Background

In British Columbia (BC), Canada, use of the integrase inhibitors (INI) in antiretroviral therapy (ART) regimens has increased rapidly in recent years.

The objective of this study was to characterize the evolution of incident and prevalent INI drug resistance mutations from 2009 to 2015, and test the hypothesis that prevalence of INI drug resistance has increased over time.

To provide context, the prevalence of drug resistance mutations to HIV protease inhibitors (PI) has increased over time.

Methods

Inclusion criteria: HIV-1-infected persons age ≥19 years were included if they received ART through the BC Centre for Excellence in HIV/AIDS (BC CIE). Drug Treatment Program between 01-Jan-2009 and 30-Oct-2015. In each year, persons were counted as “ART-treated” and included in the subset of “INI-treated” if they had at least one dispensation prescription for any ART or any INI (respectively) in the calendar year.

Drug resistance: The study included physician-ordered drug resistance tests analyzed at the BC CIE Research Laboratory, with sample dates up to 31-Oct-2015. Persons with INI, PI or RT resistance were defined as those having at least one sample with score ≥30 (intermediate or high level resistance) by the Stanford HIV drug resistance algorithm v7.0.1.

Prevalence: ART-treated persons contributed INI, RT and PI resistance data in the first, and each subsequent year following identification of study-defined drug resistance. Annual prevalence/1000 ART-treated persons was calculated at year end (31-Oct in 2015). Changes in prevalent resistance over time were tested for trend (generalized additive model, R© v3.2.2).

Incidence: Incident cases of INI resistance were counted in the first year they appeared and were categorized by the INI temporarily associated with resistance: raltegravir, elvitegravir, dolutegravir, or unclassifiable (resistance pre-dated use INI in BC).

Results

In 2014 and 2015, 8/19 (42%) new INI resistance cases were associated with dolutegravir or elvitegravir use: Five cases were associated with elvitegravir use in treatment-experienced persons (mutations: two 68A/I and one each 502D, 1455V, 1470D).

In 2014 and 2015, 8/19 (42%) new INI resistance cases followed elvitegravir or dolutegravir use: Five cases were associated with elvitegravir use in treatment-experienced persons (mutations: two 68A/I and one each 502D, 1455V, 1470D). Three cases of elvitegravir resistance were identified in 2014, two in 2015.

Conclusion

The prevalence of INI resistance remains low compared to RT and PI resistance, but is increasing with expanded INI use. Emergent INI resistance has been observed during treatment with raltegravir, elvitegravir and dolutegravir in ART naïve and experienced patients.

Correspondence: Dr. P. Richard Harrigan, prharrigan@cfenet.ubc.ca