Current and Emerging Therapies for Infectious Diseases

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Learning Objectives

1. Describe drivers for antibiotic development
2. List anti-infectives that were approved in 2017 for the treatment of multi-drug resistant organisms
3. Discuss the antibiotics that should be approved for human use in 2018/early 2019
Key Drivers
As a pharmaceutical executive, which drug would you recommend that your company bring to market?

**Drug A**
- The drug is only to be used for 5-14 days.
- The more you use the drug, the more likely it is to become less effective.
- Annual sales are $31 M.

**Drug B**
- It can be used for decades.
- The drug will never lose its efficacy.
- Annual sales are $12 B.
As a pharmaceutical executive, which drug would you recommend that your company bring to market?

Drug A: Ceftazidime/Avibactam

Drug B: Atorvastatin
What is influencing the development of drugs for resistant organisms?

• No brainer first bullet point….resistance
• Here is where I show you the graph that everyone always shows

![Graph showing the total number of new antibacterial agents from 1983-1987 to 2008-2012.]

Figure 1  Dates of discovery of distinct classes of antibacterial drugs

Illustration of the “discovery void.” Dates indicated are those of reported initial discovery or patent.

Adapted from Silver 2011 (1) with permission of the American Society of Microbiology Journals Department.

Antibacterial drugs act against bacteria and include antibiotics (natural substances produced by microorganisms), and antibacterial medicines, produced by chemical synthesis.
Legislative Drivers

Generating Antibiotics Incentives Now (GAIN Act)

- Signed into law on July 9, 2012
- Established definition of a Qualified Infectious Disease Product (QIDP)
  - Extends exclusivity for new antibiotics an additional 5 years in addition to any existing patent extensions created by other regulations
  - NDA accelerated at FDA and “fast track status”
  - Requires FDA to issue new guidance on the development of pathogen-focused antibiotics

National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB)

- March 2015

GOAL 4: Accelerate Research to Develop New Antibiotics, Other Therapeutics, Vaccines, and Diagnostics

<table>
<thead>
<tr>
<th>Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Conduct research to enhance understanding of environmental factors that facilitate the development of antibiotic-resistance and the spread of resistance genes that are common to animals and humans.</td>
</tr>
<tr>
<td>4.2 Increase research focused on understanding the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease.</td>
</tr>
<tr>
<td>4.3 Intensify research and development of new therapeutics and vaccines, first-in-class drugs, and new combination therapies for treatment of bacterial infections.</td>
</tr>
<tr>
<td>4.4 Develop non-traditional therapeutics and innovative strategies to minimize outbreaks caused by resistant bacteria in human and animal populations.</td>
</tr>
<tr>
<td>4.5 Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates.</td>
</tr>
</tbody>
</table>

### On the Horizon

A table detailing various companies and their research projects focused on drug discovery for bacterial infections, along with the bacteria they target and the stage of development.

#### Table: Bacterial Targeting and Drug Development

<table>
<thead>
<tr>
<th>Company/Research Team</th>
<th>Project</th>
<th>Novelty*</th>
<th>urgency/Priority*</th>
<th>Bacteria Targeted / Stage of Early Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achaogen</td>
<td>AKAO-LpxC</td>
<td>✔️</td>
<td>✔️</td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Antabio</td>
<td>PEI</td>
<td>✔️</td>
<td>✔️</td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Bugworks Research</td>
<td>Gyrox</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Cidara Therapeutics</td>
<td>CD201</td>
<td>✔️</td>
<td>✔️</td>
<td>Acinetobacter + P. aeruginosa + Enterobacteriaceae</td>
</tr>
<tr>
<td>ContraFect</td>
<td>Gram-negative lysisins</td>
<td>✔️</td>
<td>✔️</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>Debiopharm</td>
<td>Debio 1453</td>
<td>✔️</td>
<td>✔️</td>
<td>Neisseria Gonorhoeae</td>
</tr>
<tr>
<td>Eligchem</td>
<td>Helical AMP</td>
<td>✔️</td>
<td>✔️</td>
<td>Helical Antimicrobial Peptide</td>
</tr>
<tr>
<td>Entasis Therapeutics</td>
<td>ETX0282 CPDP</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Forge Therapeutics</td>
<td>FG-LpxC</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Itemum</td>
<td>Sulopenem</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Microbiotix</td>
<td>T3SS Inhibitor</td>
<td>✔️</td>
<td>✔️</td>
<td>Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Oppilotech</td>
<td>LPS</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Reclx Pharma</td>
<td>NB1TI</td>
<td>✔️</td>
<td>✔️</td>
<td>Acin. + P. aerug + Enterobacteriaceae</td>
</tr>
<tr>
<td>Spero Therapeutics</td>
<td>SPR741</td>
<td>✔️</td>
<td>✔️</td>
<td>Gram-negative activity</td>
</tr>
<tr>
<td>Tetraphase Pharm</td>
<td>TP-6076</td>
<td>✔️</td>
<td>✔️</td>
<td>Acinetobacter + Enterobacteriaceae</td>
</tr>
<tr>
<td>VenatoRx</td>
<td>VNIRX-PBP</td>
<td>✔️</td>
<td>✔️</td>
<td>Enterobacteriaceae</td>
</tr>
<tr>
<td>Visterra</td>
<td>VI5705</td>
<td>✔️</td>
<td>✔️</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>
2017 FDA Highlights [Antibacterials]
Approvals

- **June 19, 2017** - delafloxacin [Melinta Pharmaceuticals] approved under the trade name Baxdela

- **Indications**
  - Treatment of acute bacterial skin and skin structure infections x 5-14 days
  - Spectrum of activity includes MRSA but gaps in coverage for gram negatives exist

- **Dosing**
  - 300mg IV Q12 hours
  - 450mg PO Q12 hours
  - Renal dosing required for IV at CrCl 15-29 ml/min

- **Phase 3 ongoing** for community acquired bacterial pneumonia and Phase 1 for complicated UTI
### Breakpoint Comparisons for Selected Organisms

<table>
<thead>
<tr>
<th>Species</th>
<th>Delafloxacin MIC (mcg/mL)</th>
<th>Ciprofloxacin MIC (mcg/mL)</th>
<th>Levofloxacin MIC (mcg/mL)</th>
<th>Moxifloxacin MIC (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin susceptible S. aureus</td>
<td>≤0.25 0.5 ≥1</td>
<td>≤1 2 ≥4</td>
<td>-- -- --</td>
<td>≤2 4 ≥8</td>
</tr>
<tr>
<td>Methicillin resistant S. aureus</td>
<td>≤0.25 0.5 ≥1</td>
<td>-- -- --</td>
<td>-- -- --</td>
<td>-- -- --</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>≤0.12 0.25 ≥0.5</td>
<td>≤1 2 ≥4</td>
<td>≤2 4 ≥8</td>
<td>≤1 2 ≥4</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>-- -- --</td>
<td>≤1 2 ≥4</td>
<td>≤2 4 ≥8</td>
<td>≤1 2 ≥4</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>≤0.06 -- --</td>
<td>≤1 2 ≥4</td>
<td>≤2 4 ≥8</td>
<td>-- -- --</td>
</tr>
<tr>
<td>Enterobacteriaceae *</td>
<td>≤0.25 0.5 ≥1</td>
<td>≤1 2 ≥4</td>
<td>≤2 4 ≥8</td>
<td>≤2 4 ≥8</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>≤0.5 1 ≥2</td>
<td>≤1 2 ≥4</td>
<td>≤2 4 ≥8</td>
<td>-- -- --</td>
</tr>
</tbody>
</table>

* E. coli, K. pneumoniae, and E. cloacae
## Approvals

**August 30, 2017 – meropenem/vaborbactam [The Medicines Company/Melinta] approved under the trade name Vabomere**

**Approved indication**
- Complicated UTI (including pyelonephritis)

### Phase 3 Trial Name

<table>
<thead>
<tr>
<th>Phase 3 Trial Name</th>
<th>Population studied</th>
<th>Dosing</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>TANGO 1 (n=550)</td>
<td>cUTI, AP</td>
<td>M-V (2g/2g) via a 3 hr infusion) or P-T (4g/0.5g via a 30 min infusion) every 8 hrs. Conversion to LV allowed after 15 doses of IV</td>
<td>Primary endpoint [overall success at end of IV] 98.4% (M-V) and (94.0%) in P/T group (95% CI of difference: 0.7, 9.1). M-V statistically superior to P/T.</td>
</tr>
<tr>
<td>TANGO 2 (n=72)</td>
<td>cUTI, AP, hospital acquired bacterial pneumonia, ventilator-associated bacterial pneumonia, bacteremia, intraabdominal</td>
<td>M-V (2gm/2gm) vs. best available therapy</td>
<td>Trial stopped early after interim analysis revealed statistically significant differences favored M-V over best available therapy at test of cure in patients with CRE. Lower mortality rates were also reported in M-V patients.</td>
</tr>
</tbody>
</table>

cUTI = complicated UTI, AP = Acute pyelonephritis, M-V = meropenem/vaborbactam, P/T = piperacillin/tazobactam, LV = levofloxacin. Source: [https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209776Orig1s000SumR.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/209776Orig1s000SumR.pdf), [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
# Antimicrobial Spectrum of Activity (In-Vivo)

## Inhibitory Activity against β-Lactamases

<table>
<thead>
<tr>
<th>Class of β-Lactamases</th>
<th>Enzymes</th>
<th>Ceftolozane-tazobactam</th>
<th>Ceftazidime-avibactam</th>
<th>Meropenem-vaborbactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A (Serine)</td>
<td>TEM</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>SHV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>CTX-M</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>KPC (CRE)</td>
<td>None</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Class B (MBLs)</td>
<td>IMP/VIM</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>NDM</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Class C (Serine)</td>
<td>amp C</td>
<td>Variable</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>OXA</td>
<td>Variable</td>
<td>Variable</td>
<td>None</td>
</tr>
</tbody>
</table>

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Zerbaxa® (Ceftolozane-Tazobactam) Prescribing Information, Merck Pharmaceuticals, Inc. 2016.

Additional 2017/early 2018 FDA Activity

- **October 2017**
  - Ceftazidime/avibactam [C/A] granted priority review for supplemental New Drug Application filed to expand indication to hospital and ventilator associated pneumonia in adults
  - Supporting study: Phase 3 REPROVE study
    - C/A 2.5gm over 2 hours every 8 hours vs meropenem (M) 1gm over 30 minutes every 8 hours x 7-14 days
    - Clinically modified intention-to-treat (n=726)
      - C/A cure rate = 68.8% vs 73% in M group (-4.2% [95% CI -10.8 to 2.5])
    - Clinically evaluable (n=527)
      - C/A cure rate = 77.4% vs 78.1% in M group (-0.7% [95% CI -7.9 to 6.4])

- **January 11, 2018**
  - Reviewed inhaled ciprofloxacin for the treatment of non-cystic fibrosis bronchiectasis in patients with chronic pulmonary infections caused by *Pseudomonas aeruginosa*
  - 12 No’s; 3 Yes’

https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/ucm587657.htm
Projected approvals 2018 through early 2019
Lefamulin (Nabriva)

- New compound that is a semisynthetic derivative of pleuromutilin that is isolated from a mushroom
- Veterinary compounds in this class include tiamulin and valnemulin used in swine and poultry
- This would be the second agent for human use in this class (after retapamulin)
- Spectrum of activity
  - *S. pneumoniae, M.catarrhalis, H.influenzae, L. pneumophila, C. pneumoniae, M. pneumoniae*
  - *S. aureus* – Including MRSA
  - STDs – *N. gonorrhoeae, C. trachomatis, M. genitalium* including multidrug resistant strains
  - Minimal effects on GI flora including *B. fragilis, E.coli, and E. faecalis*
Lefamulin (Nabriva) – BC3781

- Pursing indication for community acquired bacterial pneumonia
  - 150gm IV q 12 hours over 60 minutes
  - 600mg PO q 12 hours
- Phase 2 for acute bacterial skin and skin structure infections (ABSSSI)
- Two phase 3 studies for community acquired bacterial pneumonia

**LEAP 1 (IV to Oral) Trial**
- 550 pts. with mod/severe pneumonia
- Lefamulin vs. moxifloxacin +/- linezolid
- Duration of treatment 7 days (10 if MRSA)
- Preliminary analysis shows non inferiority

**LEAP 2 (Oral) Trial**
- 740 pts. with moderate pneumonia
- Lefamulin (5 days) vs. moxifloxacin (7 days)
- Trial in progress - expect topline data in Spring 2018

Prince WT, AAC 2013;57:208-94., ID Week 2017
Eravacycline (Tetraphase)

- Novel, fully synthetic fluorocycline with activity against multiple MDROs including CRE, A. baumannii, and colistin resistant bacteria
- IV and PO (Phase 1)
- IGNITE studies
  - Ignite 1 – non inferiority vs IV ertapenem
  - Ignite 4 – non inferiority vs IV meropenem
  - Ignite 2 - didn’t meet endpoints for cUTI (inferior to levofloxacin) so company has to complete 1 more Phase 3 study. [Blamed it on PO].
  - Ignite 3- ongoing phase 3 trial comparing eravacycline IV vs ertapenem in cUTI. Enrollment completed.
- Expect NDA to be filed in Q1 18 with QIDP/fast track within 8 months

Horn P, ID Week 2017
Plazomicin (Achaogen)

Spectrum of Activity

- Enterobacteriaceae including CRE and ESBLs (*Klebsiella pneumoniae* and *E. coli*)
- *S. aureus* (in vitro)
- “greater potency that current aminoglycosides including

Phase 3 studies

EPIC – cUTI vs meropenem with conversion to PO levofloxacin

Plazomicin 15mg/kg q 24 hr

CARE – serious infections caused by CRE

- Cohort 1: plazomicin 15mg/kg q24h or colistin (plus mero or tigecycline)
- Cohort 2: plazomicin monotherapy
- Talking points: lower nephroxicity than colistin, must dose based on AUIC, lower relapse rates in cUTI
- NDA submitted – PDUFA date June 25, 2018
Fosfomycin (Zavante)

- Intravenous fosfomycin (Zolyd, ZTI-01)
- Fosfomycin has broad spectrum activity for both G+ and G-
  - ZUES (ZTI-01) Phase 2/3 trial compared fosfomycin 6gm as a one hour infusion given q8h vs piperacillin/tazobactam 4.5gms IV q8 hrs for treatment of cUTI, including acute pyelonephritis
  - Zavante intends to submit filing in early 2018 [fast track]

Table 2. Clinical Cure and Microbiologic Eradication Rates for Patients from ZEUS Trial with Antimicrobial Resistant Phenotypes (TOC, m-MITT), % (n/N)

<table>
<thead>
<tr>
<th></th>
<th>ESBL</th>
<th>Amino-R</th>
<th>CR</th>
<th>MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZTI-01</td>
<td>92%</td>
<td>57%</td>
<td>97%</td>
<td>67%</td>
</tr>
<tr>
<td>P-T</td>
<td>93%</td>
<td>47%</td>
<td>88%</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>(51/55)</td>
<td>(27/57)</td>
<td>(30/34)</td>
<td>(14/35)</td>
</tr>
</tbody>
</table>

CR: Carbapenem-resistant; ESBL: extended spectrum beta-lactamase; MDR: multidrug-resistant; m-MITT: microbiologic modified intent-to-treat

Ellis-Grosse E, et al. ID week # 1830
# Omadacycline (Paratek)

**Class:** Aminomethylcycline  
**Spectrum of activity against CDC Top Pathogen Threats**

<table>
<thead>
<tr>
<th>Category</th>
<th>Organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram positive</td>
<td>VRE, MRSA, VRSA, MDR <em>S. pneumoniae</em>, Erythromycin resistant Grp A <em>Streptococcus</em>, Clindamycin resistant Grp B <em>Streptococcus</em></td>
</tr>
<tr>
<td>Gram negative</td>
<td>Carb R <em>E. coli</em> (but limited activity against Carb R <em>K. pneumoniae</em>), ESBLs, drug resistant <em>Salmonella</em></td>
</tr>
<tr>
<td>Anaerobes</td>
<td><em>C. difficile</em> [but not developing for this indication]</td>
</tr>
</tbody>
</table>

Omadacycline (Paratek)

• Phase 3 OASIS trial – ABSSSI
  Omadacycline [100mg IV q12h x 2 doses, then 100mg IV q24hr with option to convert to 300mg PO q24h after 3 doses] vs linezolid 600mg IV/PO Q12hr

• Phase 3 OPTIC trial – CABP
  Omadacycline as above vs moxifloxacin

• Phase 2 complicated UTI - planned

• Anticipate NDA submission in quarter 1 2018 for ABSSI and CABP

Iclaprim (Motif Biosciences)

- Dihydrofolate reductase inhibitor
- Originally designed by Hoffman LaRoche to be more potent than trimethoprim. Can be given as monotherapy
- Rapidly bactericidal activity against MDR gram positive including MRSA that non susceptible vancomycin, linezolid, and daptomycin

Summary Minutes of the
Anti-Infective Drugs Advisory Committee
November 18-20, 2008
Location: Holiday Inn, The Ballrooms, 10000 Baltimore Avenue, College Park, MD

Questions to the committee:
1. Do the data presented demonstrate the safety and effectiveness of iclaprim for the treatment of cSSSI? Please vote Yes/No.

Vote: Yes = 2  No = 16  Abstain = 0

Due to problems with the electronic voting system, this vote was later found to be 2 Yes and 17 No votes. Please see the transcript for details regarding individual committee member’s votes.
Iclaprim (Motif Biosciences)

• Key trials
  – Phase 2 study (n=70) with HABP/VAP vs vancomycin for 7-14 days.
  – Two Phase 3 studies (REVIVE 1 and 2)
    ▪ Non inferior to vancomycin in both studies
    ▪ Dose = iclaprim 80mg IV q12h ; no renal dose adjustment

Phase 3 – ABSSSI Revive Trial “Read-out” April 2017
Phase 3 ABSSSI Revive 2 data “Read-out” October 2017
Expect NDA filing for ABSSSI 1Q 18
Expected approval 4Q 18

Huang ID Week 2017
Cefiderocol (Shinogi)

- Mimics natural siderophore iron complexes required by bacteria to survive. Actively transported into the periplasmic space.

- Cephalosporin that has molecular backbone from cefepime and ceftazidime and binds ferric iron.

- Broad spectrum activity against MDR gram negatives but no gram positive or anaerobes.

- Completed studies for cUTI and ongoing trial for HAP/VAP/HCAP vs carbapenem. Also have an ongoing study vs. CRE.
  
  2gms IV every 8 hours.

- Anticipate approval in 2019.

Echols R ID Week 2017
Relebactam + imipenem/cilastatin (MD-7655) – Merck

- Similar in activity to meropenem/vaborbactam
- Clinical efficacy in Phase 2 cUTI and cIAI studies
- Phase 3 ongoing in HABP/VABP

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Study Design</th>
<th>Total Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESTORE-IMI 1</td>
<td>cUTI, CIAI, or HABP/VABP caused by IMI-R, but IMI/REL and colistin susceptible isolates</td>
<td>IMI/REL 500/250mg Q 6 hrs Colistin (as CMS) given 150mg colistin base every 12 hours after 300mg loading dose + IMI 500mg every 6 hours Primary endpoint: overall response based on pre-determined criteria</td>
<td>54</td>
</tr>
<tr>
<td>(PN 013)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESTORE – IMI 2</td>
<td>HAB/VABP</td>
<td>IMI/REL 500mg/250mg every 6 hours Pip/Tazo 4.5 gms every 6 hours Can add Linezolid IV empirically for MRSA Primary endpoint is all cause mortality at day 28</td>
<td>536 (268 per group)</td>
</tr>
<tr>
<td>(PN014)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Paschke ID Week 2017
Oral drugs to Watch

- **Sulopenem**
  - Former Pfizer product purchased by Iterum pharmaceuticals in development for uncomplicated UTI but will activity against multidrug resistant gram negative organisms.
  - Moving into phase 3 in 2018 with anticipated filing in 2019
- **Ceftibuten/Clavulanate – Phase 3 cUTI trial begins in 2018**

<table>
<thead>
<tr>
<th>Organism</th>
<th>ESBL Enzyme</th>
<th>Amoxicillin-Clavulanate MIC (µg/mL)</th>
<th>Ciprofloxacin MIC (µg/mL)</th>
<th>C-Scape MIC (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>CTX-M-15,TEM-1</td>
<td>16</td>
<td>≤0.03</td>
<td>0.5</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>CTX-M-15,TEM-1</td>
<td>8</td>
<td>&gt;4</td>
<td>0.5</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>CTX-M-14</td>
<td>8</td>
<td>≤0.03</td>
<td>0.5</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>SHV-5,TEM-1</td>
<td>8</td>
<td>0.25</td>
<td>0.12</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>SHV WT,CTX-M-15, OXA-1/30-like</td>
<td>16</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>SHV-11,SHV-12,TEM-1</td>
<td>8</td>
<td>&gt;4</td>
<td>0.25</td>
</tr>
<tr>
<td><em>K. pneumoniae</em></td>
<td>SHV-30</td>
<td>8</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>CTX-M-15-like,TEM WT</td>
<td>2</td>
<td>≤0.03</td>
<td>0.03</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>CTX-M-14-like,TEM WT</td>
<td>8</td>
<td>4</td>
<td>0.03</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>None</td>
<td>0.5</td>
<td>&gt;4</td>
<td>&lt;0.015</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>None</td>
<td>1</td>
<td>≤0.03</td>
<td>&lt;0.015</td>
</tr>
<tr>
<td><em>E. coli</em></td>
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<td>&gt;4</td>
<td>0.25</td>
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<tr>
<td><em>K. pneumoniae</em></td>
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<td>&gt;4</td>
<td>0.06</td>
</tr>
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</table>

http://www.achaogen.com/cscapec
Helpful Resource

Pew Charitable Trust
