**LINEZOLID DOSE OPTIMISATION USING MONTE CARLO SIMULATION.**

**BACKGROUND:** The pharmacokinetic/ pharmacodynamic (PK / PD) index for the efficacy of linezolid is defined as the area under the plasma drug concentration-time curve (AUC$_{24}$) / minimum inhibitory concentration (MIC).

**Methods:**

PK/PD index: Linezolid $\rightarrow$ AUC$_{24}$/MIC=100

$\text{AUC}_{24}=D_{24h}/Cl_{Lin}$

- MIC data were collected of our center for the years 2013 and 2014 for Staphylococcus aureus (S. aureus) and coagulase-negative Staphylococcus (CNS) isolates.
- The method of determining the MIC was using an automated microdilution (Phoenix®BD) and the MIC > 1 was confirmed by E-test (BioMerieux®).

PK: The pharmacokinetic parameters of linezolid were obtained from published studies.

- The pharmacokinetics parameters were defined as a log-normal distribution in the Monte Carlo simulation, and in the case of MIC, a discrete distribution. A Monte Carlo simulation with 10000 subject was performed using SimulAr® program.
- Acumulative fraction of response (CFR) was calculated (CFR values of > 90% represent an optimal regimen).

**Results:**

- **S. aureus:**
  - $Cl_{Cr} < 25$ mL/min dose 900 mg/day
  - $Cl_{Cr}=25-60$ mL/min dose 1200 mg/day
  - $Cl_{Cr}=60-125$ mL/min dose 1800 mg/day
  - $Cl_{Cr}>125$ mL/min dose 2400 mg/day

One-compartment PK model was used with a first order elimination process (Matsumoto et al. 2014)

$$Cl_{Lin}=0,0258(Cl_{Cr})+2,03 \pm 30,5\%.$$  
*Cockcroft and Gault method.

- **SCN:**
  - $Cl_{Cr}<60$ mL/min dose 600 mg/day
  - $Cl_{Cr}=60-125$ mL/min do sis de 900 mg/day
  - $Cl_{Cr}>125$ mL/min dosis de 1200 mg/day

Suggested doses depending on PK / PD analysis

**CONCLUSIONS:** According to the population pharmacokinetic model and the CMI chosen, linezolid doses should be individualized based on patients $Cl_{Cr}$ and strain Staphylococcus spp. isolated.