Switching from integrase strand transfer inhibitors (INSTIs) based triple therapy to dual therapy in people living with HIV-1 infection: the French Hospital Database on HIV (ANRS CO4 FHDH) real-life experience

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Background: In PWH-1 (people living with HIV-1) with controlled HIV RNA viral load, maintenance INSTI-based dual therapy (INSTI 2-DR) has been shown in randomised trials to be non-inferior to INSTI-based triple therapy (INSTI 3-DR). Real-world data from the French ANRS CO4 FHDH cohort were used to investigate the determinants and impact of switching from INSTI 3-DR to INSTI 2-DR on virological and clinical outcomes.

Materials and methods:

Eligibility criteria: Initiation of a first INSTI 3-DR containing bictegravir, dolutegravir, elvitegravir or raltegravir between 2008-2020; controlled viral load (HIV RNA<50 cp/ml); INSTI 3-DR for ≥ 1 year $\Rightarrow$ date of eligibility for switching = date of INSTI 3-DR initiation + 1 year;

Matching switchers to non-switchers: Switchers with ≥ 1 year of follow-up were matched with up to 4 individuals who have not switched (non-switchers) at the index date (= the date of the switch). Matching criteria: eligibility for switching at the switcher's date of eligibility $\pm$ 1 month and being/to be followed in a hospital with a similar proportion of switchers.

Pseudo-population emulation: To control for indication bias, inverse probability of switch weighting (IPW) was used to identify the causal hazard ratio (HR) between switchers and non-switchers for virologic failure, defined as the first of two consecutive HIV RNA >50 copies/mL, AIDS, and death.

Results:

78 145 initiated INSTI 3-DR including BIC/DTG/EVG/RAL in 2008-2020

- 6 057 followed < 1 year

72 088

- 16 742 with ≥ 1 HIV RNA > 50 copies/mL

55 346

- 2 799 with active HBV infection
- 133 with tuberculosis
- 1 345 have switched ≤ 1 year after INSTI 3-DR initiation
- 332 initiated INSTI 3-DR during HIV primary infection

50 737

- 9 118 with history of cancer, CVD or diabetes

41 619 individuals

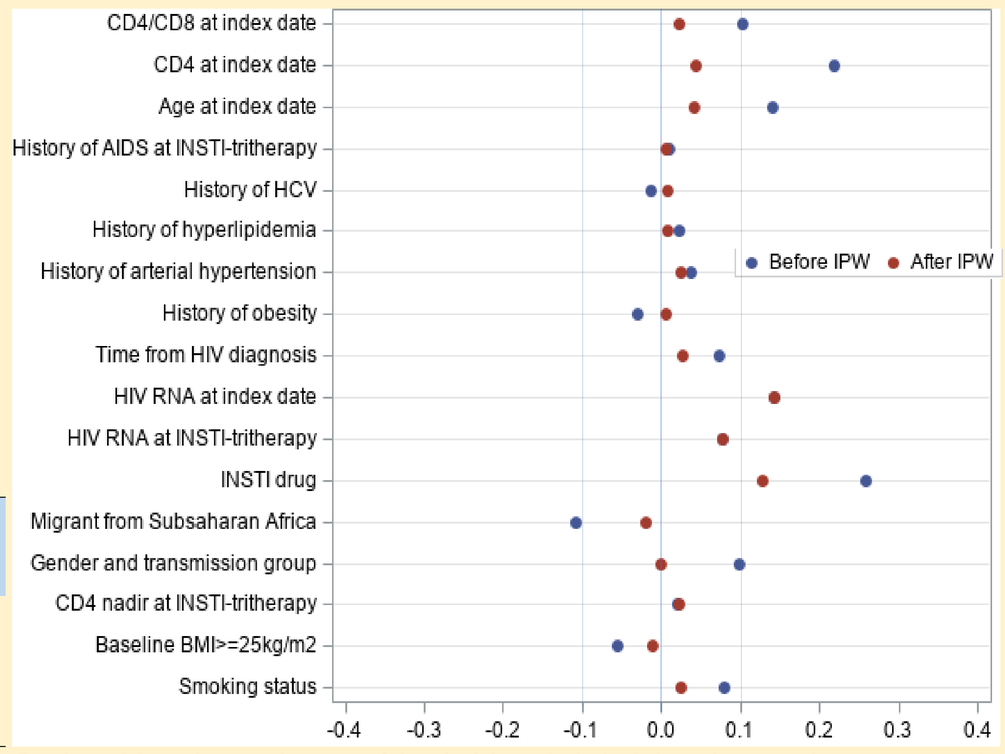
Among the 41,619 PWH under INSTI 3-DR eligible for switching, 7,673 (18,0%) switched to INSTI 2-DR. The probability of switching 4 years after starting 3-DR varied from 6.7% among PWH who started 3-DR in 2008-2011 to 7.3% among PWH who started 3-DR in 2012-2015 and 14.6% among PWH who started 3-DR in 2016-2020.

Effect of switching on outcomes	N of events	Hazard ratio [95% confidence interval]*
Death	488	0.99 [0.79;1.25]
AIDS	151	0.80 [0.52;1.23]
HIV RNA >50 copies/mL	2089	0.89 [0.79;1.00]

No difference was observed in virological and clinical outcomes between PWH on INSTI 3-DR switching to INSTI 2-DR or remaining on 3-DR (Table above).

In the pseudo-population emulated by IPW, there were 8,368 switchers and 19,452 non-switchers. The IPW mostly succeeded in balancing patients' characteristics between the two groups with most standardized differences <0.1 (see Figure below). Median age at the index date was 51 years (interquartile range (IQR) 43-57), with no difference between switchers and non-switchers, and median CD4 cell counts were 666 (476-888) and 683 (508-896)/mm^3, respectively. Median follow-up from the index date was 2.2 years in both groups. Most frequent gender and HIV acquisition group were MSM (38%) and women not using injecting drug (32%). The INSTI drugs were RAL (41%), DTG (32%), EVG (25%) and BIC (<2%).

Figure : Standardized differences in participants characteristic between those switching INSTI 3-DR and those maintaining INSTI 2-DR.



Dot lines delimit the zone between -0.1 and +0.1 in which the balance between the groups is reached

Sandwich variance estimates

Conclusion: From real-world data, after controlling for factors associated with indication of switching to INSTI 2-DR, switching from an INSTI 3-DR to an INSTI 2-DR had no impact on virological and clinical outcomes.

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https://anrs-co4.fhdh.fr

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