UNDETECTABLE PLASMA LOPINAVIR CONCENTRATIONS PREDICT VIROLOGICAL OUTCOME TO SECOND-LINE ANTIRETROVIRAL REGIMEN

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Background: Resource constraints in low and middle-income countries necessitate practical approaches to optimizing antiretroviral therapy outcomes. We hypothesized that an untimed plasma lopinavir concentration at week 12 would predict loss of virological response in those taking lopinavir as part of a second-line antiretroviral regimen

Methods: We measured plasma lopinavir levels at week 12 on stored samples from the SECOND-LINE randomized trial. We characterized lopinavir concentration as: (a) detectable and optimal (≥1000 µg/L); (b) detectable but sub-optimal (≥25 to < 1000 µg/L); (c) undetectable (< 25 µg/L). We used Cox regression to explore the relationship between undetectable lopinavir concentration and loss of virological response over 48 weeks and backwards stepwise logistic regression to adjust for baseline resistance (genotypic sensitivity score), baseline viral load, body mass index, self-reported adherence and ethnicity.

Results: At week 48 we observed virological failure in 15/32 (47%) and 53/485 (11%) of patients with undetectable and detectable plasma lopinavir concentrations, respectively, p<0.001. Both suboptimal (aHR 2.94, 95% CI 1.54 - 5.62, p=0.001), and undetectable (aHR 3.55, 95% CI 1.89 - 6.64, p<0.001) lopinavir levels were associated with higher rates of virologic failure over 48 weeks. In multivariate analysis, an independent association with loss of virologic response at week 48 and undetectable lopinavir was observed after adjustment (OR 5.48, 95% CI 2.23 - 13.42, p< 0.01)

Conclusion: In low and middle-income countries implementing a public health approach to ART treatment, untimed plasma drug levels may provide a practical method to identify those at risk of virological failure and intervene appropriately. This might preserve boosted PI-based second-line regimens and optimize the sustainability of treatment programs.

Disclosure of Interest Statement: