antibiotics

Clinical Use and Adverse Drug Reactions of Linezolid: A Retrospective Study in Four Belgian Hospital Centers

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Supplementary Material

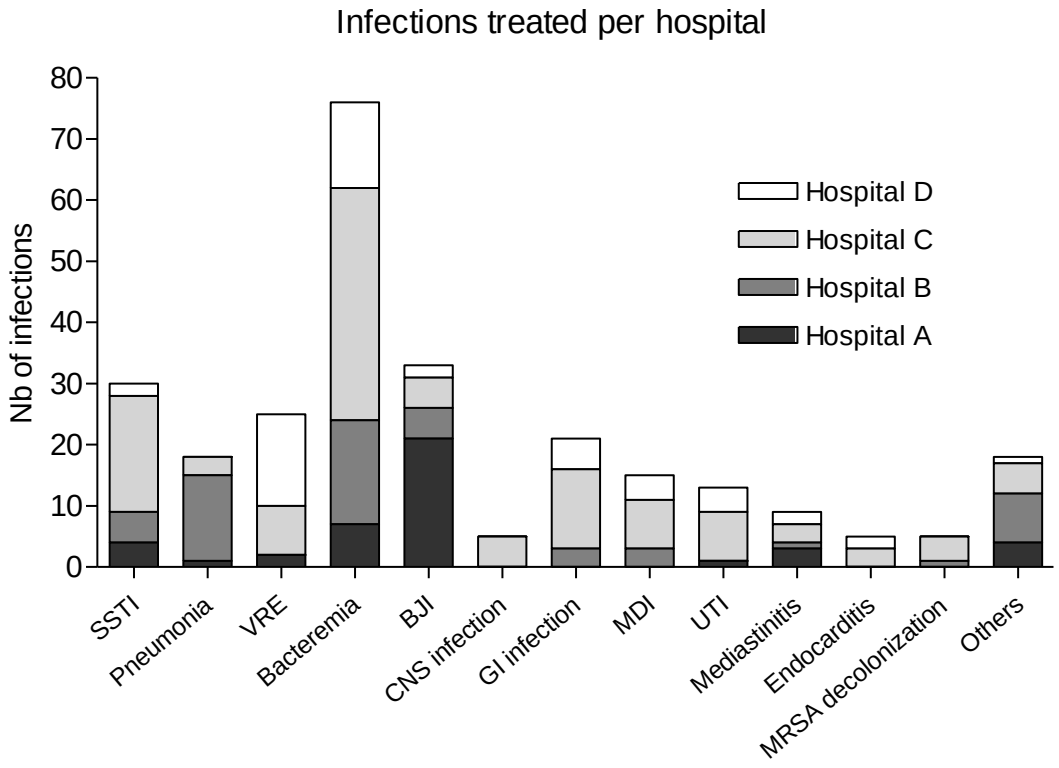


Figure S1: Distribution of the number of infections treated with linezolid among the 4 included hospital centers.
BJI, bone and joint infection; MDI, medical device infection; SSTI, skin and soft tissue infection; UTI, urinary tract infection; VRE, vancomycin-resistant Enterococcus. Each hospital is identified by a letter.

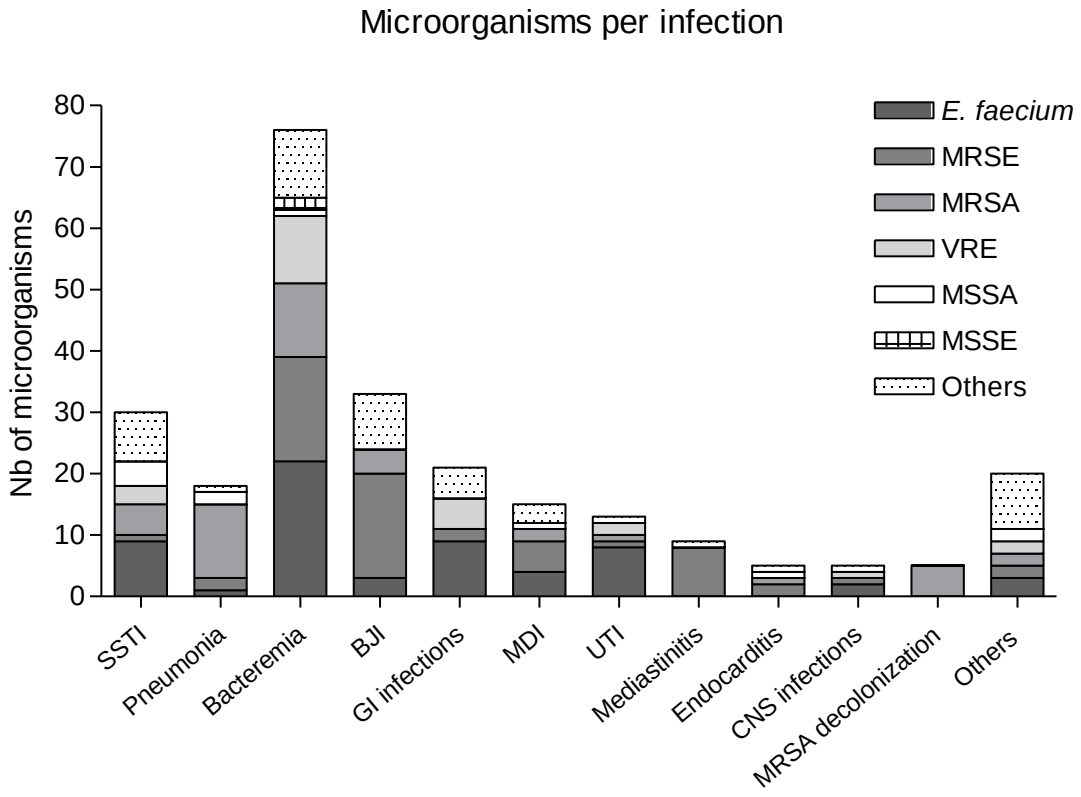


Figure S2: Distribution of the isolated microorganisms per type of infection.
BJI, bone and joint infection; CNS, central nervous system, MDI, medical infection; MRSA, methicillin resistant *Staphylococcus aureus*; MRSE, methicillin resistant *Staphylococcus epidermidis*; MSSA, methicillin sensitive *S. aureus*; MSSE, methicillin sensitive *S. epidermidis;* SSTI, skin and soft tissue infection; UTI, urinary tract infection.

Table S1. Characteristics of inpatients and outpatients

Parameters	Inpatients median (range) or nb (%)	Outpatients median (range) or nb (%)	P-value [1]
Renal function (GFR ml/min)	46.5 (10-196)	89 (15 – 195)	**0.000**
Treatment duration (days)	7 (1 – 52)	21 (2 – 90)	**0.000**
Basal platelet level	203 (1 – 1039)	297 (4 – 624)	**0.000**
Charlson index	2 (0 – 9)	2 (0-8)	0.059
Thrombocytopenia	26 (60.5)	17 (39.5)	0.142
Anemia	10 (58.8)	7 (41.2)	0.309

[1] Values in bold denote statistically significant differences ($p < 0.05$)

Table S2. Characteristics of patients with or without thrombocytopenia

Parameters	No Thrombocytopenia (n = 185) N (%) or median (range)	Thrombocytopenia (n = 43) N (%) or median (range)	P-value [3]
Male (%)	62.7	65.1	0.768
Age (year)	65 (21-95)	67 (26-86)	0.495
Weight (kg)	75 (34-178)	79 (48-132)	0.585
Body mass index (kg/m^2)	25.5 (15-47)	25.9 (16-48)	0.785
INpatients/OUTpatients	133/52	26/17	0.142
Diabetes (%)	51 (27.6)	19 (44.2)	**0.035**
Charlson index	3 (0-11)	4 (0-9)	**0.003**
GFR (ml/min)	58 (11-173)	46 (10-196)	0.087
Renal insufficiency (< 60 ml/min)	84 (52.5)	30 (69.8)	**0.043**
Treatment duration (days)	8 (1-90)	17 (3-53)	**0.000**
Basal platelet count (x10^3/ml)	243 (1-1039)	196 (29 – 507)	0.267
Previous treatment with vancomycin (%)	100 (54.1)	26 (60.5)	0.446
Route of administration (IV/PO)	81/104	19/24	0.962
Dose/Kg/Day	16 (6.7-35.3)	15.2 (9.1-25)	0.584
Isolated microorganism [1]			
MRSA (%)	29 (15.7)	8 (18.6)	0.639
VRE (%)	17 (9.2)	6 (14)	0.300
Staphylococcus aureus (%)	8 (4.3)	4 (9.3)	0.188
Enterococcus faecium (%)	55 (29.7)	10 (15.4)	0.397
Staphylococcus epidermidis (%)	50 (27)	8 (18.6)	0.390
Type of infection [2]			
Pneumonia (%)	13 (7)	1 (2.3)	0.247
SSTI (%)	20 (10.8)	8 (18.6)	0.161
Bone and joint infections (%)	27 (14.5)	4 (9.3)	0.356
Bacteremia (%)	56 (30.2)	13 (30.2)	0.996
Gastrointestinal infections (%)	15 (5.9)	5 (11.6)	0.469
Urinary tract infections (%)	9 (4.9)	2 (4.7)	0.953
IN/OFF label indication	32/153	8/35	0.839
Comedication			
Rifampin	10 (5.4)	3 (7)	0.715
Amiodarone	13 (7.1)	4 (9.3)	0.539
Amlodipine	23 (12.6)	8 (18.6)	0.301
Omeprazole	53 (29)	9 (20.9)	0.288
Pyridoxine	27 (11.8%)	7 (3.1%)	0.780
Anticancer therapy	15 (8.1%)	3 (7%)	0.797

[1] Only most frequent microorganisms are included in the table

[2] Only most frequent infections are included in the table

[3] Values in bold denote statistically significant differences

Table S3: Frequency of ADR in this study as compared to the incidence reported in the SmPC or the US label

Type of side effect	N (%)	ADR in European SmPC	ADR in US label (%)
Thrombocytopenia	43 (18.9)	≥ 1/1.000 to < 1/100	3 [1]
Anemia	17 (6.8)	≥ 1/100 to < 1/10	7.1 [1]
Gastrointestinal disorders	13 (5.2)	≥ 1/100 to < 1/10	8.3
Peripheral neuropathy	4 (1.6)	Indeterminate	Indeterminate [2]
Lactic acid serum level > 2.2mmol/L	4 (1.6)	Indeterminate	Indeterminate [2]
Paresthesia	4 (1.6)	≥ 1/1.000 to < 1/100	/ [3]
Skin disorders	3 (1.2)	≥ 1/100 to < 1/10	2.3
Fatigue	3 (1.2)	≥ 1/1.000 to < 1/100	1.8
Neutropenia	2 (0.8)	≥ 1/1.000 to < 1/100	1.1 [1]
Leucopenia	2 (0.8)	≥ 1/1.000 to < 1/100	2.2 [1]
Renal failure	1 (0.8)	≥ 1/1.000 to < 1/100	/ [3]
Taste alteration	1 (0.4)	≥ 1/100 to < 1/10	1
Serotonin syndrome	1 (0.4)	Indeterminate	Indeterminate [2]
SIADH	1 (0.4)	Indeterminate	/ [3]

[1] As mentioned in FDA label; defined as less than 75% of lower limit of normal and or/baseline. No significant difference between the comparators and linezolid in phase III comparator-controlled clinical trials.

[2] Frequency of these ADR is not reported in US label as observed in postmarketing experience.

[3] Not mentioned in the SmPC

Table S4: Comorbidities included in Charlson comorbidity index and identified in patients with thrombocytopenia

		Patients with thrombocytopenia (n=43)		
Comorbidities	**Total number of patients**	**Number of patients**	**% of the patients with thrombocytopenia**	**% of the patients with the comorbidity**
Myocardial infarction	29	7	16.2	24.1
Congestive heart failure	9	3	7.0	33.3
Peripheral vascular disease	20	6	14.0	30
Cerebrovascular disease	19	4	9.3	21
Dementia	16	4	9.3	25
Chronic pulmonary disease	55	7	16.2	12.7
Ulcer disease	13	4	9.3	30.8
Rheumatologic disease	0	0	0	0
Mild liver disease	16	5	11.6	31.2
Diabetes	78	19	44.2	24.3
Hemiplegia	3	1	2.3	33.3
Moderate or severe renal disease	20	9	20.9	45
Diabetes with chronic complications	30	6	14.0	20
Any tumor	34	8	18.6	23.5
Leukemia	9	0	0	0
Lymphoma	5	1	2.3	20
Moderate to severe liver disease	26	7	16.2	26.9
Metastatic solid tumor	10	2	4.7	20
AIDS	2	0	0	0

Table S5: Parameters tested for the development of thrombocytopenia

Patient		Comedications	Treatment	Infections
Inpatient/Outpatient	Diabetes	Rifampin	Switch from vancomycin	Type of infection
Gender	Cancer	Amiodarone	First-line treatment	In-label/off-label infection
Age	Tobacco	Amlodipine	Route of administration	Isolated microorganism
Weight	Alcohol	Omeprazole	Treatment duration	
Body mass index	GFR	Pyridoxine		
Dose/Kg/day	Creatinine level	Number of comedication		
Charlson index	Basal platelet count			