

SUB-THERAPEUTIC PLASMA LEVELS OF LINEZOLID IN THE ICU: USUAL OR UNUSUAL IN THIS SETTING?

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BACKGROUND

Linezolid is an antibiotic with a broad spectrum of activity against all clinically important gram positive bacteria, including methicillin resistant *Staphylococcus aureus* and vancomycin resistant enterococci. Standard dosing is prescribed for critical patients, regardless of their pharmacokinetic variability.

PURPOSE

To **describe** the plasma concentrations of linezolid in critical patients and its relationship with antibiotic discontinuation.

MATERIAL AND METHODS

A **prospective, observational** study was carried out in a **university hospital intensive care unit (ICU)** during **June 2017**. Patients with **linezolid treatment >48h** that signed the informed consent were included. Two blood samples, **Cmin** and **Cmax**, were taken per patient. They were analysed by **validated high performance liquid chromatography assay**. General, clinical data and analytic parameters of interest were recorded. Results were expressed in median, interquartile range and percentages. Fischer exact test for dichotomic variables was employed.



RESULTS

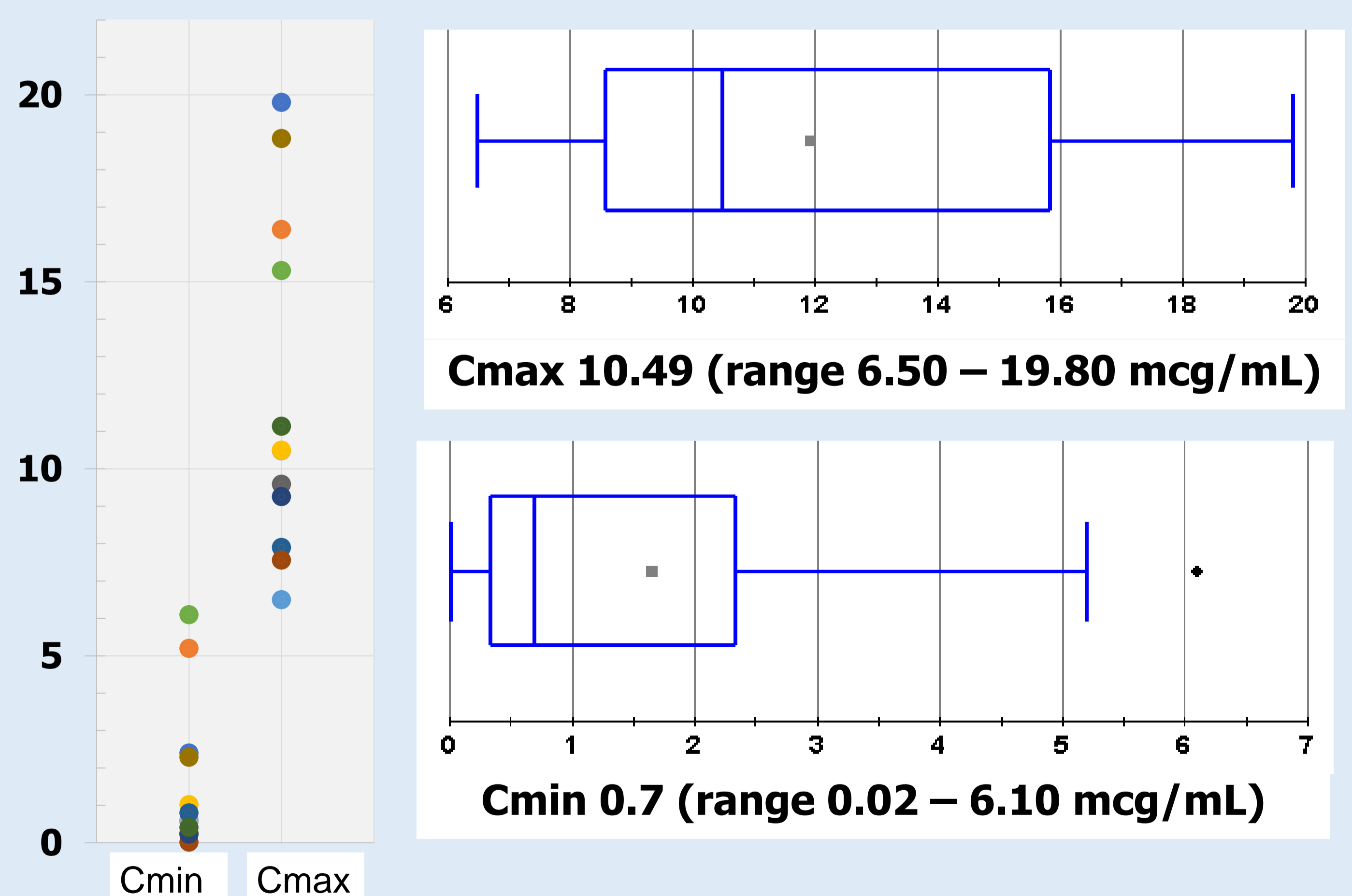
Demographic and clinical characteristics of study patients. (n=12)

Men, %	91.66
Age, years, median (IQR)	66.00 (12)
Weight kg, median (IQR)	82.50 (21)
BMI (kg/m ²), median (IQR)	26.85 (2.88)
Length of ICU stay, days, median (min-max)	18.00 (7-101)
APACHE II score, mediana (IQR)	22.00 (11)
Serum creatinine mg/dL, median (IQR)	0.95 (0.73)
Urea mg/dL, median (IQR)	0.51 (0.50)
Leukocytes x 10 ⁹ /L, median (IQR)	11.80 (10.8)
Neutrophils %, median (IQR)	89.10 (19.05)
CRP, median (IQR)	6.77 (28.49)

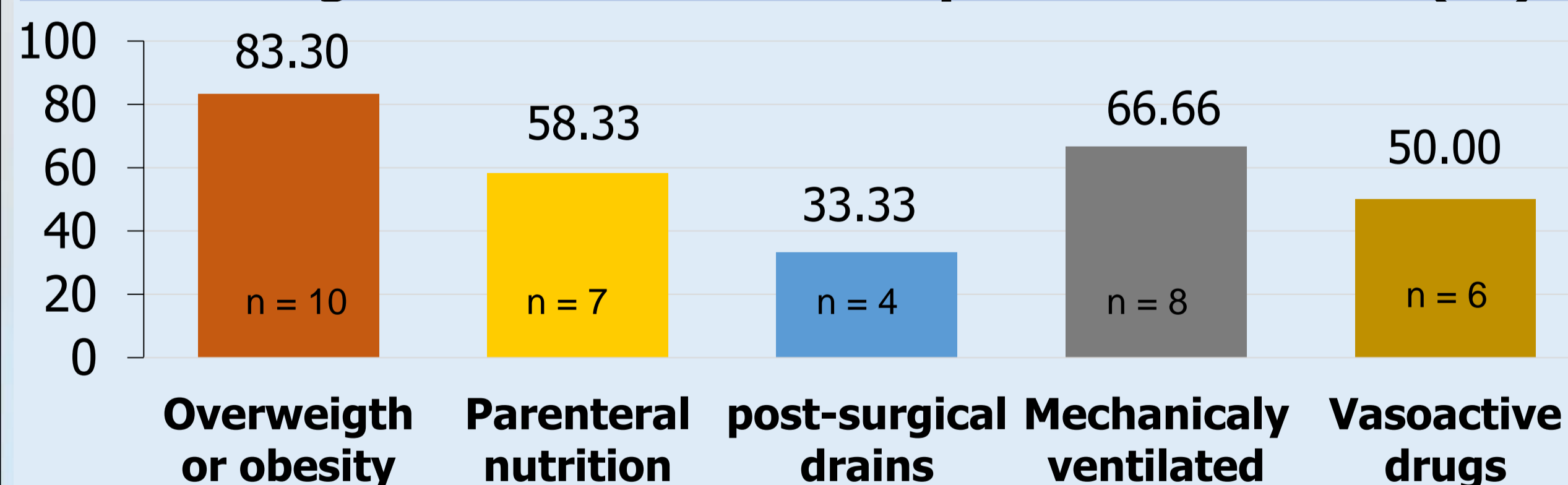
Characteristics of linezolid treatment

Dose and frequency	600 mg b.i.d.
Type of treatment, %	
Empirical regimen / targeted therapy	83.33 / 16.67
Combination therapy / monotherapy	91.67 / 8.33
Duration, days (min-max)	7 (4-20)
Plasma levels extraction dose, median (range)	7(5-11)

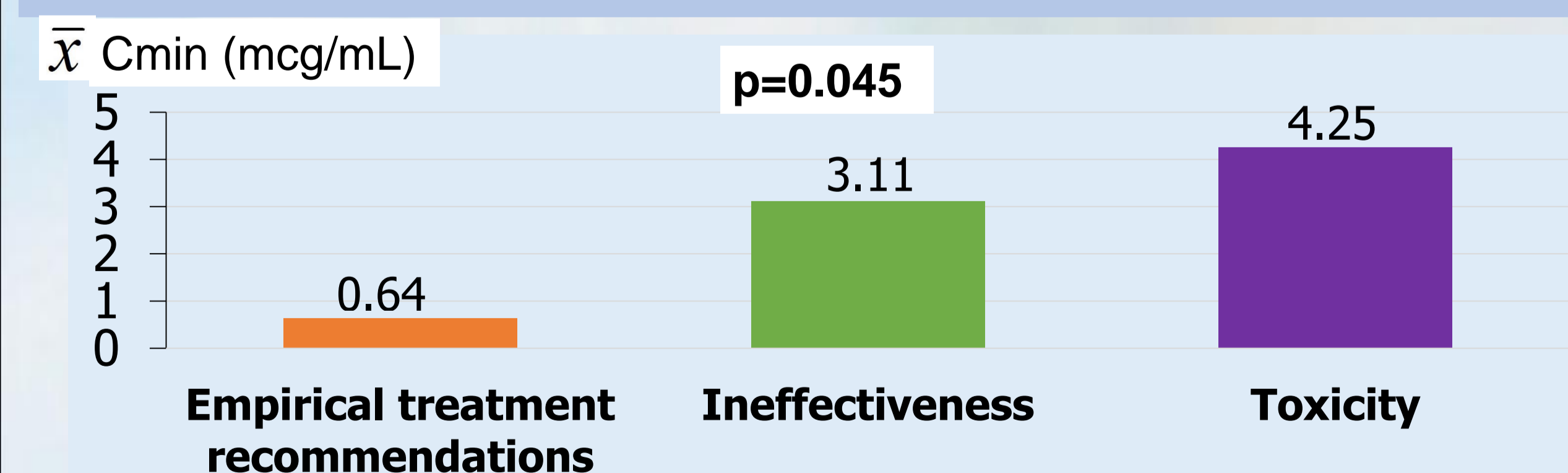
Linezolid plasma levels at steady state (mcg/mL)



Factors might influence linezolid pharmacokinetic (%)



Reasons for therapeutic discontinuation and relation with Cmin



67% → **<1 mcg/mL** **17%** → **> 18 mcg/mL**

CONCLUSIONS

A **high interindividual pharmacokinetic variability** of linezolid was observed and it could be related with the discontinuation of this antibiotic. Frequently, pharmacokinetic/pharmacodynamic targets are not achieved with standard dosing (600 mg b.i.d). Theapeutic drug monitoring should be considered to individualise linezolid dosing in ICU patients.