

Switching from integrase strand transferinhibitors (INSTI) 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-I (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:

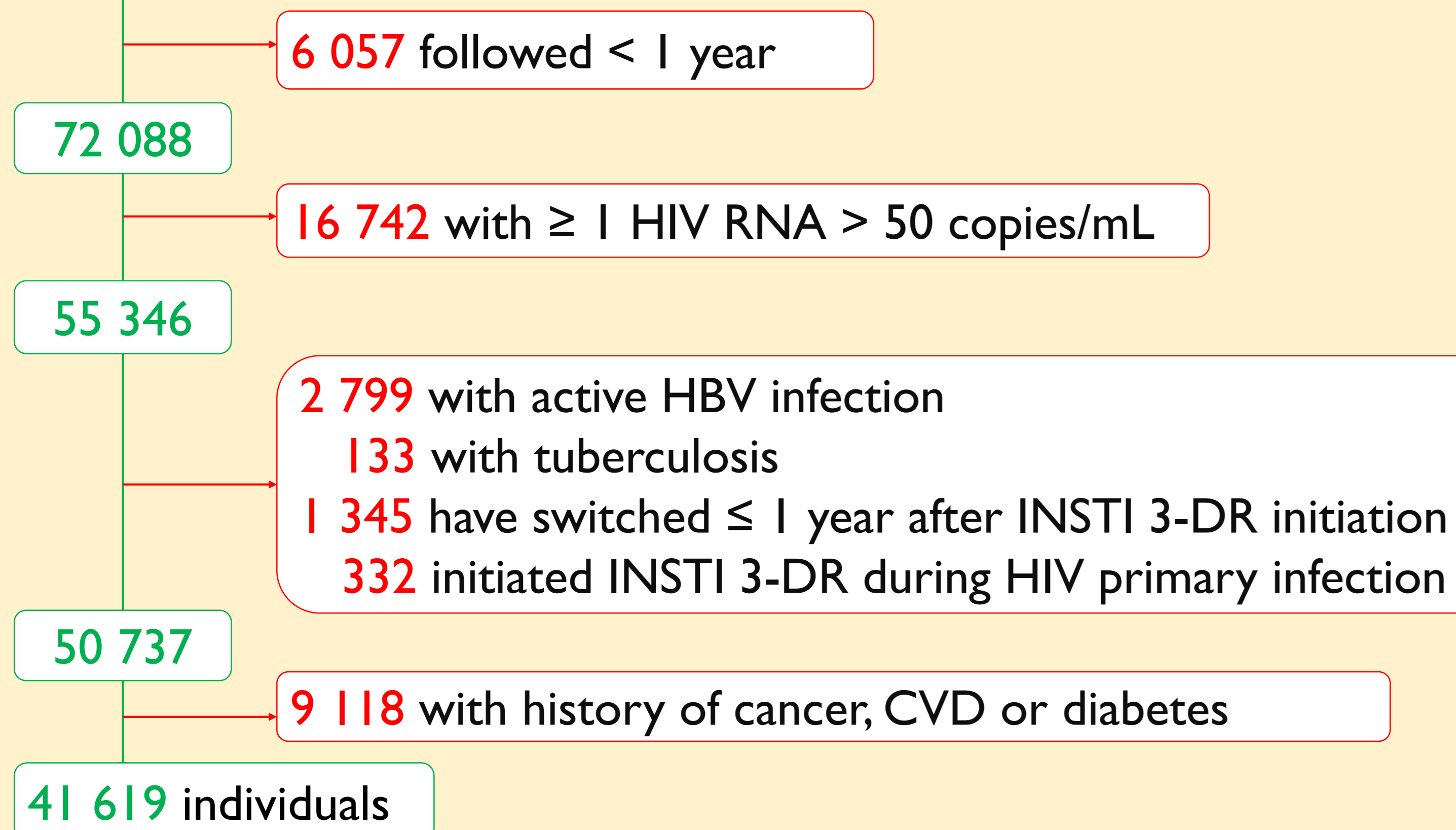
Eligibility criteria: Initiation of a first INSTI 3-DR containing bicitgravir, dolutegravir, elvitegravir or raltegravir between 2008-2020; controlled viral load (HIV RNA < 50 cp/ml); INSTI 3-DR for ≥ 1 year \Rightarrow **date of eligibility for switching** = date of INSTI 3-DR initiation + 1 year;

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 ± 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



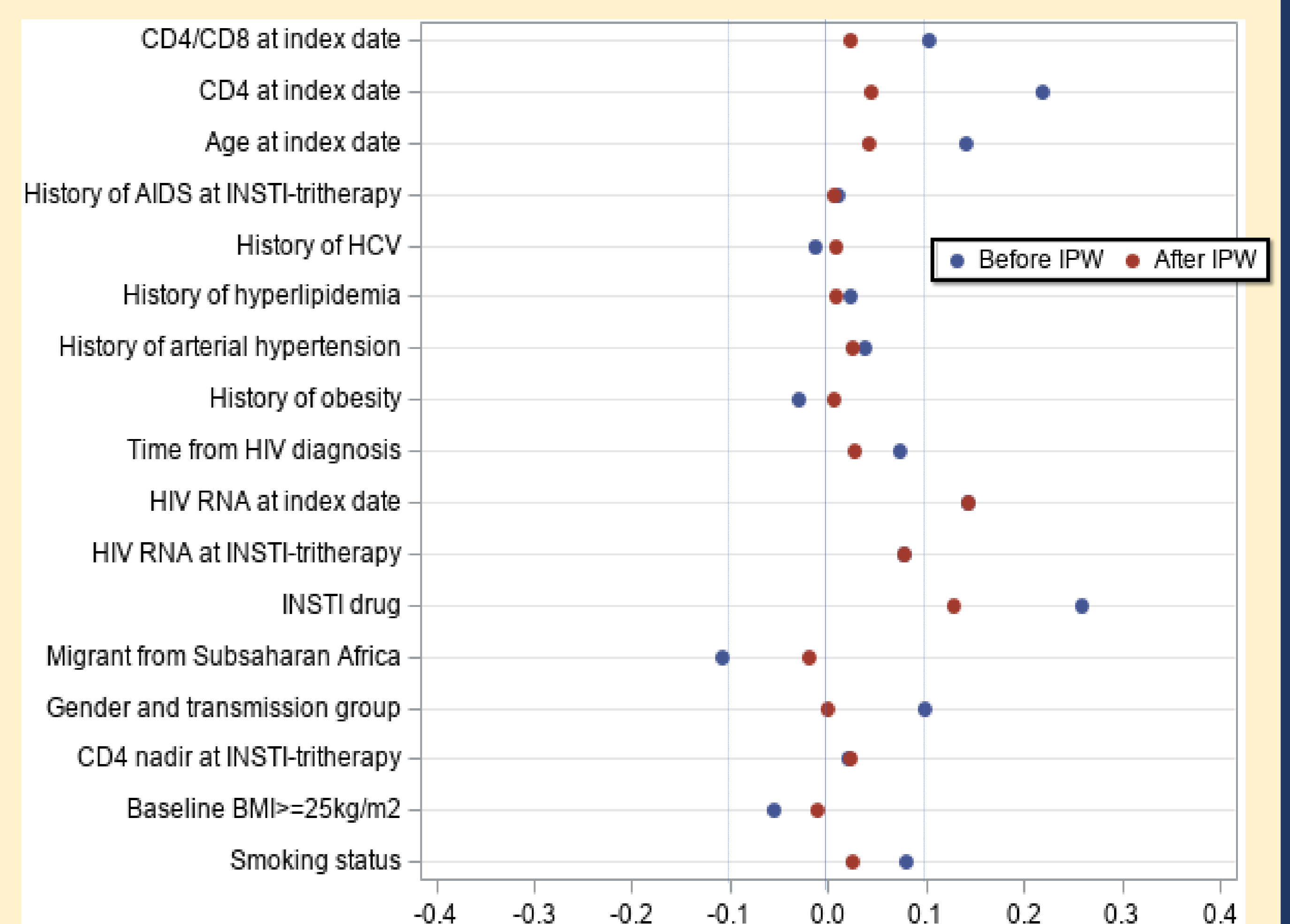
Among the 41,619 PWH under INSTI 3-DR eligible for switching, 7,673 (18,0%) switched to INSTI 2-DR. The probability of switching 4 years after starting 3-DR varied from 6.7% among PWH who started 3-DR in 2008-2011 to 7.3% among PWH who started 3-DR in 2012-2015 and 14.6% among PWH who started 3-DR in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

Effect of switching on outcomes	N of events	Hazard ratio [95% confidence interval]*
Death	501	1.05 [0.84;1.32]
AIDS	162	0.78 [0.51;1.19]
HIV RNA >50 copies/mL	2072	0.93 [0.82;1.04]

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)/mm³, 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 characteristics 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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