

Nye brydtpunkter for vancomycin

Glycopeptides - EUCAST clinical MIC breakpoints 2006-06-20 (v 1.3)

Glycopeptides		Species-related breakpoints (S</R>)										
		<i>Enterobacteriaceae</i>	<i>Pseudomonas</i>	<i>Acinetobacter</i>	<i>Staphylococcus</i> ²	<i>Enterococcus</i>	<i>Streptococcus</i> A,B,C,G	<i>S.pneumoniae</i>	<i>Other streptococci</i>	<i>H.influenzae M.catarrhalis</i>	<i>N.gonorrhoeae</i>	<i>N.meningitidis</i>
Vancomycin	RD	--	--	--	4/8 ²	4/8	4/4 ³	4/4 ³	4/4 ³	--	--	--
Teicoplanin	RD	--	--	--	4/8 ²	4/8	4/4 ³	4/4 ³	4/4 ³	--	--	--

Glycopeptides - EUCAST clinical MIC breakpoints 2009-02-16 (v 2.0)

Glycopeptides		Species-related breakpoints (S</R>)												Non-species related breakpoints S</R>	
		<i>Enterobacteriaceae</i>	<i>Pseudomonas</i>	<i>Acinetobacter</i>	<i>Staphylococcus</i>	<i>Enterococcus</i>	<i>Streptococcus</i> A,B,C,G	<i>Other streptococci</i>	<i>S.pneumoniae</i>	<i>H.influenzae M.catarrhalis</i>	<i>N.gonorrhoeae</i>	<i>N.meningitidis</i>	<i>Gram-positive anaerobes</i>		<i>Gram-negative anaerobes</i>
Vancomycin	RD	--	--	--	2/4	4/4 ^C	1/1 ^D	1/1 ^D	1/1 ^D	--	--	--	2/4	--	2/4
Teicoplanin	RD	--	--	--	2/4 4/4 ^B	2/4	1/1 ^D	1/1 ^D	1/1 ^D	--	--	--	--	--	2/4

A. Non-species related breakpoints have been determined mainly on the basis of Pk/Pd data and are independent of MIC distributions of specific species. They are for use only for species not mentioned in the table or footnotes.

B. For coagulase-negative staphylococci only, the S/I breakpoint was increased to reduce division of the wild type MIC distributions for *S. epidermidis*, *S. haemolyticus* and a few other *Staphylococcus* spp.

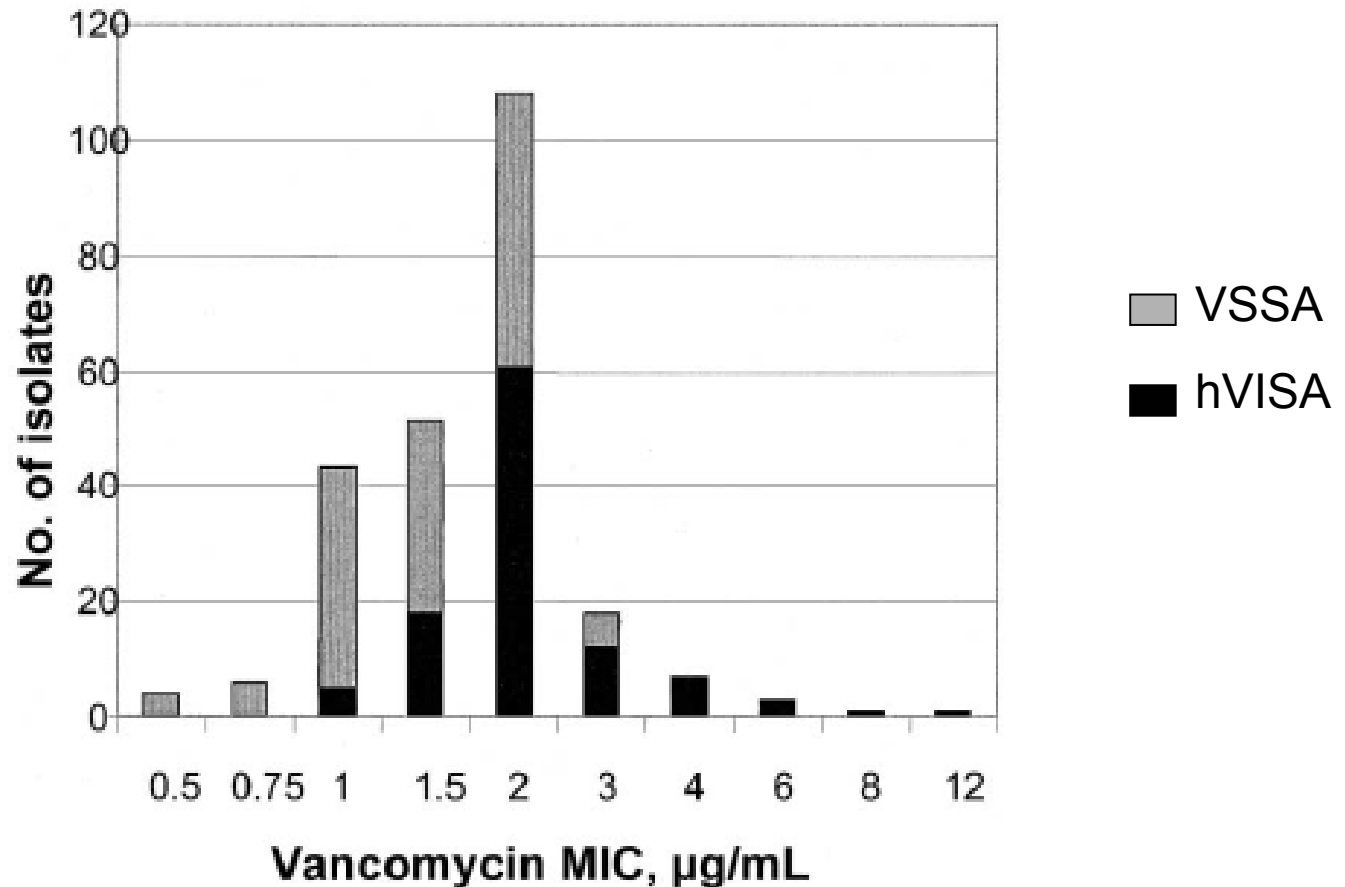
C. The S/I breakpoint was increased to avoid dividing the wild type MIC distribution.

D. Strains with MIC values above the S/I breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint (in italics) they should be reported resistant.

Resistens mekanismer i stafylokokker

- Højgradig Resistens (MIC > 16 mg/L)
 - VRSA / ((VRSE))
 - vanA pos – D-Ala-D-Lac i stedet for D-Ala-D-Ala
 - 9 (+4?) stammer i alt alle med MIC \geq 32 mg/L
- Låggradig resistens (MIC \leq 16 mg/L)
 - hVISA, VISA
 - Ændringer i cellevægs syntesen der gør at peptidoglycanlaget bliver tykkere + øget mængde monomere byggesten
 - vancomycin fanges (trapping) ved binding til disse monomerer før de når frem til virkningspunktet (på ydersiden af cellemembranen)
 - hVISA = heteroresistente VISA
 - Kun en del af kolonierne udviser resistens – dvs disse isolater kan have "følsom MIC" ved standard bestemmelse
 - Næsten udelukkende fundet i MRSA isolater, men kan teoretisk forekomme hos MSSA.

Distribution of hVISA Strains by Etest Vancomycin MIC^a



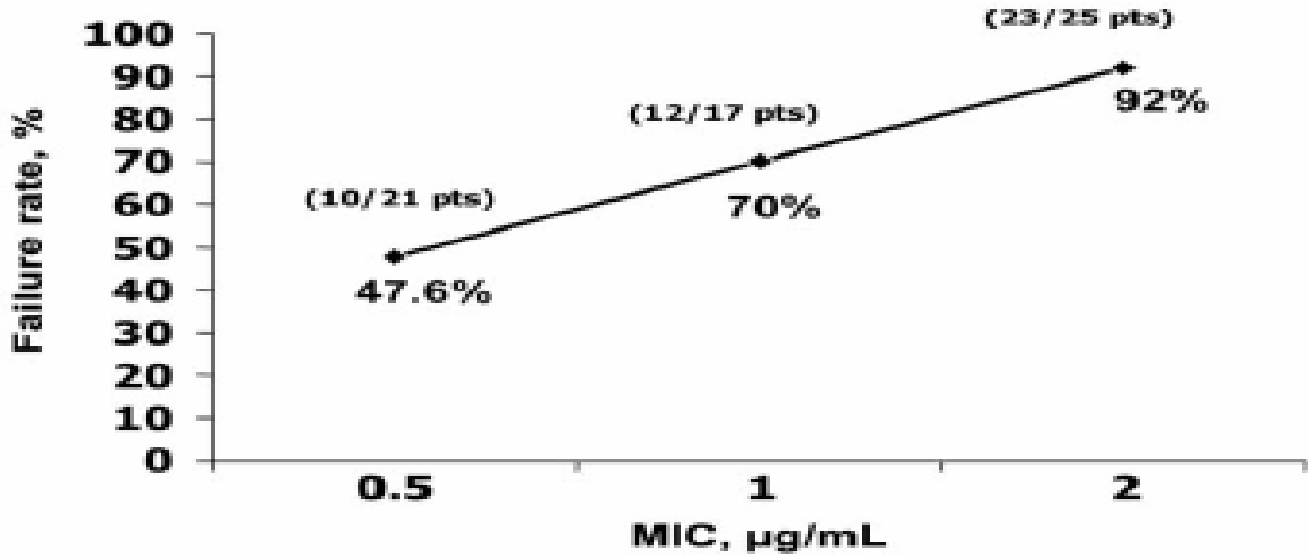
a. Tenover et al. *Clin Infect Dis* 2007; 44: 1208-1215; and Wooten et al. *Antimicrob Agents Chemother* 2005; 49: 3982-3983

Detektion

- VRSA
 - MIC (standard inokulat, MH)
 - DD
 - Obs ikke alle VRSA blev detekteret ved automatiseret resistensbestemmelse
- VISA
 - MIC (standard inokulat, MH) – MIC 4-8 mg/L
- hVISA (MIC \leq 2 mg/L)
 - Makro Etest, GRD Etest, Screenplader BHI med 5 mg/L teicoplanin
 - Konfirmeres med PAP-AUC metode

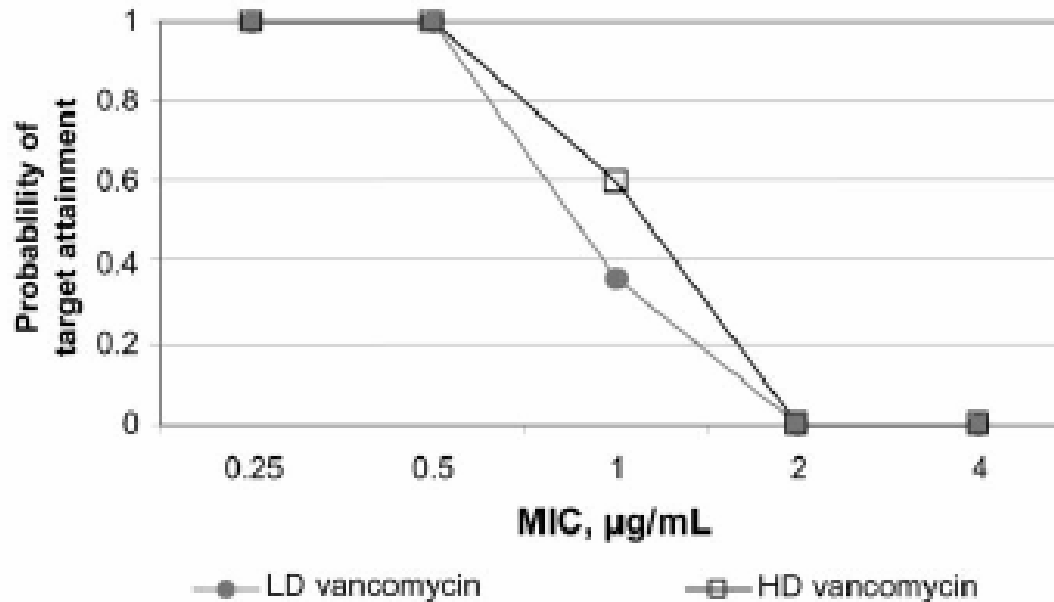
Er vanco S altid S?

Relationship of Vancomycin MIC to Clinical Failure Rates^a



a. Moise-Broder et al. *Clin Infect Dis* 2004; 38: 1700-1705.

Application of PK/PD Principles to Vancomycin Breakpoints^a



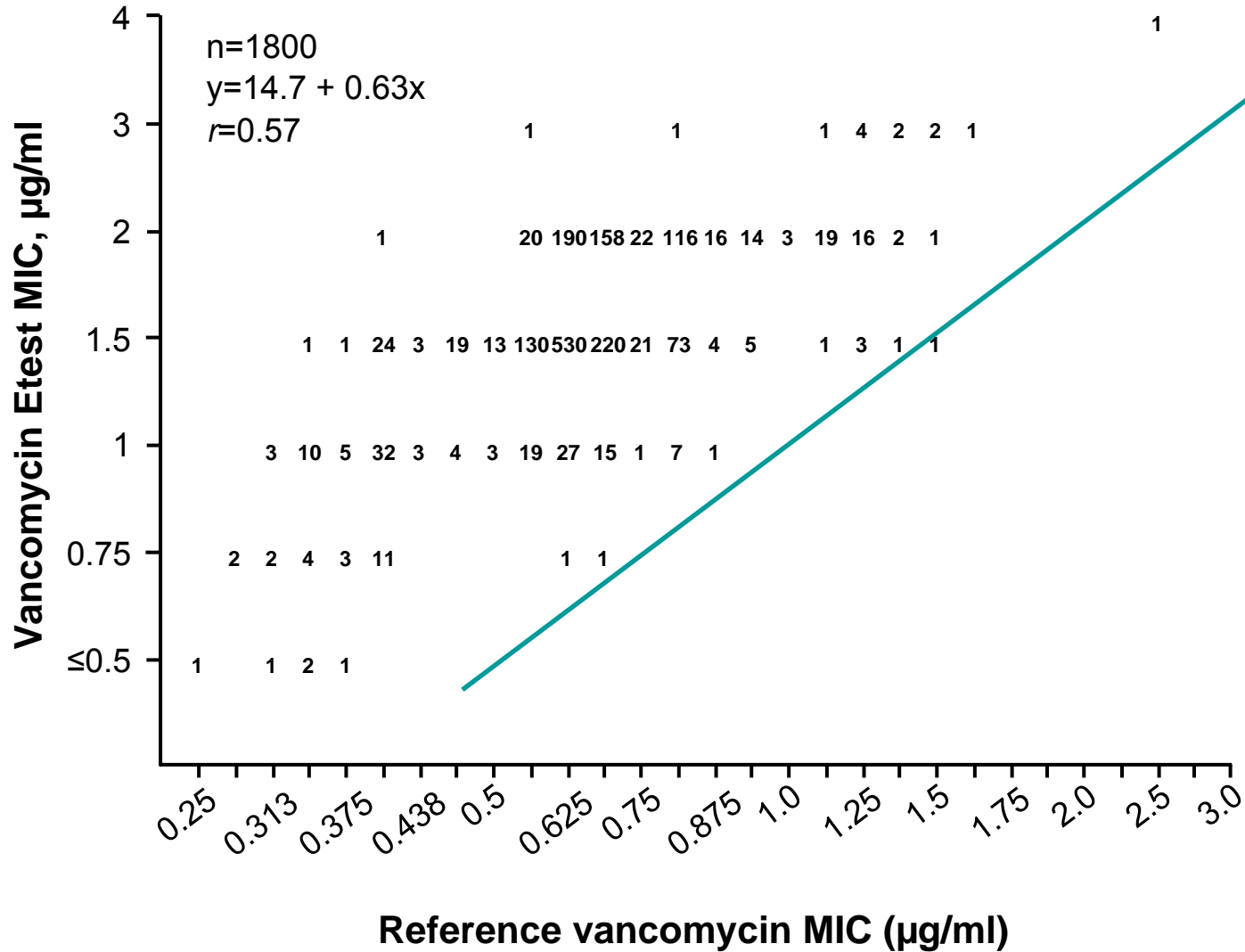
- Low dose (LD) from product package insert and US-FDA susceptible breakpoint (<4 µg/ml).
- AUC_{24}/MIC of >400 predictive of favorable outcomes^b

a. Jeffres et al. *Chest* 2006; 130: 947-955.

b. Moise-Broder et al. *Clin Pharmacokinetics* 2004; 43: 925-942



Vancomycin study 2002–2006



RAF-M anbefalinger

- MIC bør bestemmes ved vankomycin behandling af stafylokokk-infektioner
- MIC > 2 mg/L – kontakt til behandlende læge
 - Manglende respons
 - Højdosis vancomycin?
 - Byt antibiotika
- MIC ≤ 2 mg/L **og** manglende respons
 - Screening for hVISA/hVISE hvis pos da
 - Højdosis vancomycin?
 - Byt antibiotika
 - Konfirmering af hVISA (reference laboratorium)

RAF-M anbefalinger

- VISA
 - Etest or mikrobroth dilution using Mueller Hinton
- hVISA screening
 - Etest makro metode (BHI, McF 2.0, 48h)
 - Teicoplanin ≥ 12 mg/L - Screen positiv
 - Teicoplanin på 8 mg/L; suppler med vancomycin såfremt vancomycin også ≥ 8 mg/L - Screen positiv
 - Teicoplanin < 8 mg/L - screen negativ
 - BHI5T (BHI, 5 mg/L teicoplanin, McF 0.5, 48h)
 - Vækst af >2 kolonier - Screen positiv