



Linezolid-resistente *S. epidermidis* in Deutschland

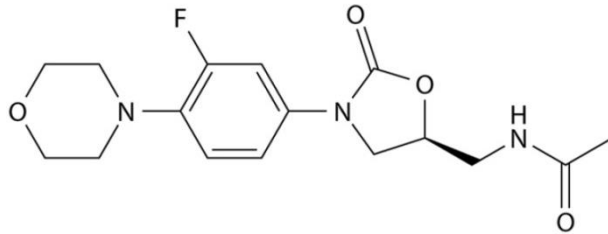
Franziska Layer

NRZ für Staphylokokken und Enterokokken
FG 13 Nosokomiale Infektionserreger und
Antibiotikaresistenzen, Abt. Infektionskrankheiten
Robert Koch-Institut, Bereich Wernigerode

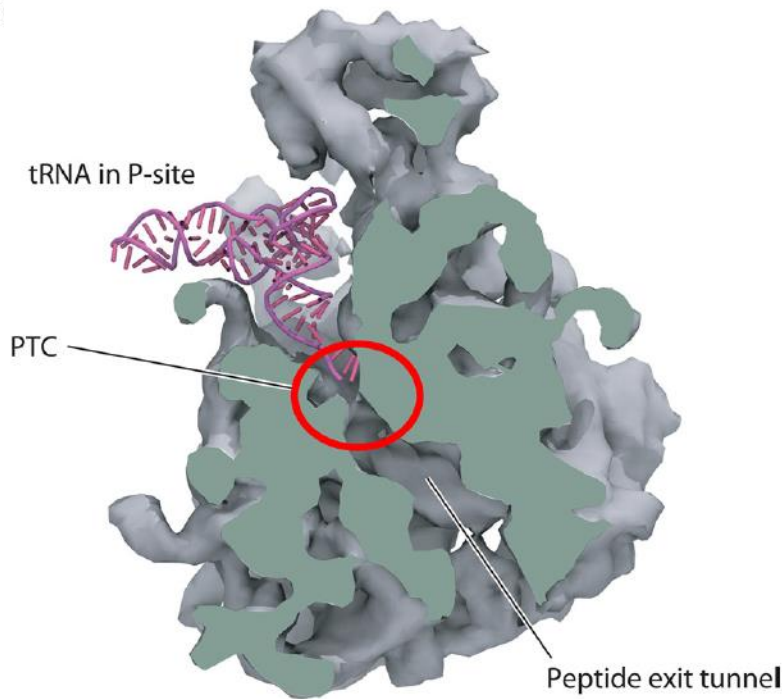
Bonn, 26.03.2018



Linezolid



- Reserveantibiotikum aus der Klasse der Oxazolidinone
- Hemmung der Proteinsynthese
- bindet spezifisch an die 23S rRNA der 50S-Untereinheit des bakteriellen Ribosoms (*PTC* Peptidyl-Transferase-Center)

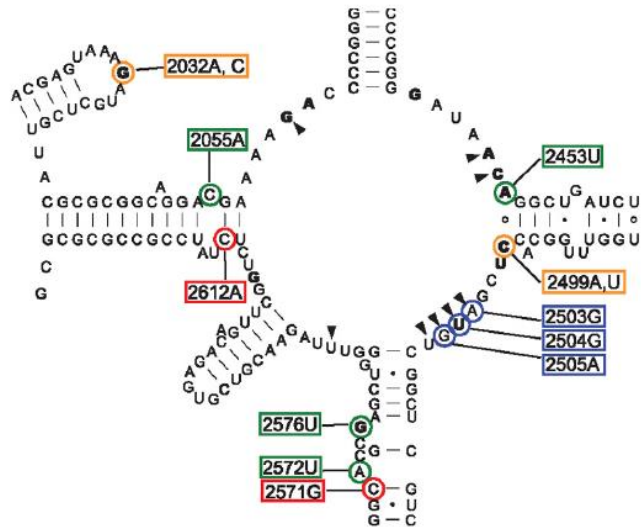


Long & Vester, Antimicrob. Agents Chemother. 2012

Linezolidresistenz

- verursacht durch Mutationen und/ oder den Erwerb von Genen

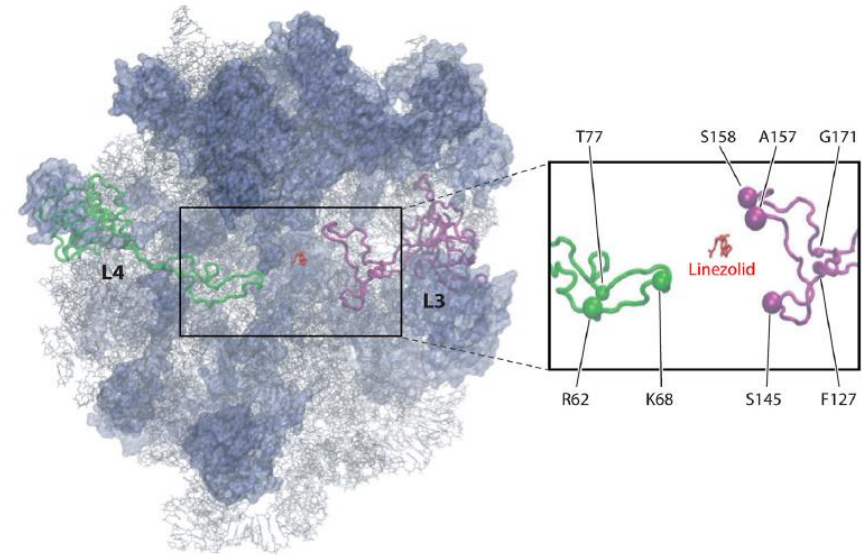
➤ Mutationen in der 23S rRNA Bindungsstelle



Long *et al.*, Antimicrob. Agents Chemother. 2010

Secondary structure of the 23S rRNA Peptidyltransferase loop; colored mutations indicate 1st (blue), 2nd (green), 3rd (orange) and outer layer (red) nucleotides with respect to linezolid

➤ Mutationen in den ribosomalen Proteinen L3, L4, L22 des PTC



Long & Vester, Antimicrob. Agents Chemother. 2012

Illustration how parts of L3 and L4 extend toward the PTC where linezolid is bound.



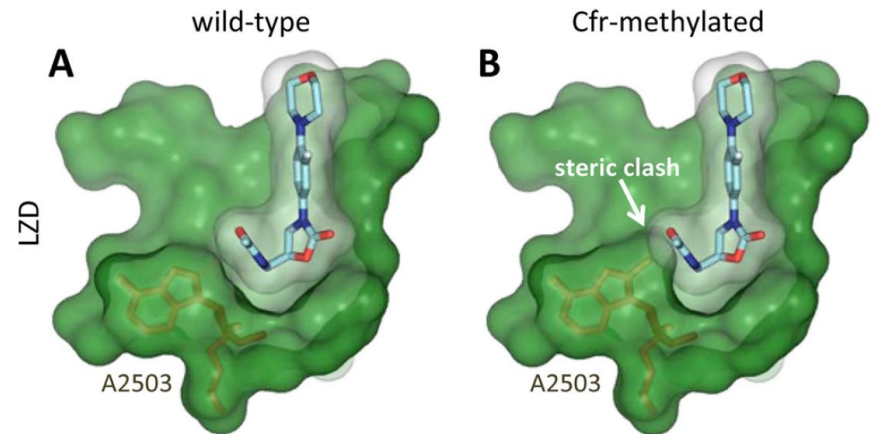
Linezolidresistenz

- ***cfr* kodiert eine Methyltransferase**
(Methylierung von Adenin an der Position A2503)

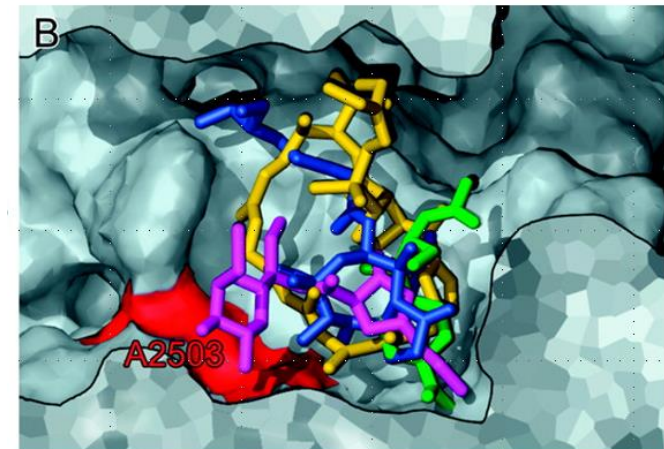
vermittelt Kreuzresistenzen
(PhLOPS_A) durch Methylierung eines
zentralen Antibiotika-
Angriffspunktes

PhLOPS_A phenotype (resistance to Phenicol,
Lincosamides, Oxazolidinones, Pleuromutilins and
Streptogramin A Antibiotics)

meistens Plasmid vermittelt und
teilweise übertragbar



Locke *et al.*, *Antimicrob. Agents Chemother.* 2010



Long K S *et al.* *Antimicrob. Agents Chemother.* 2006

Binding of Chloramphenicol (green), Clindamycin (pink), Tiamulin (blue) and Dalfofpristin (yellow) to overlapping sites at the ribosomal peptidyl transferase center.



Hospital-assoziierte Koagulase-negative Staphylokokken mit Resistenz gegenüber Linezolid werden weltweit beschrieben



- LRCoNS strains with outbreak of healthcare-associated infection
- LRCoNS strains reported

(b) Linezolid-resistant CoNS reported in North America (USA, Mexiko), South America (Brazil), Europe (Greece, Spain, Italy, France, Ireland) and Asia (India).

Gu *et al.*, J Antimicrob Chemother. 2013

J Antimicrob Chemother. 2018 Jan 1;73(1):41-51. doi: 10.1093/jac/dkx370.

Long-lasting successful dissemination of resistance to oxazolidinones in MDR *Staphylococcus epidermidis* clinical isolates in a tertiary care hospital in France.

Dortet L^{1,2,3,4}, Glaser P^{4,5}, Kassis-Chikhani N⁶, Girlich D^{2,3,4}, Ichai P⁷, Boudon M⁷, Samuel D⁷, Creton F^{2,3,4}, Imanci D⁸, Bonnin R^{2,3,4}, Fortineau N^{1,2,3,4}, Naas T^{1,2,3,4}

J Antimicrob Chemother. 2017 Dec 1;72(12):3252-3257. doi: 10.1093/jac/dkx292.

Novel multiresistance *cfr* plasmids in linezolid-resistant methicillin-resistant *Staphylococcus epidermidis* and vancomycin-resistant *Enterococcus faecium* (VRE) from a hospital outbreak: co-location of *cfr* and *optrA* in VRE.

Lazaris A¹, Coleman DC¹, Kearns AM², Pichon B², Kinnevey PM¹, Earls MR¹, Boyle B³, O'Connell B^{3,4}, Brennan G⁴, Shore AC¹.

J Antimicrob Chemother. 2018 Feb 9. doi: 10.1093/jac/dky010. [Epub ahead of print]

Emergence and control of linezolid-resistant *Staphylococcus epidermidis* in an ICU of a German hospital.

Weßels C¹, Strommenger B², Klare J², Bender J², Messler S³, Mattner F¹, Krakau M⁴, Werner G², Layer F²

Infect Control Hosp Epidemiol. 2018 Feb 12;1-3. doi: 10.1017/ice.2018.5. [Epub ahead of print]

Dissemination of *Staphylococcus epidermidis* ST22 With Stable, High-Level Resistance to Linezolid and Tedizolid in the Greek-Turkish Region (2008-2016).

Freitas AR¹, Dilek AR², Peixe L¹, Novais C¹.



Einsendungen von Linezolid-resistenten Staphylokokken an das NRZ

...Fragen der Einsender

"Kann das NRZ die Resistenz bestätigen?"

"Inwieweit sind Isolate verwandt?" (Aufklärung von Transmissionsketten)

...Routinediagnostik

Bestimmung der MHK mittels Mikrodilution

PCR zum Nachweis des *cfr*-Gens

*Sma*I-Makrorestriktion

Multilocus Sequenztypisierung (MLST)

...Forschung

Bestimmung der ribosomalen Mutationen

Analyse der *cfr*-Plasmide, Übertragbarkeit

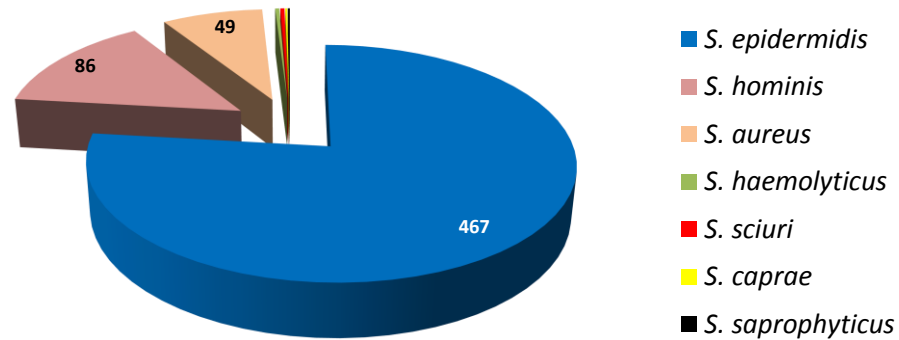
Linezolid-abhängiges Wachstum

(NGS-Daten zur Typisierung)

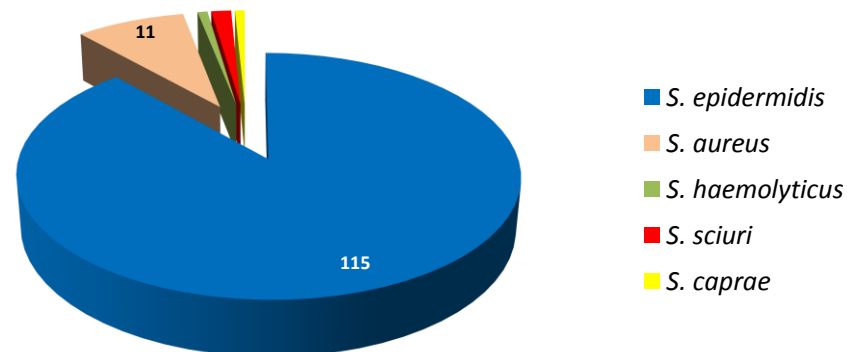


Daten aus dem NRZ

Einsendungen Linezolid-resistenter Staphylokokken an das NRZ
(2006-2017)



Nachweis des *cf*r-Gens





Charakterisierung von Linezolid-resistenten *S. epidermidis* (LRSE) aus deutschen Krankenhäusern

(Bender *et al.*, J Antimicrob Chemother. 2015)

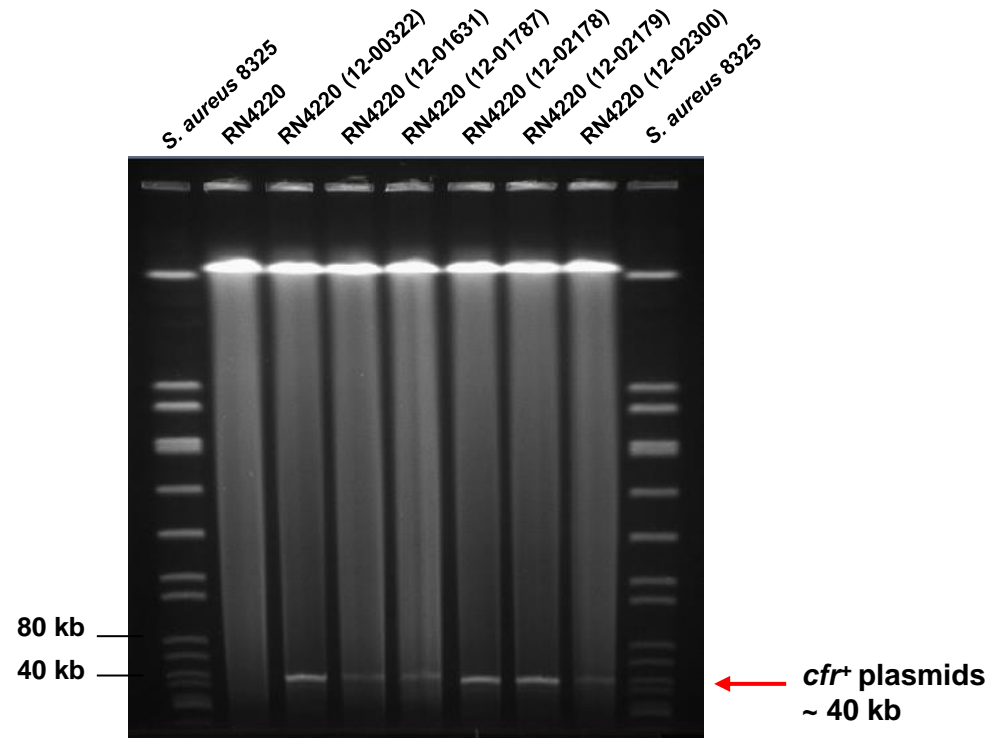
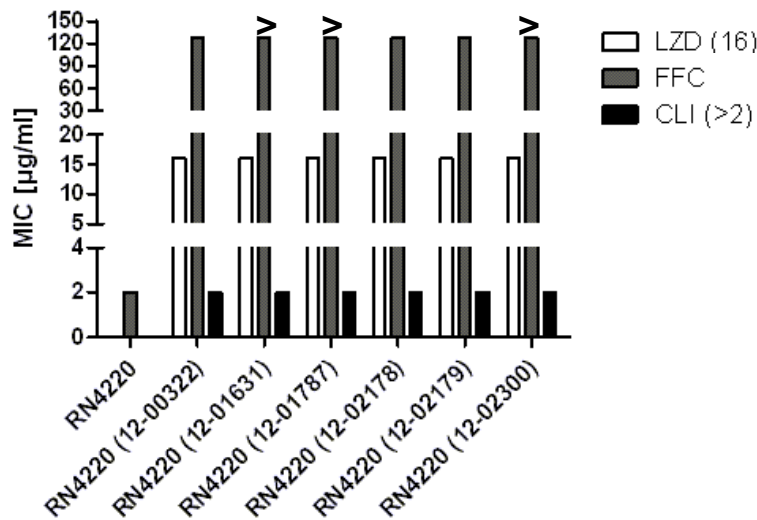
No. of isolates	Hospital	ST	PFGE type	MIC of linezolid (mg/L)	<i>cfr</i>
8	A	2	IV	16–256	–
2	A	2	IV	>256	+
1	C	2	IV	8	+
1	G	2	V	>256	+
1	B	5	II	8	–
3	F	5	II	16–32	–
1	C	22	I	16	+
14	D	22	I	>256	–
2	E	22	I	>256	–
1	E	22	I	>256	–
1	H	22	I	>256	–
1	C	23	III	8	+

- multiresistent
- LZD MHK 8 - >256 mg/L
- vier Genotypen (I – IV) nach *Sma*I-Makrorestriktion/ PFGE
- vier Sequenztypen (CC5 häufig unter nosokomialen *S. epidermidis*)
- sechs *cfr*-positive Stämme



Charakterisierung von LRSE aus deutschen Krankenhäusern

■ Analyse der *cfr*-Plasmide



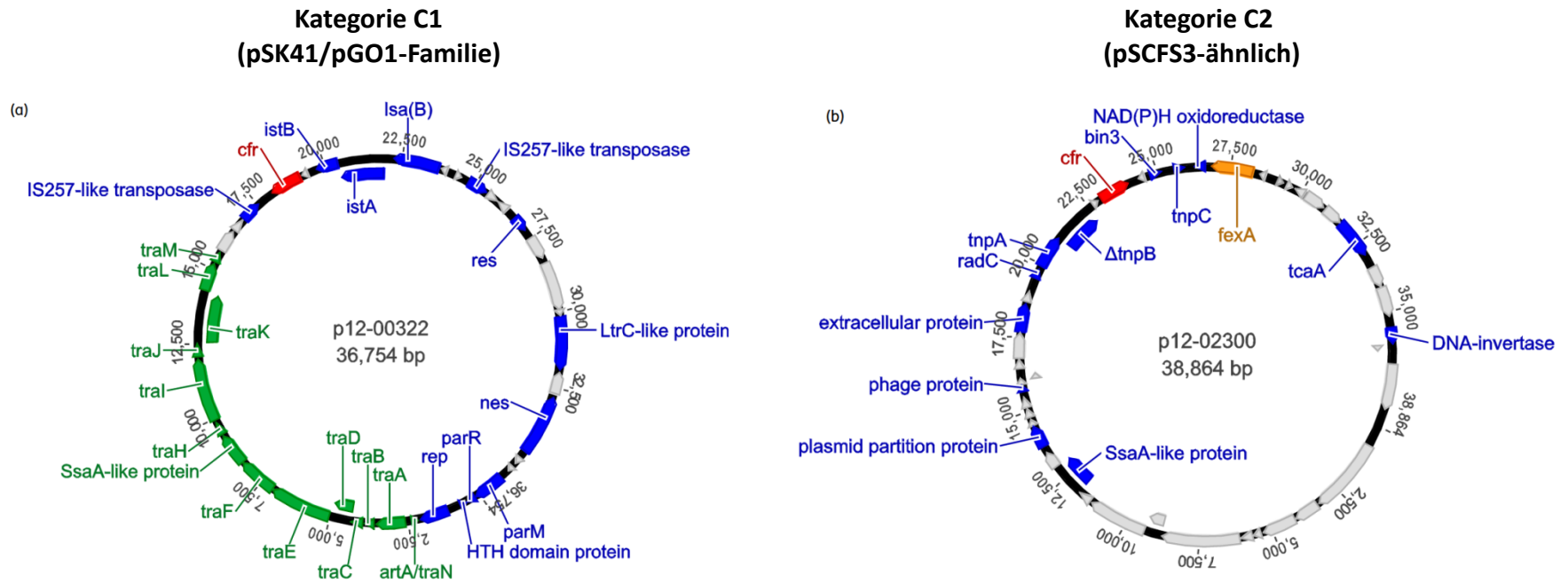
➤ Transfer der Plasmide in *S. aureus* RN4220

➤ S1 Nuclease-PFGE (+ Southern Blot hybridisiert mit einer *cfr*-Sonde)



Charakterisierung von LRSE aus deutschen Krankenhäusern

- *cfr*-Plasmide: bekannte und neue Strukturen



(a) p12-00322 (C1) shows *cfr* (red) framed by IS257-like transposases and a putative conjugation machinery (green) of vector pGO1.

LRSE ST2, ST22, ST23 aus einem Krankenhaus

(b) p12-02300 and homologues display *cfr* (red) and the additional phenicol exporter *fexA* (orange) amongst mainly unknown ORFs as defined by RAST.

LRSE ST2 aus verschiedenen Krankenhäusern

➤ klonale Verbeitung LZD-resistenter Stämme und/ oder *cfr*-tragender Plasmide

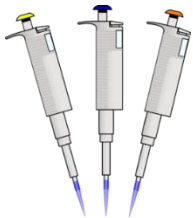


Häufung von LRSE auf einer deutschen Intensivstation

(Weßels *et al.*, J Antimicrob Chemother. 2018)



- Krankenhaus der Sekundärversorgung in NRW mit 465 Betten
- interdisziplinäre ICU mit 21 Betten
- in 15 Monaten Nachweis von LRSE bei 14 Patienten aus verschiedenen klinischen Materialien



- Resistenzbestätigung
- molekulare Typisierung
- Analyse der *cfr*-Plasmide und Resistenzmutationen



- Verschiedene Maßnahmen zur Infektionskontrolle/ Interventionen (Reduktion des Einsatzes von LZD, Information und Schulung des Personals, Umgebungsscreening, Isolationsmaßnahmen bei LRSE-positiven Patienten, u.a.)
- Review der Krankenakten und des Antibiotika-Verbrauchs des Krankenhauses und der ICU



Häufung von LRSE auf einer deutschen Intensivstation

■ Charakteristika LRSE-positiver Patienten

Patient	Sex	Age (years)	Ward	Culture site	Date of culture	Infection due to LRSE ^a	Infection ^a	MRSA (culture site)	Underlying disease and/or condition	Linezolid consumption (DDD) ^b	VRE (culture site)	LZD-R VRE (culture site)
1	male	57	ICU	blood	22/11/2013			negative	haemorrhage after ERCP	15		
2 ^c	male	71	ICU	central line tip blood central line tip	02/01/2014 07/03/2014 18/03/2014		BSI with <i>Enterococcus faecium</i>	negative	fracture of trochanter major	48	positive (urine)	
3	male	87	ICU	urine	12/12/2013			negative	cardiac decompensation, pneumonia	56		
4	female	66	ICU	central line tip	15/05/2014		BSI due to UTI and BSI with MRSA	positive (blood, tracheal secretion)	ileus	55		
5	male	61	ICU	blood	16/05/2014		BSI with MRSA	positive (blood)	myocardial infarction, CPR	26	positive (wound)	
6	male	72	ICU	wound	21/07/2014			negative	ulcus duodeni haemorrhage	17	positive (secretion drainage)	
7	male	64	ICU	secretion drainage	22/07/2014		pneumonia with MRSA	positive (punctate)	pancreatic cancer	13		
8	female	78	SU	blood	26/07/2014			positive (bronchial secretion)	pneumonia	14		
9	female	76	ICU	secretion drainage	01/08/2014			negative	peritonitis	32		
10	male	90	ICU	blood	04/08/2014		pneumonia	negative	colon cancer	15		
11	male	77	ICU	blood	07/09/2014		BSI	positive (wound)	renal failure	23		
12	male	76	ICU	axilla	19/09/2014			negative	media infarction	0		
13	female	79	ICU	decubitus	18/09/2014		UTI	negative	incarcerated hernia	65		positive (wound)
14	male	77	ICU	blood	08/01/2015			positive (screening)	pneumonia	14		

ERCP, endoscopic retrograde cholangiopancreatography; CPR, cardiopulmonary resuscitation; SU, surgical unit; BSI, bloodstream infection; UTI, urinary tract infection; LZD-R, linezolid resistant.

^aInfection: cases were defined as described elsewhere.²²

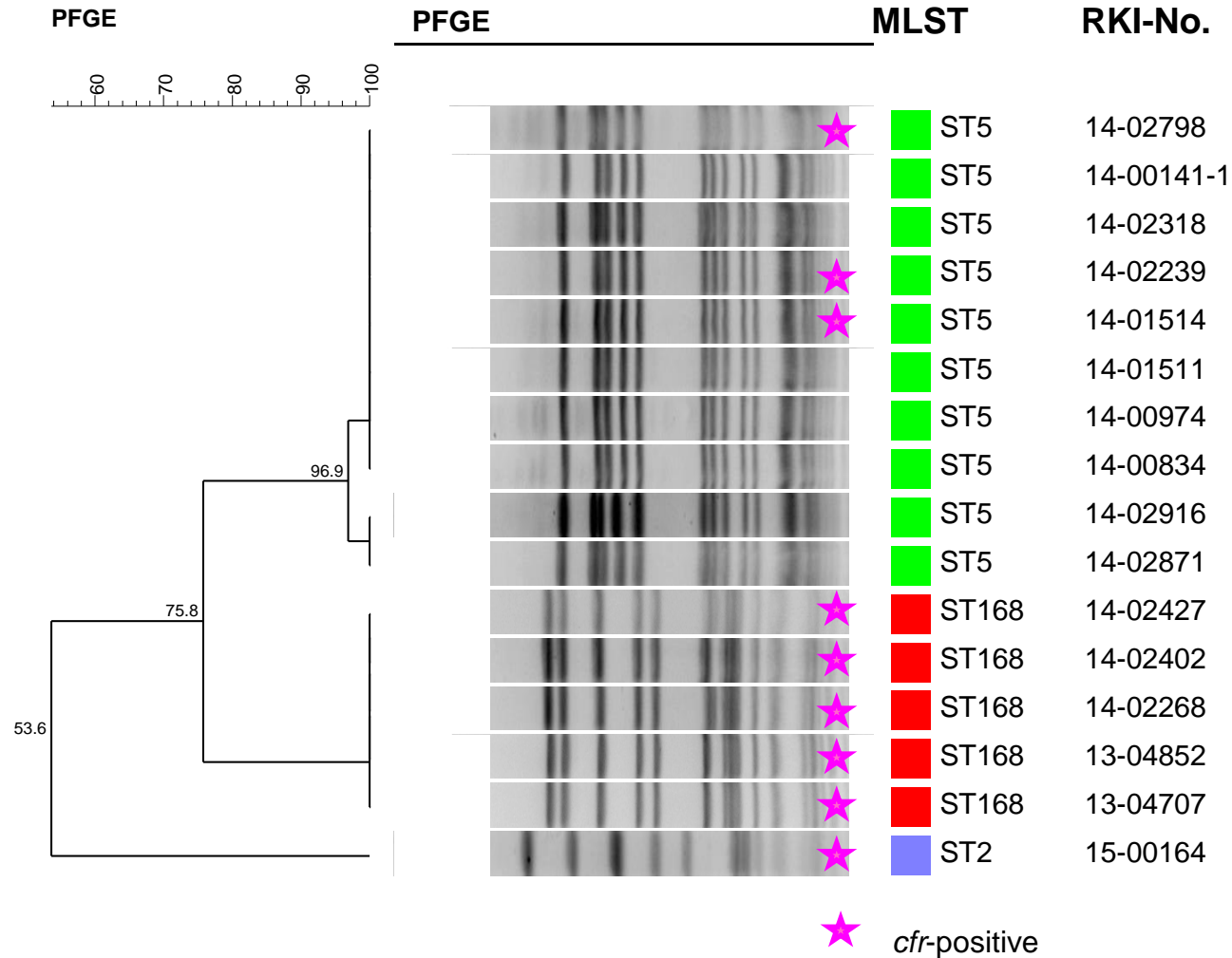
^bLinezolid consumption of the respective patient before the first LRSE was cultured. Linezolid doses of 600 mg/day were considered 1 DDD.

^cFor Patient 2, three LRSE isolates were sent to the NRC for further analysis.



Häufung von LRSE auf einer deutschen Intensivstation

- Ergebnisse der molekularen Typisierung





Häufung von LRSE auf einer deutschen Intensivstation

patient	Oct 13	Nov 13	Dec 13	Jan 14	Feb 14	Mar 14	Apr 14	May 14	Jun 14	Jul 14	Aug 14	Sep 14	Oct 14	Nov 14	Dec 14	Jan 15	strain characteristics*
1		29.10.2013 - 05.01.2014 D 08.11.2013 B* 22.11.2013 LZD															cfr-positive ST168
2			03.11.2013 - 14.03.2014 C* 02.01.2014 LZD			B* 07.03.2014 C* 18.03.2014 LZD											cfr-negative ST5
3		14.10.2013 - 02.01.2014 U* 12.12.2013 LZD															cfr-positive ST168
4					24.02. - 24.06.2014 C* 15.05.2014 LZD												cfr-negative ST5
5						09.05. - 18.06.2014 B (LZD-S) B* 18.04.2014 16.05.2014 LZD											cfr-positive ST5
6									26.06. - 16.08.2014 W* 21.07.2014 B 30.07.2014 LZD								cfr-positive ST5
7									11.06. - 03.07. + 14.07. - 05.08.2014 D* 22.07.2014 LZD								cfr-positive ST168
8										05.07. - 14.07.2014 B* 26.07.2014 LZD							cfr-negative ST5
9										27.06. - 10.11.2014 D* 01.08.2014 LZD							cfr-positive ST168
10										11.07. - 17.08.2014 B* 04.08.2014 LZD							cfr-positive ST168
11										28.08. - 20.08.2014 B* 07.09.2014 LZD							cfr-positive ST5
12											28.08. - 12.11.2014 S* 19.09.2014						cfr-negative ST5
13											27.06.2014 - 06.01.2015 DS* 18.09.2014 LZD						cfr-positive ST5
14															29.12.2014 - 20.01.2015 B* 08.01.2015 LZD		cfr-positive ST2

= ICU stay
 = LZD usage



cfr-positive



Häufung von LRSE auf einer deutschen Intensivstation

RKI-No.	MLST	MIC LZD mg/L	<i>cfr</i>	mutations in ribosomal genes / proteins								
				23SrRNA*	<i>rplC</i> (L3)			<i>rplD</i> (L4)			<i>rplV</i> (L22)	
13-04707	ST168	16	+	C2190T		Gly152Asp				-		-
13-04852	ST168	>256	+	C2190T		Gly152Asp				-		-
14-02268	ST168	>256	+	C2190T		Gly152Asp				-		-
14-02402	ST168	>256	+	C2190T		Gly152Asp				-		-
14-02427	ST168	n.d.	+	C2190T		Gly152Asp				-		-
14-00141-1	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-00834	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-00974	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-01511	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-01514	ST5	>256	+	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-02239	ST5	>256	+	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-02318	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-02798	ST5	>256	+	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-02871	ST5	>256	-	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
14-02916	ST5	>256	+	C2190T	His146Gln		Val154Leu	Ala157Arg	71-Gly-72	Ser81Arg	Asn158Ser	-
15-00164	ST2	8	+	C2190T						-		-

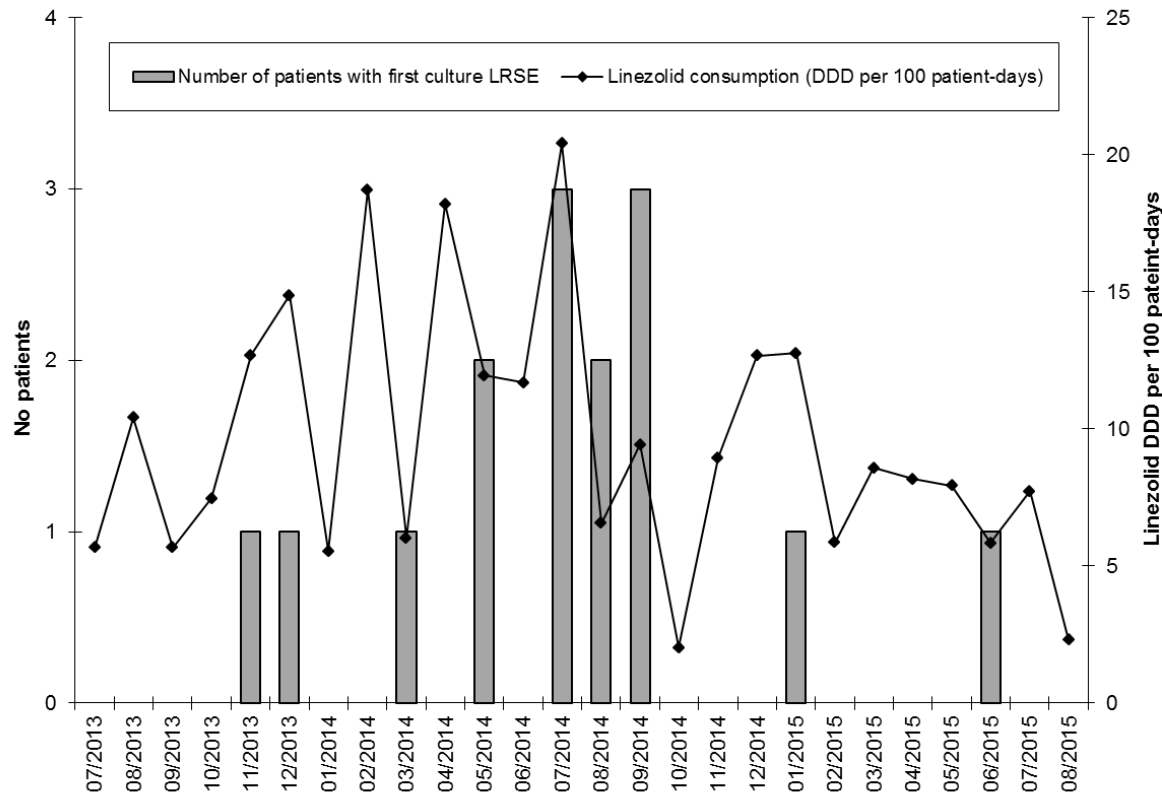
*the nucleotide positions of the mutations are listed according to *E. coli* numbering

- bekannte ribosomale Mutationen (neu Ser81Arg in L4)
- fast identische 39kb große *cfr*-Plasmide aus ST2, ST5, ST168; große Ähnlichkeit mit p12-02300 (C2)



Häufung von LRSE auf einer deutschen Intensivstation

■ Linezolid-Verbrauch auf der ICU



- 13/ 14 Patienten erhielten Linezolid (empirisch, VRE- bzw. MRSA-Infektionen)
- Anstieg von 5,55 DDDs/100 Patiententage (Januar 2014) auf 20,41 DDDs/100 Patiententage (Juli 2014)



Häufung von LRSE auf einer deutschen Intensivstation

Antibiotikaverbrauchsdaten ICU/ Krankenhaus

Table S2. Antibiotic consumption (DDD per 100 patient-days) of the effected hospital and ICU in comparison to reference values for Germany. Reference data from SARI^a were used for time spans. AVS^{b,c} reference values were used for annual benchmarks. (SARI surveillance of antibiotic use and bacterial resistance in ICUs, AVS Antibiotika-Verbrauchs-Surveillance)

	linezolid			vancomycin			glycopeptides	carbapenems	combination of penicillins and inhibitors
	2009-2013	2013	2014	2009-2013	2013	2014	2014	2014	2014
hospital	0.76 (0.6;1.1) median (min;max)		1.2	1.02 (0.81;1.48) median (min;max)		1.1	1.2	4	26.9
reference value for German hospitals			0.51 mean, AVS ^b			0.69 mean, AVS ^b	0.6 (0.4-0.8) median (IQR), AVS ^c	2.1 (1.4-3.0) median (IQR), AVS ^c	15.1 (11.1-19.4) median (IQR), AVS ^c
ICU	5.72 (3.4;8.5) median (min;max)	8.5	11.1	3.36 (2.92;6.99) median (min;max)	6.99	5.4	5.9	26	29.6
reference value for German ICUs	3.27 median, SARI ^a	2.78 mean, AVS ^b		2.28 median, SARI ^a	1.94 mean, AVS ^b		2.1 (1.1-3.6) median (IQR), AVS ^c	15.5 (10.7-20.5) median (IQR), AVS ^c	27.9 (22.7-35.2) median (IQR), AVS ^c

a: SARI: Surveillance of antibiotic use and bacterial resistance in German intensive care units 2012-2016; <http://www.sari-antibiotika.de>

b: Robert Koch-Institut: AVS, Antibiotika Verbrauchs Surveillance 2015: <http://avs.rki.de>, data status: 07.11.2017

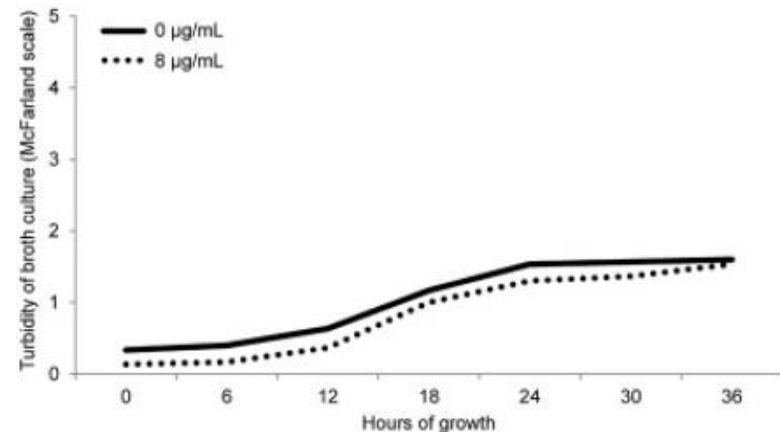
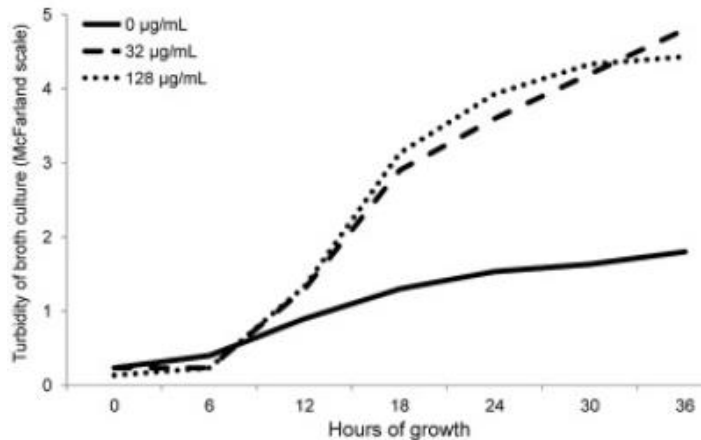
c: Marcel Feig, Michael Behnke, Luis Alberto Pena Diaz et al, Antibiotic consumption in German acute care hospitals: first data of a new web-based national surveillance system, 27th ECCMID Vienna, Austria, 22.-25. April 2017, Session: EV023 Pharmacoepidemiology, improved prescribing and antibiotic stewardship.

- der Antibiotikaverbrauch der ICU und des Krankenhauses überschritt verschiedene Referenzlevel
- Antibiotic Stewardship für adäquaten Antibiotikaeinsatz notwendig



Linezolid-abhängiges Wachstum klinischer LRSE

- LRSE werden in griechischen Krankenhäusern vermehrt nachgewiesen (2011-2013)
- vor allem LRSE ST22; diese zeigen zum größten Teil ein Linezolid-abhängiges Wachstum (Pournaras *et al.* EID 2013, Karavassilis *et al.*, J Antimicrob Chemother. 2015)



Growth curve of a representative LZD-dependent and a LZD-non-dependent isolate.

- in Anwesenheit von Linezolid ist die katalytische Aktivität der Peptidyltransferase von Ribosomen Linezolid-abhängiger LRSE höher (Kokkori *et al.* AAC 2014)



Linezolid-abhängiges Wachstum klinischer LRSE

(Layer *et al.*, J Antimicrob Chemother. 2018)

Index no./ hospital	Culture site	Infection	MLST ^a	cfr gene	Linezolid					
					MIC (mg/L)	treatment	23S rRNA	Protein L3	Protein L4	Protein L22
12-00322/C	blood	sepsis	ST22	+	16	NA	C2161T	Leu101Val Ala157Arg	WT	WT
12-01569/D	urine	UTI	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
12-02439/D	blood	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
12-03718/D	NA	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
12-03723/D	blood	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
13-00905/E	blood	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln InsHis138	WT
13-01045/E	NA	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
13-01084/H	NA	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT
14-03576/Y	blood	NA	ST2	-	>256	NA	C2190T C2561T G2603T	-	Ser61Arg Asn158Ser	WT
14-03623/Y	NA	decubitus	ST2	+	12	+	C2190T	-	-	WT
14-01514/Y	blood	endocarditis	ST5	+	>256	+	C2190T	His 146Gln Val154Leu Ala157Arg	Ser61Arg Asn158Ser	WT
14-00183/Y	NA	NA	ST23	-	8	+	C2190T	-	Ser61Arg Asn158Ser	WT
14-02427/Y	blood	NA	ST168	+	>256	+	C2190T	Gly152Asp	-	WT
13-04707/Y	blood	sepsis	ST168	+	>256	+	C2190T	Gly152Asp	-	WT

NA, data not available; UTI, urinary tract infection.

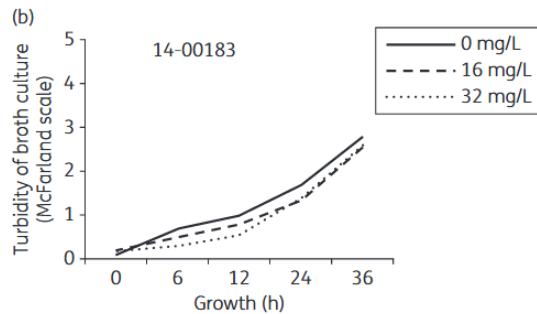
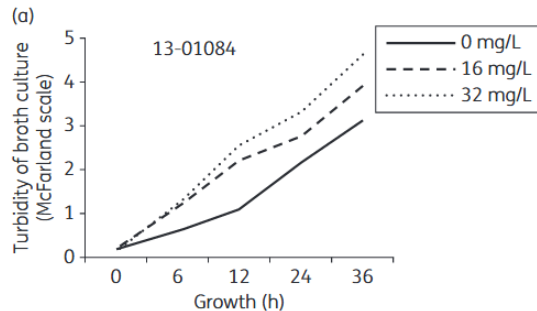
^aST2, ST5, ST22 and ST168 belong to CC5.

- 14 klinische LRSE (2012-2014) aus fünf verschiedenen Krankenhäusern
- unterschiedliche klonale Linien
- Wachstumskurven (16 und 32 mg/L LZD)



Linezolid-abhängiges Wachstum klinischer LRSE

(Layer *et al.*, J Antimicrob Chemother. 2018)



Growth curve of a representative (a) LZD-dependent and a (b) LZD-non-dependent isolate

Index no./hospital	Culture site	Infection	MLST ^a	cfr gene	Linezolid		23S rRNA	Protein L3	Protein L4	Protein L22	Linezolid dependence
					MIC (mg/L)	treatment					
12-00322/C	blood	sepsis	ST22	+	16	NA	C2161T	Leu101Val Ala157Arg	WT	WT	no
12-01569/D	urine	UTI	ST22	-	>256	NA	C2161T T2502A	Leu101Val Gly152Asp	Glu128Ala Gln174Arg	WT	yes
12-02439/D	blood	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Arg182Gln Glu128Ala Gln174Arg	WT	yes
12-03718/D	NA	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT	yes
12-03723/D	blood	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT	yes
13-00905/E	blood	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT	yes
13-01045/E	NA	NA	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT	yes
13-01084/H	NA	sepsis	ST22	-	>256	NA	C2161T T2502A C2532T	Leu101Val Gly152Asp Asp159Tyr	Glu128Ala Gln174Arg Arg182Gln	WT	yes
14-03576/Y	blood	NA	ST2	-	>256	NA	C2190T C2561T G2603T	- -	Ser61Arg Asn158Ser	WT	yes
14-03623/Y	NA	decubitus	ST2	+	12	+	C2190T	-	-	WT	no
14-01514/Y	blood	endocarditis	ST5	+	>256	+	C2190T	His 146Gln Val154Leu Ala157Arg	Ser61Arg Asn158Ser	WT	yes
14-00183/Y	NA	NA	ST23	-	8	+	C2190T	-	Ser61Arg Asn158Ser	WT	no
14-02427/Y	blood	NA	ST168	+	>256	+	C2190T	Gly152Asp	-	WT	yes
13-04707/Y	blood	sepsis	ST168	+	>256	+	C2190T	Gly152Asp	-	WT	no

NA, data not available; UTI, urinary tract infection.

^aST2, ST5, ST22 and ST168 belong to CC5.

- 10 Isolate zeigen Linezolid-abhängiges Wachstum



Zusammenfassung

- das NRZ erhält verstärkt Linezolid-resistente *S. epidermidis* (LRSE)
- ca. 30% der LRSE sind *cfr*-positiv
- LRSE tragen verschiedene ribosomale Mutationen, die ebenfalls eine Resistenz gegen Linezolid bedingen können
- *cfr* befindet sich auf bekannten aber auch neuen Plasmiden, diese sind zum Teil übertragbar
- LRSE im Rahmen von Häufungen:
 - klonale Verbreitung bestimmter Stämme
 - Übertragung *cfr*-assoziierter Plasmide wahrscheinlich
- LRSE aus deutschen Krankenhäusern weisen zum Teil ein Linezolid-abhängiges Wachstum auf
- Selektion und Ausbreitung Linezolid-resistenter Stämme wird durch den verstärkten Einsatz von Linezolid begünstigt



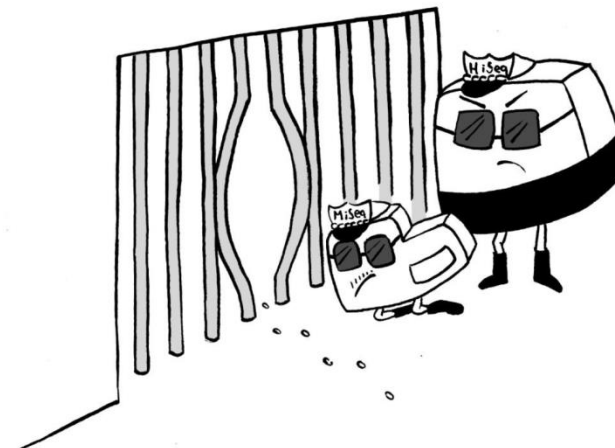
Danke!

- allen einsenden Laboren für die interessanten Stämme
- nationalen und internationalen Kooperationspartnern
- Mitarbeitern des NRZ und Fachgebietes



Quelle: RKI / Fokus-Fotostudio Wernigerode

"COULD BE AN OUTBREAK!"



NGS: MIAMI

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