access to antiretroviral therapy in developing countries has brought with it new challenges. The management of risk by the clinical pharmacist may improve HIV patient's health in poor resources setting. We assessed risk criteria for drug-drugs interactions to inform clinicians.

**Methods:** This transversal work included patients at the beginning of ART treatment. From January to August 2015, HIV seropositive attending for care at Infectious and Tropical diseases Unit of Treichville teaching Hospital at Abidjan. The guidelines for entry into the antiretroviral program has been used. All the coprescribed drugs were screened for potential for Drugs-Drugs significate interactions using the Liverpool HIV Pharmacology Group website (www.hiv-druginteractions.org). Also many others books and website have been used to analyse drugs interactions. Finally, the French Clinical pharmacy guideline allowed to stratify the pharmaceutical interventions.

**Results:** Of 562 patients screened, 228 patients were included in the final analysis, comprising 91(39.91%) male and 137(60.9%) females; aged between 35-48 years (median 41 years), unmarried 160(63.18%), 218(95.61%) HIV1, 117(51.75%) with TB, renal failure 21(9.27%), First line of antiretroviral therapy 198 (86.84%) and 27(11.6%) patients were on second line treatment, Stage C (62.39%), mean Body mass index at baseline of 17.5.1 kg/m$^2$ (range 35-48 kg). Baseline CD4 counts were 200 (IQR 25-75%) (Range 131.5-278) cells/mm$^3$.The use of 1st line regimens were as follows: TDF/3TC/EFV in 141 patients (61.34%). Antiretroviral were prescribed at standard doses, regardless of whether a CR was present or not. Physiopathology stage was identified in 83 patients (36.41%) and potential drugs-drugs interactions with antiretroviral were identified in in 145 patients (63.59%) involving anti infectives for systemic use and anti-parasitic products 131(79.88%), 18(10.98%) traditional plants. The potentials interactions 120(52.63%), contraindicated 25(10.96%) and Biological monitoring 130(57.02%) followed by Substitution/Exchange 47(20.61%) were found.

**Conclusion:** The role of pharmacist to manage patient's health is very important to decrease the mortality or morbidity linked to HIV.

**Keywords:** HIV; Xenobiotics; Physiopathology; Tenofovir Disoproxil Fumarate

## Introduction

The new challenge of the management of patients is no longer the accessibility to the therapeutic combination but rather to the improvement of the quality of life of patients [1]. A recently work showed 5.2% of 209 hospitalized HIV-infected patients were receiving a drug which was contraindicated with their antiretroviral [1]. As result, many factors may alter effectiveness of treatment such as, disease, age, polypharmacy lead to potential drug-drug interactions (PDDIs).

Non-Nucleoside Reverse Transcriptase (NNRT), Protease Inhibitors (PIs) and many others medications have the same pathways during the metabolisation of xenobiotics, which leads to adverse effects with clinically significate (DDSI). The interactions mechanism is either inducers or inhibitors of CYP enzymes. Further, PIs are substrates and/or inhibitors of drug transporters such as P-glycoprotein which may result in pharmacokinetic drug interactions [2-4]. Indeed, managing drug-drug interactions is one of the major challenges in the optimization of HIV therapy [5,6]. Also, using fixed dose combinations does not easily allow for personalization of therapy (e.g. with coadministered drugs for tuberculosis and HIV).

In many Africa's countries especially in Côte d'Ivoire, biological following and therapeutic drugs monitoring for individualization of dosage are not performed in routine. Therefore, pharmacist may play an important role for the therapeutic optimization using his knowledge and any tools. The clinical pharmacist can detect, manage the harms impacts of antiretroviral on patients' life.

DDSI have previously been reported to be prevalent in developed countries (affecting 20-41% patients) [7-11], but data from developing countries are lacking. We assessed risk factors for drug-drugs interactions perform pharmaceutical interventions by informing clinicians.

## Methods

### Study population

This transversal work included patients at the beginning of ART treatment. From January to August 2015, Due to the characteristic of prescription any ethic caution or authorization has not been needed. Patients'demographic data (Details of age, gender, baseline weight, baseline CD4 count and weight (if measured within 6 months of commencing antiretroviral therapy)) at enrolment were collected in order to confirm that antiretroviral were dispensed completely and all others co-prescription were recorded. We have validated all clinical records with pharmacy data base. Inclusion criteria for this study were: HIV seropositive followed for care at Infectious and Tropical diseases Unit of Treichville teaching Hospital at Abidjan.

We have enrolled HIV infected individuals aged 16 years, receiving antiretroviral therapy. For this study, we screened first, 560 consecutive patients According to the national Ivorian 2013 guidelines, first-line antiretroviral were defined as Tenofovir (TDF) or zidovudine (ZDV) plus lamivudine (3TC) plus nevirapine (NVP) or Efavirenz (EFV), and substitution with Tenofovir (TDF), abacavir (ABC) or didanosine (ddI) was allowed for toxicity.

Second line included any of these agents in combination with the protease inhibitors Atazanavir (ATZ), lopinavir/ritonavir (LPVr). The criteria to access the antiretroviral program were: i) WHO Stage 1 or 2 HIV disease if CD4 count is 200 cells/mm$^3$, or ii) WHO Stage 3 disease if CD4 is 350 cells/mm$^3$, or iii) WHO Stage 4 disease, irrespective of the CD4 cell count [12]. All the coprescribed drug pairs were screened for potential for DDSI using the Liverpool HIV Pharmacology Group website (www.hiv-druginteractions.org) [13].

This website comprises a comprehensive database of 5,000 drug-interaction pairs, and uses a 'traffic lights' system to flag up potential interactions. In order to avoid 'overcalling' the clinical significance of drug interactions, all interactions which flagged up as red or amber were further scrutinised, and the quality of evidence underpinning these recommendations assessed using criteria derived from the GRADE system (http://www.hivdruginteractions.org/documents/QualityOfEvidence.pdf) [14]. Also many others books and website have been used to analyse drugs interactions [15-17].

### Definition of risk criteria and antiretroviral therapy

In our study, we have defined two types of risks criteria. Physiopathology and drugs-drugs interactions are responsible of many harmful damages to patient according to illness or laboratory abnormalities, and the potential consequences of that toxicity (e.g. hospitalisation).

Also, the use of fixed dose combinations from generic manufacturers does not easily allow for individualization of dosage (e.g. with co-administered drugs for tuberculosis and antiretroviral).

### Pharmaceutical Care and pharmacist's role

French clinical pharmacy society guidelines has been used to identify the patient problems (Physiopathology stage and Contraindication and to submit pharmaceutical intervention to medical's staff.) [18].

The clinical pharmacist researches the medical anomalies and gives the solutions from Pharmaceutical interventions (Following).

Problems; Contraindication and not Guideline Respect, Potential interactions, Treatment without Monitoring Diseases, without Treatment, Surdosage.

Pharmaceutical interventions: Substitution/Exchange, Dose Adjustment, Drug Stop, Drug add, Biological Monitoring.

The classification ATC (Anatomic, Therapeutic, and Chemistry) system was also used to classify comedication drugs [19].

## Statistical Analysis

Statistical analysis used was the Software SAS 2000 statistical package. Differences in age and baseline, weight were assessed by Khi2 test, Flowchart, Patients with risk criteria.

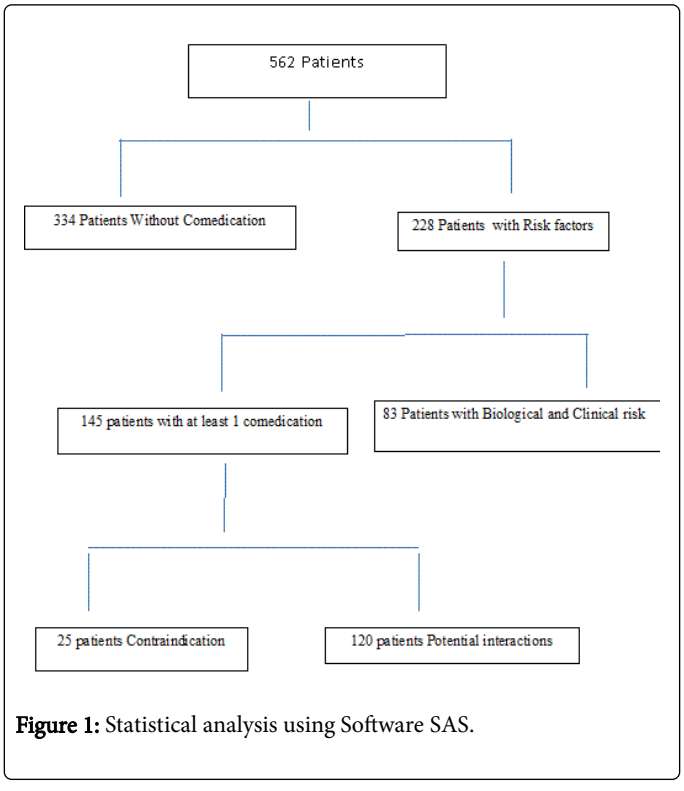


**Figure 1:** Statistical analysis using Software SAS.

## Results

Of 562 patients screened, 228 patients were included in the final analysis, comprising 91 (39.91%) male and 137 (60.9%) females; aged between 35–48 years (median 41 years), unmarried 160(63.18%), 218(95.61%) HIV1, 117(51.75%) with TB, renal failure 21(9.27%), First line of antiretroviral therapy 198(86.84%) and 27(11.6%) patients were on second line treatment, Stage C (62.39%) (Table 1).

The use of 1st line regimens were as follows: TDF/3TC/EFV in 141 patients (61.34%) (Figure 1) Antiretroviral were prescribed at standard

doses, regardless of whether a CR was present or not. Physiopathology stage was identified in 83 patients (36.41%) and potential drugs-drugs interactions with antiretroviral were identified in in 145 patients (63.59%) involving Antiinfectives for systemic use and antiparasitic products 131(79.88%), 18(10.98%) traditional plants (Figures 2 and 3) (Table 2).

Anti-infectives for systemic use and Antiparasitic products 131(79.88%), 18(10.98%) traditional plants was the most prescribed interactions (Table 3).

Potentials interactions 120(52.63%), contraindicated 25(10.96%) was found (Difference was significative).

Biological monitoring 130 (57.02%) followed by Substitution/ Exchange 47(20.61%) was observed and the difference was significative (P-value 0.001) (Table 4).

| Risk Criteria | | | | | |
|---|---|---|---|---|---|
| **Parameters** | | | | | |
| | | **Physiopathology Stage** | **Drug-Drug Interactions** | **Total** | **P-value** |
| **Sex** | Female | 53(23.25%) | 84(36.84%) | 137(60.9%) | 0.3794 |
| | Male | 30(13.16%) | 61(26.75%) | 91(39.91%) | |
| **Matrimonial Status** | Married | 20(8.77%) | 28(12.28%) | 48(21.05%) | |
| | Unmarried | 55(24.13%) | 105(46.05%) | 160(68.18%) | 0.7852 |
| | Divorced | 7(3.07%) | 11(4.82%) | 18(7.89%) | |
| | widow(er) | 1(0.44%) | 1(0.44%) | 2(0.88%) | |
| **HIV** | HIV1 | 81(35.53%) | 137(60.09%) | 218(95.61%) | 0.6783 |
| | HIV2 | 3(1.31%) | 7(3.07%) | 10(4.38%) | |
| **Tuberculosis** | Yes TPM- | 4(1.75%) | 7(3.07%) | 10(4.82%) | 0.0001 |
| | Yes TPM+ | 24(10.53%) | 83(36.40%) | 107(46.93%) | |
| | No | 55(24.12%) | 55(24.12%) | 110(48.24%) | |
| **Renal Failure** | Yes | 6(2.69%) | 15(6.58%) | 21(9.27%) | 0.0296 |
| | No | 77(33.77%) | 130(57.02%) | 207(90.73%) | |
| **Treatment Line** | First | 69(30.26%) | 129(56.58%) | 198(86.84%) | 0.095 |
| | Second | 14(6.14%) | 13(5.70%) | 27(11.84%) | |
| | Third | 0(0%) | 3(1.32%) | 27(11.84%) | |
| | | 83(36.41%) | 145(63.59%) | | |
| **WHO stage** | A | | | | 24(11.01%) |
| | B | | | 57(26.15%) | |
| | C | | | 136(62.39% | |
| Age (Years) Median IQR 25-75% | 41[35-48] | | | | |
| Total | 228 | | | | |

**Table 1:** Characteristics sociodemographic and risk criteria.

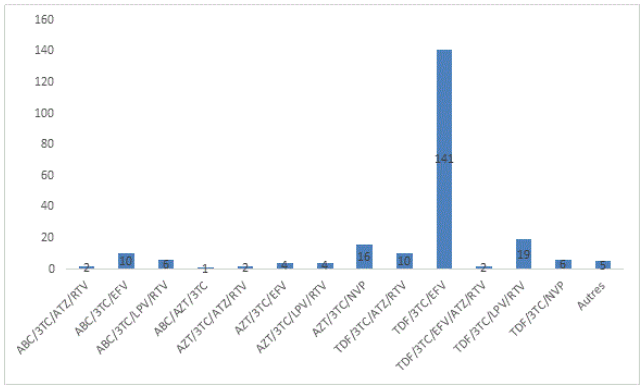


**Figure 2:** Antiretroviral involving drug-drug Interactions. ABC: Abacavir; 3TC: Lamivudine; ATZ: Atazanavir; RTV: Ritonavir; EFV: Efavirenz; LPV: Lopinavir; AZT: Zidovudine; NVP: Nevirapine; TDF: Tenofovir Disoproxil Fumarate.

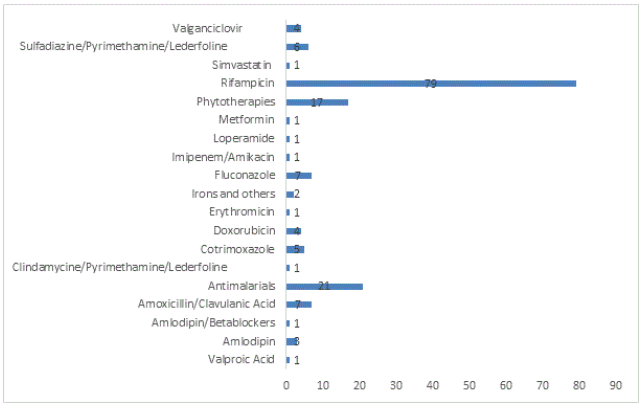


**Figure 3:** Drugs involving interactions with antiretroviral.

Rifampicin was the most prescribed interactions drugs.

| Classification | Physiopathology | Drug-Drug Interactions | Total |
|---|---|---|---|
| Alimentary tract and metabolism | - | 2(1.22%) | 2(1.22%) |
| Blood and blood forming organs | - | 3(1.83%) | 3(1.83%) |
| Cardiovascular system | - | 5(3.05%) | 5(3.05%) |
| Anti infectives for systemic use and Anti parasitic products | - | 131(79.88%) | 131(79.88%) |
| Nervous system | - | 4(2.44%) | 4(2.44%) |
| Antineoplastic and immune modulating agents | - | 1(0.16%) | 1(0.16%) |
| Others (Traditional plants) | - | 18(10.98%) | 18(10.98%) |
| Total | | | |

**Table 2:** Classification ATC and risk criteria (From French Clinical Pharmacy Guideline).

| Problem | PS | DDI | P-Value |
|---|---|---|---|
| Contraindicated | 0(0%) | 25(10.96%) | <0.0001 |
| Diseases without Treatment | 5(2.19%) | 0(0%) | - |
| Treatment without Monitoring | 20(8.77%) | 0(0%) | - |
| No guideline respected | 53(23.25%) | 0(0%) | - |
| Potentiel Interactions | 0(0%) | 120(52.63%) | - |
| Surdosage | 5(2.19%) | 0(0%) | - |
| Total | 83(36.40%) | 145(63.60%) | |

**Table 3:** Risk criteria and problem (Using French Clinical Pharmacy society guideline).

| PI | Physiopathology | Drug-Drug Interactions | | P-Value |
|---|---|---|---|---|
| Substitution/Exchange | 38(16.67%) | 9(3.95%) | 47(20.61%) | <0.0001 |
| Dose Adjustment | 9(3.95%) | 8(3.51%) | 17(7.45%) | - |
| Drug Stop | 10(4.39%) | 18(7.89%) | 28(12.28%) | - |
| Drug add | 5(2.19%) | 1(0.44%) | 6(2.63%) | - |
| Biological Monitoring | 21(9.21%) | 109(47.81%) | 130(57.02%) | - |

| | | | | |
|---|---|---|---|---|
| Total | 83(36.40%) | 145(63.60%) | 228(100%) | |

**Table 4:** Pharmaceutical interventions according French Clinical Pharmacy Guideline.

## Discussion

In developed countries, the harmful of drug-drug interactions are one of the most occurring reasons of hospitalization, and antiretroviral are among the most therapeutically risky drugs for clinically significant drug interactions (CSDI) and its impact on clinical and physical disorders. Any kinds of this studies has not been done before in resources limited settings where risk is arguably increased as a result of less laboratory monitoring including Therapeutic Drug Monitoring (TDM). High prevalence of background illness (which may result in adverse effects being missed), lack of affordable alternative treatments, use of fixed dose combinations (that offer less flexibility for managing interactions) and lack of pharmacovigilance data make very difficult the personalization of treatment. The purpose of our study was to investigate the role of clinical Pharmacy to reduce prescription errors in an HIV outpatient cohort in Côte d'Ivoire.

Our estimate of risk (27.57%) is similar to G. Kigen results (27.00%) [20] and our observation was same to the previous surveys from the Netherlands, the United States, and Kenya where potential CSDIs were reported in 14-41% patients [2-5]. We observed that, risk for CSDIs have affected about 30% of patients. Of particular concern, these risks could have resulted in lowering of plasma concentrations of antiretroviral (thus increasing the risk of HIV treatment failure) in over a third of patients with CSDIs. Although the lists of available drugs, risk of adverse outcome resulting from CSDIs and patients particularity are arguably higher in resource-poor settings due to lack of intensive laboratory monitoring, presence of overlapping syndromes such as fever (which may confound the correct identification of adverse events), late presentation of HIV, high background of other illness and use of traditional medicines and antimalarial in the community.

According to WHO recommendations early treatment lines were TDF/3TC/EFV 141(61.6%), fixed combinations to improve adherence and optimize patient's care. Access to health care has been improved with the support of partners in development: Supplying Chain Management System (SCMS), (Elisabeth Glaser Pediatric Aids Foundation (EGPAF).

They allowed from the strengthening of the logistics management system to promote access to treatment and to scale the availability of the most remote areas country. Most of the major interactions involved interactions between antiretroviral and rifampicin (HIV/TB). Despite the growing number of clinical trials assessing novel TB drugs, there is still not credible alternative to rifampicin-based therapy, and this remained the predominant cause of CSDIs in our study. Also TB is the first co-infected disease during the AIDS in Côte d'Ivoire [12].

The majority of identified potential drug-drug interactions occurred between Protease inhibitors or Non Nucleosides Reverse Transcriptase to anti-infective for systemic use/antiparasitic products 79(34.6%), followed by antimarials 21(9.2%), and 18(7.5%) traditional plants. This high proportion of anti-infective is explain by the fact that Côte d'Ivoire is an area of infectious and tropical diseases, but also that HIV is an infection with a high prevalence (3.4%) with its corollary of comorbidity (opportunistic infection). The same outcome has been found by Kigen et al in Kenyan Cohort and the same reasons were mentioned concerning drug interactions [20].

In develop countries the data are different. Two most prescribed therapeutic classes (Central Nervous System, and Cardiovascular drugs) were usually founded. We observed in the occidental cohort, the patients with psychiatric illness, including substances abuse, represent a considerable part of the infected population and also cardiovascular drugs results from the ageing HIV population and the increased risk for cardiovascular diseases associated with the ART itself and possible HIV [21,22].

In therapy for HIV infection, pharmacokinetic interactions are often multifactorial. They may involve alterations in drug metabolism mediated by the cytochrome P-450 system, modulation of P-glycoprotein (a cellular transport protein), change in renal elimination, changes in gastric pH and drug absorption, and fluctuations in intracellular drug concentrations (mechanism). These processes may take place at various sites in the body. Pharmacodynamics interactions alter the pharmacologic response to a drug. The response can be additive, synergistic, or antagonistic [23] So, by using scientific knowledge and judgement, the clinical pharmacist may be finally improve care in resource-poor settings by the detection and the management of patient's therapeutic problems [24].

Some risk criteria has been observed. (e.g.) Cotrimoxazole and lamivudine association lead the Lamivudine AUC increased by 44 percent due to inhibition of tubular secretion by erasing lamivudine concentrations. The coadministration of Zidovudine and ganciclovir leads additive bone marrow suppression. It may require discontinuation or reduced doses of one or both drugs or addition of G-CSF [25].

Therapeutic drug monitoring (TDM) of antiretroviral is a strategy used to reduce viral resistance and the incidence of drugs side effects. In Africa unfortunately and especially in Cote d'Ivoire TDM is not available. So, the only way to avoid HIV drugs resistances is to prevent it. Clinical pharmacist can allowed many harmfulness effects of drugs using his judgement. In our study we founded potentials interactions 120(52.63%), contraindicated 25(10.96%) with are needed pharmaceutical interventions (130(57.02%) Biological monitoring, followed by Substitution/Exchange 47(20.61%)).

The pharmaceutical intervention of clinical pharmacist has certainly helped avoiding complications. The role of pharmacist to manage patient's health is very important to decrease the mortality or morbidity [24].

The computer tools will be needed to ease the managements of the problems. Computerized systems can support electronic prescribing; however, a systematic review of such systems showed that 55-91.2% of drug interaction alerts are ignored by physicians [26,27].

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Until such systems can be made more usable, we recommend that physicians are vigilant to the risks of CSDIs, use available drug information resources, and that the pharmacy department aid in identification of CSDIs and regularly audit prescribing practice.

We think that community pharmacist is a key factor in providing a correct and effective antimicrobial therapy, by investigating diagnostic, treatment concordance, detecting prescribing errors and offering solutions for those errors.

## References

1. Berrey MM, Schacker T, Collier AC, Shea T, Brodie SJ, et al. (2001) Treatment of primary human immunodeficiency virus type 1 infection with potent antiretroviral therapy reduces frequency of rapid progression to AIDS. J Infect Dis 183: 1466-1475.
2. Smith PF, DiCenzo R, Morse GD (2001) Clinical pharmacokinetics of nonnucleoside reverse transcriptase inhibitors. Clin Pharmacokinet 40: 893-905.
3. De Maat MM, Ekhart GC, Huitema AD, Koks CH, Mulder JW, et al. (2003) Drug interactions between antiretroviral drugs and comedicated agents. Clin Pharmacokinet 42: 223-282.
4. Huang L, Wring SA, Woolley JL, Brouwer KR, Serabjit-Singh C, et al. (2001) Induction of P-glycoprotein and cytochrome P450 3A by HIV protease inhibitors. Drug Metab Dispos 29: 754-760.
5. Young B (2005) Review: mixing new cocktails: drug interactions in antiretroviral regimens. AIDS Patient Care STDS 19: 286-297.
6. Evans-Jones JG, Cottle LE, Back DJ, Gibbons S, Beeching NJ, et al. (2010) Recognition of Risk for Clinically Significant Drug Interactions among HIV-Infected Patients Receiving Antiretroviral Therapy. Clinical Infectious Diseases 50: 1419-1421.
7. Robertson SM, Penzak SR, Pau A (2007) Drug interactions in the management of HIV infection: an update. Expert Opinion Pharmacother 8: 2947-2963.
8. De Maat MM, de Boer A, Koks CH, Mulder JW, Meenhorst PL, et al. (2004) Evaluation of clinical pharmacist interventions on drug interactions in outpatient pharmaceutical HIV-care. J Clin Pharm Ther 29: 121-130.
9. Shah S, McGowan J, Opulski B, Lieblein A, Saperstein A (2007) Identification of Drug Interactions Involving ART in New York City HIV Specialty Clinics, In: Program and abstracts of the 14th conference on Retroviruses and Opportunistic Infections.
10. Miller CD, El-Kholi R, Faragon JJ, Lodise TP (2007) Prevalence and risk factors for clinically significant drug interactions with antiretroviral therapy. Pharmacotherapy 27: 1379-1386.
11. Marzolini C, Elzi L, Gibbons S, Weber R, Fux C, et al. (2010) Prevalence of comedications and impact of potential drug-drug interactions in the Swiss HIV Cohort Study. Antiviral Ther 15: 413-423.
12. Evans-Jones JG, Cottle LE, Back DJ, Gibbons S, Beeching NJ, et al. (2010) Recognition of risk for clinically significant drug interactions among HIV infected patients receiving antiretroviral therapy. Clin Infect Dis 50: 1419-1421.
13. WHO (2013) World Health Organization. Guideline HIV.
14. http://www.hiv-druginteractions.org
15. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, et al. (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ Apr 26;336(7650): 924-926.
16. Dictionnaire Vidal (2006) OVP. Paris: Vidal.
17. Dorosz P (2014) Guide pratique des médicaments. Paris: Maloine.
18. Therausus drug interactions. French Agency for Safety of Health Products.
19. Conort O, Bedouch P, Juste M, Augereau L, Charpiat B, et al. (2004) Validation d'un outil de codification des interventions de pharmacie clinique. J Pharm Clin 23: 141-147.
20. Guidelines for ATC classification and DDD assignment (2013) WHO Collaborating Centre for Drug Statistics Methodology (16th edn.) Norwegian Institute of Public Health.
21. Gabriel Kigen, Sylvester Kimaiyo, Winstone Nyandiko, Brian Faragher, Edwin Sang, et al. (2011) Prevalence of Potential Drug-Drug Interactions Involving Antiretroviral Drugs in a Large Kenyan Cohort.
22. Meade CS, Sikkema KJ (2005) Risk behaviour among adults with mental illness: a systematic review. Clin Psychol Rev 25: 433-457.
23. Friis-Møller N, Sabin CA, Weber R, d'Arminio Monforte A, El-Sadr WM, et al. (2003) Combination Antiretroviral Therapy and the Risk of Myocardial Infarction. N Engl J Med 349.
24. Nelson DR, Kamataki T, Waxman DJ (1993) The P450 superfamily: update on new sequences, gene mapping, accession numbers, early trivial names of enzymes, and nomenclature. DNA Cell Biol 12: 1-51.
25. Burke JM, Miller WA, Spencer AP, Crank CW, Adkins L, et al. (2008) Clinical pharmacist competencies. Pharmacotherapy 28(6): 806-815.
26. Barry M, Mulcahy F, Merry C, Gibbons S, Back D (1999) Pharmacokinetics and potential interactions amongst antiretroviral agents used to treat patients with HIV infection. Clin Pharmacokinet 36: 289-304.
27. Eslami S, Abu-Hanna A, de Keizer NF (2007) Evaluation of outpatient computerized physician medication order entry systems: a systematic review. J Am Med Inform Assoc 14: 400-406.