Abstract #1627

Tedizolid is Well-tolerated Among Patients Receiving Prolonged Treatment Courses, Including Those Who are Intolerant of Alternative Agents

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INTRODUCTION

- Tedizolid is a second generation oxazolidinone antibiotic with activity against Gram-positive bacteria, *Nocardia spp*. and mycobacteria
- Tedizolid has been approved by the Food and Drug Administration (FDA) for acute bacterial skin and skin structure infections (ABSSSI), but is often used off-label for more complicated infections
- Tedizolid's predecessor, linezolid, has an established track record for favorable clinical outcomes, but its long-term tolerability and risk of serotonin syndrome limits its utility
- Currently, evidence for long term tolerability of tedizolid is limited to case reports and published abstracts; but suggests that this agent has an improved tolerability profile compared to linezolid
- The aim of this study was to assess and characterize the real-world long-term tolerability of tedizolid

METHODS

Study design and patients:

- Retrospective cohort study of patients receiving >72 hours of tedizolid at UPMC from June 1, 2015 and March 3, 2020

Definitions:

- Thrombocytopenia was defined as a >50% decrease in baseline platelet count or an absolute platelet count <50,000 cells/L
- Serotonergic agents were those agents documented to interact with linezolid predisposing to an increased risk for serotonin syndrome
- A favorable clinical outcome was defined as completion of intended therapy without readmission for the same infection within 30 days

RESULTS

Patient Demographics and Clinical Characteristics

- Overall 86 patients receiving 102 distinct treatment courses were included

Demographics	Unique patients (n = 86)
Age (years, mean ± standard deviation)	Mean: 55 ± 14
Female	50 (58.1%)
Immunosuppression	36 (41.9%)
Solid Organ Transplant	27 (31.4%)
Chronic Inflammatory Demyelinating	1 (1.2%)
Polyneuropathy	1 (1.2%)
Splenectomy	1 (1.2%)
Crohn's Disease	2 (2.3%)
Acute Myeloid Leukemia	2 (2.3%)
Systemic Lupus Erythematosus	1 (1.2%)
Chronic steroids	1 (1.2%)
Hidradenitis (Anakinra)	1 (1.2%)

	Unique Treatment Courses (n = 102)
Duration Ranges	
4 - 14 days	69 (67.6%)
15 – 30 days	15 (14.7%)
31 – 60 days	13 (12.7%)
≥ 60 days (range 119-350+)	5 (4.9%)
Indication	
Skin and Soft Tissue Infection	42 (41.2 %)
Bloodstream Infection	12 (11.8 %)
Intra-abdominal Infection	11 (10.8 %)
Respiratory Infection	10 (9.8 %)
Osteomyelitis	9 (8.8 %)
Mycobacterium abscessus (respiratory & disseminated)	6 (5.9 %)
Other	12 (11.8 %)
Pathogen	
Vancomycin Susceptible Enterococci	3 (2.4%)
Vancomycin Resistant Enterococci (VRE)	27 (26.5%)
Methicillin Susceptible *Staphylococcus aureus* (MSSA)	4 (3.9 %)
Methicillin Resistant *S. aureus* (MRSA)	21 (20.6%)
Vancomycin Intermediate *S. aureus* (VISA)	2 (2.0%)
Streptococcus spp.	8 (7.8 %)
Coagulase negative staphylococcus (CoNS)	7 (6.9 %)
Mycobacterium abscessus	5 (4.9 %)
No pathogen isolated	32 (33.4 %)
Baseline Platelet Counts	
Platelets < 100 K	17 (16.6%)
Platelets < 50 K	7 (6.9%)
Concomitant Serotonergic Agents	78 (76.0%)
One	44 (43.1%)
Two	18 (17.6%)
Three	11 (10.8%)
Other	5 (6.4%)

Prior Treatment Failures

Antibiotics Associated with Failures	Reasons for Failure Prior failure in 44% of treatment courses (45/102)
Amoxicillin	Failed *E. faecalis* suppression (n=1)
Ceftaroline	Clinical progression (n=1)
Cephalexin	Clinical progression (n=1)
Daptomycin	Clinical progression (n=2), CPK elevation without rhabdomyolysis (n=1), Eosinophilic pneumonia (n=1), Hallucinations (n=1)
Doxycycline	Breakthrough on suppression therapy (n=1), Clinical progression (n=5), GI intolerance (n=2)
Linezolid	Cytopenias + lactic acidosis (n=1), Lactic acidosis (n=1), Mixed cytopenias (n=3), Thrombocytopenia (n=8)
Quinupristin/Dalfopristin	Myopathy (n=1)
Sulfamethoxazole/trimethoprim	Clinical progression (n=3), Fever (n=1), Hyperkalemia (n=2)
Televancin	Acute Kidney Injury (n=1)
Tigecycline	Clinical progression (n=2), Nausea (n=1)
Vancomycin	Acute Kidney Injury (n=2), Clinical progression (n=3), Rash (n=1)
Combination (≥ 3 antibiotics)	Clinical progression (n=2)

Tolerability of Tedizolid

- Forty-four percent (45/102) of tedizolid courses were preceded by treatment failure or adverse events associated with alternative therapies
  - 13 patients demonstrated adverse events with linezolid
- A favorable treatment outcome was documented following 82/102 (80.4%) of tedizolid courses which included completion of therapy without documented adverse reaction, retreatment or readmission
- Overall 8% (8/102) of tedizolid treatment courses were discontinued prematurely due to adverse events
- Tolerability of tedizolid was demonstrated among 78% (14/18) and 80% (4/5) of patients receiving > 30 and > 100 days of treatment, respectively
- Among patients who experienced adverse events to linezolid, 61.5% (8/13) completed their intended course of tedizolid
  - Two patients had persistent thrombocytopenia and three patients experienced clinical failure

Outcomes	Unique Treatment Courses (n = 102)
Favorable Outcome	82 (80.4%)
Adverse events requiring discontinuation	8 (8.0%)
Thrombocytopenia	3
Gastrointestinal intolerance	2[a]
Confusion	1[b]
Eosinophilia	1[b]
Thrombocytopenia + lactic acidosis	1
In hospital death/transfer to hospice	5 (4.9%)
Failed therapy/readmission	2 (2.0%)
Ongoing Suppression (>350 days in total)	1 (1.0%)
Thrombocytopenia	
>50% decrease during treatment course	11 (10.8%)
Total platelets < 50K (Baseline platelet range 16 – 86)	11 (10.8%)
>50% decreased AND total platelets <50K ▪ 83K →40K ▪ 16K →5K ▪ 86K →26K	3 (2.9%)
Baseline Platelets > 100K with >50% decrease	8/85 (9.4%)
Baseline Platelets < 100K with >50% decrease	3/17 (17.6%)

[a] Both cases were the same patient who subsequently tolerated a 31 day treatment course
[b] Persisted after tedizolid discontinuation and later determined to be unrelated to tedizolid

CONCLUSIONS

- **In our real-world experience tedizolid was well-tolerated across patients, including those who did not tolerate or failed alternative agents**
  - **Thrombocytopenia leading to treatment discontinuation was rare**
  - **Most patients experiencing adverse events to linezolid were able to tolerate subsequent treatment with tedizolid**
- **Tedizolid was well-tolerated for prolonged courses, including patients who received > 3 months of treatment**
- **Despite high rates of concomitant serotonergic agents, no patient in this study experienced serotonin syndrome while receiving tedizolid**

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