Poster #2275

# Novel Therapeutic Options for the Treatment of Multi-Drug Resistant *Achromobacter* Respiratory Infections

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## Background

- Respiratory infection due to *Achromobacter spp.* has become increasingly more common, especially in patients with cystic fibrosis (CF).[1]
- Recurrent infections in this patient population contribute to significant morbidity and mortality.
- Frequent antibiotic exposure may lead to subsequent expression of intrinsic multi-drug resistant (MDR) mechanisms.[1]
- Antibiotics available with potential activity against MDR *Achromobacter spp.* infections are limited and lack approved susceptibility breakpoints.
- Several recently approved antimicrobials target MDR gram-negative pathogens, but none are FDA approved for *Achromobacter spp.* respiratory infections.

## Objective

- **Purpose:** To examine clinical outcomes with novel therapeutic agents for the treatment of respiratory infections due to MDR *Achromobacter spp.*

## Methods

- Multi-center (7 acute care hospitals across AdventHealth Central Florida Division)
- Retrospective chart review
- Study Period: 8/1/17 to 3/31/19
- Inclusion Criteria:
- Culture confirmed MDR *Achromobacter spp.* respiratory infection

and

Treatment with at least one of the following:
eravacycline (ERV),
meropenem/vaborbactam (MEM/VAB),
ceftolozane/tazobactam (TOL/TAZ),
ceftazidime/avibactam (CZA),
cefiderocol (CFD)

| *Achromobacter spp.* MDR Criteria |
|---|
| Intermediate or resistant to 1 active antimicrobial in at least 3 antimicrobial classes |

## Results

| Patient # - Treatment Course | Age & Gender | Relevant PMH | Culture Source | Organism | Treatment Summary* | MIC Values | Concomitant Organisms in Respiratory Culture | Concomitant Antibiotics | Total Duration of Therapy (Days) | Length of Stay (Days) | Inpatient All-Cause Mortality | 30-Day Infection-Related Readmission |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 80 y/o F | chronic bronchiectasis | Sputum | *A. xylosoxidans* | **MEM/VAB: D1-20** | NR | None | None | 20 | 8 | N | N |
| 2 – a | 40 y/o M | CF | Sputum | *A. xylosoxidans* | **MEM/VAB: D1-14**<br>COL: D1-14 | MEM/VAB: 32<br>COL: 0.12 | MDR *P. aeruginosa* | None | 14 | 14 | N | N |
| 2 – b | 40 y/o M | CF | Sinus | *A. xylosoxidans* | **ERV: D1-22** | NR | None | None | 22 | 13 | N | N |
| 2 – c | 41 y/o M | CF | Sputum | *A. xylosoxidans* | **ERV: D1-31**<br>**CFD: D10-31** | ERV: 2<br>CFD: 0.06 | MDR *P. aeruginosa* | TOL/TAZ: D4-10<br>MEM: D5-10<br>DELA: D10-31 | 31 | 31 | N | N |
| 2 – d | 41 y/o M | CF s/p BOLT/OLT | Lung Tissue | *A. xylosoxidans* | **ERV: D1-36**<br>**CFD: D1-22** | ERV: 1<br>CFD: NR | MDR *P. aeruginosa* | PIP/TAZ: D5-21<br>DELA: D6-7 | 36 | 28 | N | N |
| 3 | 63 y/o M | COPD | Sputum | *A. xylosoxidans* | TZP: D1-2<br>TOB: D1<br>MEM: D2<br>MINO: D2-4, 6-9, 24-34<br>COL: D6-9, 35-37<br>CIP: D9-27<br>**CZA: D22-35**<br>TS: D27-34<br>**ERV: D29-34** | TZP: 16<br>TOB: 8<br>MEM: ≥16<br>MINO: 4<br>COL: 2<br>CIP: 4<br>CZA: 8<br>TS: ≤20<br>ERV: NR | MDR *P. aeruginosa*, MDR *S. maltophilia*, MRSA | VANC: D1-2, 6, 22-29<br>TOL/TAZ: D2-17<br>METRO: D2-17, 22-29 | 37 | 37 | Y | N/A |
| 4 | 45 y/o F | chronic respiratory failure | Sputum | *A. xylosoxidans* | **CZA: D1-15, 23-27**<br>**MEM/VAB: D22-23, 42**<br>TZP: D42-57, 61-79, 114-121<br>**ERV: D106-108, 112-114** | CZA: 4<br>MEM/VAB: 8<br>TZP: 8 to ≥128<br>ERV: NR | None – Enterobacter cloacae complex in separate respiratory specimen | MEM: D1, 41-42, 57-59, 105-109, 112-114<br>VANC: D1-8, 22-24, 41-43, 57-61, 72-78, 106-119<br>CFP: D109-112<br>CIP: D114-116 | 74 | 121 | Y | N/A |
| 5 | 75 y/o F | COPD, chronic bronchiectasis | Bronch wash | *A. species* | MEM: D1-4<br>**ERV: D4-13** | MEM: S<br>ERV: NR | None | None | 13 | 7 | N | Y |
| 6 – a | 29 y/o F | CF | Sputum | *A. xylosoxidans* | **MEM/VAB: D1-10**<br>COL: D2-10 | MEM/VAB: NR<br>COL: NR | None | None | 10 | 2 | N | N |
| 6 – b | 29 y/o F | CF | Sputum | *A. xylosoxidans* | **MEM/VAB: D1-14**<br>COL: D1-14 | MEM/VAB: NR<br>COL: NR | None | None | 14 | 4 | N | N |
| 6 – c | 30 y/o F | CF | Sputum | *A. xylosoxidans* | **ERV: D1-7**<br>TIG: D7-11 | ERV: NR<br>TIG: NR | None | None | 11 | 6 | N | N |
| 7 | 26 y/o M | CF | Sputum | *A. denitrificans* | MEM: D1-2<br>MINO (PO): D1-5<br>**MEM/VAB: D3-5** | MEM: 4<br>MINO: NR<br>MEM/VAB: NR | MRSA, *E. coli* | CFT: D5-16 | 16 | 7 | N | N |
| 8 | 52 y/o F | CF | Sputum | *A. xylosoxidans* | CIP: D1-15<br>MINO (PO): D1-15<br>**TOL/TAZ: D1-15** | CIP: 4<br>MINO: NR<br>TOL/TAZ: NR | ESBL *E. coli*, *P. aeruginosa* | None | 15 | 4 | N | N |
| 9 | 22 y/o M | CF | Bronch wash | *A. xylosoxidans* | TOB: D1-5<br>CFP: D1-5<br>**ERV: D2-11, 14-18**<br>TS: D5-25<br>TZP: D5-7<br>COL: D10-18 | TOB: ≥16<br>CFP: ≥64<br>ERV: 2<br>TS: 40<br>TZP: 256<br>COL: 0.5 | Group A Strep | LZD: D1-2 | 18 | 18 | N | N |

*Does not include any inhaled antibiotics (i.e. colistin, tobramycin, aztreonam) or antibiotics used for anti-inflammatory effects (i.e. azithromycin).
Abbrevations: CF = cystic fibrosis, BOLT = bilateral orthotopic lung transplant, OLT = orthotopic liver transplant
Antibiotics: cefepime (CFP), cefiderocol (CFD), ciprofloxacin (CIP), ceftazidime/avibactam (CZA), ceftolozane/tazobactam (TOL/TAZ), colistin (COL), eravacycline (ERV), meropenem (MEM), meropenem/vaborbactam (MEM/VAB), minocycline (MINO), piperacillin/tazobactam (TZP), tigecycline (TIG), trimethoprim/sulfamethoxazole (T/S), tobramycin (TOB)

| Antibiotic | Number of Treatment Regimens | Lowest MIC (mcg/mL) | Mean MIC (mcg/mL) | Highest MIC (mcg/mL) |
|---|---|---|---|---|
| **Eravacycline** | 8 | 1 | 2 | 2 |
| **Meropenem/vaborbactam** | 6 | 0.25 | 64 | 256 |
| **Cefiderocol** | 2 | S* | - | - |
| **Ceftazidime/avibactam** | 1 | 2 | 8 | 16 |
| **Ceftolozane/tazobactam** | 0 | 16 | 256 | 256 |

* Interpretation based on *P. aeruginosa* disk diffusion breakpoints provided by Shinogi (Cefiderocol Susceptibility Testing Protocol).

## Summary

| Characteristic | Value |
|---|---|
| Unique patients | 9 |
| Age (years), mean | 45 |
| Female | 56% |
| Cystic fibrosis | 56% |
| Polymicrobial infection | 50% |
| Duration of all antibiotic therapy (days), median | 16 |
| Length of stay (days), median | 8 |
| Treatment completed outpatient | 64% |
| Inpatient all-cause mortality | 14% |
| 30-day infection-related readmission | 8% |

- 10/14 (71%) of cases were treated with combination therapy
  - 5/10 (50%) of combination therapy included IV colistin
- 3/4 (75%) of monotherapy was eravacycline

## Conclusion

Novel agents, such as eravacycline or meropenem/vaborbactam, may be viable treatment options for patients with MDR *Achromobacter spp.* respiratory infections.

**References:**
1. Parkins MD, Elborn JS. Newer antibacterial agents and their potential role in cystic fibrosis pulmonary exacerbation management. *J Antimicrob Chemother*. 2010;65(9):1853-1861. doi:10.1093/jac/dkq245

Disclosures: Authors of this presentation have the following 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: All authors have nothing to disclose.

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