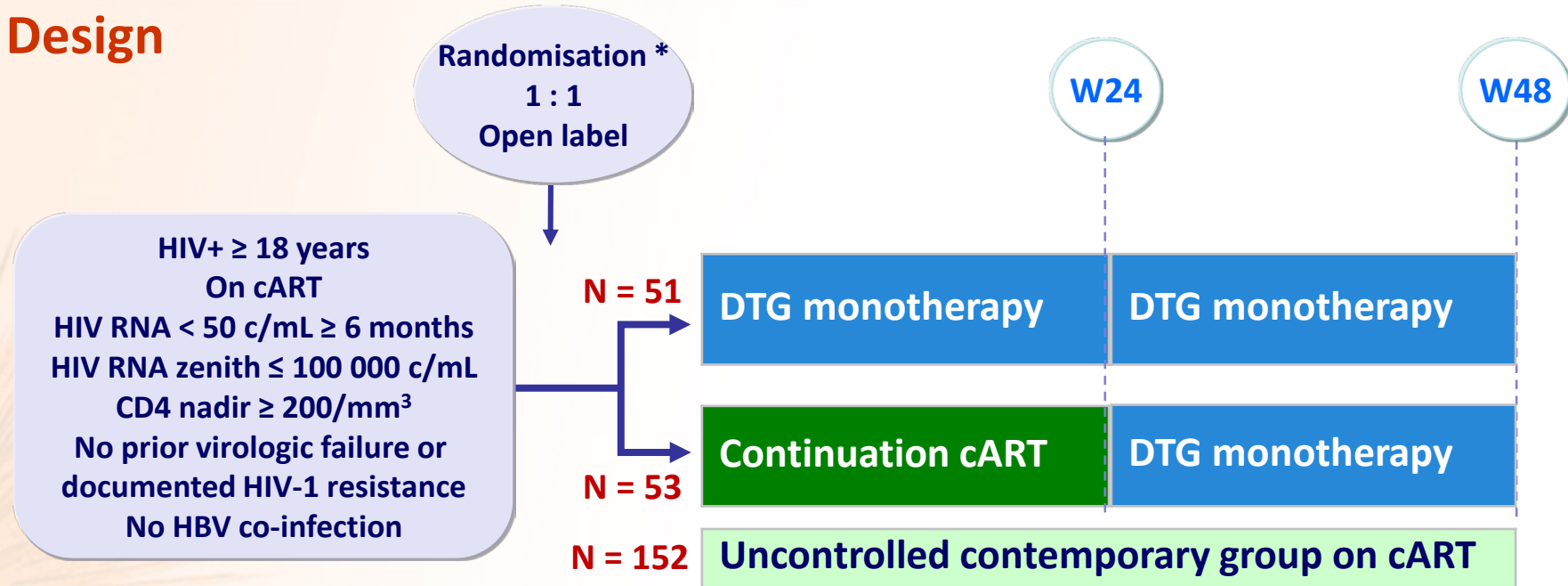


Switch to DTG monotherapy

- **DOMONO Study**
- MONCAY Study
- EARLY-SIMPLIFIED Study

DOMONO Study: Switch to dolutegravir monotherapy

■ Design



* Randomisation stratified by HIV RNA zenith (< or ≥ 50 000 c/mL)

■ Primary endpoint

- Proportion of patients with HIV RNA < 200 c/mL at W24 in on-treatment population; non-inferiority if lower margin of a one-sided 97.5% CI for the difference = - 12%, 80% power

- **Secondary endpoints:** % with HIV-RNA < 50 c/mL at W24, % with HIV-RNA < 200 c/mL at W48, emergence of resistance

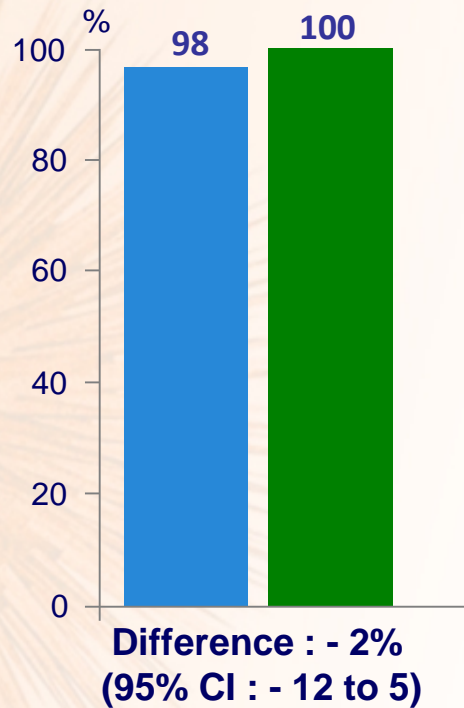
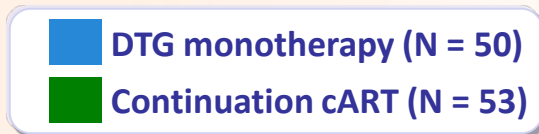
DOMONO Study: Switch to dolutegravir monotherapy

Baseline characteristics and patient disposition

	DTG monotherapy N = 51	Continuation cART N = 53
Median age, years	47	48
Female, %	8	9
White, %	86	79
CD4/mm ³ nadir, median	320	380
HIV RNA zenith, c/mL, median	29 300	44 877
ART regimen before switch, %		
2 NRTI + NNRTI	80	81
2 NRTI + PI	4	2
2 NRTI + INSTI	14	17
Other	2	0
Time on ART, months, median	35	43
Time suppressed on ART, months, median	31	39
Did not switch to DTG monotherapy at W24, N	Not applicable	6
Discontinued between W24 and W48 (AE), N	1	2
On-treatment population at W48	50	45

DOMONO Study: Switch to dolutegravir monotherapy

HIV RNA < 200 c/mL at W24



HIV RNA < 200 c/mL at W48

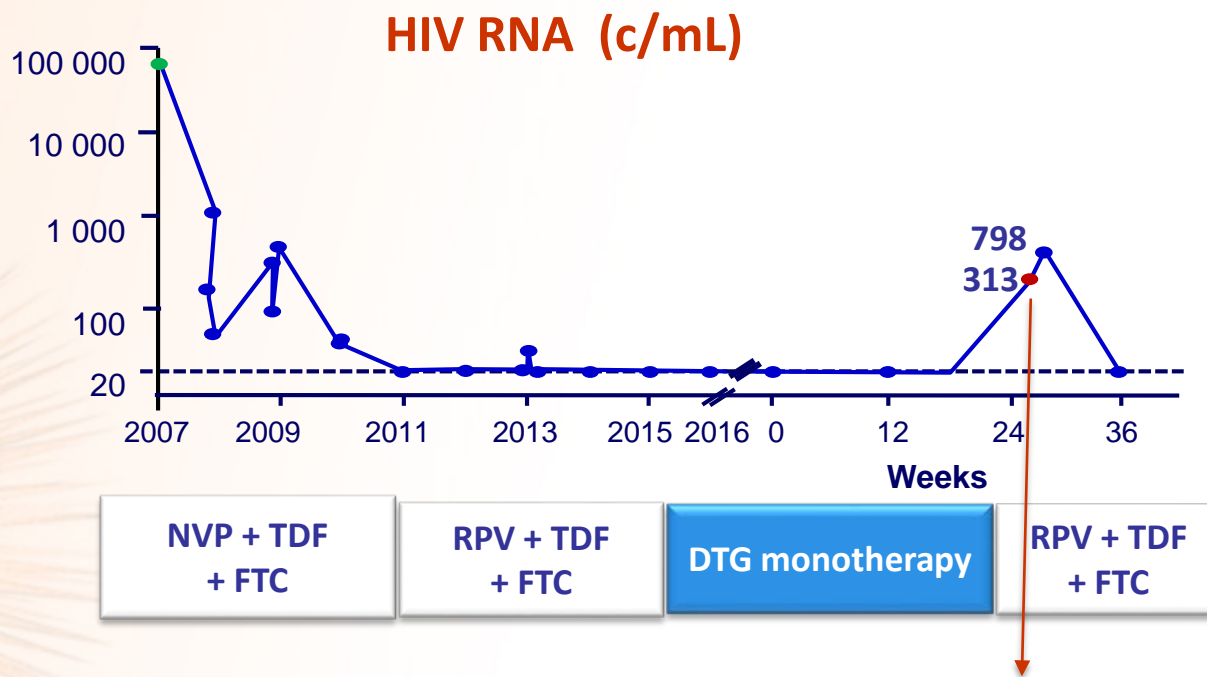
- DTG monotherapy (immediate and deferred switch group) = 87/95 (92%)
- Concurrent uncontrolled group on cART = 149/152 (98%)
- Difference = - 6% (95% CI: - 14.5 to - 0.5)

Follow-up on DTG monotherapy (immediate and deferred switch group)

- 8 virologic failures (2 before W24, 6 after W24)
- Integrase genotype at failure successful in 6/8: emergence of resistance mutations in 3/6 [N155H ; S230R ; R263K]
- In all patients with virologic failure, DTG plasma concentrations were therapeutic and self-reported adherence was > 95%

DOMONO Study: Switch to dolutegravir monotherapy

- 1 patient with no new resistance mutations in integrase gene at virologic failure, but with mutations in nef/LTR region (Sanger sequencing)



Changes in the G-stretch of the 3'-PPT (nef)

Position	9067	//	9078	9079	9080	9081	9082	9083
Reference (HXB2) - 2007	T	//	G	G	G	G	G	G
Sequence at failure (Oct 2016), DOMONO	T	//	G	G	G	A	G	C

DOMONO Study: Switch to dolutegravir monotherapy

■ Conclusion

- DTG monotherapy, as switch strategy in virologically suppressed patients, is
 - Suboptimal
 - Associated with virologic failure in a relatively high number of patients
 - And emergence of INSTI resistance