Linezolid versus Tedizolid for the Treatment of Nontuberculous Mycobacteria in Solid Organ Transplant Recipients: An Assessment of Safety

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BACKGROUND

- Treatment options for nontuberculous mycobacteria (NTM) infections are limited by the long-term tolerability of antimicrobials.
- The oxazolidinones, linezolid and tedizolid, display *in vitro* activity against many NTM species and demonstrate excellent oral bioavailability.[1-3]
- This study compares the hematologic safety profile of linezolid versus tedizolid for the treatment of NTM in solid organ transplant (SOT) recipients.

METHODS

STUDY DESIGN
- Retrospective cohort study from January 1, 2010 to August 31, 2019 at the University of Texas Southwestern Medical Center.

INCLUSION CRITERIA
- SOT recipients who received at least one dose of linezolid or tedizolid as part of an NTM multi-drug regimen.
- Organism identified as *Mycobacterium abscessus* complex or *Mycobacterium chelonae.*

PRIMARY ENDPOINT
- Hematologic effects of linezolid versus tedizolid from therapy initiation to week 7 using a mixed-effects ANOVA model.

Table 1. Hematologic Effect Definitions

Hematologic Effect	Definition
Thrombocytopenia[4]	• PLT < 150,000 / µL or > 50% reduction from baseline
Neutropenia[5]	• ANC < 1500/ µL or > 50% reduction from baseline
Anemia[6]	• Hgb < 13.5 (male) or 12 (female) g/dL or > 30% reduction from baseline

ANC, absolute neutrophil counts, Hgb, hemoglobin; PLT, platelets.

SECONDARY ENDPOINT
- Proportion of non-hematological adverse effects and discontinuation.
- Adverse effects include gastrointestinal effects, peripheral neuropathy, and serotonin syndrome.

RESULTS

Table 2. Baseline Characteristics

Treatment Group	Linezolid (n = 9)	Tedizolid (n = 15)
Age, years, median (range)	66 (61-72)	64 (43-71)
Male, n (%)	8 (89)	9 (60)
Lung transplant, n (%)	9 (100)	14 (93)
Days since transplant, median (range)	361 (27-1041)	200 (0-1343)
Site of Infection, n (%)		
Bacteremia	1 (11)	4 (27)
Disseminated	1 (11)	4 (27)
Osteomyelitis	0	2 (13)
Pulmonary	7 (78)	12 (80)
Skin and soft tissue	2 (22)	3 (20)
Surgical site	0	4 (27)

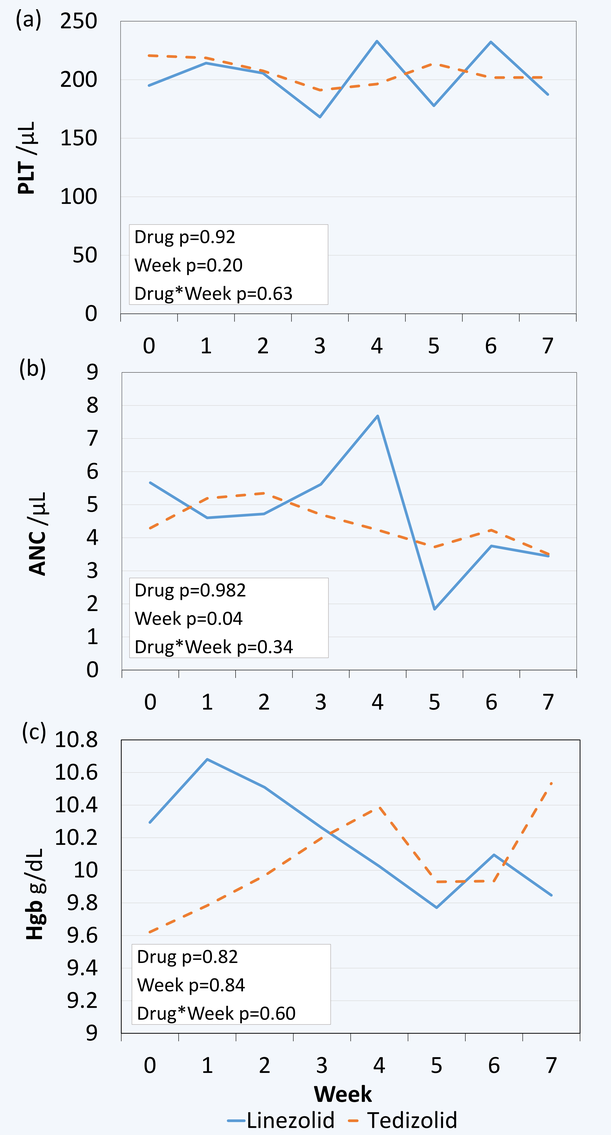
PRIMARY ENDPOINT (Figure 1)
- In the mixed-effects ANOVA, the ANC decreased in both groups after 7 weeks of therapy (p=0.04).
- No other significant effects for week, treatment group, or interaction between week and treatment group were found.

SECONDARY ENDPOINT (Table 3)
- One patient experienced non-hematological adverse effect in the tedizolid group.
- Approximately one-fifth of patients in each group discontinued the medication due to adverse effects.

Table 3. Non-Hematological Adverse Effects and Discontinuation of Therapy

Treatment Group	Linezolid (n = 9)	Tedizolid (n = 15)
Gastrointestinal effects (nausea and/ or vomiting), n (%)	0 (0)	1 (7)
Peripheral neuropathy, n (%)	0 (0)	0 (0)
Serotonin syndrome, n (%)	0 (0)	0 (0)
Discontinuation due to ADEs, n (%)	2 (22)	3 (20)
Discontinuation due to non-ADEs, n (%)	2 (22)	2 (13)
Deceased, n (%)	0 (0)	1 (7)
Lost to follow up, n (%)	1 (11)	0 (0)

Figure 1. Hematologic Effects of Linezolid versus Tedizolid during the Initial 7 Weeks of Therapy



CONCLUSIONS

- No statistical significant differences were found comparing the effects of linezolid versus tedizolid for PLT, ANC, and Hgb.
- ANC decreased significantly in both groups after 7 weeks of therapy.
- Larger cohort studies are required to compare the hematologic adverse effect profile of the oxazolidinones for the treatment of NTM infections in SOT recipients.

1. Longworth SA et al. *Clin Transplantation*. 2019; e13588.
2. Brown-Elliott BA et al. *J Clin Microbiol.* 2017;55(6):1747-54.
3. Winthrop KL et al. *Eur Respir J*. 2015;45(4):1177-9.
4. Rabon AD et al. *Ann Pharmacother*. 2018;52(11):1162-4.
5. Gerson SL et al. *Antimicrob Agents and Chemother*. 2002; 46(8), 2723-6.
6. Hanai Y et al. *J Infect Chemother*. 2016; 22(8), 536-42.

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