We recently analyzed, in our real-life cohort of 2260 HIV-infected patients, the reasons for discontinuation of dolutegravir-based combined antiretroviral therapies (cARTs) [1]. Of 517 patients, 55 (10.6%) discontinued this cART due to adverse effects. Unexpectedly, four (7%) of these adverse effects were abnormal weight gain, which ranged between 4 and 12 kg. This prompted us to assess, retrospectively, the evolution of weight and BMI (kg/m$^2$) among the 462 patients who received this cART for more than 6 months. Mean age of these patients was 50.1 years, and 65% were men. At baseline, mean CD4$^+$ lymphocyte cell count was 591 cells/μl (range 5–2010). Most patients (94%) were already receiving cART, and plasma HIV-1 RNA was suppressed for 92% of them. Dolutegravir was mostly associated with abacavir/lamivudine (48%) or tenofovir/emtricitabine (32%) [1]. Finally, BMI was less than 18 kg/m$^2$ (class I) for 6% of the patients, ranging between 18 and 25 kg/m$^2$ (II) in 59%, and between 25 and 30 kg/m$^2$ (III) in 24%, and was more than 30 kg/m$^2$ (IV), indicating obesity, in 6%.

Mean time from baseline to weight/BMI assessments was 276 ± 79 days. At this time point, mean weight gain was 3 kg ($P = 0.009$) and mean BMI increase was 1 kg/m$^2$ ($P = 0.002$) (Fig. 1). We observed, for 20% of the patients, a more than 10% weight increase compared with baseline, whereas a 4–10% weight increase was observed for 27% of the patients. In addition, during follow-up, in 13% of the patients, BMI increased from class II to class III, and, in 9% of the patients with class III, BMI increased toward class IV. We further found that mean increases in BMI and weight were significant for women, whereas they only showed a tendency toward significance for men. Finally, these increases were particularly significant for women receiving abacavir/lamivudine and dolutegravir, in whom weight increased from 57 to 62 kg ($P = 0.009$) (Fig. 1a) and BMI increased from 22 to 24 kg/m$^2$ ($P = 0.01$) (Fig. 1b).

A recent study conducted in 41 149 HIV-infected patients from the D:A:D cohort showed that a high level of BMI may be associated with serious non-AIDS events [2]. In addition, body fat changes can be deleterious to self-perception and HAART adherence [3]. Gains in central fat in HIV-positive patients were strongly associated with protease inhibitors of earlier generation. However, McComsey et al. [4] showed recently, in a large randomized ART-initiation trial including 328 patients, that central and peripheral fat changes did not differ after 96 weeks of treatment containing either two boosted protease inhibitors (including darunavir and atazanavir) or the integrase strand transfer inhibitor (INSTI) raltegravir ($+1$ kg/m$^2$ in 3.8–4.7% of the patients). There are, to our knowledge, no data on the effect of other INSTIs on body composition. Nevertheless, an in-vitro study showed that, in contrast with raltegravir, elvitegravir altered adipocytes differentiation and function, although less than efavirenz [5].

Hence, our preliminary finding incites the need to monitor, in other large cohorts, the effect of dolutegravir on body weight, BMI, and fat changes at various body sites. Pharmacological assessments may be helpful to explain the more significant rise observed for BMI and weight in women on dolutegravir/abacavir/lamivudine.

**Acknowledgements**

**Conflicts of interest**

The authors have no conflicts of interest to declare. Funding sources had no role in the design and conduct
Evaluation of non-sexual, non-needlestick, non-occupational HIV post-exposure prophylaxis cases

Potential exposures to HIV outside of the workplace are a common reason for individuals to seek medical care for non-occupational HIV post-exposure prophylaxis (nPEP). Published guidelines from public health agencies recommend standardized diagnostic testing, follow-up, and initiating a 4-week course of antiretroviral (ARV) medications for higher risk HIV exposures if patients present within 72 h [1–4]. The vast majority of exposures are sexual, followed by needle exposures [5]. Here, we evaluate the clinical presentation, management decisions, and outcomes of non-sexual, non-needlestick exposures from a large nPEP cohort.

The current retrospective cohort study took place in a dedicated HIV Prevention Clinic at the Toronto General Hospital (Toronto, Ontario) between January 2013 and August 2015. Research Ethics Board approval was obtained from the University Health Network. All cases were referred from one of three affiliated emergency departments. Based on standardized clinical algorithms, patients presenting to affiliated emergency departments for potential HIV exposures received baseline screening investigations and a 3–6 day ‘starter pack’ of a three-drug nPEP regimen. The patient was then contacted by the HIV Prevention Clinic prior to completing the starter pack and was evaluated by an HIV specialist. Exclusion criteria included sexual and needlestick exposures of all varieties, and all other nPEP cases were included. Standardized data were collected from identified charts and included the type of exposure, risk of HIV transmission (as deemed by the HIV specialist), nPEP use, and adherence to follow-up appointments.

Of the 255 cases referred to the HIV Prevention Clinic, 15 (5.9%) were non-sexual, non-needlestick, non-occupational exposures. Of the 15 cases, five (33.3%) were women and 10 (66.7%) were men, with an age range of 21–48 years (mean 33.1 years). The exposure in nine (60%) cases was blood on skin that was either not intact or perceived to be not intact at the time of exposure. Five (33.3%) cases involved bite wounds, and one (6.7%) involved exposure of a mucous membrane to sputum that was possibly contaminated with blood.

Table 1 summarizes these exposures. Of the nine cases involving exposure to blood on non-intact skin, seven involved minor skin defects or abrasions and were determined to have a negligible HIV transmission risk. In four cases, nPEP was prescribed for a 28-day course, often at the request of the patient. In one case, nPEP was discontinued when the source patient tested negative. nPEP was discontinued in one case as the patient was off ARVs for 5 days prior to presentation in clinic. One patient had nPEP discontinued at their clinic appointment due to the negligible risk of transmission and side effects from the regimen. Two cases were determined to be non-exposures as the patients’ skin was intact, and nPEP was not continued in the HIV Prevention Clinic.

The few cases of non-sexual, non-needlestick exposures were generally characterized as having a negligible risk of HIV transmission as determined by patient history and physical exam. However, management of some of these cases is complicated by uncertainty regarding the accuracy of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Amélie Menard, Line Meddeb, Herve Tissot-Dupont, Isabelle Ravaux, Catherine Dhiver, Saadia Mokhtari, Christelle Tomei, Philippe Brouqui, Philippe Colson and Andreas Stein, URMITE, Aix Marseille Université, UM63, CNRS 7278, IRD 198, INSERM 1095, IHU Méditerranée Infection, Marseille, France.

Correspondence to Amélie Menard, URMITE, Aix Marseille Université, UM63, CNRS 7278, IRD 198, INSERM 1095, IHU, Méditerranée Infection, 19–21 boulevard Jean Moulin, 13005 Marseille, France.
Tel: +33 4 13 73 20 01;
e-mail: amelie.menard@ap-hm.fr

Received: 24 March 2017; accepted: 28 March 2017.

References


DOI:10.1097/QAD.0000000000001495