# AST in 2016: New Drugs

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# Declarations

- Dr. Romney Humphries is a full time employee of the University of California, Los Angeles.

- Dr. Romney Humphries is a paid consultant to Merck, Allergan, Cepheid, Roche, SlipChip, MicrobeDx, DiaSorin, and receives grant support from bioMerieux, Beckman Coulter, BD, GenMark, Accelerate Diagnostics, Luminex, Merck, Allergan, Curetis, and Applied BioCode.

- Dr. Romney Humphries is on the Allergan and Merck speaker's bureau.

# Case

62 year old woman with advanced pancreatic cancer

↓

Vomiting & fever after surgery

↓

CT scan: fluid collection in liver, inflammatory ascites

↓

Blood cultures: Gram negative rods

ID Team:
"This patient had CRE in the past –can you test ceftazidime-avibactam for us?"

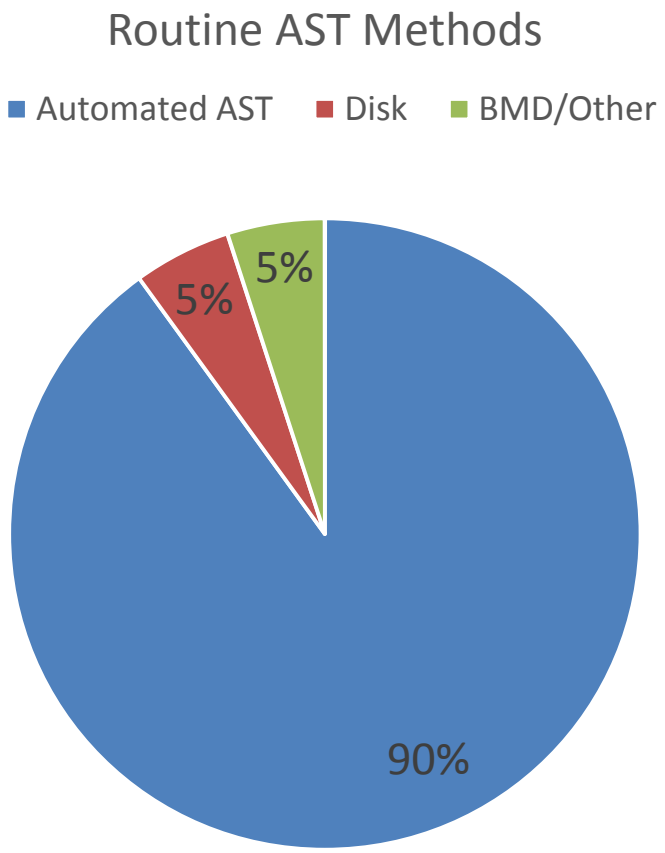
# *Clinical & Laboratory Standards Institute Guidance*

"…each laboratory should develop a protocol to address isolates that are confirmed as resistant to all agents on their routine test panels. This protocol should include options for testing additional agents in-house or sending the isolate to a reference laboratory."

(Also a College of American Pathologist certification requirement - MIC.21944)

**M100S 26. "Instructions for Use"**

# Susceptibility Testing in U.S. Clinical Laboratories




Almost all labs use an automated AST system (Vitek 2/MicroScan >> Phoenix/Sensititre) for routine AST

Some use alternative methods for select reasons:

- Difficult organisms
- Difficult drugs
- No FDA claim for drug/bug

# Testing options: New Gram-negative agents

| Agent | FDA cleared tests | Reference laboratories |
|---|---|---|
| Ceftazidime-avibactam | • Disk (Hardy)<br>• Trek Sensititre (ThermoFisher)<br>  • Custom panel<br>  • Must order n=100 or n=500 | • Laboratory Specialists, Inc.<br>  • No testing of FL, NY or CA patients<br>  • 2-4 day TAT from receipt of isolate<br>  • Delay if R, mixed culture or testing issues |
| Ceftolozane-tazobactam | • Disk (Hardy)<br>• MIC Strip (Liofilchem)<br>• Trek Sensititre (ThermoFisher)<br>  • Custom panel<br>  • Must order n=100 or n=500 | • Laboratory Specialists, Inc.<br>  • Only urine & intra-abdominal sources<br>  • No testing of FL, NY or CA patients<br>  • 2-4 day TAT from receipt of isolate<br>  • Delay if R, mixed culture or testing issues |

TAT, turnaround time

# Poll of LA area laboratories: "How do you test Avycaz®?"

| Small community hospital (no Micro-specific Director) | Private Hospital (PhD Director) | County Hospital (PhD Director) | Large Reference Laboratory |
|---|---|---|---|
| - Perform RUO Etest, no verification (but QC ok)<br>- Report results to chart | - Perform RUO Etest, after verification<br>- Prior to reporting result, physician phoned to discuss RUO & limitations | - Cannot test<br>- Hospital policy = no RUO<br>- LSI → not licensed for CA patients<br>- ARUP → does not test<br>- Quest → does not test | - Cannot test<br>- no non-RUO reagents<br>- disk reproducibility poor |

QC, Quality Control
RUO, research use only

# Why not use the disk?

“reproducibility was poor”

“physicians want an MIC”

“there are no disk breakpoints for the organism I am being asked to test”

# Verification Studies

- Laboratories must verify performance of all new tests (including FDA-cleared ones), in-house, prior to performing patient testing

  - CLIA 493.1253

QC is not sufficient

- Must also test
  - Accuracy: minimum 30 isolates
  - Precision: 5 isolates in triplicate x 3 days

# Other considerations for implementing a new test

- Standard Operating Procedure
  - When to test; how to interpret; any special reporting considerations (body site reporting, intrinsic resistance, etc)
- Information Technology
  - Must build test & interpretations in Lab IT system
  - Interface?
- Quality Control
  - Including new IQCP requirement or daily QC
- Training & Competency of staff
- UCLA: time to implement new test = 6 months – 1 year

IQCP, individualized quality control plan

# Back to case…

| | | |
|---|---|---|
| Amikacin | 2 | S |
| Ampicillin | >128 | R |
| Cefazolin | >128 | R |
| Cefepime | 16 | I |
| Ceftazidime | >128 | R |
| Ceftazidime-Avibactam | 1 | S |
| Ceftriaxone | >128 | R |
| Ciprofloxacin | >4 | R |
| Colisin | 1 | S |
| Ertapenem | >4 | R |
| Gentamicin | >16 | R |
| Imipenem | 4 | I |
| Meropenem | >16 | R |
| Pip-tazo | >128 | R |
| Tigecycline | 1 | S |
| Tobramycin | 1 | S |
| Trim-sulfa | >4 | R |

Comments

| Lab using RUO test | Lab that can't use RUO & can't send to reference lab | Lab using reference lab |
|---|---|---|
| Result reported 3 days after routine AST known<br><br>? If RUO test would detect "R" | "R" result never reported (or tested)<br><br>- Use drug in combo?<br>- Don't use drug? | "R" result received 7 days after routine AST known<br>- Delay of shipping<br>- Reference lab confirms all R results |

# THANK YOU!

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