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Background

- Ceftolozane/tazobactam (C/T): novel cephalosporin formulated with a beta-lactamase inhibitor
- FDA-approved indications: treatment of complicated intra-abdominal and urinary tract infections
- Clinical utilization of C/T appears to be towards multi drug-resistant (MDR) pathogens (especially *P. aeruginosa*)
- At our institution C/T is restricted to the department of Infectious Diseases
- Objective: This evaluation aimed to characterize the use of C/T at a large academic medical health system

Objectives

- Primary Objective:** Characterize utilization of C/T throughout the Cleveland Clinic Health System
- Secondary Objectives:**
 - Characterize the dosing of C/T
 - Calculate rates of clinical and microbiological cure in patients receiving C/T
 - Determine percent susceptibility of *P. aeruginosa* in patients receiving C/T

Methods

- Retrospective case series including all patients who received ≥ 1 dose of C/T from April 2015 – February 2016.
- Study Site: Cleveland Clinic Health System (10 hospitals including 1400-bed academic medical center and 9 community hospitals)
- Susceptibility interpreted using FDA Breakpoints
- Statistics: Descriptive Statistics

Definitions

Clinical cure: complete resolution of index infection (no further escalation of antimicrobial therapy or need for additional source control) in patients that received at least 72 hours of inpatient therapy

Clinical Failure: not meeting criteria for clinical cure after receiving at least 72 hours of inpatient therapy

Indeterminate Clinical Status: insufficient data to categorize as clinical cure or failure

Microbiological cure: eradication of baseline pathogen in microbiologically evaluable patients

Results

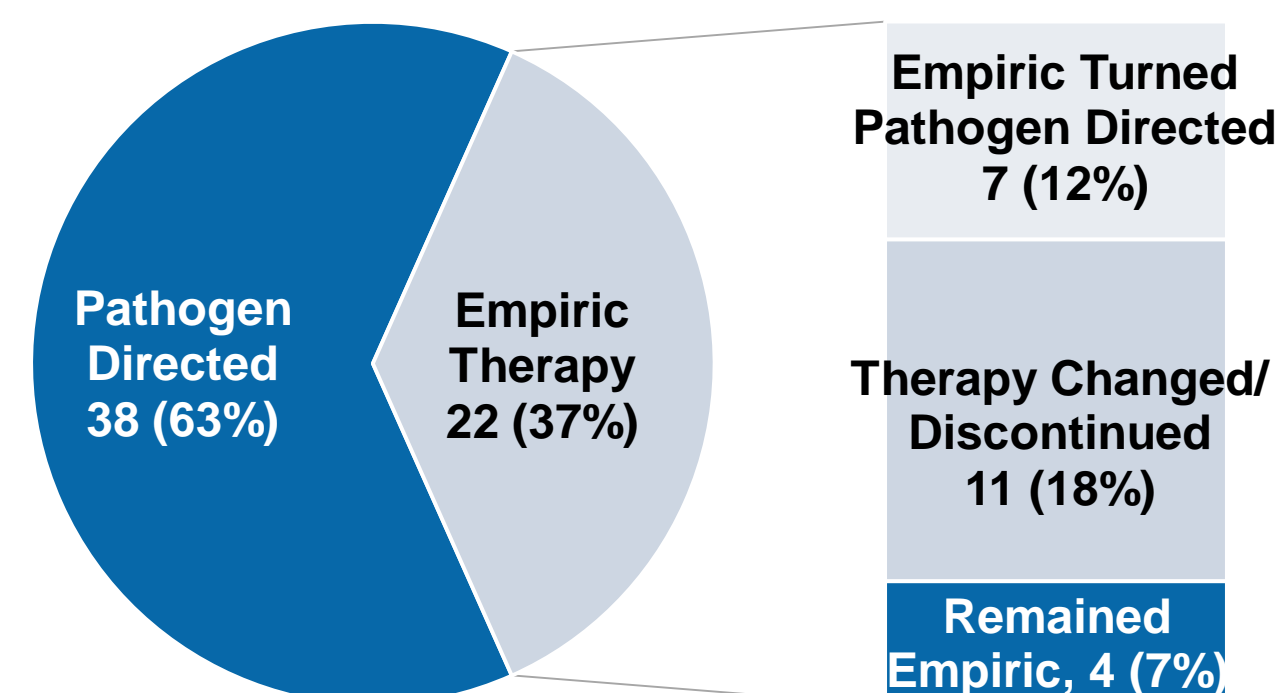
- 60 patient encounters included (50 unique patients)
- Baseline Characteristics**
 - Male, n (%): 38 (63)
 - Mean age, years: 61 \pm 16.1
 - ICU Location, n (%): 37 (61.7)
- Source of infection**
 - Pneumonia: 34 (56.7%)
 - Intra-abdominal: 11(18.3%)
 - Unknown: 6 (10%)
 - SSTI: 3 (5%)
 - Primary Bacteremia: 4 (6.7%)
 - Bone & Joint: 2 (3.3%)
 - Other: 2 (3.3%)
- Concomitant Bacteremia:** 12 (20%)
- No Pathogen Isolated:** 6 (10%)
- Source Control:** 9 / 17 (52.9%)

Ceftolozane/Tazobactam Dosing

C/T Initial Dose, n (%)	3 g Q8h	1 (1.7)
	1.5 g Q8h	31 (51.7)
	750 mg Q8h	16 (26.7)
	375 mg Q8h	5 (8.3)
	150 mg Q8h	7 (11.7)
	Standard Dosing*	52 (86.7%)
	High Dosing	6 (10%)
	Other Dosing	2 (3.3%)
IHD Dosing, n (%)	N=9 patients	
	150 mg Q8h	7 (77.8)
	375 mg Q8h	1 (11.1)
	1.5 mg Q8h	1 (11.1)
CRRT Dosing, n (%)	N=14 patients	
	750 mg Q8h	11 (78.6)
	1.5g Q8h	2 (14.3)
	375 mg Q8h	1 (7.1)

*Standard dosing=dosing recommendations from product package insert

Ceftolozane/Tazobactam Utilization

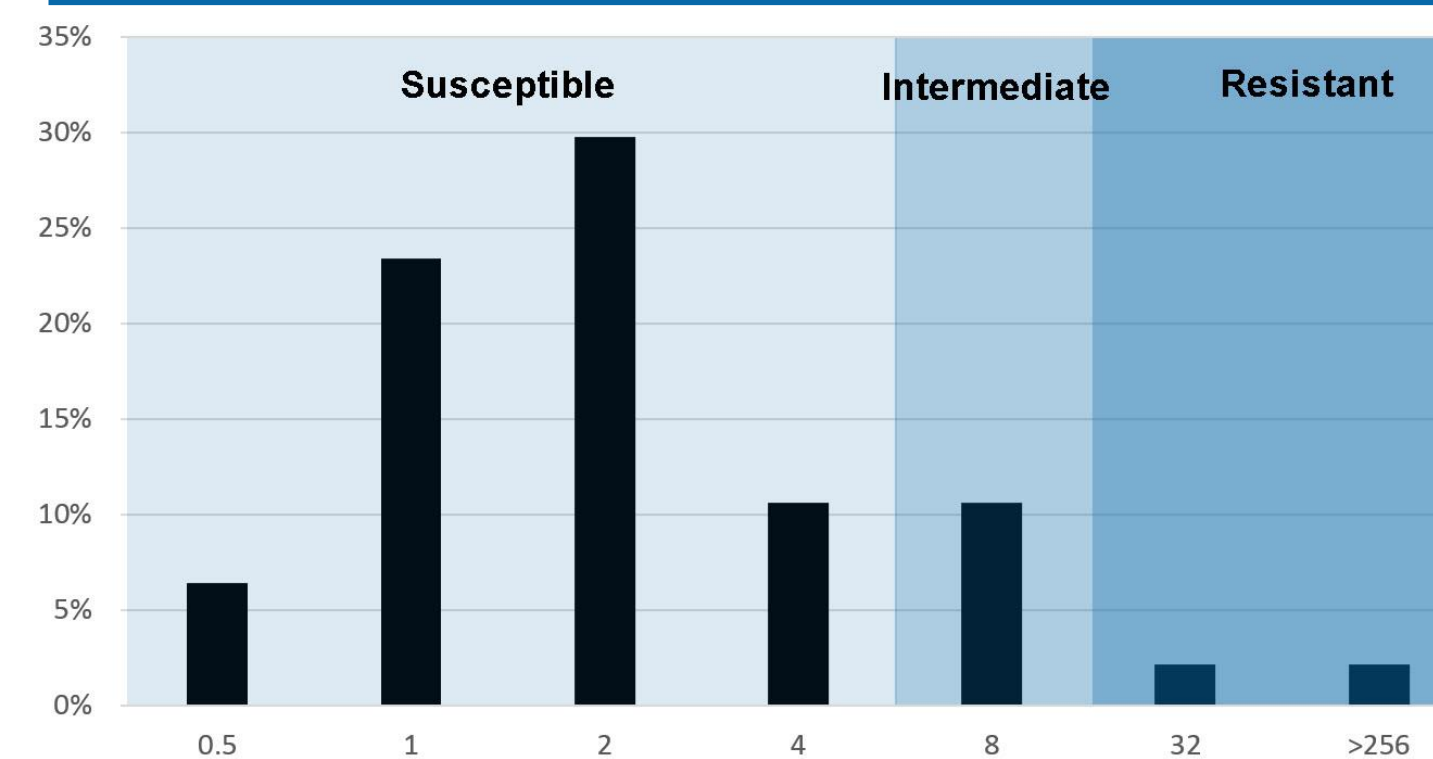


Infection Results

Organism Isolated, n (%)	N=52*
<i>P. aeruginosa</i>	52 (86.7)
Polymicrobial	1 (3.3)
Resistance of Pathogen, n (%)	N=52*
Non-MDR	18 (34.6)
MDR	21 (40.4)
XDR	13 (25)
Susceptibility to C/T, n (%)	N=47 tested
Susceptible	39 (83)
Intermediate	5 (10.6)
Resistant	3 (6.4)
Susceptibility not Tested	n=5

*Only includes patients with isolated *P. aeruginosa* as appropriate indication for C/T

MIC Distribution for *P. aeruginosa*



Susceptibility to C/T by Phenotype

Non-MDR	MDR	XDR
94.1%	94.7%	45.5%

Outcomes

Clinical Cure, n (%)	Overall	N=39*
	Monotherapy (n=22), n (%)	25 (64.1)
	Combination Therapy (n=17), n (%)	17 (77.3)
Clinical Failure, n (%)		8 (47.1)
Indeterminate Clinical Status, n (%)		10 (25.6)
Microbiological Cure (N=13), n (%)		4 (10.3)
	Intra-abdominal	5 (38.5)
	Primary Bacteremia	3
	Pneumonia	1
Microbiological Failure (N=13), n (%)		8 (61.5)
	Pneumonia	7
	Intra-abdominal	1
Patient Disposition, n (%)		N=60
	Completed Therapy in Hospital	22 (36.7)
	Discharged on C/T	11 (18.3)
	Died in Hospital on C/T	10 (16.7)
	Therapy Changed	13 (21.7)
	De-escalation of Therapy	2 (3.3)
	Therapy Discontinued	1 (1.7)

*Only calculated in patients with isolates susceptible to C/T

Conclusions

- At the Cleveland Clinic C/T is used primarily for pseudomonal infections, with the major source being pneumonia.
- Overall, the susceptibility rate of *P. aeruginosa* isolated from patients receiving C/T was 83%.
- Antimicrobial susceptibility testing, especially for MDR and XDR *P. aeruginosa* isolates, will be important in stewarding the use of this new antimicrobial.