Vancomycin dose adjustment based on pharmacokinetic-pharmacodynamic approach is required in critically ill oncological patients against isolated strains MIC 1-2 mg/L

Authors: Estela M Oliveira[1], Juliano P Almeida[1], João M Silva Junior[1], Alberto H Sabanai[1], Luana C Silva[1], Rejane S Siqueira[1], David S Gomez[2], Silvia RCJ Santos[3]

Institutions: [1]Cancer Institute of Sao Paulo HCFMUSP, [2]Division of Plastic Surgery and Burns, postal code 05800-090, [3]Clinical Pharmacokinetics Center, School of Pharmaceutical Sciences, postal code 05508-000, University of Sao Paulo, Sao Paulo, SP Brazil.

Contact: estela.oliveira@hc.fm.usp.br

Introduction: Vancomycin empiric dose regimen recommended usually cannot reach the target once pharmacokinetic changes can occur during the septic shock in critically ill patients from the Intensive Care Unit (ICU) against the most common MIC> 1 mg/L Gram-positive strains.

Objective: Rational of study was to compare vancomycin empirical dose regimen 1g q12h with dose adjusted regimens based on the individualization of drug therapy by pharmacokinetic-pharmacodynamic (PK/PD) approach in ICU oncological septic patients.

Methods: Ethical approval was obtained, and consent form was signed by each patient's responsible included in the study.
Caracteristics of 42 (20F/22M) patients included

- Renal function preserved (39/42)
- Renal dysfunction (3/42)
- ICU clinical patients (36/42) ICU surgical patients (6/42)

Patients undergoing vancomycin therapy 1g q12h at the earlier period of septic shock received initially the empirical dose and dose adjustments were done if required.
Blood sampling at the steady state 3rd and 11th hr of start vancomycin infusion for drug serum measurements done by immunoassay in hospital.

Pharmacokinetics (PK): noncompartimental data analysis

- PK-data of septic patients x healthy volunteers [1].

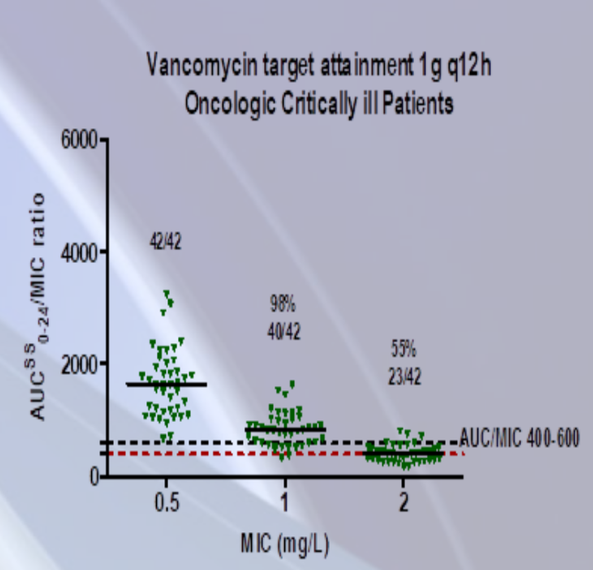
PK/PD approach for target attainment (PTA) based on the predictive index of effectiveness AUC^{ss}_{0-24}/MIC ratio for target (ratio >400) considered [2]

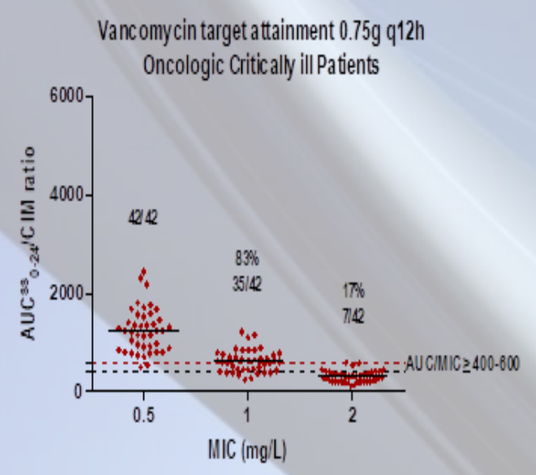
References
[1] Boeckh *et al*. AAC.1988; 32 (1):92-95.
[2] Rybak *et al*. USA Consensus, 2020.

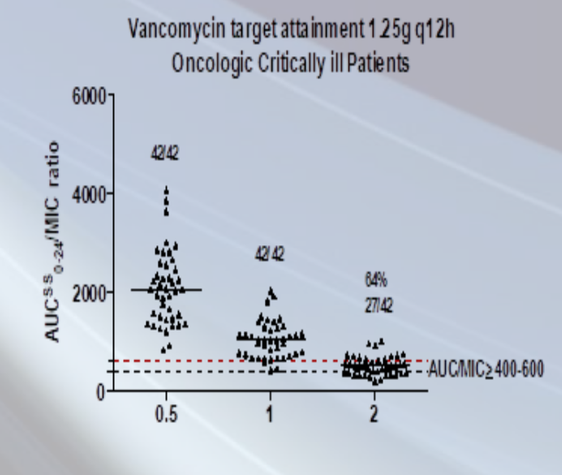
Results: Oncological critically ill patients included, and the characteristics of them at ICU admission med(IQR):
59yrs, 54kg, BSA 1.72 m2, BMI 25 kg/m2, Clcr 92 ml/min, SAPS3 37
SAPS Simplified Acute Physiology Score

Target was reached at the empirical dose regimen 1g q12h for all patients against Gram-positive MIC 1 mg/L and extended up to MIC 2mg/L in 23/42 patients.

After dose adjustment 1.25g q12h was reached for all patients against MIC 1 mg/L, and in 27/42 to MIC 2mg/L.
After a reduction of daily dose to 0.75g q12h the target was reached for all patients against strains MIC 0.5 mg/L, and for 35/42 patients against Gram-positive pathogens MIC 1mg/L.







Conclusion: Since the clinical cure by vancomycin against Gram-positives MIC 1 mg/L strains occurred for all patients, the desired outcome was reached by applying PK/PD approach, an important tool based on drug serum monitoring to guarantee drug effectiveness.
If vancomycin PK is unpredictable in those ICU patients, PK/PD approach done in a real time based on drug serum monitoring must be done earlier to eradicate gram-positive pathogens with cure of infection, and to avoid the microbial resistance.

Contact: estela.oliveira@hc.fm.usp.br