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# O424 Resistance development in virological failures with DRV/r or LPV/r: 96-week analysis of the Phase III TITAN trial in treatment-experienced patients

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## Purpose of the study

In the randomised, controlled, Phase III TITAN trial, at week 96, significantly more patients on darunavir co-administered with low-dose ritonavir (DRV/r) than on lopinavir/r (LPV/r) achieved HIV-1 RNA <400 copies/mL (67.5% vs. 59.5%; difference 8%, 95% CI 0.1–15.8), confirming non-inferiority ($p < 0.001$) and superiority of DRV/r over LPV/r ($p = 0.034$). A detailed resistance characterisation of virological failures (VFs) was performed.

## Methods

Treatment-experienced, LPV-naïve patients with HIV-1 RNA >1,000 copies/mL were randomised to DRV/r 600/100 mg BID (n = 298) or LPV/r 400/100 mg BID (n = 297) combined with an optimised background regimen (NRTIs ± NNRTI). VFs were defined as patients who lost or never achieved HIV-1 RNA <400 copies/mL after week 16. Genotyping and phenotyping (Antivirogram®) were performed by Virco.

## Summary of results

The VF rate in the LPV/r arm (25.6%, n = 76) was higher than in the DRV/r arm (13.8%, n = 41). Among VFs with an available genotype at baseline and endpoint (72 for LPV/r and 39 for DRV/r), more patients developed primary protease inhibitor (PI) mutations at end-point in the LPV/r arm (n = 25) than in the DRV/r arm (n = 7). Primary PI mutations developing in DRV/r VFs were V32I in three patients, I47V and L76V in two patients and M46I, I54L, I54M and L90M in one patient. All but the M46I and L90M mutations were 2007 DRV RAMs. In addition, more VFs developed NRTI RAMs in the LPV/r arm (n = 20) than in the DRV/r arm (n = 4). Phenotypically, more LPV/r VFs than DRV/r VFs lost susceptibility to the study PI (17/55 vs. 3/36) or any PI (25/69 vs. 7/37). Among the DRV/r VFs, the majority retained susceptibility to amprenavir (31/31), atazanavir (29/30), indinavir (31/32), LPV (33/33), nelfinavir (24/26), saquinavir (31/31) and tipranavir (34/35). Furthermore, more LPV/r VFs than DRV/r VFs lost susceptibility to the NRTI(s) used in the OBR (20/55 vs. 4/35) or any NRTI (27/66 vs. 7/38). Similar results were obtained when patients with LPV FC >10 or patients who previously used ≥2 PIs were excluded from the analysis.

## Conclusion

In this treatment-experienced, LPV-naïve patient population, the overall VF rate with DRV/r was half compared to LPV/r. Furthermore, the majority of DRV/r VFs did not develop primary PI mutations or NRTI RAMs and preserved susceptibility to PIs and NRTIs.