ABSSSI e fascite necrotizzante

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AO Santa Croce e Carle
Cuneo

Il sottoscritto Valerio Del Bono ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009

dichiara

che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

MSD
Advanz
Correvio
Angelini
Biotest
Thermo Fischer

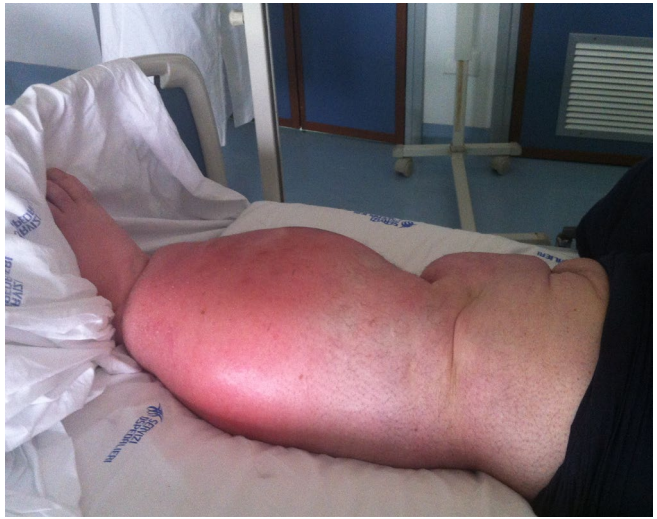
FDA definitions for cSSTIs

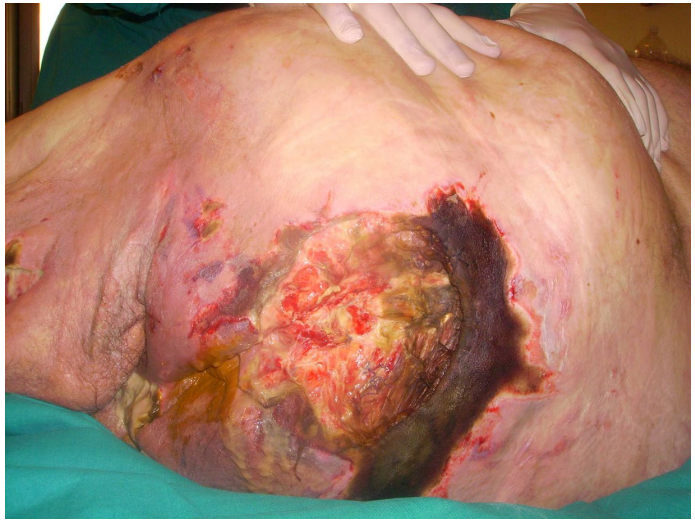
- coinvolgimento dei piani profondi
- manifestazioni cliniche di sepsi
- immunodepressione del paziente
- necessità di intervento chirurgico

An ABSSSI is defined as a bacterial infection of the skin with a lesion size area of at least 75 cm_2 (lesion size measured by the area of redness, edema, or induration)

Casistica Malattie Infettive AO S.Croce e Carle, Cuneo

- **Ricoveri 2019** **586**
- **SSTI** **59 (10%)**
- **Degenza media rep** **10,7 gg**
- **Degenza media SSTI** **14,5 gg**
- **DRG medio rep** **1,90**
- **DRG medio SSTI** **1,42**





Score LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis)

Indici di laboratorio	*Score (≥ 6 forte sospetto di FN)*
➢PCR >150	4 punti
➢GB >15.000 < 25.000	1
➢GB > 25.000	2
➢Na ≤ 135	1
➢Creatinina ≥ 1.6	2
➢Glucosio ≥ 180	2

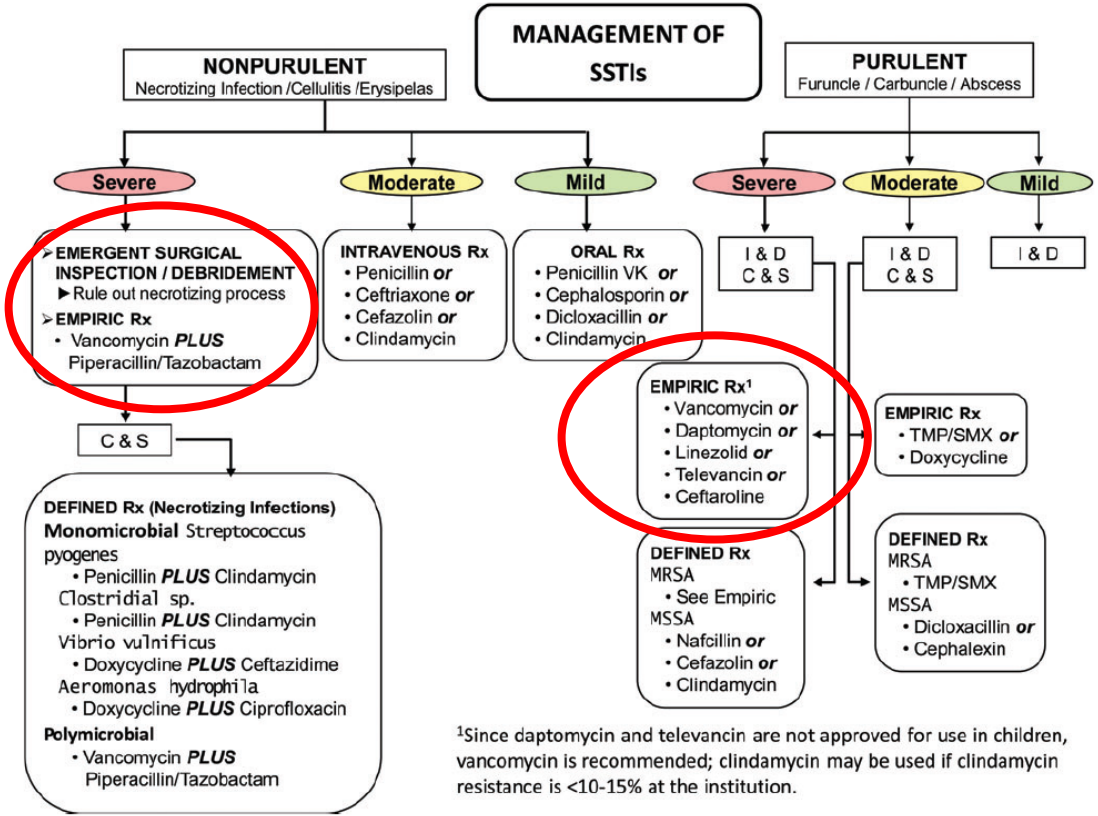
Approccio terapeutico

Clinical Infectious Diseases Advance Access published June 18, 2014

IDSA GUIDELINE

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,[1] Alan L. Bisno,[2] Henry F. Chambers,[3] E. Patchen Dellinger,[4] Ellie J. C. Goldstein,[5] Sherwood L. Gorbach,[6] Jan V. Hirschmann,[7] Sheldon L. Kaplan,[8] Jose G. Montoya,[9] and James C. Wade[10]



[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

caveat

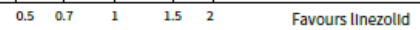
- ***Vancomicina*** **bassa batteriocidia, performance inferiore a betalattamici vs MSSA, finestra terapeutica ristretta, prevedibile fallimento clinico con MIC per *S.aureus* ≥ 1.5**

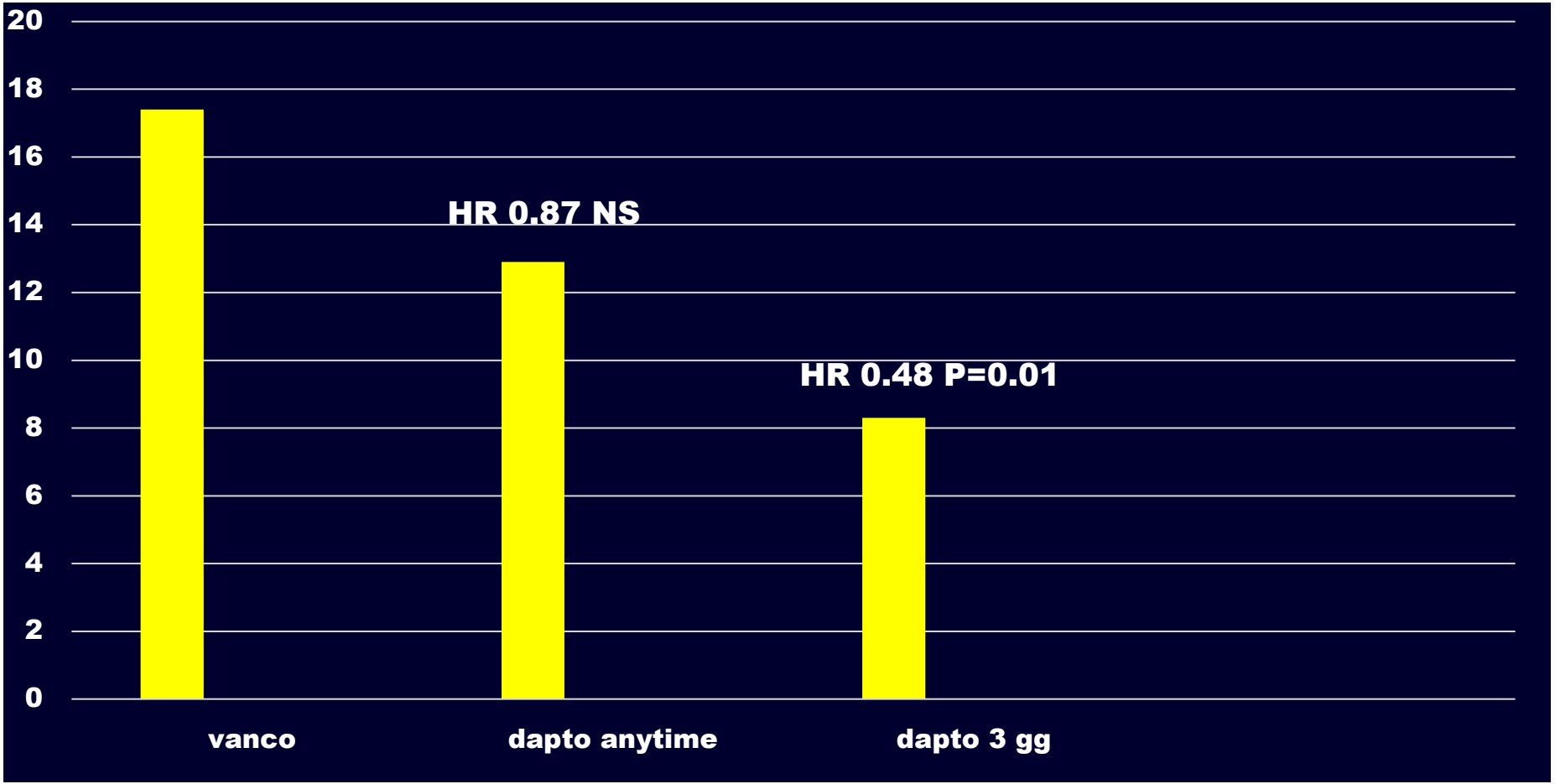
Linezolid versus vancomycin for skin and soft tissue infections

Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD008056

Analysis 1.1. Comparison 1 Clinical cure, Outcome 1 All participants.

Study or subgroup	Linezolid n/N	Vancomycin n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Itani 2010	223/537	196/515		23.11%	1.09[0.94,1.27]
Jaksic 2006	19/27	14/20		1.86%	1.01[0.69,1.47]
Kohno 2007	14/31	6/17		0.9%	1.28[0.6,2.71]
Lin 2008	30/33	19/29		2.34%	1.39[1.04,1.85]
Sharpe 2005	15/30	6/30		0.69%	2.5[1.12,5.56]
Stevens 2002	64/122	54/108		6.62%	1.05[0.81,1.35]
Weigelt 2005	439/592	402/588		46.59%	1.08[1.01,1.17]
Wilcox 2009	123/164	113/151		13.59%	1[0.88,1.14]
Yogev 2003	64/80	28/40		4.31%	1.14[0.91,1.44]
Total (95% CI)	**1616**	**1498**		**100%**	**1.09[1.03,1.16]**
Total events: 991 (Linezolid), 838 (Vancomycin)					
Heterogeneity: $Tau^2=0$; $Chi^2=9.19$, df=8(P=0.33); $I^2=12.98\%$					
Test for overall effect: Z=3.06(P=0)					




20
18
16
14
12
10
8
6
4
2
0
HR 0.87 NS
HR 0.48 P=0.01
vanco
dapto anytime
dapto 3 gg

Drug	*Design*	*Comparator*	*Main results*	*Ref*
CPT 600 mg BID	RCT, double blind, NI	VAN +ATM	NI reached	Corey, CID 2010
ICL 80 mg BID	RCT, double blind, NI	VAN	NI reached	Huang, CID 2018
DLX 300 mg BID x 3 dd + 450 mg OD	RCT, double blind, NI	VAN + ATM	NI reached	O'Riordan, CID 2018
TZD 200 mg OD 6 dd	RCT, double blind, NI	LZD (10 dd)	NI reached	Prokocimer, JAMA 2013
DAL 1000 mg D1 + 500 mg D 8	RCT, double blind, NI	VAN	NI reached	Boucher, NEJM 2014
ORI 1200 mg single dose	RCT, double blind, NI	VAN	NI reached	Corey, NEJM 2014
OMC IV→oral (100 mg BID LD, then 100 QD, 300 mg orally after 3 dd) OMC oral (450 mg QD x 2 dd, then 300 QD)	RCT, double blind, NI	LZD	NI reached	O'Riordan NEJM 2019 O'Riordan LID 2019
BPR 500 mg TID	RCT, double blind, NI	VAN + ATM	NI reached	

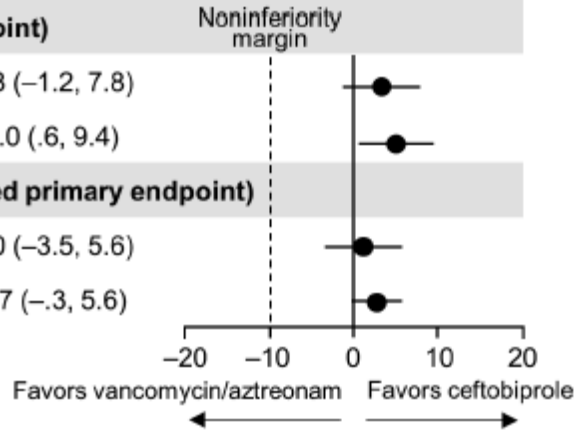
Ceftobiprole Compared With Vancomycin Plus Aztreonam in the Treatment of Acute Bacterial Skin and Skin Structure Infections: Results of a Phase 3, Randomized, Double-blind Trial (TARGET)

Clinical Infectious Diseases 2021;73(7):e1507–17

679 pazienti
335 BPR (500 mg x 3)
344 VAN + ATM (1g x 2)
Primary endpoints
FDA: *early clinical response* at 48–72 hrs (20% or greater reduction from baseline in the area of the primary lesion, survival for 72 hours or more from the initiation of the study drug, no unplanned surgical procedures for the ABSSSI after the start of treatment).
EMA: *investigator-assessed clinical success* at the TOC visit, both in the ITT and CE populations. Clinical success was defined as complete, or near complete, resolution of baseline signs and symptoms of the primary infection, with no further need for antibacterial treatment.
Secondary:
80% or greater reduction in lesion area at the EOT visit and
90% or greater reduction at the TOC visit

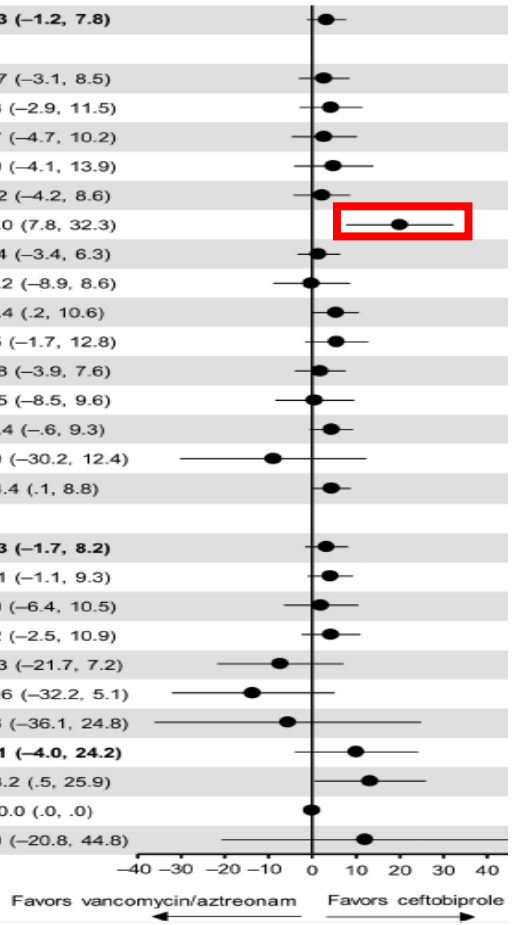
NI margin 10%

	Ceftobiprole n/N (%)	Vancomycin/ aztreonam n/N (%)	Adjusted difference (ceftobiprole minus vancomycin/aztreonam) (95% CI)[a]
Early clinical response (FDA-defined primary endpoint)			
ITT	306/335 (91.3)	303/344 (88.1)	3.3 (–1.2, 7.8)
CE[b]	267/283 (94.3)	262/293 (89.4)	5.0 (.6, 9.4)
Investigator-assessed clinical success (EMA-defined primary endpoint)			
ITT	302/335 (90.1)	306/344 (89.0)	1.0 (–3.5, 5.6)
CE	277/283 (97.9)	279/293 (95.2)	2.7 (–.3, 5.6)



(A) Early clinical response (FDA-defined primary endpoint)

		Ceftobiprole n (%)	Vancomycin/ aztreonam n (%)	Adjusted difference (ceftobiprole minus vancomycin/aztreonam) (95% CI)[a]
ITT population				
Overall		**306 (91.3)**	**303 (88.1)**	**3.3 (–1.2, 7.8)**
Subgroup analysis, n/N (%)				
Region	North America	185/203 (91.1)	190/215 (88.4)	2.7 (–3.1, 8.5)
	Europe	121/132 (91.7)	113/129 (87.6)	4.3 (–2.9, 11.5)
Baseline ABSSSI type	Wound infection	115/127 (90.6)	123/140 (87.9)	2.7 (–4.7, 10.2)
	Cellulitis erysipelas	99/112 (88.4)	93/111 (83.8)	4.9 (–4.1, 13.9)
	Major cutaneous abscess	92/96 (95.8)	87/93 (93.5)	2.2 (–4.2, 8.6)
Diabetes mellitus	Yes	36/36 (100.0)	35/42 (83.3)	20.0 (7.8, 32.3)
	No	270/299 (90.3)	268/302 (88.7)	1.4 (–3.4, 6.3)
Injection drug use	Current	94/108 (87.0)	102/117 (87.2)	–0.2 (–8.9, 8.6)
	Never	203/216 (94.0)	188/212 (88.7)	5.4 (.2, 10.6)
Fever	Yes	111/120 (92.5)	105/120 (87.5)	5.5 (–1.7, 12.8)
	No	194/214 (90.7)	198/224 (88.4)	1.8 (–3.9, 7.6)
Baseline WBC count	Abnormal	96/113 (85.0)	107/126 (84.9)	0.5 (–8.5, 9.6)
	Normal	210/222 (94.6)	196/218 (89.9)	4.4 (–.6, 9.3)
Baseline immature neutrophils	>10%	19/27 (70.4)	30/36 (83.3)	–8.9 (–30.2, 12.4)
	≤10%	261/275 (94.9)	245/271 (90.4)	4.4 (.1, 8.8)
mITT population				
Gram-positive	**Overall**	**213/228 (93.4)**	**220/244 (90.2)**	**3.3 (–1.7, 8.2)**
	Staphylococcus aureus	186/197 (94.4)	185/205 (90.2)	4.1 (–1.1, 9.3)
	MRSA	77/82 (93.9)	67/73 (91.8)	2.0 (–6.4, 10.5)
	MSSA	106/112 (94.6)	112/124 (90.3)	4.2 (–2.5, 10.9)
	β-Hemolytic streptococci	23/26 (88.5)	30/32 (93.8)	–7.3 (–21.7, 7.2)
	Streptococcus pyogenes	17/20 (85.0)	23/24 (95.8)	–13.6 (–32.2, 5.1)
	Viridans streptococci	14/17 (82.4)	15/17 (88.2)	–5.6 (–36.1, 24.8)
Gram-negative	**Overall**	**26/27 (96.3)**	**33/37 (89.2)**	**10.1 (–4.0, 24.2)**
	Enterobacterales	16/16 (100.0)	24/27 (88.9)	13.2 (.5, 25.9)
	Klebsiella spp.	9/9 (100.0)	10/11 (90.9)	0.0 (.0, .0)
	Pseudomonas spp.	7/7 (100.0)	4/5 (80.0)	12.0 (–20.8, 44.8)



Terapia empirica per SSTI

Emocolture o altri esami colturali prima di inizio antibiotico

SSTI non complicata

↓

Terapia orale (se possibile)
Amoxi-clavulanico (LZD, TDZ, DLX, CTX, DOXI se FR per MRSA)

oppure

Terapia e.v. "leggera"
Ceftriaxone (amoxi-clavulanico,ampi-sulbactam, cefazolina)

SSTI complicata, FR per MDR

(comorbidità, associazione con pratiche assistenziali, FR per MRSA)

↓

Terapia e.v.

↓

***Vanco o Teico (??)*, Dapto, Ceftarolina, Ceftobiprolo* +/- copertura per Gram neg e anaerobi (clinda)**

**** Non indicazione in RCP***

↘ ↙

Rivalutazione dopo 3-5 gg, de-escalation, switch per os, Dalba/Orita per dimissione rapida

E le infezioni del piede diabetico?

- **Possibile utilizzo nuovi farmaci (ceftobiprolo, delafloxacina) in monoterapia (con switch a terapia orale)?**
- **Oppure long-acting in associazione con anti gram neg?**

Grazie per l'attenzione!