No evolution of HIV-1 Total DNA and 2-LTR Circles After 48 Weeks of Raltegravir-Containing Therapy in Patients With Controlled Viremia: A Sub-study of the ANRS 138 ARMS Trial

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With Controlled Viremia: a sub-study of randomized multicentric study

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Week 24

Virological and immunological outcome (n=60)

W0 W24 W48

W24

2.5 0 100 200 300 400

HIV-1 Total DNA evolution

W0 W24 W48

HIV-1 2LTR circle quantification

W24-W0

Discussion

In patients virologically controlled with potent regimens, including integrase inhibitor, the evolution of the viral reservoir illustrated by the HIV-1 DNA level is stable and non-dynamic within the 48-week short-term follow-up.

References

For all these patients, plasma HIV-1 RNA remained sustained between W0 and W24.

- No 2LTR circles were detected at W48 in the 29 patients under RAL-containing regimen.

- Median HIV-1 total DNA at D0 (3.1 log10/106 PBMC) was high in these heavily pretreated patients compared to values in patients at an earlier stage of HIV infection (2.7 log10/106 PBMC, Kostrikis J Virol 2002). This higher level may be related to the low nadir of CD4 count (37 cells) (Burland AIDS 2009).

- In this randomized trial, we found no difference in HIV-1 total DNA evolution after 24 weeks under raltegravir compared to enfuvirtide in patients with a sustained plasma HIV-1 RNA below 50 cop/mL.

- No significant individual HIV-1 viral load difference was observed after 48 weeks of RAL, suggesting a stable HIV-1 DNA amount in successfully treated patients as previously described with standard HAART (Vard AIDS 2004).

- HIV-1 2LTR DNA does increase at 24 or 48 weeks on raltegravir. This result may be related to the sample timing, the 2-LTR increase being described earlier after the integrase inhibitor (Buzon et al. CROI 2009).

- However, HIV-1 2LTR DNA detection was observed in 9 patients (5 at W0 and 3 at W24) despite controlled viremia below 50 cop/mL, suggesting an ongoing replication.

- HIV-1 2LTR DNA circles quantification could not be proposed as a sensitive surrogate marker of antiretroviral activity of raltegravir in controlled patients except in the early steps of the inhibition of integration (ie. at week 2).

1. Avettand-Fènoël V., Buzon MJ, Houin J et al., et al., CROI 2009 (423a)
6. de Castro et al. CROI 2009
7. May Thierry, Bordeaux
8. Meynard Jean Luc, Paris
9. Morlat Philippe, Bordeaux
10. Viard JP., et al., CROI 2009 (423a)

Virological and immunological outcome

- Median HIV-1 DNA level at D0 was 2.7 log10/106 PBMC (Arm ENF) and 2.5 log10/106 PBMC (Arm RAL) in the early steps of the inhibition of integration (ie. at week 2).
- After the raltegravir initiation, integrase inhibition kept a high level of HIV-1 DNA that was maintained for 24 weeks (Arm ENF) or 48 weeks (Arm RAL).
- This effect of the raltegravir, on the virus reservoir was followed by a transient significant increase in episomal HIV-1 DNA at W2 in patients with RAL.
- Following this early increase, the HIV-1 DNA level tended to decrease in Arm RAL but remained constant in Arm ENF.

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