Comment on: Persistence and adherence to single-tablet regimens in HIV treatment: a cohort study from the French National Healthcare Insurance Database

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Sir,

We read with interest the article by Raffi et al.,1 entitled Persistence and adherence to single-tablet regimens in HIV treatment: a cohort study from the French National Healthcare Insurance Database. We are also interested in studying HIV management in France with adherence estimation and assessment using a health insurance database. In fact, we conducted an observational study using the French National Healthcare Insurance Database (CPAM), based on the complete local CPAM database of HIV-infected patients having at least two prescriptions of specific ART from March 2009 to December 2010.2

This exhaustive database allowed collection of the following for each patient: hospital or extra-hospital practice for prescribers; hospital or extra-hospital dispensation of treatments; hospital or extra-hospital biological tests; and antiretroviral agents prescribed. Our database, more specifically than the General Sample of Social Security Beneficiaries (French acronym EGB) used by Raffi et al.,1 allows study of the care consumption of HIV-infected patients in the community and hospital. One of the strengths of our study is that our database includes both biological analyses and prescription.

Our study represented 575 patients; the prescriptions were exclusively hospital issued for 76.2% of the patients. Compared with EGB, mean adherence was higher in our study (>.90%, only one patient out of five had adherence <80% whatever the ART used). The patients with adherence >80% were significantly older (46.1 versus 42.7 years, \( P = 0.03 \)), with a greater yearly frequency of biological tests (3 versus 2.5, \( P = 0.004 \)). They switched their ART more frequently, but this difference was not significant (35.4% versus 26.0%, \( P = 0.07 \)).

In our study, we were able to analyse the trajectory of care with hospital or extra-hospital management. There was a trend for HIV infection to shift to extra-hospital management, but the prescriber remains almost exclusively hospital based (76%).

Raffi et al.,1 concluded, in their study supported by Gilead, based on a healthcare insurance database, that persistence is higher in HIV-infected patients treated with a single-tablet regimen (STR) compared with other administration schedules. Lack of clinical or biological data necessitates careful interpretation about antiretroviral persistence. These study limitations were not considered. Combination ART (cART) persistence is an interesting composite marker of toxicity and efficacy if reasons to switch are recorded. For example, many hospital centres in France still recommend a PI/ritonavir induction NNRTI maintenance strategy for treatment-naive patients in their local guidelines. In these centres, PI/ritonavir persistence is low, but not associated with toxicities or lack of efficacy and could not be compared with first-line NNRTI persistence. The strategy in the study of Raffi et al.1 underestimates persistence with PI/ritonavir. Moreover, many clinical situations require physicians to stop a non-STR strategy (AIDS events like TB, pregnancy, chemotherapy). These clinical events were not recorded and could also underestimate persistence if a non-STR strategy is used.

Raffi et al.1 found a significant benefit in terms of adherence with the STR in comparison with regimens with more than one daily intake, but no difference when compared with regimens involving more than one pill once daily. A recent meta-analysis of randomized studies evaluated the impact of regimen type on adherence.3 Adherence was better with once- versus twice-daily regimens, but the difference was modest, without virological suppression difference. Viral load is probably a stronger endpoint than adherence for a cART strategy. Furthermore, lack of clinical details could also result in misinterpretation of adherence data. All patients were considered antiretroviral naive because of an absence of cART in the 3 years before inclusion. However, treatment-experienced patients lost to follow-up for >3 years could be considered treatment naive. In the study of Raffi et al.,1 more than a third (15/41) of raltegravir-based regimens were NRTI sparing with PI/ritonavir and/or NNRTI, suggesting a high proportion of treatment-experienced patients with risk factors of moderate adherence.

Clinical trials are not representative of real life. A healthcare insurance database allows adherence analysis in real life. However, the tenofovir disoproxil fumarate/emtricitabine/efavirenz STR, the only STR analysed in the study of Raffi et al.,1 has been available in France since 5 May 2009. Almost one-third of STR patients (23/76) started cART before 2009 and French availability. These patients were probably included in clinical trials with a heavy follow-up programme and better adherence than in real life.

Finally, results must be viewed with caution according to the database and its exhaustivity. Our study used a complete regional database as compared with real life. Mean adherence was higher whatever the ART regimen and the previous treatment experience than in the study of Raffi et al.1 and no significant differences were found between administration schedules. The study by Raffi et al.,1 together with our exhaustive results, demonstrates the potential use of a healthcare insurance database to analyse adherence to ART. The current information systems covering the entire population health services allow data analysis and production of indicators,4 and really could allow a large-scale and exhaustive assessment of management modalities and mean adherence for HIV-infected patients. However, lack of interface with clinical and biological characteristics requires careful
interpretation. Future collaborations with healthcare insurance are needed to cross-reference this database with clinical data.

**Transparency declarations**
None to declare.

**References**