

Pharmacokinetic changes can impact vancomycin target attainment in critically ill oncologic patients

Authors: Estela M Oliveira¹, Juliano P Almeida¹, João M Silva Junior¹, Alberto H Sabana¹, Luana C Silva¹, Rejane S Siqueira¹, David S Gomez², Silvia RCJ Santos³

Institutions: ¹Cancer Institute of Sao Paulo HCFMUSP, ²Division of Plastic Surgery and Burns, postal code 05800-090, ³Clinical 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: Pharmacokinetics of vancomycin is altered in septic patients from the Intensive Care Unit (ICU) that could impact the desired outcome related to drug effectiveness and safety.

Objective: Rationale of study was to investigate changes on pharmacokinetics of vancomycin after the empirical dose regimen 1g q12h that could impact desired outcome done 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. Characteristics 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): noncompartmental 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_{0-24}/MIC ratio for target (ratio >400) considered [2]

References

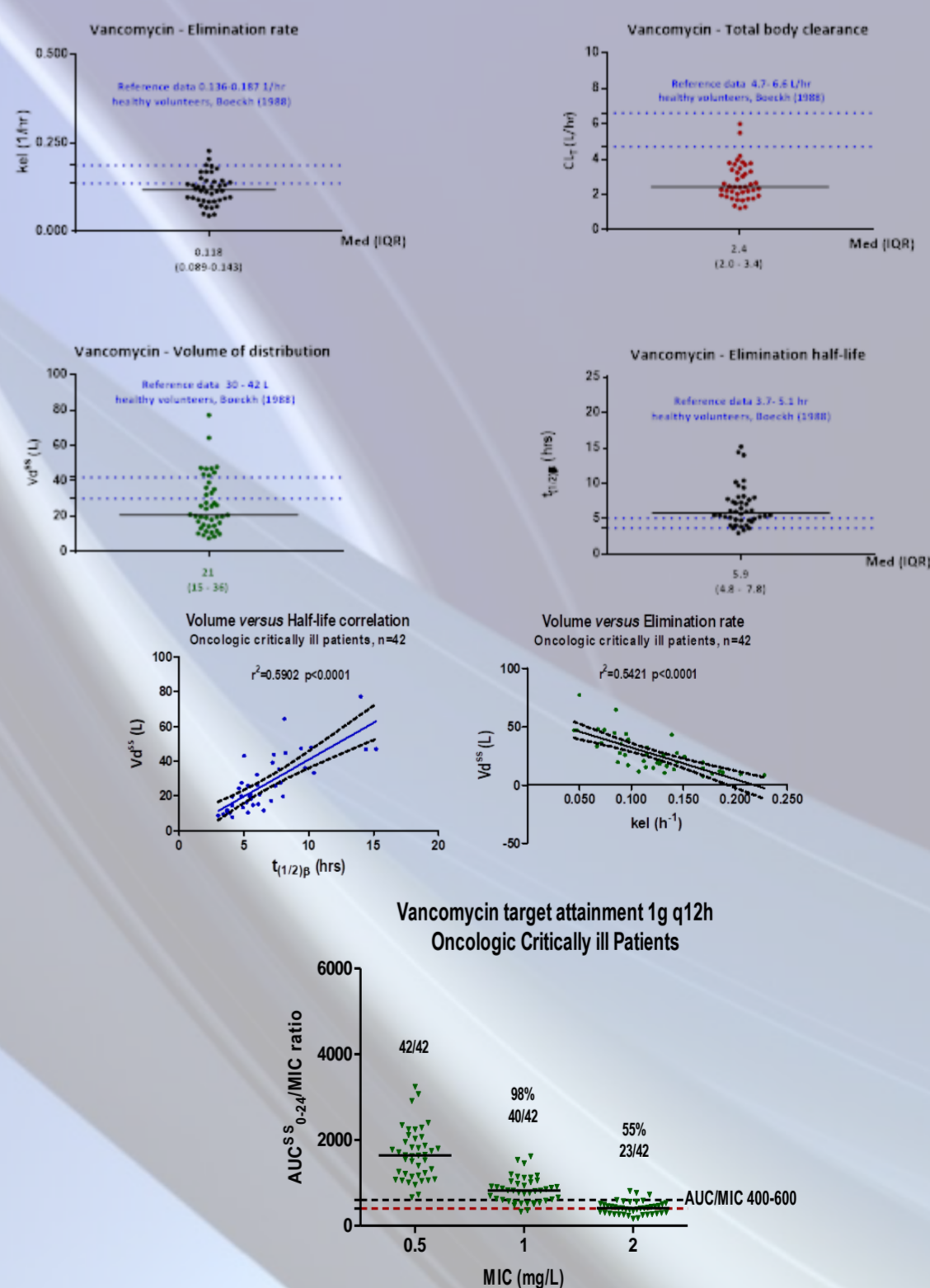
- [1] Boeckh et al. AAC.1988; 32 (1):92-95.
[2] Rybak et al. USA Consensus, 2020.

Results: Oncological critically ill patients included, and the characteristics of them at ICU admission med(IQR): 63(59-71) yrs, 55 (48-62) kg, BSA 1.79 (1.59-1.87)m², BMI 24 (21-28 kg/m² Clcr 88 (68-108) ml/min, SAPS3 38 (34-42) SAPS

SAPS Simplified Acute Physiology Score

High variability on PK parameters: proportional changes on elimination half-life versus volume of distribution, and reduction on total body clearance related to elimination rate also occurred.

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



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.