P369

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A New Era of Pharmacovigilance: Challenges and Opportunities

Occurrence and Characteristics of Linezolid Toxicity in Clinical Practice: Interim Analysis of a Prospective Multicentric Study.

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Background

The antibiotic linezolid (LZD) is a last-resort drug against multiresistant Gram-positive bacteria.

LZD is known to cause adverse drug reactions (ADRs). Among them, the most serious are hematological disorders (anemia and thrombocytopenia), or peripheral and optic neuropathy. Gastro-intestinal disorders and metallic taste are less risky, but still highly uncomfortable.

The probability Naranjo score [1] is an established tool to define whether ADR will be possibly, probably or definitely associated to a given drug.

Buzelé et al. proposed another score that specifically predicts the risk of developing ADRs to LZD [2]. This score includes an age-adjusted Charlson comorbidity index [3] and the treatment duration; a value ≥ 7 is associated with a risk of developing ADRs.

Monitoring of LZD trough levels (C_{min}) may also help to predict to toxicity, with values > 9 mg/L associated to a higher risk of hematological toxicity [4].

Objectives

To assess in clinical practice

- The rate of all observed **ADRs** and their **association** with LZD
- The **risk factors** associated with their development
- The relation between the most frequent ADRs and **C_{min}** values

Methods

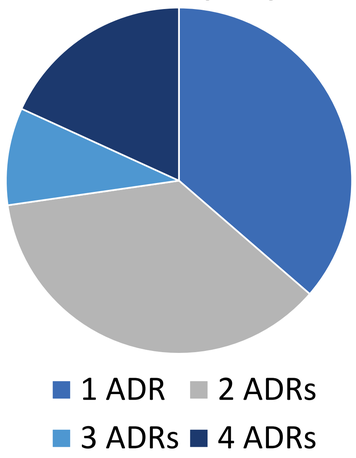
- Prospective multicentric study in 2 Belgian hospitals (May 2021 – March 2022 [still ongoing study])
- Inclusion of patients treated with LZD (IV or oral)
- Data collection in electronic medical records and via phone calls
- ADRs during the treatment and causality assessment through Naranjo ADR Probability scale.
- Risk evaluation of developing ADRs based on the Buzelé score
- C_{min} values (every 7 days for inpatients and at follow-up visits for outpatients) [5]
- Statistics: Mann-Whitney U test in SPSS (version 26)

Results

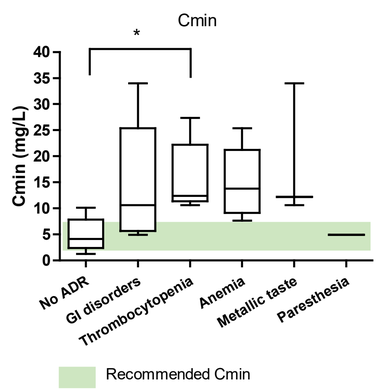
Patients' data and treatment characteristics

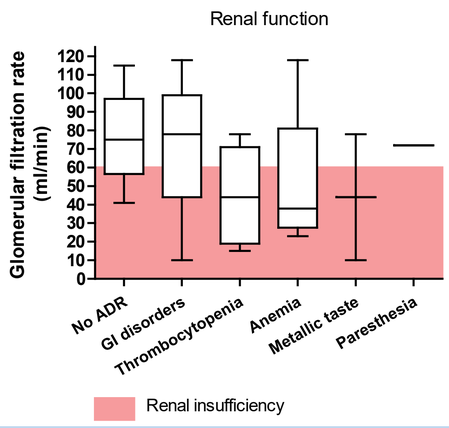
N =19	Median (Min – Max)
♀ ♂	8 / 11
AGE	62 years (33-69)
	68 ml/min (10-108)
	100 kg (42-154)
Charlson index	1 (0-5)
	600 mg 2x/day
	15 days (4-121)

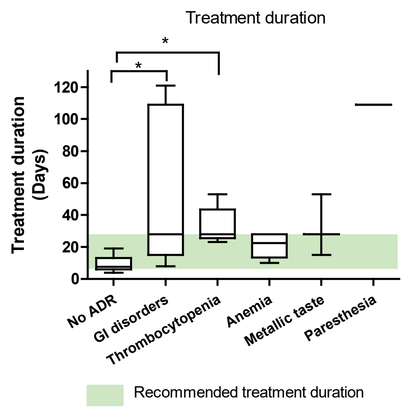
ADR number per patient

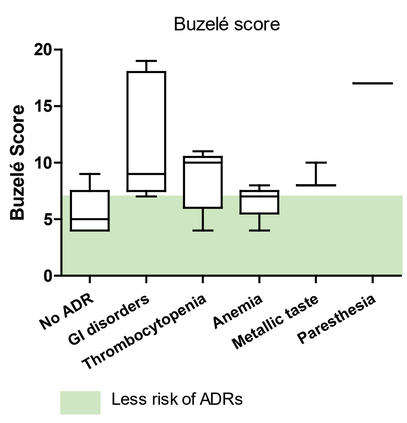


- **23 ADRs** in **19 patients**
- **Causality**: 16/23 probably associated – 7/23 possibly associated to LZD based on Naranjo probability score
- **4** stops for toxicity









- **C_{min}**: Higher, and higher than the recommended range of 2-7 mg/L in patients with ADRs (except for paresthesia)
- **Treatment duration**: Longer in patients with ADRs (median still in the maximal recommended duration of 28 days)
- **Glomerular filtration:** Trend to lower values (< 60 ml/min) in patients with hematological disorders and metallic taste
- **Buzelé score**: median ≥ 7 for all ADRs

Conclusion

Preliminary data → larger sample is required to confirm the trends:

- ADRs more **frequent** in clinical practice than reported in the SmPC [6] and the Naranjo score tends towards **LZD causality**
- Buzelé score tends to be > 7 in patients with ADRs versus patients without ADR
- High **C_{min}** and long **treatment duration** seem to be associated with the development of ADRs
- Detection of at-risk patients possible via therapeutic drug monitoring, follow-up of blood cell counts and renal function

References

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