Newer Intravenous Antibiotics in the Intensive Care Unit

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- Connor KA. Newer Intravenous Antibiotics in the Intensive Care Unit: Ceftaroline, Ceftolozane-Tazobactam, & Ceftazidime-Avibactam. *AACN Adv Crit Care*. 2016. Oct;27:353-357.
  - Designated for Nursing CE, Pharmacology

Ceftaroline, Ceftolozane-Tazobactam, & Ceftazidime-Avibactam

Examples of Disease-Causing Microbes

How Antibiotic Resistance Happens

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How Antibiotic Resistance Happens

How Antibiotic Resistance Spreads

Lives Devastated/Lost due to Antibiotic-Resistant Organisms

**Timothy Mok, Univ.
of KY pharmacy
resident falls ill from
E. coli on rotation in
MD**

**Bryce Smith, 14
months old,
almost died from
MRSA lung
infection in ICU**

**Meredith Littlejohn,
19 years old, cancer
survivor, died from
antibiotic-resistant
Pseudomonas
infection**

Premature Death

Rebecca Lohsen
(17 yr)--Dead

Mariana Bridi da Costa
(22 yr)--Dead

Carlos Don
(12 yr)--Dead

Ricky Lannetti
(21 yr)--Dead

Life-altering Disability

Tom Dukes: colostomy, lost 8" colon

Addie Rereich, 11yo
Double lung transplant
Stroke, nearly blind
\$6 million hospital bill

Challenge of Antibiotic Resistance

- Infections due to multidrug-resistant (MDR) pathogens ↑ world-wide
  - Carbapenem-resistant Enterobacteriaceae (CRE)
  - Extended-spectrum β -lactamase (ESBL)–producing organisms
  - Multidrug-Resistant *Pseudomonas aeruginosa* & *Acinetobacter spp*
  - Methicillin-resistant *Staphylococcus aureus* (MRSA)
  - Vancomycin-resistant *enterococci* (VRE)
  - Penicillin-resistant *Streptococcus pneumoniae*

Challenge of Antibiotic Resistance

MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = Vancomycin-resistant *enterococci*
FQRP = Fluoroquinolone-resistant *Pseudomonas aeruginosa*

McArdle M. "[How Superbugs Will Affect Our Health Care Costs.](#)" The Atlantic 2011.

FDA-Approved Antibacterial Agents

CDC: Get Smart for Healthcare

**Know
When
Antibiotics
Work**

Encouraging Antibiotic Development: IDSA 10 x '20 Initiative

10
9
8
7
6
5
4
3
2
1

Bad Bugs
Need Drugs

10x'20

Oritavancin, 2014
Ten New ANTIBIOTICS by 2020

Dalbavancin, 2014

Tedizolid, 2014

1 ceftaroline fosamil: Forest Laboratories, Inc.
Approved October 29, 2010

Encouraging Antibiotic Development: IDSA 10 x '20 Initiative

**Bad Bugs
Need Drugs**

Ten new **ANTIBIOTICS** by 2020

Encouraging Antibiotic Development: IDSA 10 x '20 Initiative

Number	Drug Name	FDA-Approval Date
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10	???	

APPROVALS OF SYSTEMIC ANTIBACTERIALS SINCE 2010¹

#	DRUG	YEAR	NOVEL COMPOUND	COMMENT
1	<u>ceftaroline</u>	Nov 2010	N	MRSA benefit
2	dalbavancin	May 2014	N	PK differentiation
3	<u>tedizolid</u>	Jun 2014	N	PK differentiation
4	<u>oritavancin</u>	Aug 2014	N	PK differentiation
5	<u>ceftolozane/tazobactam</u>	Dec 2014	N	<u>P.aerug</u> , ESBL
6	ceftazidime/avibactam	Feb 2015	Y	ESBL + CPE

Ceftaroline, Ceftolozane-Tazobactam, & Ceftazidime-Avibactam

- Indications/Uses
- Place in Therapy
- Spectrum
- Pharmacokinetics
- Administration and Monitoring
- Safety
- Dosing & adjustments

Ceftaroline, Ceftolozane-Tazobactam, & Ceftazidime-Avibactam

Generic Name	Brand Name	Class	Role	New MOA	New Class
Ceftaroline	Teflaro	5 th Generation cephalosporin	- Additional options to treat severe/resistant infections - Extend spectrum of coverage against resistant organisms relative to other antibiotics	No	No
Ceftolozane-tazobactam	Zerbaxa	Cephalosporin/ beta-lactamase inhibitor combination			
Ceftazidime-avibactam	Avycaz	Cephalosporin/ beta-lactamase inhibitor combination			

Antibiotic Market

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[IDSA Incentives for Antibiotic Development](#)

T H E W A Y F O R W A R D

The National Action Plan for Combating Antibiotic Resistant Bacteria (CARB) is organized around the following five goals to turn the tide against the threat of antibiotic resistance:

- Slow the emergence of resistant bacteria and prevent the spread of resistant infections
- Strengthen national One-Health surveillance efforts to combat resistance
- Advance development and use of rapid and innovative diagnostic tests or identification and characterization of resistant bacteria
- Accelerate basic and applied R&D for new antibiotics, other therapeutics, and vaccines
- Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control, and antibiotic R&D

Ceftaroline (Teflaro)

Novel 5th generation cephalosporin

FDA-approved in 2010

Indications

Community-acquired pneumonia

ABSSSI

Place in Therapy

Potential salvage therapy for severe MRSA/ORSA
bacteremia, endocarditis, other severe infections

Ceftaroline

Spectrum

Staphylococci (including MRSA/ORSA), most *streptococci*, gram negative bacteria, *Enterococcus faecalis*

No activity against *Pseudomonas aeruginosa*

Ceftaroline

Mechanism of Action

Ceftaroline binds to penicillin-binding proteins

Prevents synthesis of peptidoglycan

Pharmacokinetics

Half-life: ~2h

Prolonged in renal dysfunction

Primarily eliminated renally

Requires dose adjustment in renal insufficiency

CrCl <50mL/min

Ceftaroline

Dosage/Administration

600mg q12hr

Higher doses potentially for severe infections

Adjust for renal dysfunction

Administer over 1hr

Ceftaroline

Monitoring

Renal function

Safety

Adverse Reactions

Positive Coombs' test without hemolysis

Diarrhea, nausea, rash

Conclusion

- Resistant organisms cause infections in hospital & community-settings
  - Associated with high rates of death, disease & complications
- Several newer antibiotics recently approved to help treat resistant infections
- Appropriate antibiotic use + Research & Development continue to be vital in turning tide of antibiotic resistance

Conclusion

- Several new antibiotics have come to market recently to help fight difficult to treat infections
  - Especially MDR organisms
- Antibiotic resistance remains a huge challenge
  - Several initiatives aim to help ameliorate this, but work is ongoing

Additional Resources

- Infectious Disease Society of America (IDSA)
  - [http://www.idsociety.org/Topic Antimicrobial Resistance/](http://www.idsociety.org/Topic%20Antimicrobial%20Resistance/)
- Centers for Disease Control & Prevention (CDC)
  - <https://www.cdc.gov/drugresistance/index.html>
- World Health Organization (WHO)
  - <http://www.who.int/campaigns/world-antibiotic-awareness-week/en/>

Additional Resources

- What You Can Do
  - <http://www.who.int/campaigns/world-antibiotic-awareness-week/posters/you.pdf?ua=1>
- What Policy Makers Can Do
  - <http://www.who.int/campaigns/world-antibiotic-awareness-week/posters/policy-makers.pdf?ua=1>
- What Nurses Can Do
  - <http://www.who.int/campaigns/world-antibiotic-awareness-week/poster-nurses.pdf?ua=1>
- What Pharmacists Can Do
  - <http://www.who.int/campaigns/world-antibiotic-awareness-week/poster-pharmacists.pdf?ua=1>

Questions/Discussion

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