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Study of Prescribing patterns and Effectiveness of Ceftolozane/Tazobactam Real-world Analysis (SPECTRA): Results from a multinational, multicenter observational study

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Background

- Hospital-acquired Gram-negative (GN) infections cause significant morbidity and mortality. These infections are often difficult to treat because they are caused by organisms resistant to common therapy[1]
- Ceftolozane/tazobactam (C/T) is a novel antipseudomonal cephalosporin (ceftolozane) combined with an established β-lactamase inhibitor (tazobactam) used for the treatment of serious Gram-negative bacterial infections[2,3]
- C/T has demonstrated efficacy in registration trials to treat complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), and hospital-acquired bacterial and ventilator-associated bacterial pneumonia[1,4,5]
- Real-world evidence on C/T is important to physicians, providers, and other stakeholders including payers to help inform clinical decisions and optimize healthcare resource use

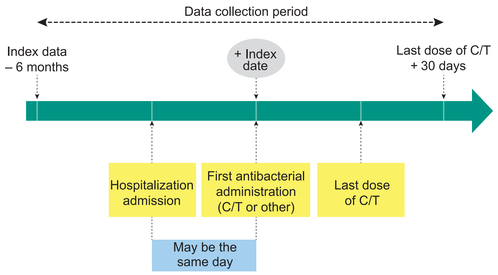
Objective

- To describe the real-world clinical use and outcomes of C/T in a multinational, multisite study

Methods

- SPECTRA is a multinational, multicenter, retrospective inpatient observational study of patients treated with C/T in Australia, Austria, Germany, Italy, Mexico, Spain, and the UK
- Adult patients treated for ≥48 hours with C/T from 15 January 2016 to 21 November 2020 were included in the study
- Demographics, clinical characteristics, treatment management patterns, clinical outcomes, and resource utilization were analyzed in the study

Figure 1. Study design



Results

- There were 687 patients from 38 participating hospitals in 7 countries
- 42.1% of patients were immunocompromised, 28.4% had chronic pulmonary disease

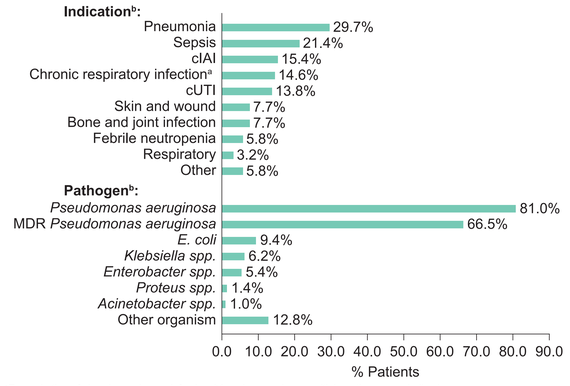
Table 1. Patient characteristics

	(N = 687)
Age (years), mean (SD)	57.6 (17.3)
Male, n (%)	456 (66.4%)
At least one comorbidity, n (%)	563 (82.0%)
Number of comorbidities, mean (SD)	2.0 (1.6)
Immunocompromised, n (%)	289 (42.1%)
Heart disease, n (%)	208 (30.3%)
Chronic pulmonary disease, n (%)	195 (28.4%)
Diabetes mellitus, n (%)	178 (25.9%)
Chronic kidney disease	136 (19.8%)
Previous hospitalizations in the 6 months prior to the index date, n (%)	376 (54.7%)
ICU stay in the 6 months prior to the index date, n (%)	87 (23.1%)
Surgeries in the 6 months prior to the index date, n (%)	217 (31.6%)

Microbiological findings

- The most common indications were pneumonia (29.7%), sepsis (21.4%), and cIAI (15.4%)
- 23.6% of patients had multiple sites of infection and 245 (35.7%) were polymicrobial infections
- The most common pathogen was *Pseudomonas aeruginosa* (81.0%), with 66.5% of samples positive for multidrug-resistant *Pseudomonas aeruginosa*

Figure 2. Indication for C/T treatment and pathogen



[a]Exacerbation of chronic respiratory infection. [b]A patient can have multiple pathogens or indications.

Treatment management findings

- Median C/T treatment duration was 12.0 days (11.0 [IQR])
- C/T was administered empirically in 28.8% of the overall cohort and in 31.8% of patients with respiratory infections
- Initial C/T dose adjustment was observed in 12.1% of patients

Table 2. Therapy characteristics

	Overall (N = 687)	Respiratory infections	
		Yes (N = 305)	No (N = 365)
Previous antibiotics in past 30 days, n (%)	463 (67.4%)	190 (62.3%)	260 (71.2%)
Previous carbapenem in past 30 days, n (%)	217 (31.6%)	90 (29.5%)	121 (33.2%)
C/T duration (days), median (IQR)	12.0 (11.0)	12.0 (8.0)	11.0 (14.0)
C/T empiric therapy, n (%)[a,b]	171 (28.8%)	83 (31.8%)	83 (25.8%)
C/T definitive therapy, n (%) [a,b]	423 (71.2%)	178 (68.2)	239 (74.2%)
Initial dose of C/T 3 g/8H, n (%)	138 (20.1%)	100 (33.0%)	37 (10.1%)

[a]Based on a lower denominator as some patients could not be categorized as empiric or definitive due to missing or indeterminate values.
[b]Empiric refers to initiation of C/T prior to susceptibility testing.
[c]Definitive refers to initiation of C/T after susceptibility testing.

Table 3. Treatment duration (days) by indication for index event

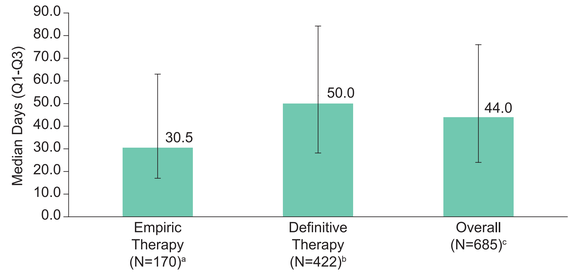
C/T duration (days)	Indication for index event										
	cIAI (n=106)	cUTI (n=95)	Pneumonia (n=204)	Exacerb. of CRI (n=100)	Sepsis (n=147)	Febrile neutro. (n=40)	B&J infection (n=40)	Respiratory illness (n=22)	Bacteremia (n=20)	Wound (n=35)	Overall (n = 687)
Median	12.0	10.5	11.0	14.0	10.0	8.5	24.0	10.5	14.0	11.0	12.0
Q1;Q3	7.0;22.0	7.0;15.0	7.0;16.0	8.0;16.0	7.0;17.0	6.0;14.5	12.0;44.0	7.0;16.0	6.5;20.5	6.0;22.0	7.0;18.0

CRI, chronic respiratory infection; B&J, bone and joint; Neutro., Neutropenia; Exacerb., Exacerbation.

Resource utilization

- Approximately one-half (49.9%) of patients were admitted to the ICU, 43.4% were related to the infection
- Most patients (71.3%) had an infectious disease consultation with an average of 9.3 (SD 14.3) consultations per patient
- Lower median duration of hospital length of stay in patients who received empiric C/T therapy 30.5 days (Q1-Q3: 17.0-63.0) compared to definitive therapy 50.0 days (Q1-Q3: 28.0-84.0)

Figure 3. Hospital length of stay

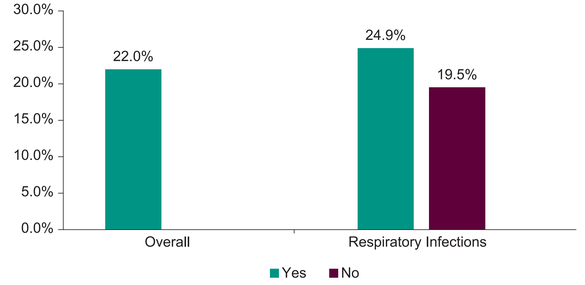


[a]One patient receiving empiric therapy had missing hospital length of stay data.
[b]One patient receiving definitive therapy had missing hospital length of stay data.
[c]Overall sample includes patients who could not be categorized as receiving empiric or definitive therapy but contributed length of stay data.

Table 4. Outcomes of overall cohort

Outcomes (N=687)	N (%) or mean (SD)
Clinical success	454 (66.1%)
In-hospital all-cause mortality	151 (22.0%)
Time from index date to death (in days)	41.0 (57.1)
In-hospital infection-related mortality	60 (8.7%)
30-day all cause re-admission	67 (9.8%)
30-day infection-related re-admission	32 (4.7%)

Figure 4. Mortality overall and by respiratory infections



Conclusions

- Many patients receiving C/T were critically ill, and immunocompromised
- C/T was used to treat multisource, polymicrobial infections, with pneumonia being the most common indication and *P. aeruginosa* the most common pathogen
  - Two-thirds of samples were positive for multidrug-resistant *P. aeruginosa*
- In this multicountry, multicenter real-world analysis, C/T treated patients demonstrated clinical success and mortality rates consistent with clinical trial results despite the complexity of patient types and pathogen resistance profiles

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Disclosures

This study was sponsored by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.
AHW and ENO are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.
LPK was an employee of Merck Sharp & Dohme Corp at time of study

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