

## **Case study**

### **Use of Tedizolid for the Treatment of *Staphylococcus aureus***

#### **Bacteremia – an off labelled indication**

##### **Abstract**

##### **Aims**

We aim to share our experience in the successful use of tedizolid for the treatment of *staphylococcus aureus* bacteremia in two of our patients.

##### **Presentation of cases**

Our first patient has methicillin-resistant *staphylococcus aureus* (MRSA) bacteremia. The MRSA isolated was sensitive to linezolid and vancomycin (MIC=2), resistant to daptomycin (MIC=2). In view of the documented drug allergy to ceftriaxone and drug interaction with daptomycin, the patient was initially initiated on intravenous vancomycin but developed a breakthrough fever with rising inflammatory markers. However, upon initiation of tedizolid, fever lysed, and the patient improved clinically.

Our second patient has ~~end-end~~ stage renal failure on hemodialysis. ~~Patient~~ The patient has methicillin-susceptible *staphylococcus aureus* (MSSA) catheter-related bloodstream infection. The MSSA isolated was sensitive to vancomycin (MIC=2) and ceftaroline (MIC=0.50), but resistant to daptomycin (MIC=2). Vancomycin was initiated in view of documented drug allergy to ceftriaxone but repeated blood cultures showed the persistence of MSSA. Antibiotics were switched to linezolid for 3 days before switching to tedizolid due to previous neutropenia with linezolid. Blood cultures had documented clearance with tedizolid.

## 23 Discussion and conclusion

24 In both our patients, tedizolid was introduced after [a](#) few days of vancomycin therapy. Hence, [the](#)  
25 efficacy of tedizolid as the first-line therapy for [the](#) treatment of staphylococcus bacteremia  
26 remains unknown. Nevertheless, in both patients, there was no relapse of staphylococcus  
27 bacteremia and infections when tedizolid was used to complete the antibiotic therapy. The  
28 optimal treatment duration of staphylococcus bacteremia with tedizolid also remains unknown.

## 30 Introduction

31  
32 For decades, vancomycin has been the cornerstone for treatment of methicillin-resistant  
33 *staphylococcus aureus* (MRSA) infections, but increasingly, creeping minimum inhibitory  
34 concentration (MIC) of MRSA has resulted in treatment failure [1]. In view of the lack of  
35 clinical experience in the use of tedizolid for off-labelled indications, we describe two patients  
36 with MRSA/MSSA bacteremia and were treated with tedizolid successfully.

## 38 Case Presentation

39 The first patient was a 51-year-old Chinese male. His medical history was significant for  
40 diabetes mellitus, depression and alcohol dependency with Child's B alcoholic liver cirrhosis. He  
41 presented with giddiness and was febrile (37.7°C) on admission. He was recently admitted for  
42 mild pancreatitis, was given ceftriaxone but developed fixed drug eruption (diagnosed by [a](#)  
43 dermatologist). MRSA screen came back positive and blood cultures subsequently grew MRSA  
44 – sensitive to linezolid and vancomycin (MIC=2), resistant to daptomycin (MIC=2). Heart echo  
45 revealed no vegetation.

46

47 | Despite the high MIC, the patient was initiated on vancomycin due to limited therapeutic options  
48 | – loading dose of 20mg/kg, followed by 20mg/kg Q12h. Despite receiving high doses of  
49 | vancomycin (25mg/kg Q12h) after several titrations, serum vancomycin troughs remained  
50 | persistently sub-therapeutic (4.4 – 13mg/L). Patient’s renal function remained good throughout  
51 | with no change in urine output. Blood cultures were negative on day 3 of vancomycin but on day  
52 | 13 of vancomycin therapy, patient spiked fever (39.9°C) and repeated inflammatory markers  
53 | (pro-calcitonin, C-reactive protein, and white cell count) were up-trending. As the patient was  
54 | taking escitalopram for depression, concurrent use with linezolid was not recommended due to  
55 | the risk of serotonin syndrome. Ceftaroline was contraindicated as the patient is allergic to  
56 | ceftriaxone. In light of the poor response to vancomycin with breakthrough fever and limited  
57 | therapeutic options, intravenous tedizolid 200mg once-daily was initiated. Thereafter, fever  
58 | normalized and inflammatory markers were down-trending. Repeated blood cultures remained  
59 | negative, the patient completed one week of tedizolid, was discharged well without antibiotics  
60 | and there was no relapse of infection on follow up.

61

62 | Our second patient was a 58-year-old Chinese male who presented with fever (39°C), chills and  
63 | rigors. ~~Patient~~ The patient had end-stage renal failure; on thrice-weekly hemodialysis since 2010.  
64 | Due to recurrent vascular access issues, the patient had been dialyzing through permanent  
65 | catheters. He was recently admitted and given 1 week of intravenous vancomycin for catheter  
66 | exit-site infection, and blood cultures were negative then. In this current admission, blood  
67 | cultures sent on admission grew MSSA – sensitive to vancomycin (MIC=2), ceftaroline  
68 | (MIC=0.50), resistant to daptomycin (MIC=2). Heart echo revealed no vegetation. Vancomycin

69 | was initiated as the patient had type I hypersensitivity reaction to ceftriaxone. ~~Infected-The~~  
70 | infected permanent catheter was removed on day 2 of admission but repeated blood cultures  
71 | showed the persistence of MSSA up to day 6 of admission (two sets of blood cultures were  
72 | repeated on a daily basis). Hence, in view of treatment failure with vancomycin and patient's  
73 | drug allergy, linezolid was initiated but was later switched to tedizolid 200mg once-daily after 3  
74 | days – taking into account patient's previous history of known thrombocytopenia with linezolid.  
75 | On the day of the switch from linezolid to tedizolid therapy, repeat blood cultures came back  
76 | negative. While using tedizolid, the patient's platelet count was monitored closely. Platelet  
77 | counts were normal initially and the patient was planned for 2-weeks course of tedizolid.  
78 | However, on day 11 of tedizolid therapy, platelet count dropped to  $<100 \times 10^9/L$  and tedizolid  
79 | was stopped. ~~Patient-The patient~~ was subsequently discharged well without antibiotics. Two  
80 | weeks post-discharge, patient's platelet counts normalized, and there was no relapse of  
81 | infections.

82

### 83 | **Discussion**

84 | In both our patients, alternative anti-MRSA/anti-MSSA therapies (daptomycin, ceftaroline,  
85 | linezolid) within our formulary were taken into consideration in view of therapeutic failure with  
86 | vancomycin. Both our patients had severe allergic reactions to ceftriaxone and this prohibits the  
87 | use of ceftaroline. Daptomycin could not be used both of MSSA/MRSA from our patients  
88 | exhibit a high MIC of 2 to daptomycin (resistant). Linezolid was not used or continued in view  
89 | of drug interactions and adverse drug effects observed.

90

91 Multiple studies have demonstrated tedizolid's potent *in-vitro* activity against MSSA/MRSA [2].  
92 Tedizolid's long elimination half-life (10-12h) and its improved potency allows for a lower dose  
93 to be used. This contributes to a lower incidence of thrombocytopenia, when compared to  
94 linezolid [3]. In addition, tedizolid does not appear to have a significant drug interaction with  
95 serotonergic agents [4].

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97 In both our patients, tedizolid was introduced after a few days of vancomycin therapy. Hence, the  
98 efficacy of tedizolid as the first-line therapy for the treatment of staphylococcus bacteremia  
99 remains unknown. Nevertheless, in both patients, there was no relapse of staphylococcus  
100 bacteremia and infections when tedizolid was used to complete the antibiotic therapy. The  
101 optimal treatment duration of staphylococcus bacteremia with tedizolid also remains unknown.

## 102 103 **Conclusion**

104 To date, tedizolid is only licensed for the treatment of ABSSSI, with investigational use in  
105 nosocomial pneumonia. While evidence for its use in bacteremia is lacking, we reported that  
106 tedizolid is effective and safe in the treatment of *staphylococcus aureus* bacteremia, with no  
107 relapse.

Comment [DM1]: Full form followed by abbreviation

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113 **Ethical Approval:** Not required

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116 **References**

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