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ORAL COMMUNICATION

Tailored approaches to antiretroviral therapy

OC 34 Clinical outcome of switching to a dual drug regimen (2DR) vs. switching or remaining on a triple (3DR) regimen in the setting of a viral load ≤50 copies/mL

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ABSTRACT

Background: Dual drug regimens (2DR) have been proposed to reduce the emergence of toxicities in individuals with viral load (VL)≤50 copies/mL. A possible drawback of 2DR is greater inflammation, possibly leading to higher incidence of cardiovascular disease (CVD) and cancer. There are no randomised trials with clinical endpoints comparing 2DR vs. 3DR in the VL≤50 copies/mL setting.

Methods: We included PWH enrolled in the Icona Foundation Study who after November 2014 had kept a VL≤50 copies/mL for >6 months on a 3DR ART. HBsAg+ participants and pregnant women were excluded. PWH were followed up until they newly developed a clinical composite outcome (CCO) of CVD, cancer or death or their last visit with VL≤50. We aimed to emulate a parallel trial with primary endpoint the time to experience CCO by 48 months. Secondary endpoints were time to CVD and cancer alone, no deaths. The treatment strategies were defined as to switch to 2DR regimen (DRV/r/c+3TC or ATV/r/c+3TC or DTG+RPV or DTG+3TC) within 6 months from enrolment vs. switch or remain on a 3DR regimen. Participants' characteristics were compared according to the observed treatment strategy. The effect of switch to 2DR vs 3DR was quantified by the difference in the Kaplan-Meier estimated risk of CCO at 48 months (per protocol analysis). We used cloning to control for immortal time and confounding bias and inverse probability of censoring weights (IPW) to control for informative censoring bias. Factors used in the IPW model are reported in the footnote of Table 1B. The 95% CIs were calculated using 100 bootstrap replicates. Sensitivity analyses were performed after restricting to 3TC/DTG as the sole 2DR and in the subset of those with no prior evidence of failure to 3TC.

Results: We included 7,820 PWH of Icona, 595 (7%) who switched to a 2DR (502 to 3TC+DTG) within a median of 92 days (IQR:31-153) of enrolment. PWH who were switched to 2DR in the natural course were more likely to be MSM (48% vs 44%, p=0.03), more likely to be Italian (78% vs 73%, p=0.002) entered the target trial 2 years earlier, were more likely to be receiving INSTI-based regimens at baseline (51% vs 37%) and showed shorter previous gaps in care (6.3 vs. 7.5 months, p<0.001). The breakdown (n;%) of the 278 observed primary endpoint events was AIDS cancers (27;0.4%), CVD (52;1%), non-AIDS cancer (141;2%) and death (58;1%). Table 1A shows the KM estimates of the risk of CCO at 48 months from enrolment: in the weighted analysis the risk of CCO was 2.0% lower (95% CI: 0.6-2.9%) in participants who switched to 2DR vs. those switching/remaining on 3DR. This difference was similar in sensitivity analyses (not shown) but was attenuated after excluding deaths from the endpoint (Table 1B).

Conclusions: In our real-world switch setting, under our assumptions, a switch to modern 2DR regimens appears to lead to a small reduction in 2-year risk of CVD/cancer/death (2% difference) which seemed to be mainly driven by a difference in mortality.

Table 1A

Strategy	2-year risk of CVD/cancer (AIDS, non-AIDS)/death (%)	95% CI
	Original cohort	
KM estimates		
Switch to 2DR[£]	2.48	1.66, 3.18
Switch to or continue on a 3DR	3.98	3.49, 4.58
Difference[1]	-1.51	-2.49, -0.74
	Emulated cohort (clones only)	
KM estimates		
Switch to 2DR[£]	2.16	1.26, 3.43
Switch to or continue on a 3DR	3.63	3.18, 4.13
Difference[2]	-1.47	-2.44, -0.13
	Emulated cohort (cloned and weighted)	
Weighted[&] KM estimates		
Switch to 2DR[£]	1.86	1.04, 3.37
Switch to or continue on a 3DR	3.90	3.41, 4.48
Difference[3]	-2.04	-2.96, -0.56

[*]The 95% CI were calculated using 100 bootstrap replicates

[1]These differences are prone to both confounding and immortal-time biases

[2]These differences are prone to informative censoring

[3]These differences account for all types of biases, under the assumptions detailed in methods

Table 1B

Strategy	2-year risk of morbidity (%)	95% CI
	Emulated cohort (CVD events only)	
Weighted[&] KM estimates		
Switch to 2DR[£]	1.63	0.77, 3.12
Switch to or continue on a 3DR	2.71	2.29, 3.21
Difference[3]	-1.08	-2.01, 0.44
	Emulated cohort (Cancer events only[**])	
Switch to 2DR[£]	1.52	0.74, 3.16
Switch to or continue on a 3DR	2.15	1.82, 2.52
Difference[3]	-0.64	-1.38, 1.01

[&]Weighted for calendar year, age, sex, mode of transmission, age, AIDS, nadir CD4, most recent CD4, peak HIV-RNA, duration of ART, class of anchor drug at baseline and adherence score and traditional risk factors for CVD/cancer (BMI, smoking, total cholesterol, hypertension)

[£]DRV/r/c+3TC or ATV/r/c+3TC or DTG+RPV or DTG+3TC

[**]Includes one death due to cancer (missed diagnosis)