Three-year Efficacy of Lopinavir/ritonavir Monotherapy in the OK04 Trial

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Abstract

Background: The OK04 trial showed that 96-wks of lopinavir-ritonavir (LPV/r) monotherapy (MT) with reinduction of nucleosides as needed was noninferior to triple therapy (TT) for maintenance of HIV suppression. After 40 patients randomized to MT switched to TT. We report data on 144 patients who were followed for up to 144 weeks.

Methods: Patients were eligible if they had no history of virological failure (VF) while receiving a protease inhibitor (PI) (primaquine-resistant or not), and had switched to LPV/r in the previous 14 weeks. Patients with confirmed VF > 50 copies/mL while on LPV/r MT without nucleoside-resistance to PI were re-initiated with nucleosides (NF).

Results: Of the 144 patients originally randomized to MT, 140 patients were virally suppressed (VS) at Week 144. Of these, 114 patients were reinitiated with nucleosides. Outcomes after re-initiation: 11 sustained viral suppression (1 with VF reinduced); 1 lost viral suppressor due to failure; 3 viral suppression failed due to PI mutations (1 of whom developed major PI mutation). Outcomes after re-initiation: 40 patients were reinitiated with nucleosides. Of these, 33 patients were VS at Week 144 (11 sustained viral suppression, 1 lost viral suppressor due to PI mutations, and 13 viral suppression failed).

Conclusions: After 3 years of follow-up the OK-04 study shows that lopinavir/ritonavir monotherapy can maintain HIV viral suppression in a very large proportion of patients. This result supports the long-term efficacy and safety of LPV/r MT for maintenance of HIV suppression.

Objective

To report final 144 wk data of patients originally randomized to MT in the OK04 trial.

Methods-I

- From week 96 to week 144 of patients were on Lopinavir/ritonavir tablets by mouth, switched from SSIC.
- After week 96 all patients randomized to triple therapy were switched to monotherapy (results of this switch are not reported here).
- Based on the first year results, protocol was amended to allow intensification with nucleosides (if necessary) for patients who failed to achieve viral suppression at Week 96 (24 patients with nucleosides).

Methods-II

- Forty patients (17%) were reinitiated with nucleosides at Week 144. Of these, 11 patients were VS at Week 144 (3 sustained viral suppression, 1 lost viral suppressor due to PI mutations, and 7 viral suppression failed).

Efficacy Analysis

A. Time to HIV-1 RNA > 50 copies/mL (ITT M = F, Reinduction ≠ F) 71%

B. Time to HIV-1 RNA > 50 copies/mL, On Treatment, Reinduction = Failure, Missing or Change in therapy other than reinduction = censored 82%

C. Time to HIV-1 RNA > 50 copies/mL (TT M = F, Reinduction ≠ F, Missing or Change in therapy = censored) 80.7%

Genotypic testing through Week 144

After three years of follow up the OK-04 study shows that lopinavir/ritonavir monotherapy can maintain HIV viral suppression over prolonged periods of time. Sixteen patients (11%) were reinitiated with nucleosides. Of the 100 patients initially randomized to lopinavir/ritonavir monotherapy, 71% remained on monotherapy with HIV RNA < 50 copies/mL after four years of follow-up (J Antimicrob Chemother. 2008;61:1359-61)

Conclusions

Three year results of OK04 trial supports long term efficacy and a minimal risk of resistance of the strategy lopinavir/ritonavir monotherapy with reintroduction of nucleosides as needed.

Subject disposition

By week 96

- MT: 100
- TT: 40

By week 144

- MT: 71
- TT: 30
- MT reinitiated with nucleosides: 11

* Patients who reached and maintained < 50 c/mL after resuming baseline nucleosides are considered as successes (n=11)

** Patients who reached and maintained < 50 c/mL after resuming baseline nucleosides are considered as failures (n=11)