

## Introduction and background

Linezolid (LZD), commercialized in 2000, is an antibiotic active against Gram-positive bacteria including multiresistant strains like vancomycin-resistant enterococcus (VRE) and methicillin-resistant staphylococcus aureus (MRSA) [1].

LZD is known to bind to the active site of monoamine oxidases and to inhibit their activity [2], which can increase the risk of developing a serotonin syndrome (SS) if co-administered with serotonergic drugs, i.e. drugs that inhibit serotonin catabolism or its recapture [3] [4]. Based on its current Belgian Summary of Product Characteristics (SmPC), LZD is contra-indicated in patients treated with this kind of drugs. However, the occurrence of real cases of serotonin syndrome remains unsettled in patients to whom LZD is co-prescribed with serotonergic drugs [1] [5], especially since LZD is often used off-label and for longer periods than recommended.

## Objective

- To assess the real risk of developing a serotonin syndrome in patients receiving routine LZD treatment together with a serotonergic drug

## Method

- Observational, retrospective, and multicentric study:
  - 4 Belgian hospital centers
- Analysis of medical files from adult patients (>18 years) treated with LZD between January 2016 and December 2016
- Collected key pieces of information:
  - Patient's characteristics, treatment modalities, indications
  - Adverse drug reaction data
  - Registration of all concomitant medications with emphasis on those known to increase the risk of developing a serotonin syndrome (SS).

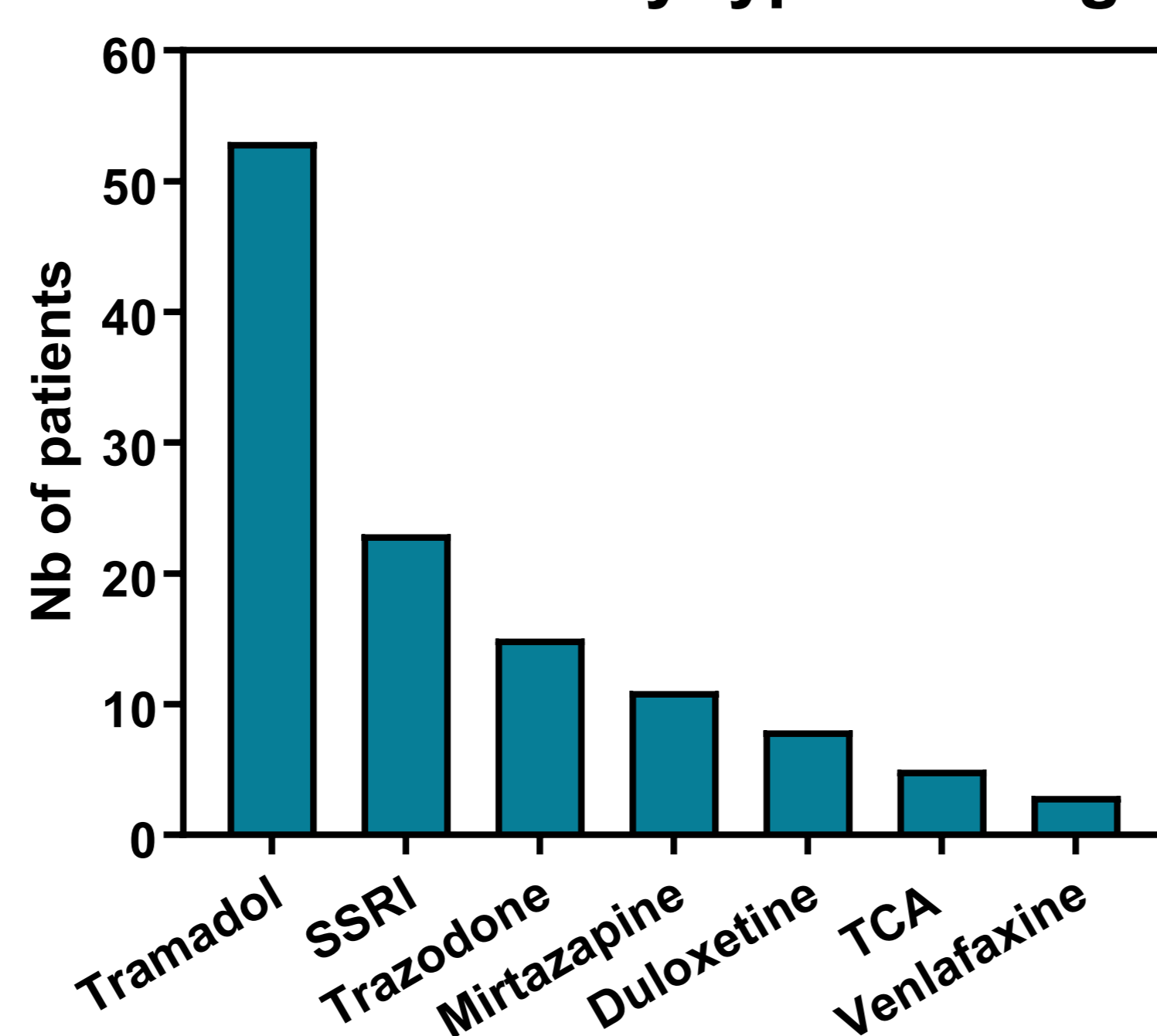
## Results

### Patients' data and treatment modalities:

Patients	230
Treatments	248
Male/Female	143/87
Age (year)	65 (21-95) <sup>a</sup>
Weight (kg)	76 (34-178) <sup>a</sup>
Renal function (GFR in ml/min)	57 (10-96) <sup>a</sup>
Posology	600mg 2x/day
Oral route/IV route	141/89
Treatment duration	10 (1-90) <sup>a</sup>

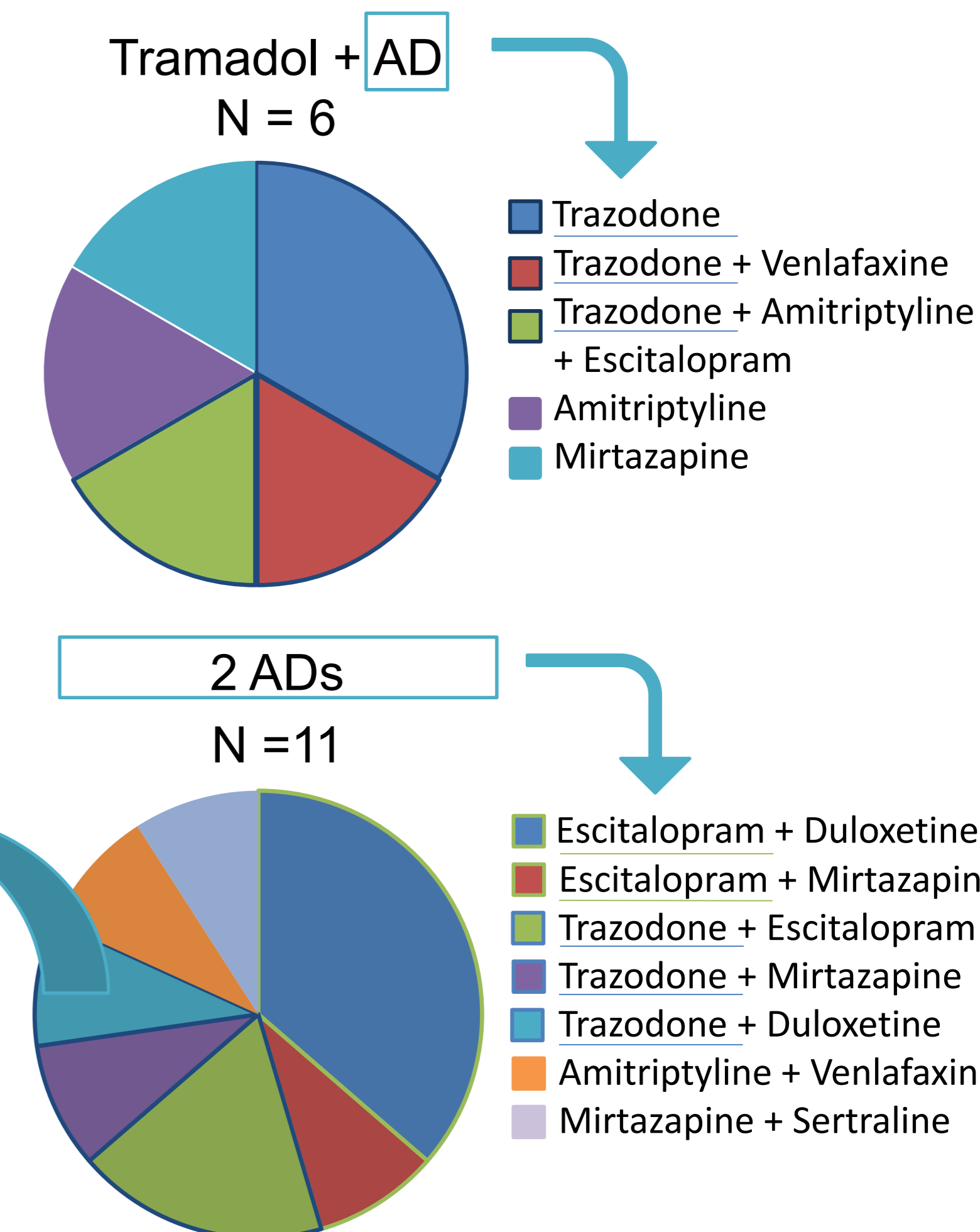
<sup>a</sup> Median (range)

### Patients with co-prescription of one or several serotonergic drug(s) stratified by type of drug



- 100 patients (40%) were prescribed one or several serotonergic drugs (susceptible to cause a SS).
- Tramadol (analgesic) was the most serotonergic co-prescribed drug.
- All other co-prescribed serotonergic drugs were antidepressants (AD).

### Patients with 2 or more drugs at risk of developing a serotonin syndrome



### Only 1 patient developed what was diagnosed as a serotonin syndrome:

This patient received trazodone (100 mg/day) + duloxetine (60 mg/day) and showed  
 → agitation and delirium after 7 days of concomitant treatment with LZD (600 mg BID);  
 → full recovery after LZD withdrawal.

## Main Message and Conclusion

- Serotonin syndrome occurrence in this large retrospective cohort of linezolid-treated patients (n=230) was very low (only 1 case) despite the frequent co-administration of contra-indicated serotonergic drugs (40% of all patients).
- The co-administration of linezolid with serotonergic drug(s) could be safer than anticipated in routine clinical practice but clinicians may, nevertheless, need to be warned about possible severe side effects of such co-administration.

## References

- [1] Linezolid Belgian Summary of Product Characteristics (SmPC - ZYVOXID® RCP - updated in 2014 - available in French from <https://goo.gl/zjKqZv> ; see also the UK ZYVOX® SPC - updated in 2016 - available in English from <https://goo.gl/CuyGzJ> ).
- [2] Jones *et al.* Biochem Pharmacol (2005) 70 (3): 407-416 – PMID: [15950194](https://pubmed.ncbi.nlm.nih.gov/15950194/)
- [3] Frykberg *et al.* J Am Podiatr Med Assoc (2015) 105 (3): 244-248 – PMID: [26146971](https://pubmed.ncbi.nlm.nih.gov/26146971/)
- [4] Sutton *et al* Proc (Bayl Univ Med Cent ) (2016) 29 (2): 214-215 – PMID: [27034576](https://pubmed.ncbi.nlm.nih.gov/27034576/)
- [5] Preston (2016) Stockley's Drug Interactions. Pharmaceutical Press, London, UK - ISBN 978 0 85711 270 5 - <https://goo.gl/y6nXzX>

