

Sistema Socio Sanitario



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ASST Santi Paolo e Carlo

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Predictors of treatment choice in the management of ABSSSIs. (Dalbavancin versus SoC)



UNIVERSITÀ
DEGLI STUDI
DI MILANO

LA STATALE

ABSSSI: how to manage

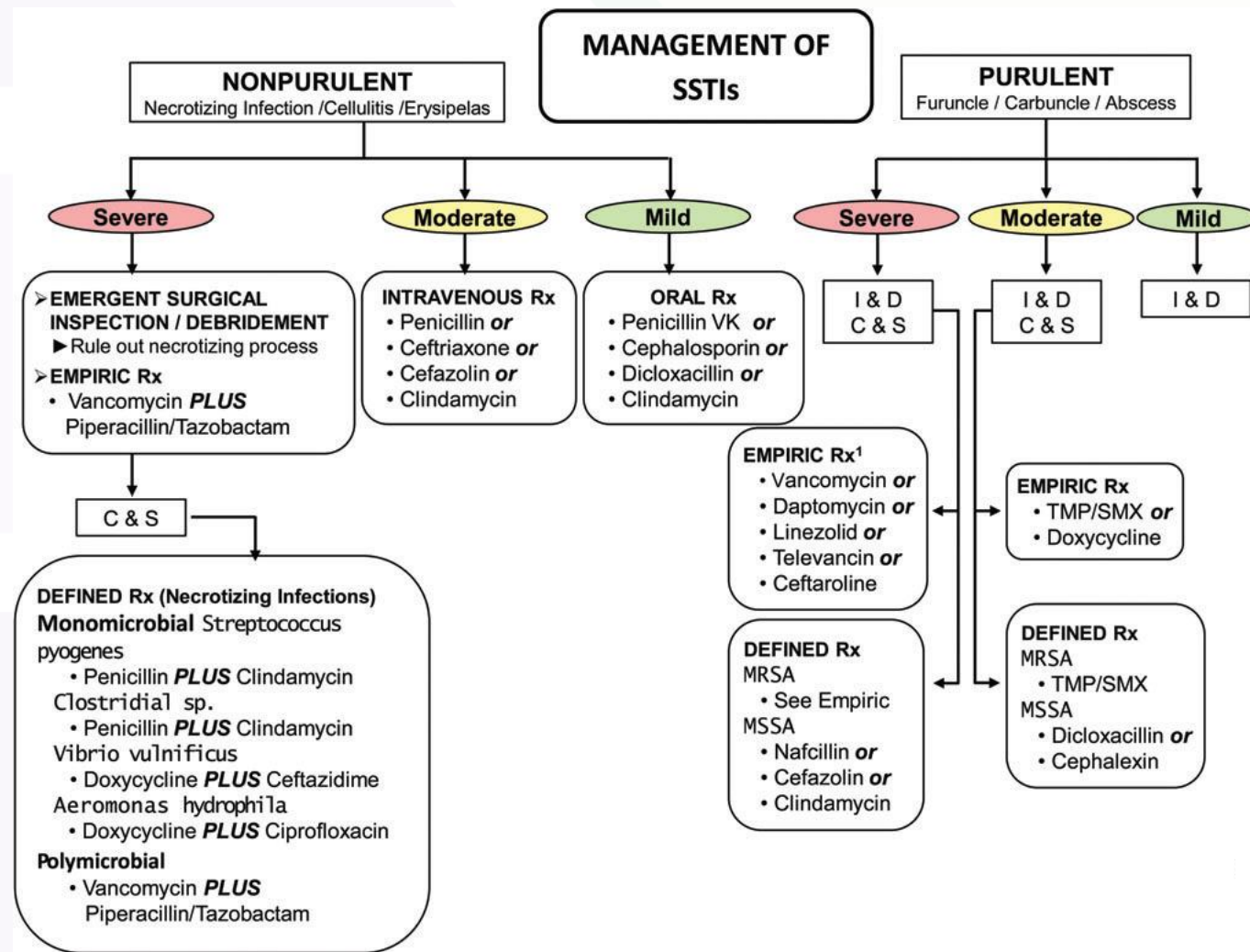
IDSA GUIDELINE

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. Wade¹⁰

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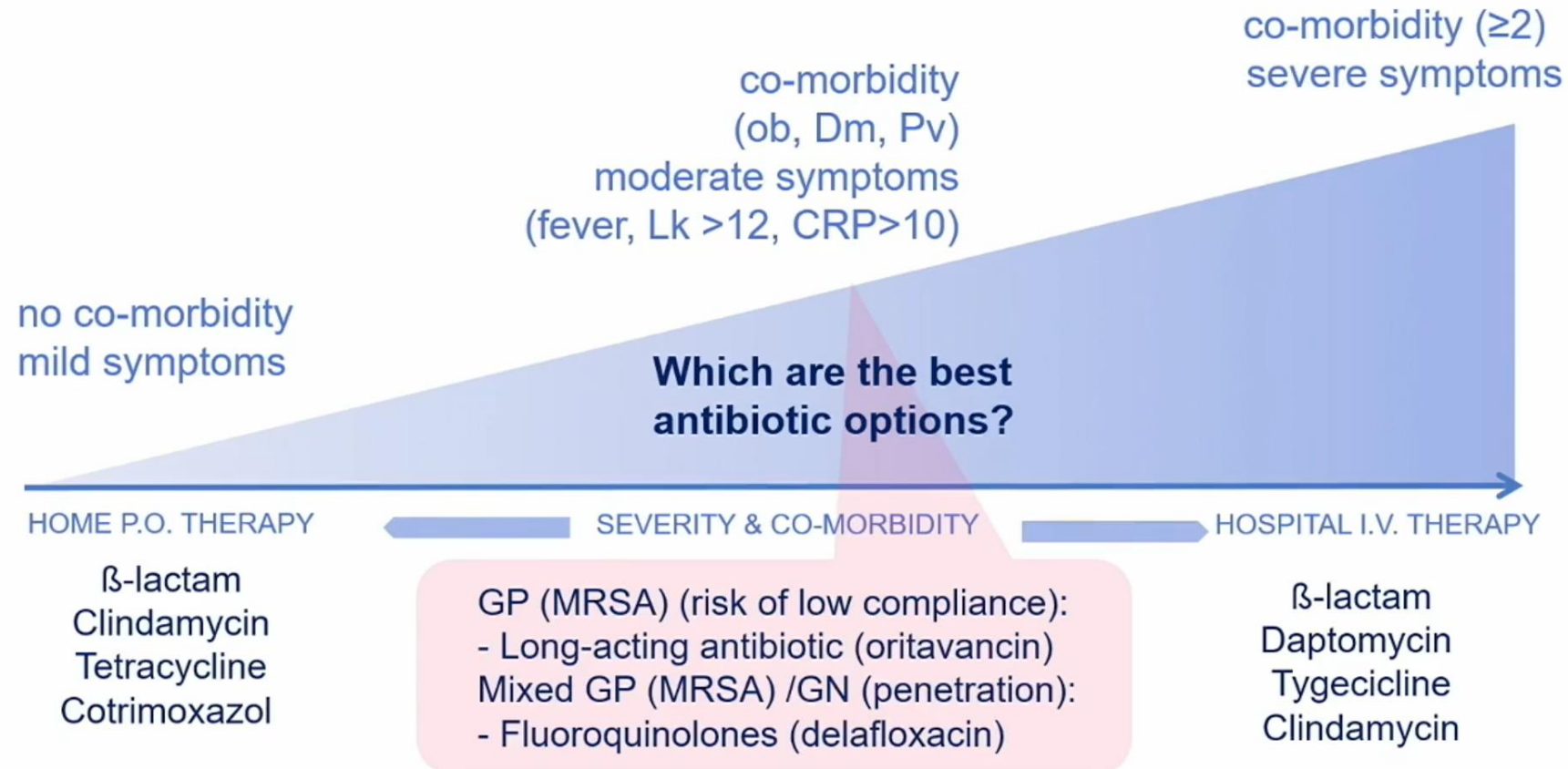
	PURULENT	NON PURULENT
MILD	Purulent SSTI	typical cellulitis/erysipelas with no focus of purulence
MODERATE	Purulent SSTI with systemic sign of infection*	typical cellulitis/erysipelas with systemic signs of infection*
SEVERE	Patients who have failed incision and drainage plus oral antibiotics or those with systemic signs of infection*, or immunocompromised patients	Patients who have failed oral antibiotic treatment or those with systemic signs of infection*, or those who are immunocompromised, or those with clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction.



* temperature >38°C, tachycardia (heart rate >90 beats per minute), tachypnoea (respiratory rate >24 breaths per minute) or abnormal white blood cell count (<12 000 or <400 cells/μL)

BACKGROUND

Potential antibiotic strategies for patients with SSTI



DALBAVANCIN: Bactericidal activity and good antimicrobial profile.

- Dalbavancin forms a stable complex with the C-terminal D-alanyl-D-alanine subgroup in the peptidoglycan, interfering with cell wall synthesis;
- Bactericidal activity
- It has an antimicrobial profile comparable to older glycopeptides:
 - *S. aureus* (MRSA)
 - *S. pyogenes*, *S. agalactiae* (also MDR)
 - *E. faecalis*, *E. faecium* (even ampicillin-R)
- In vitro activity against:
 - VISA
 - *Enterococcus* spp vancomycin-R (Van-B)

<https://www.ema.europa.eu/en/medicines/human/EPAR/xydalba>

DALBAVANCIN: Bactericidal activity and good antimicrobial profile.

- **Dosing:** 1 dose 1500 mg (or 2 dose: 1st dose 1000 mg; 2nd dose 500 mg)
- **Half-life:** 346 h
- **Dalbavancin** has demonstrated **non-inferiority** compared to standard of care (**SoC**) antibiotics in the treatment of ABSSSI in randomized controlled trials and observational real-life studies.
- However, **in real-life setting** this long-acting antibiotic **is often used in second or higher line of treatment** and in **combination** with other antibiotics; furthermore, reasons of dalbavancin use in clinical practice may be different compared to SoC.

*New Engl J Med. 2014 Jun 5;370(23):2169-79. doi: 10.1056/NEJMoa1310480.
Clin Infect Dis. 2016 Mar 1;62(5):545-51. doi: 10.1093/cid/civ982. Epub 2015 Nov 26.*

AIM of the study:

- To investigate **efficacy and safety** of dalbavancin vs SOC in treatment of ABSSSI
- To investigate **predictors of treatment choice** (dalbavancin vs SoC) for ABSSSI

STUDY DESIGN

- **Retrospective** cohort study
- **STUDY POPULATION**: Patient diagnosed with ABSSSIs (both hospitalized and outpatients) at San Paolo Hospital, ASST Santi Paolo e Carlo, Milan, from March 2016 to April 2023
- **OUTCOMES**:
 - Primary: efficacy (clinical recovery vs death vs recurrence/not symptoms resolution at end of treatment) comparing Dalbavancin and SoC
 - Secondary: Factors associated with clinical recovery at end of treatment
- Demographic and clinical characteristics will be collected from clinical records (age, gender, comorbidities, type of ABSSSI, setting: hospitalization, outpatient service, blood test at ABSSSI diagnosis and end of treatment, outcome at end of treatment, adverse events, date of start and date of end of antibiotic treatment)
- **STATISTICAL ANALYSIS**: Mann Whitney, Kruskal Wallis and Chi-square test – logistic regression analysis to investigate predictors of clinical recovery.
 - A logistic regression model will be used including variables hypothesized to be determinants of antibiotic treatment and propensity scores for dalbavancin and SoC initiation will be derived from this logistic regression model

1.1. Demographic and clinical characteristics of patients diagnosed with ABSSSI and comparison between DALBAVANCIN and SOC

Characteristics	Study population N 220	Dalbavancin N 80 (36.4%)	SOC N 140 (63.6%)	p value
Female, n (%)	100 (45.5%)	44 (55%)	56 (40%)	0.032
Age, median (IQR)	56 (43-71)	57 (45-69)	54 (42-72)	0.663
BMI, median (IQR)	26 (23.5-31)	27 (24-32.9)	25.4 (23.2-29.6)	0.155
Comorbidities, n (%)	175 (79.5%)	63 (78.7%)	112 (80%)	0.514
ABSSSI, n (%):				
Abscess	49 (22.3%)	15 (18.8%)	34 (24.3%)	0.358
Erysipelas	38 (17.3%)	18 (22.5%)	20 (14.3%)	
Cellulitis	62 (28.2%)	19 (23.8%)	43 (30.7%)	
Wound infection	58 (26.4%)	24 (30%)	34 (24.3%)	
Animal bite	10 (4.5%)	3 (3.7%)	7 (5%)	
Unknown	3 (1.4%)	1 (1.2%)	2 (1.4%)	
ABSSSI site, n (%):				
Arms/Legs	139 (63.2%)	55 (68.8%)	84 (60%)	0.060
Face	40 (18.2%)	8 (10%)	32 (22.9%)	
Trunk	39 (17.7%)	16 (20%)	23 (16.4%)	
Unknown	2 (0.9%)	1 (1.2%)	1 (0.7%)	
Setting:				
Hospital admission	101 (45.9%)	25 (31.3%)	76 (54.3%)	0.001
Outpatient service	110 (50%)	51 (63.7%)	59 (42.1%)	
Unknown	9 (4.1%)	4 (5%)	5 (3.6%)	
Length of hospital stay, median (IQR)	7 (4-11)	7 (4-11)	6 (4-10)	0.651

RESULTS

1.2. Demographic and clinical characteristics of patients diagnosed with ABSSSI and comparison between DALBAVANCIN and SOC

Characteristics	Study population N 220	Dalbavancin N 80 (36.4%)	SOC N 140 (63.6%)	p value
BMI, n (%):				
Underweight	3 (1.4%)	1 (1.3%)	2 (1.4%)	0.554
Normal weight	37 (16.8%)	9 (11.3%)	28 (20%)	
Overweight	30 (13.6%)	11 (13.8%)	19 (13.6%)	
Obese	26 (11.8%)	11 (13.8%)	15 (10.7%)	
Unknown	124 (56.4%)	48 (60%)	76 (54.3%)	
Comorbidities, n (%):	N 175	N 63	N 112	
Cardiovascular diseases	96 (43.6%)	37 (58.7%)	59 (52.7%)	0.652
Chronic renal diseases	21 (9.5%)	10 (15.9%)	11 (9.8%)	0.447
Chronic liver disease	27 (12.3%)	6 (9.5%)	21 (18.8%)	0.253
Neurological diseases	29 (13.2%)	12 (19%)	17 (15.2%)	0.727
Diabetes	41 (18.6%)	12 (19%)	29 (25.9%)	0.555
Immunodeficiencies	24 (11%)	7 (11.1%)	26 (23.2%)	0.138
Age >65 years	70 (31.8%)	25 (39.7%)	45 (40.2%)	0.917
Other	110 (50%)	41 (65.1%)	69 (61.6%)	0.802

Blood exams at ABSSSI diagnosis, comparison between DALBAVANCIN and SOC

Blood exams	Study population N 220	Dalbavancin N 80 (36.4%)	SOC N 140 (63.6%)	p value
Hemoglobin, g/dL, median (IQR)	12.9 (11.4-14.3)	12.7 (11.6-13.9)	13.1 (11.3-14.4)	0.405
WBC/mmc, median (IQR)	11150 (74250-14777)	11490 (7495-15510)	10730 (7320-14160)	0.239
Platelets, 10*9/mmc, median (IQR)	241 (185-299)	249 (186-307)	231 (184-299)	0.523
Neutrophils/mmc, median (IQR)	8290 (4830-11710)	9105 (5687-12407)	7450 (4350-10705)	0.073
CRP, mg/L, median (IQR)	47.7 (21.3-102.3)	41.3 (17.6-102.6)	49.3 (25.5-100)	0.369
Procalcitonin, ug/L, median (IQR)	0.11 (0.04-0.66)	0.5 (0.08-6.27)	0.11 (0.03-0.56)	0.216
Creatinine, mg/dL, median (IQR)	0.8 (0.69-1.00)	0.8 (0.6-0.95)	0.89 (0.7-1.1)	0.046
Total bilirubin, mg/dL, median (IQR)	0.63 (0.45-0.89)	0.66 (0.45-0.87)	0.62 (0.45-0.89)	0.917

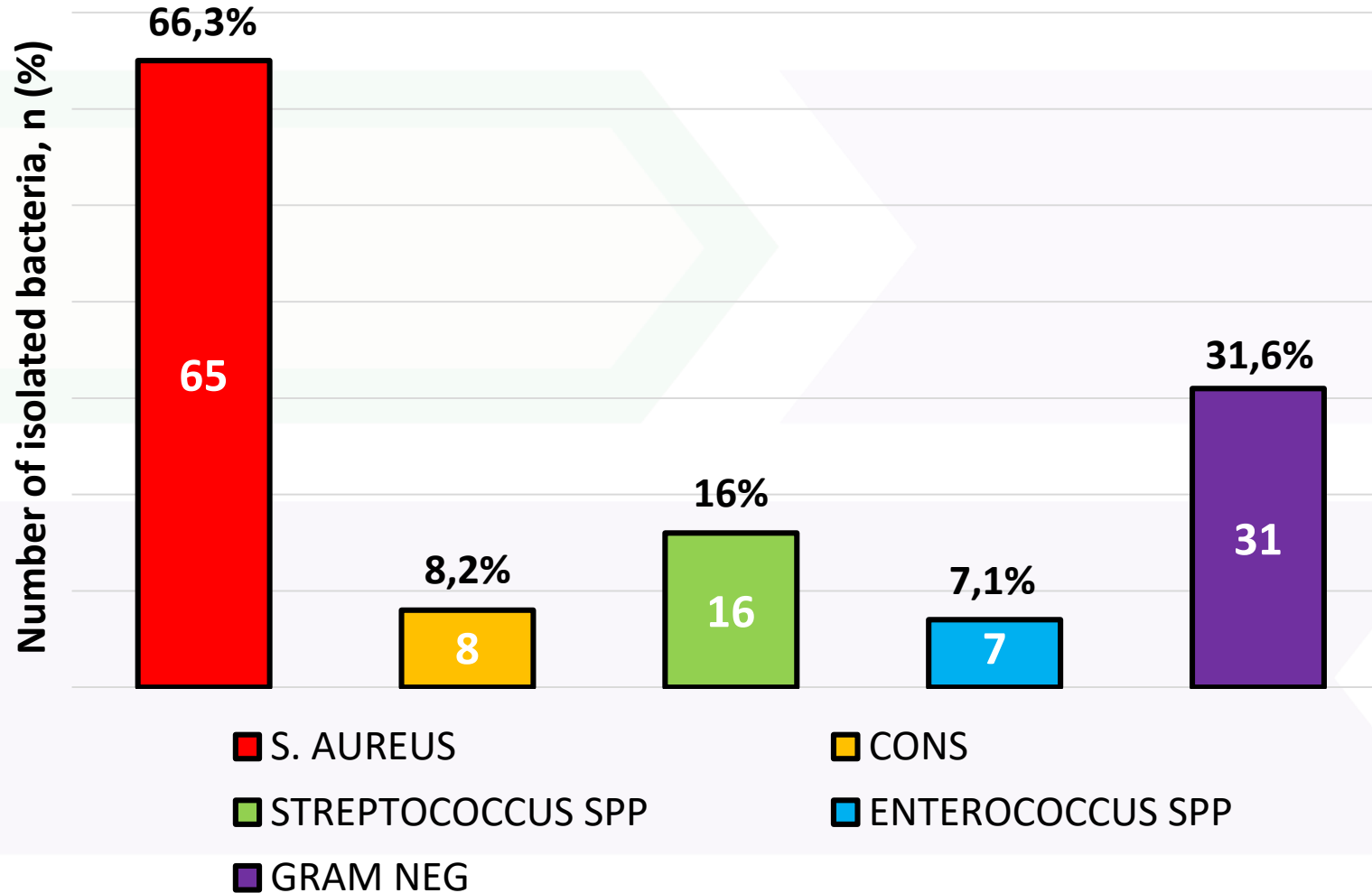
RESULTS

Microbiological data , comparison between DALBAVANCIN and SOC

Characteristics	Study population N 220	Dalbavancin N 80 (36.4%)	SOC N 140 (63.6%)	p value
Culture, n (%):	166 (75.5%)	59 (73.8%)	107 (79.9%)	0.301
Skin swab	73 (44%)	26 (44%)	47 (44%)	
Deep biopsy	41 (24.7%)	9 (15.2%)	32 (30%)	
Blood culture	85 (51.2%)	36 (61%)	49 (45.8%)	
Other	45 (27.1%)	15 (25.4%)	30 (28%)	
Isolation, n (%):				0.714
Yes	98/166 (59%)	35 (60.3%)	62 (57,4%)	
Gram, n (%):				1.000
positive	70 (71.4%)	25 (71.4%)	45 (71.4%)	
negative	14 (14.3%)	5 (14.3%)	9 (14.3%)	
mixed	14 (14.3%)	5 (14.3%)	9 (14.3%)	
Polymicrobial infections, n(%)	24 (24.5%)	9 (25.7%)	15 (23.8%)	0.834

RESULTS

Microbiological isolations in ABSSSI



DRUG-RESISTANT ISOLATIONS

MRSA → 36/98, 36.7% (**55.4%** of all S. Aureus isolations); more frequent on skin swab (22/36, 61,1%)

MRSE → 1/98, 1% (**1,2%** of all CoNS isolations); on blood culture.

VRE → 1/98, 1% (**1.4%** of all Enterococcus spp. Isolations); on blood culture.

RESULTS

Associated factors with Gram negative infections

Parameters	Gram pos N 70	Gram neg/mixed N 28	p value
Comorbidities	45 (64.3%)	27 (96.4%)	0.001
Age	50 (34-64)	57 (46-79.5)	0.047
LOS	6.5 (3.5-9)	14 (5.5-24.7)	0.056

RESULTS

Antibiotic treatment: number of antibiotic lines and combination therapy

Characteristics	Dalbavancin N 80	SOC N 140	p value
N lines, n (%):			
1	21 (26.3%)	63 (45%)	
2	41 (51.2%)	50 (35.7%)	0.002
3	15 (18.8%)	20 (14.3%)	
4	2 (2.5%)	5 (3.6%)	
5	1 (1.3%)	2 (1.4%)	
N lines, n (%):			0.003
1	20 (25%)	63 (45%)	
≥ 2	60 (75%)	77 (55%)	
Monotherapy, n (%)	63 (78.7%)	96 (68.6%)	0.075

RESULTS

Parameters to identify moderate/severe ABSSSI

Characteristics	Total population	Dalbavancin	SOC	p value
Age				
<70 yrs	164 (74.5%)	60 (75.9%)	104 (74.3%)	0.785
≥ 70 yrs	56 (25.5%)	19 (24.1%)	36 (25.7%)	
Comorbidities				
0	45/220 (20.5%)	17 (21.3%)	28 (20%)	0.952
1	49/220 (22.5%)	17 (21.3%)	32 (22.9%)	
≥2	126/220 (57.3%)	46 (57.5%)	80 (57.1%)	
Immunodeficiency	33	7 (11.1%)	26 (23.2%)	0.13
Diabetes	41	12 (19%)	29 (25.9%)	0.555
Cirrhosis/Liver disease	27	6 (9.5%)	21 (18.8%)	0.253
BMI ≥30	26 (11.8%)	11 (13.8%)	15 (10.7%)	0.554
WBC				
<12.000/mmc	115/192 (59.9%)	39 (53.4%)	76 (63.9%)	0.152
≥12.000/mmc	77/192 (40.1%)	34 (46.6%)	43 (36.1%)	
CRP				
<100 mg/L	137/187 (62.3%)	50 (70.4%)	87 (75%)	0.492
≥100 mg/L	50/187 (22.7%)	21 (29.6%)	29 (25%)	
Isolation (swab, biopsy, blood):				
MRSA	35/98 (15.9%)	16 (45.7%)	19 (30.2%)	0.124
Gram neg - mixed	28/98 (28.6%)	10	18	1.000
Positive blood culture	7/98 (7.1%)	3/35 (8.6%)	4/62 (6.4%)	0.123

RESULTS

Outcome of ABSSSI according to treatment (Dalbavancin vs SOC)

Characteristics	Study population N 220	Dalbavancin N 80	SOC N 140	p value
Outcome, n (%):				
Recovery	192 (87.3%)	64 (80%)	128 (91.5%)	0.005
Recurrence/Not resolution	26 (11.8%)	16 (20%)	10 (7.1%)	
Death	0	0	0	
Unknown	2 (0.9%)	0	2 (1.4%)	
Adverse events, n (%)	20 (9.1%)	8 (10.1%)	12 (8.6%)	0.701

Factors associated with clinical recovery by fitting a multivariable logistic regression analysis

Parameters	OR	95%CI	p	AOR	95%CI	p
Dalbavancin vs SOC	0.313	0.13-0.73	0.007	0.399	0.15-1.08	0.071
1 line vs ≥2 lines	2.232	0.86-5.81	0.100			
Combination vs monotherapy	0.67	0.28-1.599	0.367			
Age, each year more	0.977	0.95-1.001	0.056	0.983	0.94-1.02	0.362
Male vs female	1.717	0.75-3.93	0.201			
Hospital admission vs Outpatient	3.34	1.18-9.49	0.024	3.006	0.84-10.73	0.09
ABSSSI: Trunk Arms/legs Face	Ref 0.921 5.588	 0.32-2.65 0.62-50.25	 0.879 0.125			
WBC <12.000/mmc vs ≥12.000/mmc	0.579	0.23-1.47	0.251			
CRP <100 mg/L vs ≥100 mg/L	0.226	0.051-1.003	0.06			
Comorbidities: ≥2 1 None	Ref 8.113 1.623	 1.06-62.36 0.57-4.60	 0.044 0.363	Ref 3.879 0.734	 0.37-41.08 0.19-2.87	 0.260 0.656
BMI: Non obese Obese Unknown	Ref 0.039 0.084	 0.005-0.34 0.01-0.64	 0.017 0.003	Ref 0.044 0.162	 0.005-0.42 0.02-1.34	 0.007 0.091
MRSA: Yes vs no	0.497	0.13-1.94	0.314			
Gram: Pos vs Neg/mixed	1.685	0.5-5.68	0.400			

RESULTS

Limitations:

- **Small sample size**
- **Retrospective** study
- Unavailability of some data: fever, SIRS/sepsis, **characteristics of the lesion** (deepness, extension, oedema), comorbidities (presence of peripheral vasculopathy, IVDU), **surgical drainage** of abscesses, antibiotic length
- *Ongoing data collection*



CONCLUSIONS

- In our experience, Dalbavancin was administered more commonly as **second or more line of antibiotic treatment** and not always as monotherapy, thus losing its possible advantages (no hospital admission and cost savings)
- After adjusting for possible confounders, **efficacy of Dalbavancin was comparable to SoC** in the treatment of ABSSSI.
- In ABSSSI management a **better classification of patients according to severity and risk of gram-negative infection may help identify who deserves a LA therapy**, avoiding hospitalisation and improving patients' quality of life.

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TO BE CONTINUED ...

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