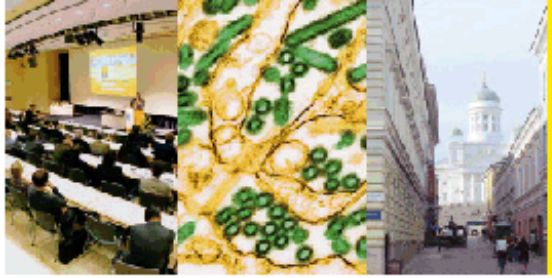

Determination of pharmacokinetic/pharmacodynamic index for patients treated with high-dose vancomycin by continuous infusion

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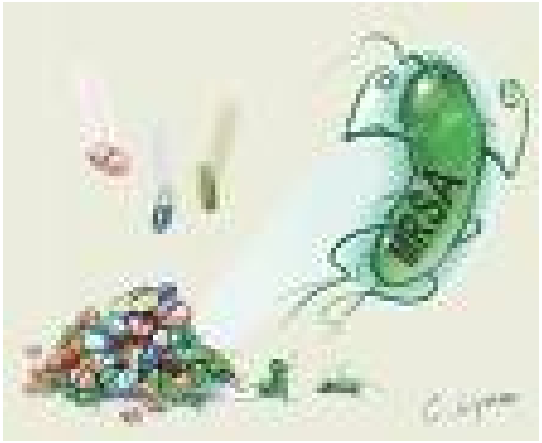
Background

- a vancomycin AUC_{24h}/MIC ratio ≥ 400 (h^{-1}) is necessary for optimal therapy (Moise-Broder et al. Clin Pharmacokinet. 2004;43:925-42)
- we have to take into account *Staphylococci* with decreased susceptibility to vancomycin (Tenover FC et al. CID 2007; 44: 1208-1215)
  - associated with higher rates of clinical failure
  - not always detected by standard laboratory methods
- continuous infusion is easier for nursing and for therapeutic drug monitoring (TDM) than every 12h dosing (Wysocki et al AAC 2001; 45:2460-2467)

Aim of the study

Does high dose vancomycin, administered by continuous infusion, allow to attain an AUC_{24h}/MIC ratio ≥ 400 (h^{-1}) in patients with infections caused by organisms with increased MIC's?



Which vancomycin serum concentration should we target?

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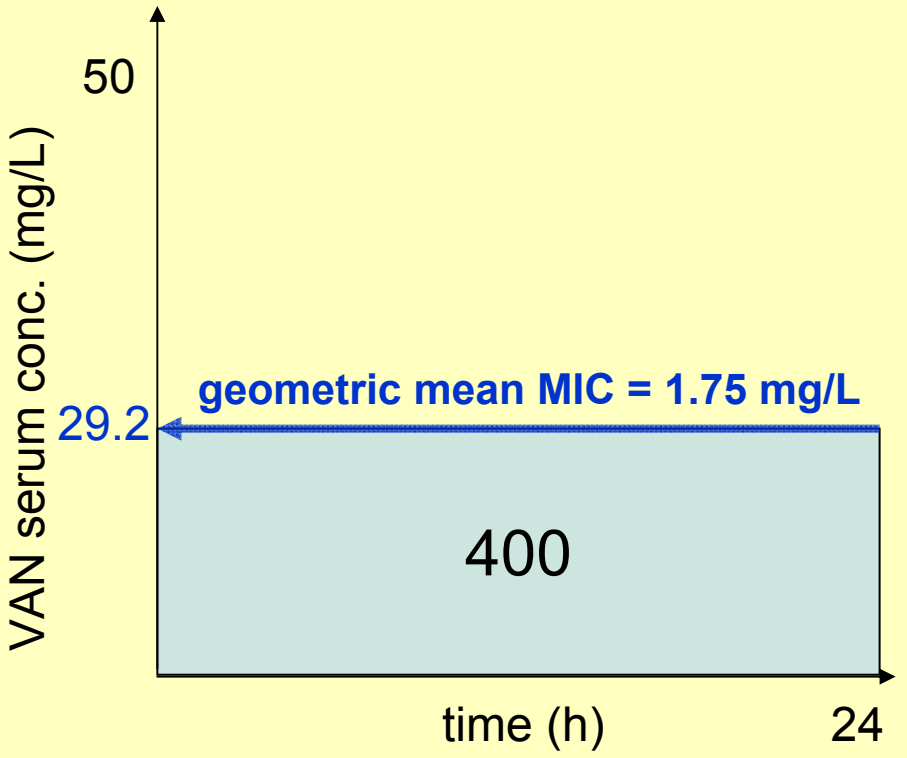

Moise-Broder et al. Clin Pharmacokinet. 2004;43:925-42

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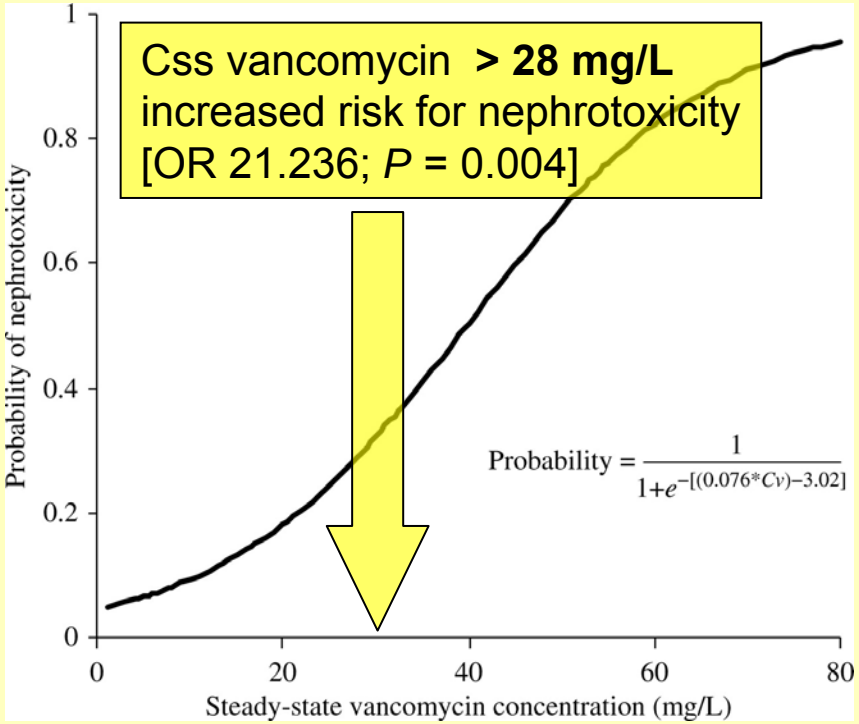
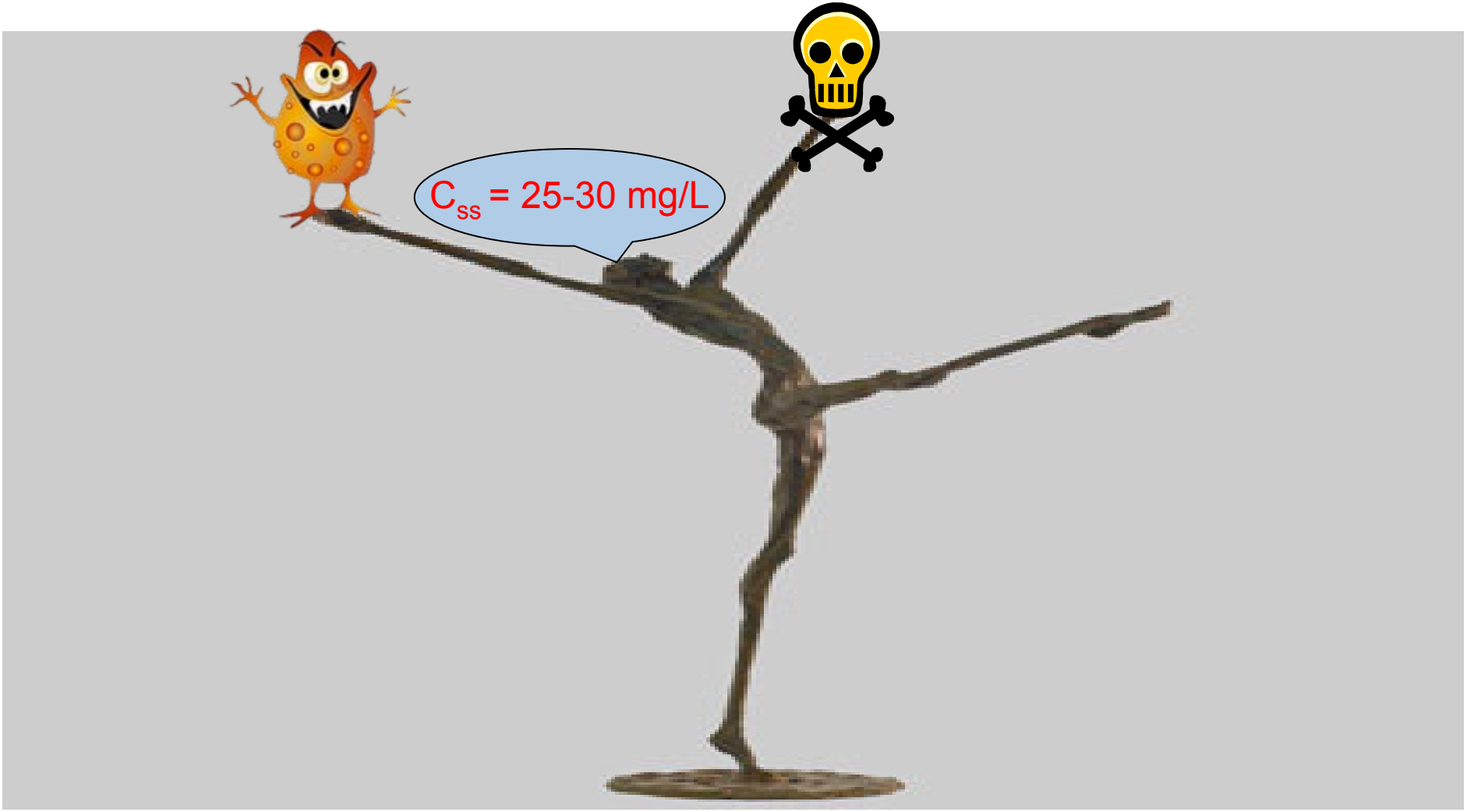


Ingram, P. R. et al. J. Antimicrob. Chemother. 2008 Jul;62 (1): 168-71.

Which vancomycin serum concentration should we target?



statue of Fred Bellefroid, Louvain

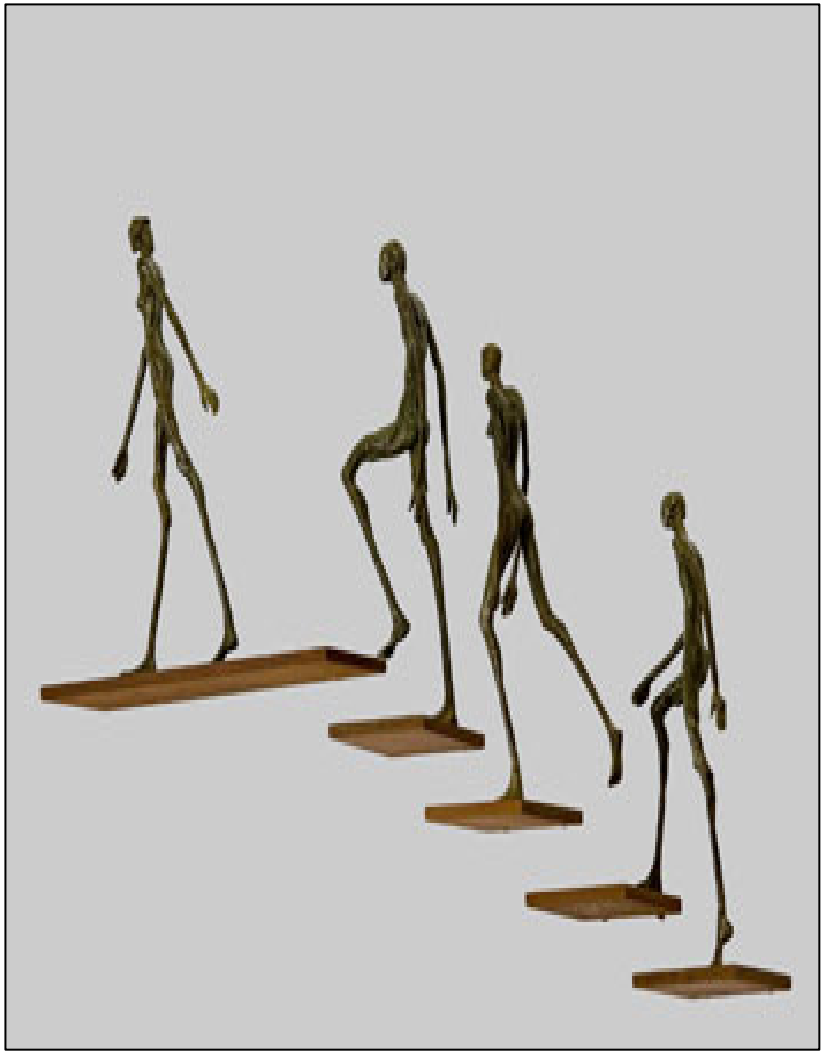
Methods

- administration scheme
  - loading dose: 20 mg/kg
  - infusion rate: 2.5 g/day adapted to renal function and adjusted by a clinical pharmacist

Methods: (2)

- determination of total vancomycin serum levels:
  - CMIA: Architect®, Abbot Diagnostics, Solna, Sweden
- determination of MIC's:
  - E-test: AB BIODISK, Solna, Sweden

Results

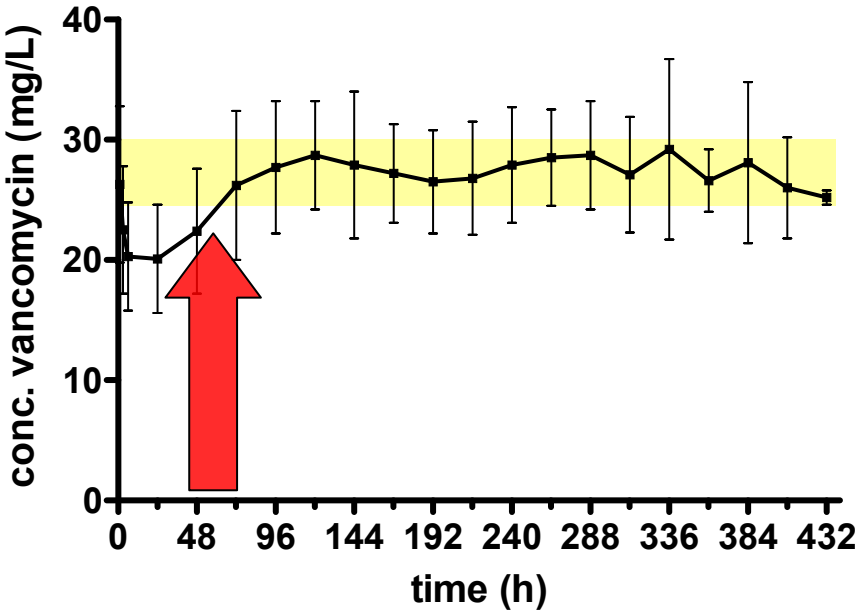


statue of Fred Bellefroid, Louvain

- patients: n=54 (40 documented infections)
- treatment duration:
  - 1 to 37 days
  - mean: 12 ± 10 days
- isolates
  - MRSA: 14
  - MSSA: 6
  - coagulase negative Staphylococci: 16
  - Other: 4
- MIC-range: 0.25 - 3 mg/L

Results (2)

vancomycin concentrations measured over time in patients treated by continuous infusion



Target concentration range was reached and remained constant after 48h (infusion rate adjusted by a clinical pharmacist)

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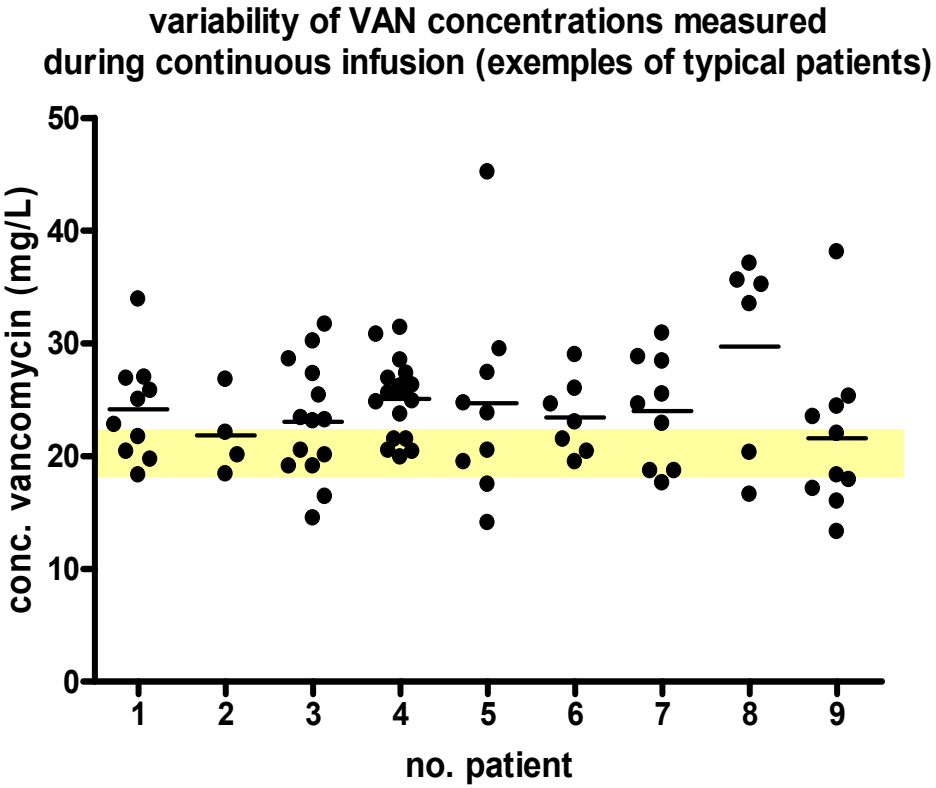
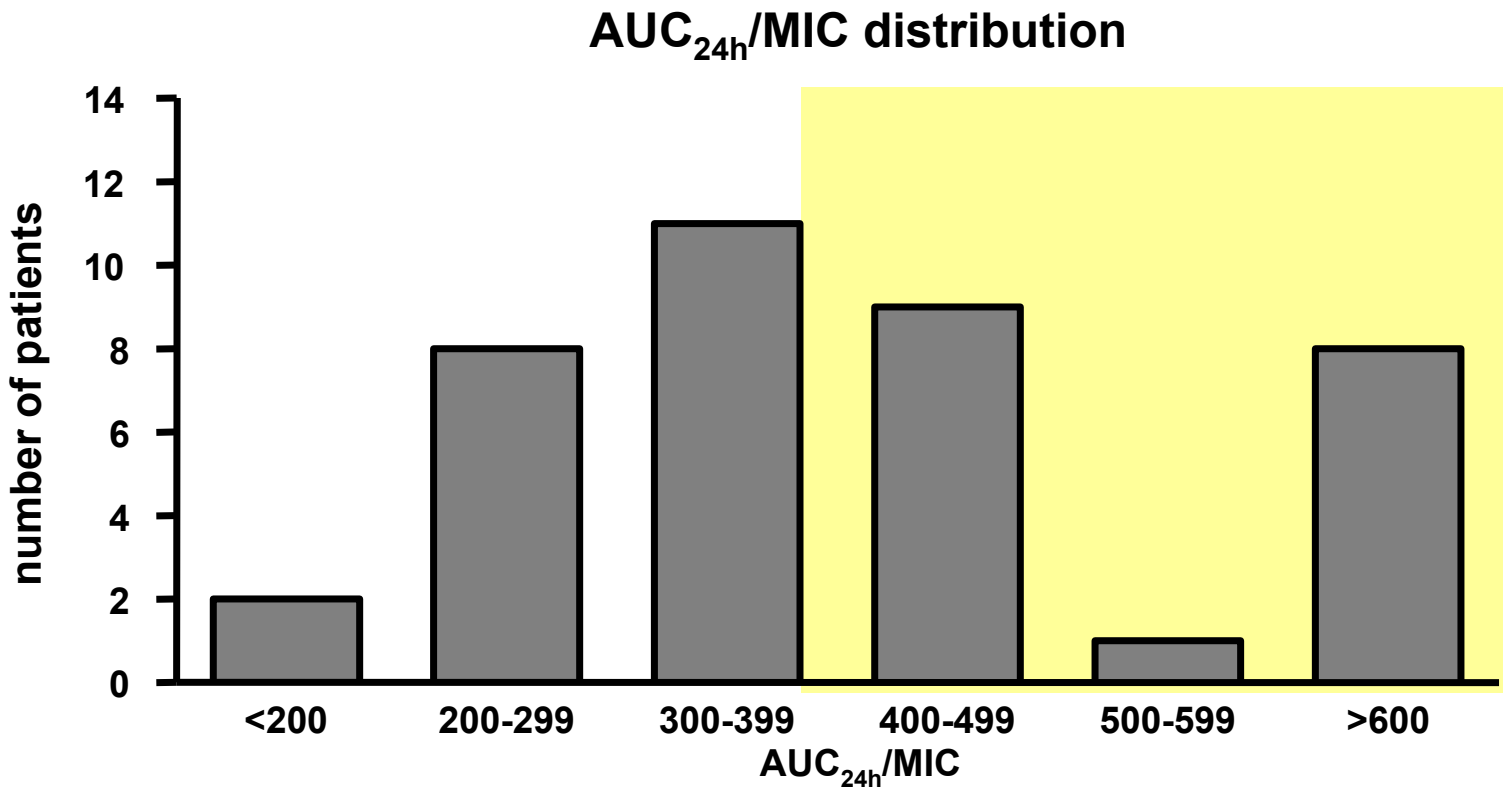
Results (3)



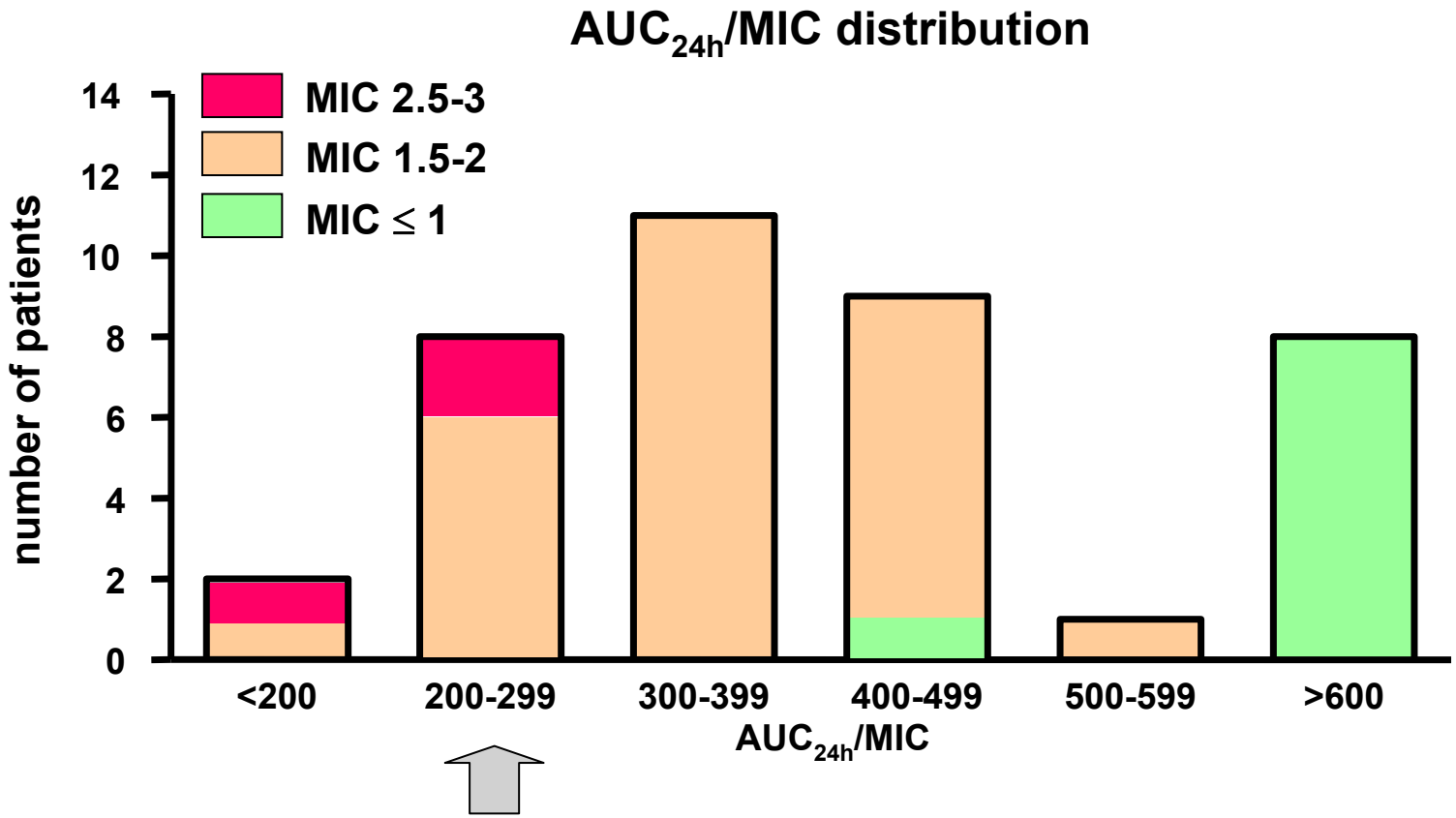
Important inter- and intra-individual variability in vancomycin serum concentrations measured despite dose adjustment by clinical pharmacist

Results (4)



- AUC_{24h}/MIC ratio
  - mean: 525 +/- 83.4 h^{-1} [196 - 2684 h^{-1}]
  - AUC_{24h}/MIC of 400 h^{-1} was achieved in only 46% of cases

Results (5)



low target attainment in patients infected with organisms having MIC's ≥ 1,5 mg/L

Conclusion

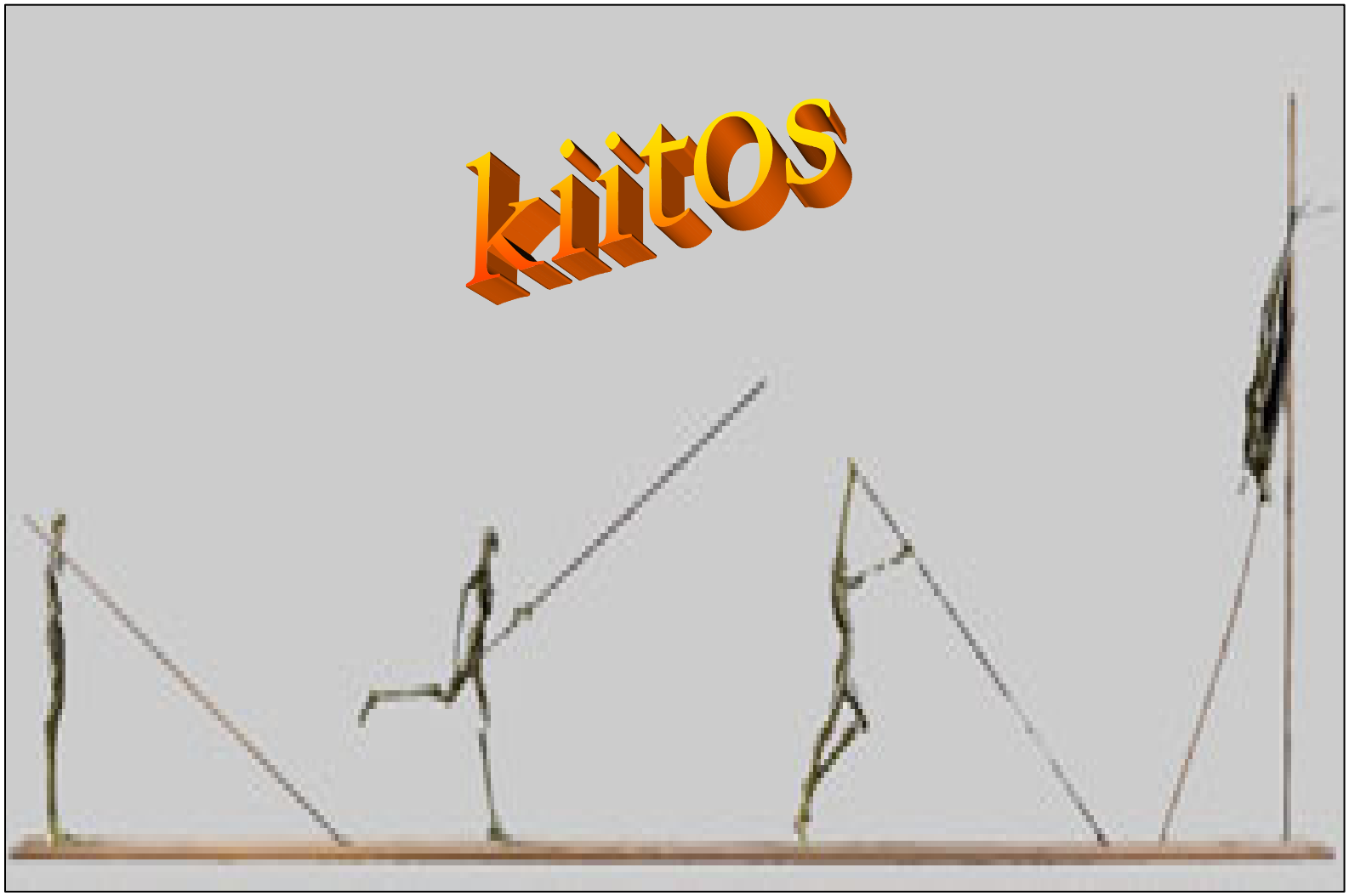
- high dose VAN by CI with dose adjustment by TDM did allow to maintain the mean VAN concentration within the target concentration range after the first 48h

- a high variability in VAN concentrations measured was observed despite dose adjustment by a clinical pharmacist

- due to this variability and the high prevalence of organisms with reduced susceptibility to VAN, an AUC_{24h}/MIC ratio ≥ 400 (h^{-1}) was not reached in all patients

- patients infected with organisms having MIC's >1.5 mg/L should be considered at risk for treatment failure

- the PK/PD data observed in this study further suggest that lowering the current susceptibility breakpoint of VAN is justified
  - EUCAST: susceptible if MIC ≤ 4 mg/L
  - CLSI: susceptible if MIC ≤ 2 mg/L



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