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SOUTH CAROLINA COLLEGE OF PHARMACY

Evaluation of Meropenem Dosing in Adult Patients

Lauren Haney, PharmD
PGY1 Resident
MUSC Medical Center and College of Pharmacy
Residency Program

Introduction

- Review of carbapenem class conducted
  - Anti-infective subcommittee
  - Meropenem restrictions removed
  - Imipenem/cilastatin removed from formulary
- Automatic therapeutic substitution (ATS)
  - Protocol develop based on Monte Carlo simulation data

Background

- Monte Carlo simulation data
  - 5000 subjects
  - Compared 1 gram Q8H with 500 mg Q6H based on susceptibility breakpoint of 4 microgram/mL
- Pharmacodynamic results
  - Percent time above minimum inhibitory concentration (MIC) for both regimens were similar
- Similar concentrations achieved
  - Use less drug and reduce drug costs

Am J Health-Syst Pharm 2003;60:565-568
J Clin Pharmacol. 2003;43:1116-1123

Adult Dosing Guidelines

- Most conditions (500 mg IV Q6H)
  - Determine indication
  - Calculate creatinine clearance
  - Write medication order
- Central nervous system (CNS) infections
  - 2 grams IV Q8H
- Cystic fibrosis (CF) and febrile neutropenia (FN)
  - 1 gram IV Q8H

MUSC ATS Imipenem/cilistation to Meropenem. 2007

Renal Dosing Guidelines

Creatinine Clearance (mL/min)	Dose	Dosing Interval
≥ 51	500 mg	Q6H
26 to 50	500 mg	Q8H
10 to 25	500 mg	Q12H
< 10, hemodialysis (HD)	500 mg (after HD)	Q24H

MUSC ATS Imipenem/cilistation to Meropenem. 2007

Objectives

- Primary outcome
  - Compare clinical outcomes between patients receiving imipenem/cilastatin and meropenem
- Secondary outcomes
  - Compare the dosing parameters between patients receiving imipenem/cilastatin and meropenem
  - Assess adherence to ATS protocol

Methods

- Identified patients using pharmacy order entry computer system and medical records
  - International classification of diseases (ICD-9) codes
  - Excluded CNS, CF, and FN patients
- Data collection
  - Patient demographics
  - Clinical outcomes
    - Length of stay, ICU days, mortality, length of therapy
  - Serum creatinine, dose, dosing interval
- Calculated creatinine clearance to categorize dose and dosing interval

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Baseline Characteristics

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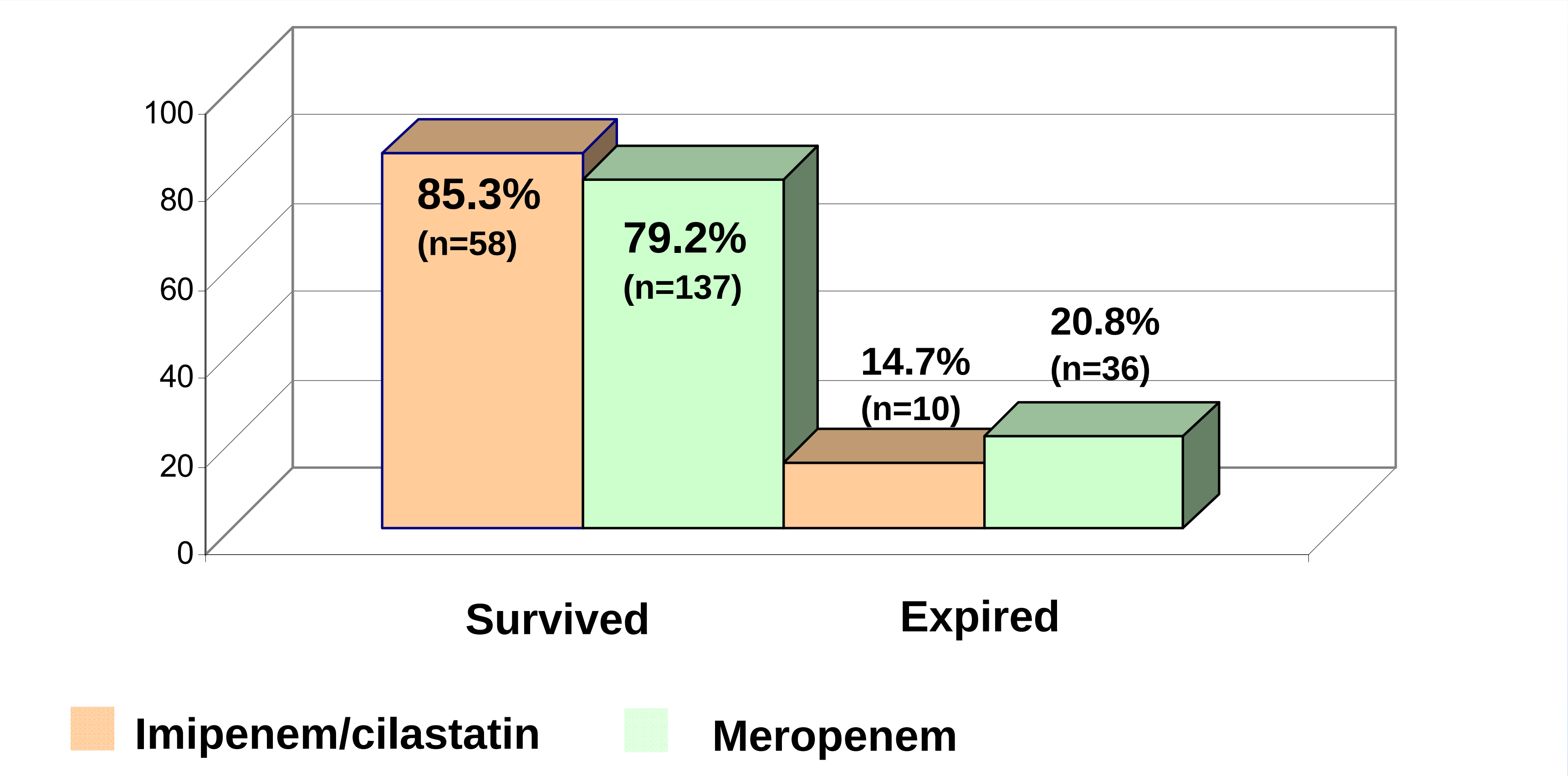
	Meropenem (n=182)	Imipenem/cilastatin (n=68)
Mean age (SD)	51.6 (16.7)	52.0 (17.6)
Male (%)	112 (61.5)	43 (63.2)
Race (%)		
Caucasian	117 (64.2)	41 (60.3)
African-American	54 (29.7)	26 (38.2)
Other	7 (3.8)	1 (1.5)

Results



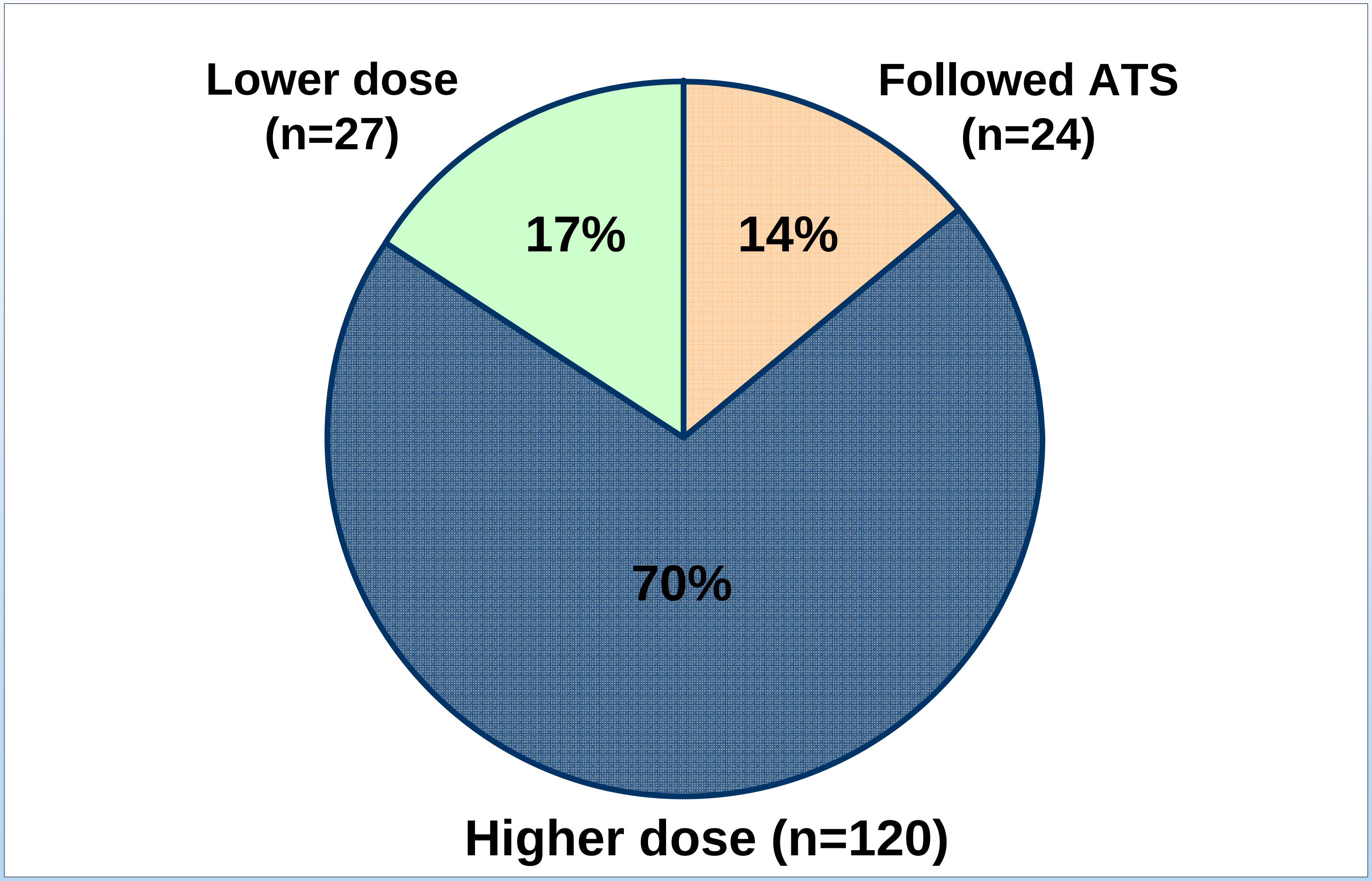
100
80
60
40
20
0
85.3%
(n=58)
79.2%
(n=137)
14.7%
(n=10)
20.8%
(n=36)
Survived
Expired
Imipenem/cilastatin
Meropenem

Results

	Meropenem (n=182)	Imipenem/ cilastatin (n=68)
Mean length of stay (d)	24.6 (23.6)	31.6 (39.8)
ICU stay (days)	10.9 (17.5)	15.2 (33.3)
Mortality	21%*	15%
Mean length of therapy (d)	7.2 (8.3)	8.2 (8.1)

*** p-value = 0.2779**

Adherence with ATS Protocol



Conclusions

- Implementation of ATS in adult patients did not change clinical outcomes
  - Further analyses are needed to evaluate clinical outcomes based on Monte Carlo simulation
    - 1 gram Q8H versus 500 mg Q6H
- Adherence of ATS protocol occurred less than 15% of time in eligible patients

Limitations

- Severity of illness
- Retrospective chart review
- Modified creatinine clearance equation
- Weight
- Use of ICD-9 codes
- Culture and sensitivities
- MIC data

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Future Directions

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- Further analysis needed for comparison of doses based on Monte Carlo model
- Specific dosage regimens
- Resistance mechanisms
- Extended infusion time

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