# Long Term Follow up of Dolutegravir as Single Antiretroviral Agent in patients with suppressed HIV viremia.

G. Tebano [1,2], L. Schneider [1,2], C. Soulié [2,3], C. Blanc C [1,2], R. Agher [1,2], S. Seang [1,2], MA. Valantin [1,2], R. Tubiana [1,2], L. Assoumou [1,2], AG. Marcelin [2,3], C. Katlama [1,2]

*1. Pitié-Salpêtrière Hospital, AP-PH, Infectious Diseases Department, Paris France*
*2. Sorbonne University, UPMC Université Paris 06, INSERM, IPLESP (UMRS 1136), Paris, France*
*3. Pitié-Salpêtrière Hospital, AP-PH, Department of Virology, Paris France*

## Background

- Drug reduced regimens (mainly dual-therapy) are increasingly investigated to reduce drug exposure and long term toxicity in HIV infected patients.
- As pilot approach, dolutegravir (DTG) has been evaluated in monotherapy, given its high potency, long half-life and high genetic barrier to resistance. However concerns have been recently raised about emergence of resistance in case of virological failure [1-3].
- We report here our experience with long term follow-up in patients receiving DTG monotherapy.

1. Katlama C. et al., JAC 2016; 71: 2646–50
2. Gubavu C. et al., JAC 2016; 71: 1046-50
3. Wijting I. et al., Lancet HIV. 2017;4: e547-e554

## Methods

This was an observational, single-centre retrospective study.
Patients included were ≥ 18 years old and HBsAg negative; they received DTG monotherapy (50 mg, 1 pill/day) after a period of viral suppression ≥ 6 months (VS: < 50 copies/mL). Previous history of therapeutic failure during integrase inhibitors (INIs)-based regimen or known resistance mutations to INIs were considered as exclusion criteria.

- **The primary endpoint** was the rate of viral suppression at Week 12, W24, W48, W96.
- **The secondary endpoints** were time to viral suppression loss, resistance profile in case of rebound, evolution of HIV-DNA quantification

## Patients Characteristics at Baseline

| 63 patients were enrolled in the cohort study | Value |
|---|---|
| Meeting AIDS defining criteria, n (%) | 10/63 (15,9) |
| ART duration in years, median [IQR] | 15,5 [6,4-20,0] |
| Duration of viral suppression (<50 cp/ml) in years, median [IQR] | 5,9 [3,2-10,4] |
| CD4+ count in cells/mmc, median [IQR] | 679 [487-847] |
| HIV-DNA Log $_{10}$ copies/$10^6$ cells, median [IQR] (within 6 months prior DTG monotherapy) n= 26 | 2,3 [1,9-2,8] BLD (<1,82 log) : 5 pts |
| Ongoing ART at time of switch to DTG monotherapy, n (%) | |
| - protease inhibitor monotherapy | 24/63 (38,1%) |
| - dual-therapy | 17/63 (27,0%) |
| - 3 drug regimen | 22/63 (34,9%) |
| - INI containing regimen, n (%) | 14/63 (22,2%) |
| Pre-exposed to any integrase inhibitor, n (%) | 25/63 (39,7%) |

## Results

**Virological Efficacy**

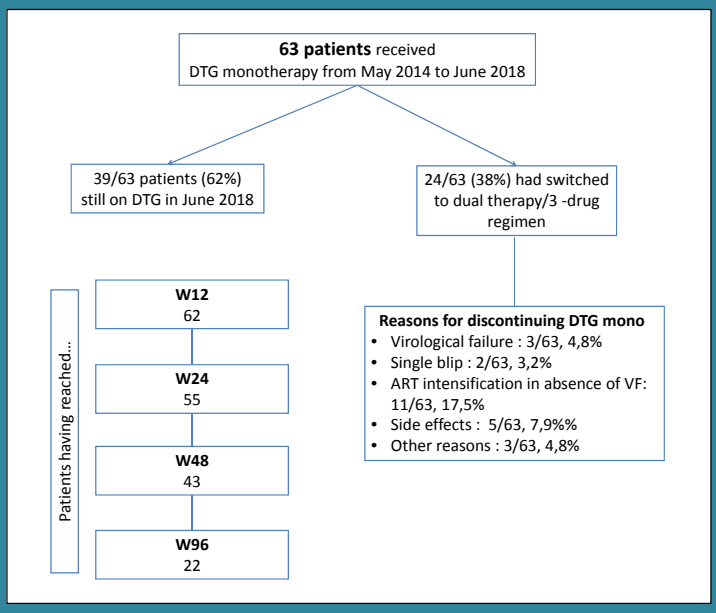
- Overall VS was maintained in 98% (95%CI:91-99) of patients at W12; 95% (95%CI:85-99) at W24; 100% (95%CI:92-100) at W48; 95% (95%CI:77-100) at W96 (Figure 2).

- Virological failure **(VF)** occurred in 3 patients (4,8%, 95%CI:1-13): at W12 (n=1) and W24 (n=2), with emergence of INI resistance (previously reported[1], see also Figure 2 for details). All had been exposed to INIs, including one having INI resistance-associated mutation retrospectively detected on baseline HIV-DNA genotype resistance.
  No VF was observed after W24.

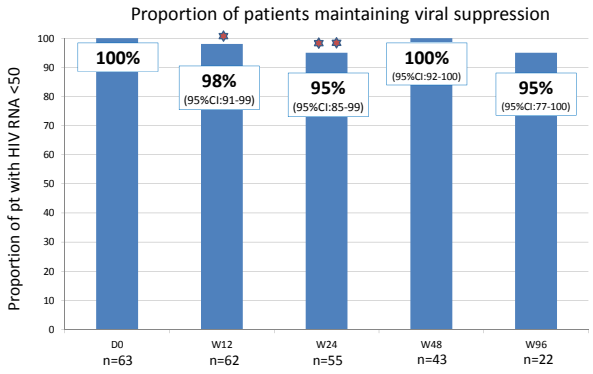
- A single blip occurred in 2 patients (54 cp/ml and 67 cp/ml respectively), which were consequently switched to dual therapy for precaution.

**HIV-DNA quantification** was available at baseline and during DTG monotherapy for 26 and 17 patients respectively (median value: 2,3 log vs 2,1 log, p 0,48). For 8 patients HIV-DNA quantification was available both at baseline and during DTG-monotherapy and did not increase during DTG monotherapy (median value: 2,1 log vs 2,1 log, p 0,8).

## Study Flowchart




## Proportion of patients maintaining viral suppression




* Already reported, *Katlama C et al., JAC 2016; 71: 2646–50:*

- **pt#1** at W12, 138 cp/ml, resistance mutations (RM): 74I+92Q;
- **pt#2** at W24, 2210 cp/ml, RM: 138K+140A+148R;
- **pt#3** at W24, 291 cp/ml, RM: 155H.

## Conclusion

- Long term viral suppression is achievable with DTG given as monotherapy.
- After initial report of 3 VF (4,8%), prior to 24 weeks, none was observed over a median follow-up of 18 months
- Enrolled patients were characterized by:
  - a long duration of viral suppression;
  - mostly a drug reduced regimen prior to DTG monotherapy;
  - a low HIV-DNA load.
- Predictive factors of success with drug reduced strategies should be investigated, in order to optimize treatment individualization.
- In a context of dual DTG based regimen, those findings are reassuring with regards to potential unknown resistance to 3TC or RPV.

**Contact**: christine.katlama@aphp.fr gianpiero.tebano@aphp.fr