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Treating Hospital-Acquired, Ventilated Hospital-Acquired and Ventilatory-Associated Bacterial Pneumonia in Canada with Ceftolozane/Tazobactam (C/T): Final Results from the CLEAR (Canadian LEadership on Antimicrobial Real-life usage) Registry

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Introduction

Over the past several years in Canada, when new IV antimicrobials are approved and introduced onto the market, they are used primarily by infectious diseases/medical microbiology specialists and frequently used to treat "off-label" infectious indications. There is commonly limited data sharing between clinicians regarding why they chose to use these new IV antimicrobials (i.e., because of failure, resistance, or adverse effects associated with use of other antimicrobial agents), the types of infections treated, and how (i.e., dosage regimen, duration of therapy, as monotherapy or in combination with one or more other antimicrobial agents) they use new IV antimicrobial agents in real world scenarios.

The CLEAR (Canadian LEadership on Antimicrobial Real-life Usage) registry is an initiative coordinated by the Canadian Antimicrobial Resistance Alliance (CARA). CLEAR is a national usage registry platform that enables the accumulation of knowledge regarding the clinical usage of new IV antimicrobials recently introduced into the Canadian marketplace. In this study, CLEAR is accumulating data on the usage of IV ceftolozane/tazobactam across Canada in treating hospital acquired bacterial pneumonia (HABP), ventilated hospital-acquired bacterial pneumonia (vHABP) and ventilatory-associated bacterial pneumonia (VABP).

CLEAR also has IV ceftobiprole, IV dalbavancin, and IV fosfomycin in the registry. Links to access these surveys:
https://rcsurvey.radyfhs.umanitoba.ca/surveys/?s=A8EHM8JJRF;
https://rcsurvey.radyfhs.umanitoba.ca/surveys/?s=F7JXNDFXEF;
https://rcsurvey.radyfhs.umanitoba.ca/surveys/?s=TPMWJX98HL

Materials and Methods

An IV ceftolozane/tazobactam usage questionnaire was developed using the input of infectious disease/medical microbiology specialists (physicians and pharmacists) across Canada. The CLEAR registry protocol/questionnaire was submitted to and received approval by the Human Ethics Committee at the University of Manitoba (Winnipeg, Canada; April 2019).

Using the web-based research data management program, REDCap™ (Research Electronic Data Capture), clinicians (physicians and clinical pharmacists) responded directly to the usage questionnaire online starting June 2019. The REDCap™ online survey link (https://rcsurvey.radyfhs.umanitoba.ca/surveys/?s=WHWT7RDK7X) was distributed via email to >400 CLEAR participants (members of the Association of Medical Microbiology and Infectious Diseases Canada [AMMI] and Canadian Society of Hospital Pharmacists [CSHP]). Clinicians were sent an email every 2-3 months encouraging their participation in CLEAR. A series of drop-down menus and short answer questions allowed for rapid (~3 minutes) completion of the survey. Clinicians were encouraged to voluntarily complete usage questionnaires for as many patients as possible. The CLEAR IV ceftolozane/tazobactam questionnaires received by March 7, 2024 were tabulated and results presented are based on 54 patient treatment surveys for treating HABP, vHABP and VABP. The survey link was then disabled as all study objectives have been met.

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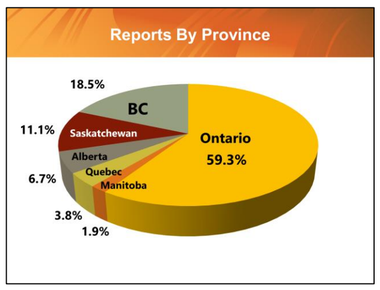
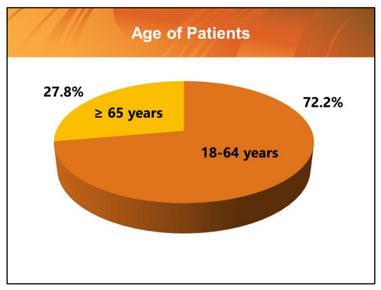
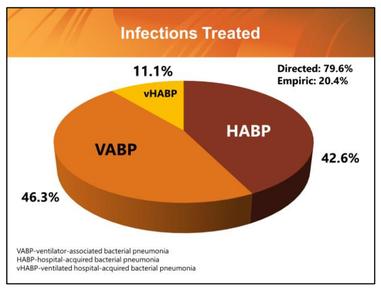
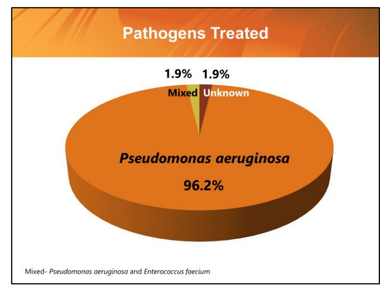
Results

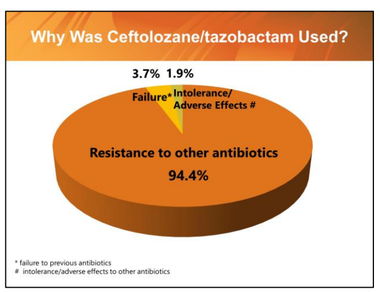
Below are the cumulative tabulated results of the questions asked in the CLEAR IV ceftolozane/tazobactam usage survey questionnaires as of March 7, 2024. The following tables are based on a total of 54 patient treatment surveys.

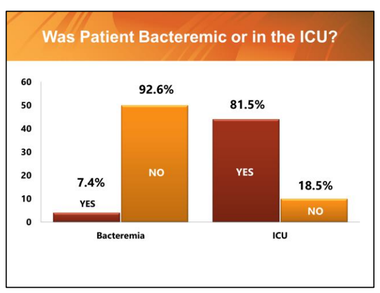


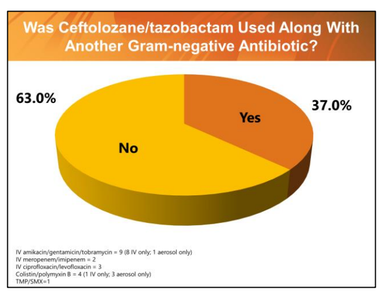


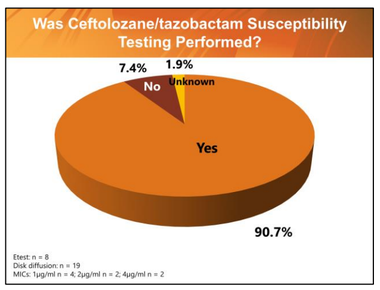


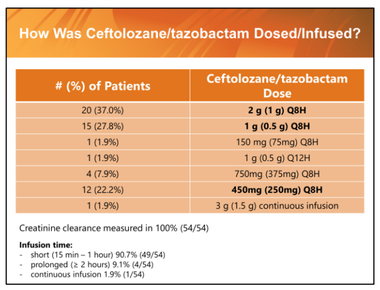


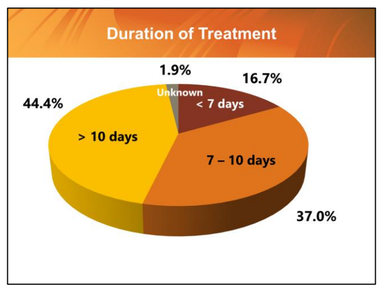


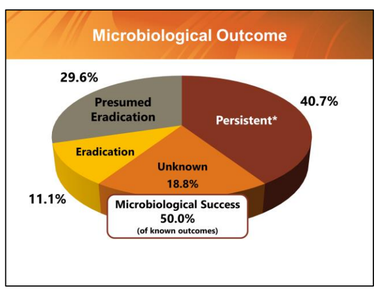


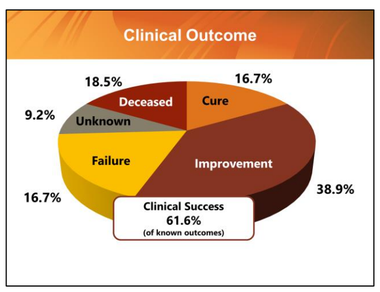


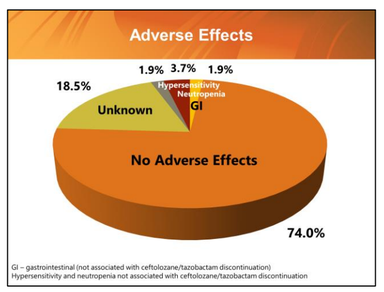












Conclusions

1. Ceftolozane/tazobactam was used to treat HABP (42.6%), VABP (46.3%) and less commonly vHABP (11.1%) of which 81.5% were treated in the ICU.
2. Ceftolozane/tazobactam was primarily used as directed (but at times as empiric) treatment of HABP, VABP and vHABP caused or presumed to be caused by *Pseudomonas aeruginosa.*
3. Ceftolozane/tazobactam was primarily used due to resistance to other antibiotics.
4. Ceftolozane/tazobactam was mostly used with antimicrobial susceptibility testing.
5. Ceftolozane/tazobactam was frequently combined with a second anti-Pseudomonal agent such as an aminoglycoside (IV or aerosolized), colistin (IV or aerosolized), or a fluoroquinolone.
6. The most common IV doses administered were 1 g (0.5 g) Q8H and 2 g (1 g) Q8H using a short infusion (≤ 1 hour), but dosing was customized based on renal clearance in all patients.
7. Ceftolozane/tazobactam was frequently used for durations >10 days.
8. Ceftolozane/tazobactam treatment was associated with relatively good rates of clinical success, though bacterial persistence did occur and was at times associated with clinical failure and resulting death due to infection.
9. Adverse events were uncommon, which is consistent with the good safety profile of ceftolozane/tazobactam.
10. The CLEAR IV ceftolozane/tazobactam study objectives have been met and the survey link disabled as of March 7, 2024.

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