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Short-Cycle Therapy comprising a lamivudine and dolutegravir regimen of 5 days on and 2 off in a small cohort of suppressed HIV-infected patients

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Introduction/Summary

- Short-cycle therapy (SCT) has proven to be a safe and effective alternative to the standard every-day regimen for HIV-1 infected patients, as demonstrated in several previous studies both in high- and in low-income countries[1,2].
- By reducing the number of doses taken by the patient, short cycle antiretroviral therapy has the advantage of improving tolerability and quality of life, as well as reducing the cost of antiretroviral therapy (ART).
- While many previous studies on SCTs focused on combinations containing efavirenz, in this study we focused only on combination containing lamivudine and dolutegravir , which are known to be better tolerated.

Study Design

- We conducted a prospective cohort study in the Infectious Disease Outpatient Clinic of G.B. Rossi Hospital in Verona with the aim of monitoring virological suppression (viral load <50 copies/ml) in a cohort of patients treated with a short regimen of dolutegravir and lamivudine.
- The regimen consisted of five days on therapy (from Monday to Friday) and two days (Saturday and Sunday) off.

Materials and Methods

- Inclusion criteria of our study were:
  - be on daily ART with dolutegravir plus lamivudine for over one year;
  - presence of >12 months of virological suppression (<50 copies/ml) and a CD4 cell count > 200/µl for over 6 months;
  - no evidence of drug resistance mutations or failures with the regimens before the beginning of the short-cycle therapy;
  - written informed consent.
- For the first three months after deintensification, plasma HIV-RNA level and dolutegravir concentration were checked monthly on Monday (over 48 hours after the last dose of lamivudine and dolutegravir). Dolutegravir concentration was determined through a liquid chromatography coupled to atmospheric pressure ionization tandem mass spectrometry method (LC-MS/MS).
- The level of satisfaction of the new regimen was assessed through anonymous questionnaires.

Results

PATIENT CHARACTERISTICS

- 27 patients were included in the study:
  - the mean age was 47.3 years (range 25-65);
  - the mean time since HIV diagnosis was 14.2 years (range 2-34);
  - the mean number of previous antiretroviral regimens was 1.8 (range 1 to 4);
  - the mean length of viral suppression was 10.4 years (range 2-23).

Results

OUTCOMES

- After a mean follow-up of 10.4 months (range 4-33) on the short-cycle antiretroviral treatment, HIV-RNA was undetectable (<50 copies/ml) in all patients.
- The pharmacokinetic analysis showed that in 49 out of 81 (60%) examined samples, the C-trough, 60 to 72 hours after the last dose, was below the in vitro protein-adjusted 90% inhibitory concentration (IC 90) of dolutegravir for wild type virus (64 ng/mL).
- All the patients reported to prefer the SCT over the past standard daily treatment regimen.

Discussion

- The dual antiretroviral therapy combining dolutegravir and lamivudine was recently approved for use in antiretroviral naïve people living with HIV with certain features and, as maintenance regimen, in suppressed individuals with no evidence of resistance to either drug and without HBV coinfection[3].
- In our small cohort, an intermittent short-cycle maintenance dual drug therapy has been effective on mantaining HIV viral suppression.
- Our pharmacokinetic results have shown a plasma concentration of dolutegravir below the IC90 in 60% of the samples while maintaining HIV virological suppression. This may be explained by the fact that lower levels of drug exposure are required to prevent viral rebound because the overall viral burden declinesover time[4].

Conclusion

- SCT with two-drugs ART containing dolutegravir could be a feasible option for optimization of ART in selected HIV patients.
- The advantages of SCT, combined with its effectiveness, could make it a good option especially in low-resource settings.

Reference

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