Burkholderia Returns: Are Two Drugs Better or Back to Bactrim?

Jason Hedvat, PharmD; Monica Mehta, PharmD, MPH, BCPS, BCIDP; Christine Kubin, PharmD, BCPS-AQID, BCIDP
Columbia University Irving Medical Center, New York, NY

Contact information:
Jason Hedvat
28 Elkwood Terrace
Tenafly, NJ 07670
jdhedvat@gmail.com

BACKGROUND

- *Burkholderia cepacia complex* (Bcc) is a group of non-lactose fermenting gram-negative bacteria[1]
- Bcc can cause colonization and infection in individuals resulting in respiratory tract, central nervous system, bloodstream, and urinary tract infections[2]
- Bcc is intrinsically resistant to multiple classes of antibiotics including polymyxins and aminoglycosides[3]
- Antibiotics with in-vitro activity include trimethoprim-sulfamethoxazole (TMP-SMX), ceftazidime, meropenem, levofloxacin, and minocycline[2]
- Use of TMP-SMX remains limited due to real and perceived treatment-related adverse effects[2]
- Combination therapy is frequently utilized despite limited clinical evidence supporting this practice[2]
- The objective of this study is to compare outcomes associated with different regimens for the treatment of Bcc infections

METHODS & STUDY DESIGN

- IRB-approved, retrospective, single-center study
- Columbia University Irving Medical Center
- Timeline: January 2015 to September 2019

Inclusion	Exclusion
• ≥ 18 years of age • First positive culture for Bcc of any source per patient within 90 days • Received at least one susceptible antibiotic within 5 days of culture	• Polymicrobial infection from the same site within 3 days • Death within 3 days • Cystic fibrosis • Untreated concurrent infections • Colonization based on NHSN criteria

- Comparisons were performed using Chi - squared or Fischer's exact test for categorical variables and Student's t test or the Mann - Whitney U test for continuous variables, as appropriate
- Multivariable logistic regression analysis was used to identify independent risk factors for overall treatment failure

OUTCOMES

Primary	Secondary
• Composite of overall treatment failure defined as clinical failure, microbiologic failure, or mortality at 30 days	• Mortality at 14, 30 and 90 days • Clinical failure at 30 days • Microbiologic failure at 30 days • Development of resistance while on initial treatment regimen • Recurrence at 90 days • Treatment related adverse drug reactions (ADR) while on initial treatment regimen

RESULTS

Figure 1. Initial Treatment Regimens

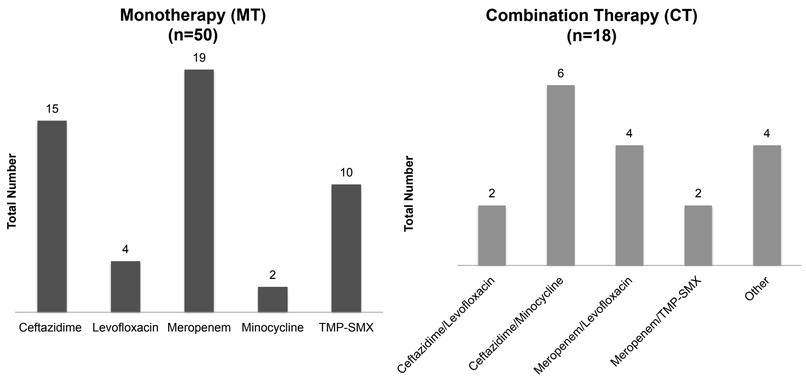

Table 1. Baseline Characteristics

	MT (n=50)	CT (n=18)	P value
Age (years), median	63	56	.075
Male, n (%)	28 (56)	12 (67)	.611
Comorbidities			
Diabetes, n (%)	20 (40)	4 (22)	.252
Renal disease, n (%)	19 (38)	1 (6)	.014
End stage renal disease, n (%)	8 (16)	1 (6)	.427
Severe liver disease, n (%)	4 (8)	2 (11)	1.000
Cardiac disease, n (%)	21 (42)	5 (28)	.434
Chronic obstructive pulmonary disease, n (%)	16 (32)	7 (39)	.811
Charlson comorbidity index, median	3	2	.021
Immunosuppressive conditions, n (%)	16 (32)	15 (83)	.001
Neutropenia, n (%)	0 (0)	1 (6)	.265
Chemotherapy	7 (14)	5 (28)	.340
Active malignancy, n (%)	5 (10)	5 (28)	.150
Organ transplant, n (%)	9 (18)	10 (56)	.006
ICU admission within 48 hours of infection onset, n (%)	34 (68)	8 (44)	.139
SOFA score at infection onset, mean	8	4	.003
First episode of Bcc, n (%)	46 (92)	17 (94)	1.000
Type of infection, n (%)			.314
Hospital acquired pneumonia	38 (76)	15 (83)	
Urinary tract infection	1 (2)	0 (0)	
Intra-abdominal infection	1 (2)	2 (11)	
Primary bacteremia	8 (16)	1 (6)	
Other	2 (4)	0 (0)	
Appropriate empiric therapy, n (%)	16 (32)	5 (28)	.972
Infectious diseases consult, n (%)	38 (76)	13 (72)	1.000

Table 2. Primary and Secondary Outcomes

Outcome	MT (n=50)	CT (n=18)	P value
Overall treatment failure at 30 days, n (%)	18 (36)	7 (39)	.947
Clinical failure at 30 days, n (%)	13 (26)	5 (28)	1.000
Microbiologic failure at 30 days, n (%)	13 (27)	4 (24)	.972
Development of resistance, n (%)	4 (31)	1 (25)	1.000
Recurrence/ongoing Infection at 90 days, n (%)	5 (10)	1 (6)	.569
Mortality at 14 days, n (%)	2 (4)	1 (6)	1.000
Mortality at 30 days, n (%)	4 (8)	2 (11)	1.000
Mortality at 90 days, n (%)	10 (28)	5 (29)	1.000
Discontinuation due to ADR, n (%)	4 (8)	2 (11)	1.000

Table 3. Multivariable Logistic Regression Analysis for Overall Treatment Failure

	Univariable			Multivariable	
Variable	Overall Treatment Success (n=43)	Overall Treatment Failure (n=25)	P Value	OR (95% CI)	P Value
Renal disease, n (%)	13 (31)	7 (27)	.936	.102 to 2.273	.355
Total CCI, median	3	3	.764	.603 to 1.278	.496
Immunosuppressive condition, n (%)	17 (41)	14 (54)	.409	.129 to 12.656	.834
SOFA score at infection onset, mean	6	9	.002	1.150 to 1.766	.001
Monotherapy, n (%)	31 (74)	19 (73)	1.000	.249 to 5.969	.808
ICU admission, n (%)	24 (57)	18 (69)	.459	.077 to 2.007	.261

CONCLUSIONS

- No differences in outcomes between monotherapy and combination therapy groups for the treatment of Bcc infection
- Treatment outcomes appeared to be driven primarily by disease severity
- Additional studies are needed to identify the optimal treatment regimens

DISCLOSURES

- Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

REFERENCES

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