Kaletra® is a fixed dose coformulation of two HIV-1 protease inhibitors (lopinavir [LPV] 400mg/ritonavir [RTV] 100mg). The pharmacoenhancing effect of RTV on LPV resulted in a highly potent, clinically effective antiretroviral drug with a high genetic barrier to viral resistance.

Having the population model previously obtained for LPV with the same data-set (D Santos Buelga. PAGE 2009), the aim of this study was to develop and validate a population pharmacokinetic (PK) model for RTV used as a booster in HIV-infected patients treated with Kaletra®

### Methods

**Patients:** HIV-infected subjects, treated with Kaletra® twice daily.

**Analytical Assay:** HPLC with UV detection.

**Pharmacokinetic Analysis:**
- **PK Model:** one-compartment model with first-order absorption and elimination including the absorption lag-time (ALAG).
- **PK parameters estimated:** Clearance (CL/F), distribution volume (V/F), Ka, ALAG.
- **Error model:** Proportional (interindividual) and additive (residual).
- **Software:** NONMEM V.I (FOCE, Interaction); Xpose (GAM).

**Covariates:** age, sex, height, body mass index (BMI), LPV trough concentration (CLLPV), LPV clearance (CLLPV), total bilirubin, hepatitis C virus co-infection (HCV), and concomitant saquinavir (SQV), tenofovir (TFV) and atazanavir (ATV).

**External Validation:** Comparison of model-predicted and observed concentrations obtained in the validation data. Mean prediction error (MPE) and standardised mean prediction errors (SMPE) were used.

**Inclusion of the absorption lag-time** leads to the best fitting for the basic model.

- The inclusion of CLLPV in the model elicited a decrease in the objective function value (-658.656 to -820.039).

**Validation results obtained** confirm the adequacy of the proposed model.

### References