

AST in 2016: New Drugs

Romney Humphries, PhD D(ABMM)

UCLA Clinical Microbiology

rhumphries@mednet.ucla.edu

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

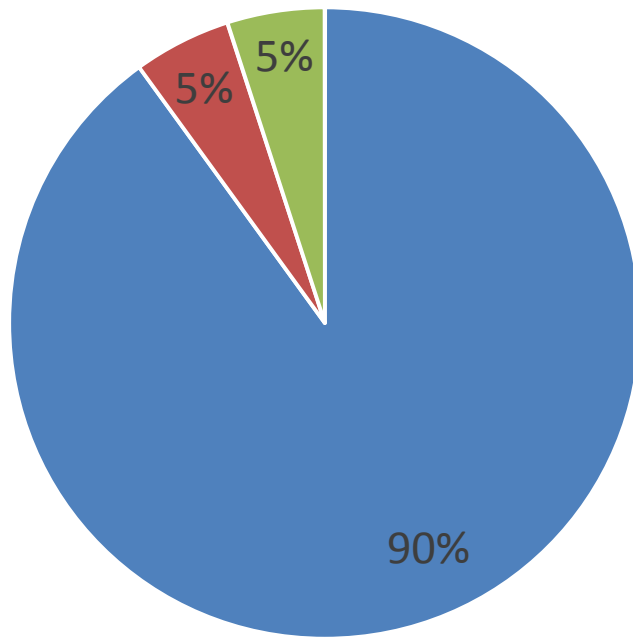
“...each laboratory should develop a protocol to address isolates that are confirmed as resistant to all agents on their routine test panels. This protocol should include options for testing additional agents **in-house** or sending the isolate to a **reference laboratory**.”

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

Susceptibility Testing in U.S. Clinical Laboratories

Routine AST Methods

■ Automated AST ■ Disk ■ BMD/Other



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	<ul style="list-style-type: none">• Disk (Hardy)• Trek Sensititre (ThermoFisher)<ul style="list-style-type: none">• Custom panel• Must order n=100 or n=500	<ul style="list-style-type: none">• Laboratory Specialists, Inc.<ul style="list-style-type: none">• No testing of FL, NY or CA patients• 2-4 day TAT from receipt of isolate• Delay if R, mixed culture or testing issues
Ceftolozane-tazobactam	<ul style="list-style-type: none">• Disk (Hardy)• MIC Strip (Liofilchem)• Trek Sensititre (ThermoFisher)<ul style="list-style-type: none">• Custom panel• Must order n=100 or n=500	<ul style="list-style-type: none">• Laboratory Specialists, Inc.<ul style="list-style-type: none">• Only urine & intra-abdominal sources• No testing of FL, NY or CA patients• 2-4 day TAT from receipt of isolate• 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
<ul style="list-style-type: none"> - Perform RUO Etest, no verification (but QC ok) - Report results to chart 	<ul style="list-style-type: none"> - Perform RUO Etest, after verification - Prior to reporting result, physician phoned to discuss RUO & limitations 	<ul style="list-style-type: none"> - Cannot test - Hospital policy = no RUO - LSI → not licensed for CA patients - ARUP → does not test - Quest → does not test 	<ul style="list-style-type: none"> - Cannot test - no non-RUO reagents - disk reproducibility poor

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

Back to case...

	2	S	Comments
			Lab using RUO test
			Lab that can't use RUO & can't send to reference lab
			Lab using reference lab
Amikacin			
Ampicillin			
Cefazolin			
Cefepime			
Ceftazidime			
Ceftazidime-			
Ceftriaxone			
Ciprofloxacin			
Colisin			
Ertapenem			
Gentamicin			
Imipenem			
Meropenem			
Pip-tazo	>128	R	
Tigecycline	1	S	
Tobramycin	1	S	
Trim-sulfa	>4	R	

THANK YOU!

rhumphries@mednet.ucla.edu