Darunavir (DRV)/r-Based PEP Versus Standard of Care (SOC) - the Randomized PEPDar Study

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Background: Post exposure prophylaxis (PEP) for 4 weeks is state-of-the-art following exposure to HIV with high risk of transmission. None of the recommended regimens has been studied in prospective randomized studies in this indication so far, discontinuations rates due to side effects are high. Darunavir/r has a favorable safety profile and high antiviral potency. It could therefore be an alternative to currently used drugs (mainly lopinavir (LPV)/r).

This study was designed to generate data on safety and tolerability of DRV/r-based PEP compared to SOC-PEP.

Methodology: PEPDar was an open-label, randomized multicenter prospective noninferiority study enrolling patients following high risk exposure to HIV in Germany. Recommended SOC as per 2008 National Guidelines included 2 NRTIs plus LPV/r or EFV. Patients were stratified by risk of exposure (occupational [OE] vs. non-occupational [NOE]) to receive DRV/r + 2 NRTIs or SOC-PEP within 72 hours following high risk contact for 28-30 days.

Primary endpoint was the early discontinuation rate (% subjects who discontinued HIV-PEP for >2 consecutive days prior to day 28) for any reason except documented negative HIV-status of the index person. The trial had 80% power to show non-inferiority (overall significance level 5% [two-sided], non-inferiority margin 12%).

Results: Between 11/2011 and 05/2013 306 patients were enrolled at 22 centers. 82.7% were male (median age 33 years [range: 18-62]); 17.3 % were female (median age 31 years [range 18-55]). Median time between risk contact and start of PEP was 2 hours (range 0.1 - 22) after OE (n=62 [20.3%]) and 14 hours (range 0 -71.9) after NOE (n=244 [79.7%]). 155 patients received DRV/r + 2 NRTIs, 151 patients received SOC (LPV/r-based in all patients) + 2 NRTIs. 97% (n=298) received TDF/FTC as backbone. Early discontinuation rate was 5.8% (n=9) in the DRV/r-arm and 9.4% (n=14) in the SOC-arm showing non-inferiority (CI: -0.148; 0.078). Adverse events (AEs) related to DRV/r or SOC were reported in 106 DRV/r-patients (68.4%) and in 114 SOC-patients (75.5%) (p=0.203). Most common AEs (all grades) were diarrhoea (28 vs. 42 patients [p=0.056]), nausea (16 vs. 26 patients [p=0.097]) and fatigue (17 vs.22 [p=0.393]). SOC-patients experienced more sleep disorders (0 vs. 6 [p=0.014]). Rash was reported in 6 DRV/r- patients and 5 SOC-patients. No seroconversion was documented.

Conclusions: DRV/r showed noninferiority with regard to early discontinuation of PEP when compared to SOC (LPV/r in all SOC-patients). Both regimens were well tolerated. We conclude that DRV/r-based PEP is an alternative to SOC including LPV/r.