P072

Dual therapy with dolutegravir plus ritonavir-boosted or unboosted atazanavir as a maintenance treatment in highly experienced HIV-1-infected patients

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Background

Dolutegravir (DTG) and atazanavir (ATV) are two drugs with high antiviral potency, good tolerability profile and synergistic pharmacological interaction with a boosting effect of ATV on DTG.

Objectives

We aimed to evaluate whether a dual therapy based on the association DTG/ATV ± ritonavir (DTG/ATV±r) can control HIV replication in pretreated and virologically controlled HIV-infected patients.

Methods

This observational study included all HIV-1-infected patients with plasma viral load (pVL) <50 cp/ml having started DTG/ATV±r combination between June 2014 and December 2017 at Pitié-Salpêtrière hospital. This strategy was proposed by a multidisciplinary committee, and based on individuals treatment past histories.

- The primary endpoint was the proportion of patients without virological failure (one HIV pVL >200 cp/ml or two consecutive pVL >50 cp/ml) at week (W)24.
- The secondary endpoint was the proportion of patients without virological failure at W48 for patients having completed at least 48 weeks from the switch.

Results

- Twenty patients were included

Patients' characteristics at baseline

N = 20 patients	Median (IQR)
Age (years)	58 (52-64)
CD4 nadir (/mm^3)	154 (56-197)
CD4 count at baseline (/mm^3)	450 (350-551)
CD4/CD8 ratio at baseline	0.55 (0.38-0.70)
Time from HIV diagnosis (years)	26 (20-28)
Time of virological suppression (years)	7 (3-9)
Previous exposition to different ART classes	
NRTIs	100%
NNRTIs	90%
PIs	100%
INSTIs	85%
Last ART regimen (before DTG/ATV±r initiation)	
1 drug regimen	1/20 (5%)
2 drugs regimen	10/20 (50%)
3 drugs regimen	8/20 (40%)
4 drugs regimen	1/20 (5%)

NRTIs : nucleoside reverse transcriptase inhibitors. NNRTs : non nucleoside reverse transcriptase inhibitors. PIs : protease inhibitors. INSTIs : integrase strand transfer inhibitors.

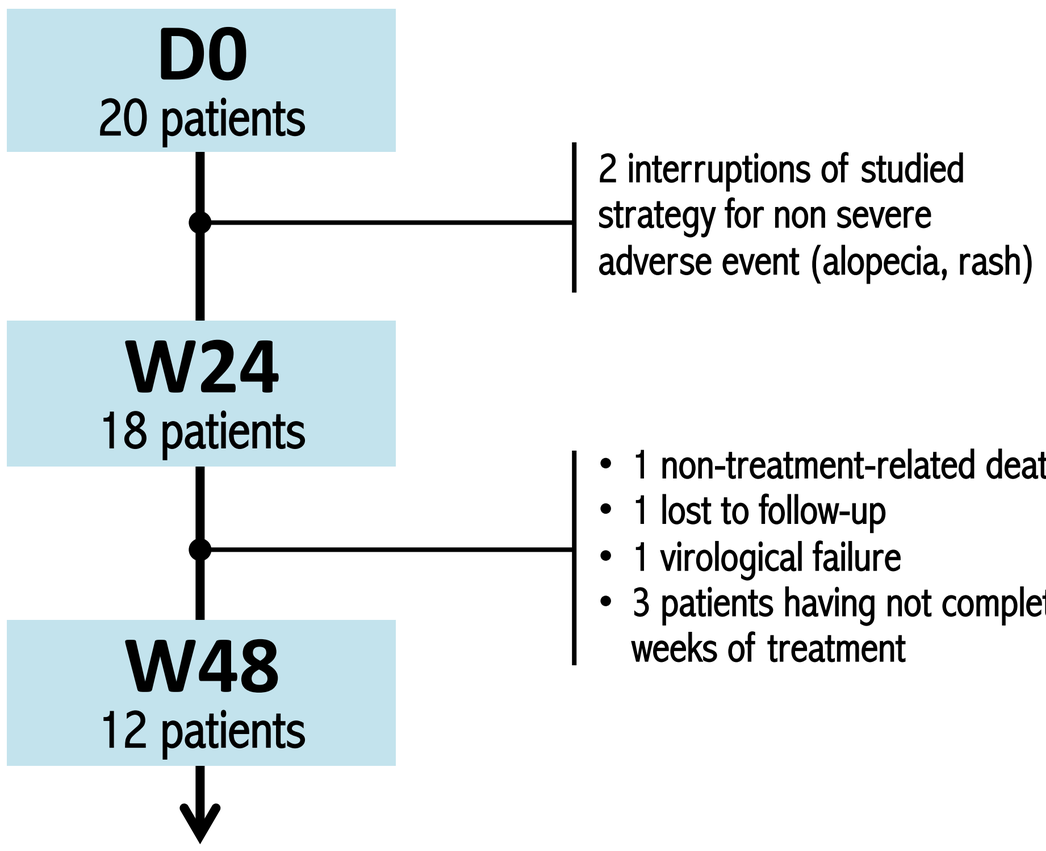
Proportion of HIV strains with resistance-associated drugs (RAMs) at baseline*

NRTIs		NNRTIs	
Lamivudine/ emtricitabine	14/16 (88%)	Nevirapine	11/16 (69%)
Abacavir	14/16 (88%)	Efavirenz	11/16 (69%)
Tenofovir	10/16 (63%)	Rilpivirine	11/16 (69%)
		Etravirine	10/16 (63%)

PIs		INSTIs	
Lopinavir/r	2/16 (13%)	Raltegravir	3/9 (33%)
Atazanavir/r	3/16 (19%)	Elvitegravir/c	4/9 (44%)
Darunavir/r QD	2/16 (13%)	Dolutegravir QD	3/9 (33%)
Darunavir/r BID	1/16 (6%)	Dolutegravir BID	1/9 (11%)

* From history of RNA genotypes for each patient. Data is given as Number of HIV strains with RAMs / Number of patients with available genotype(s) for analysis (%). ANRS algorithm, v.28, April 2018, was used to perform the analysis. QD : once a day (800 mg 1/d for darunavir/r and 50 mg 1/d for dolutegravir). BID : Twice a day (600 mg 2/d for darunavir/r and 50 mg 2/d for dolutegravir

- ATV at baseline was ritonavir-boosted in 10/20 patients (50%) and ritonavir-unboosted in 10/20 patients (50%). Ritonavir was removed in one patient during the study period
- DTG was 50 mg 1/d in all patients. ATV was 300 mg 1/d in 15/20 patients, 400 mg 1/d in 3/20 patients and 200 mg 1/d in 2/20 patients
- Fifteen patients were pre-exposed to ATV and 6 were pre-exposed to DTG



Only one virological failure occurred, at W48: pVL=6,760 cp/ml (treatment breakage during 2 months; no drug detected in plasma), without acquired RAM, and recovered virological control 2 months after the resumption of the same treatment.

The proportion of patients without virological failure was 100% (CI95% 80-100) at W24, and 92% (CI95% 77- 100) at W48

Conclusion

This pilot study shows that DTG/ATV±r dual therapy is able to maintain sustained virological control in patients with multiresistance. This strategy could be relevant to lighten the treatment of highly experienced patients, for whom NRTIs and NNRTIs use is not possible.

ATV present a boosting effect on DTG, doubling at least the plasma concentration of ATV. ATV can be used with low dose (200 mg) for the boosting effect on DTG, or with a higher dose (300-400 mg ± ritonavir 100 mg) for the antiretroviral effect. This strategy is interesting in patients with previous INSTI RAMs.

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