ARLG Update
Antibacterial Resistance Leadership Group

To prioritize, design, and execute clinical research that will reduce the public health threat of antibacterial resistance

ARLG Update

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For more information about the ARLG, its leaders, or its current projects, please visit **arlg.org**

Meet our Committees

Gram-Positive Bacteria


Sara Cosgrove

Chair: Sara Cosgrove

The ARLG research agenda focuses on four high priority areas: rapid diagnostics, stewardship of our remaining antibiotics, infections caused by gram-negative bacteria and infections caused by gram-positive bacteria, primarily MRSA and VRE.

MRSA is a leading cause of soft-tissue infection, bacteremia, hospital-acquired pneumonia, and endocarditis. Despite availability of several antibacterials active against MRSA, comparative studies are needed to identify which agent or agents might improve outcomes of patients with invasive MRSA infections. Infections caused by vancomycin-resistant enterococci (VRE) are seen primarily in immunocompromised patients, transplant recipients, and in patients with surgical disruption of the urinary or gastrointestinal tract. Enterococci are intrinsically resistant to most antibacterials, making treatment challenging and studies of new approaches to management essential. Optimizing use of current antibiotics in the treatment of suspected or confirmed Gram positive infections, while minimizing overuse of broad-spectrum antibiotic therapy, is critical to preserve the value of existing antibiotics. Novel approaches to antimicrobial stewardship targeted at such optimization of therapy are needed. The objectives of the Gram Positive Committee are to:

- Investigate strategies or therapies, including narrow-spectrum oral antimicrobials, for treatment of infections predominantly caused by Gram-positive bacteria, including skin and soft tissue infections, bone and joint infections, and bacteremia in adults and children.
- Compare the effectiveness of available antibiotics alone or in combination with other agents for infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin resistant enterococci (VRE).
- Optimize administration of antimicrobial agents for treatment of Gram-positive infections with respect to dose, dosing interval, and duration of therapy in adults or children.

Committee Member	Institution
Sara Cosgrove (Chair)	Johns Hopkins University
Cesar Arias	University of Texas
Helen Boucher	Tufts University
Ralph Corey	Duke University
Robert Daum	University of Chicago
George Eliopoulos	Harvard University
Scott Evans	Harvard University
Frank Lowy	Columbia University
Loren Miller	University of California, Los Angeles
Barbara Murray	University of Texas
David Snydman	Tufts University

ARLG Project Spotlight

PROVIDE

Thomas Lodise

Prospective Observational Evaluation of the Association between the Day 2 Vancomycin Exposure and Failure Rates among Adult Hospitalized Patients with MRSA Bloodstream Infections (PROVIDE)

Principal Investigator: Thomas Lodise

The goal of PROVIDE is to prospectively evaluate the previously identified Day 2 AUC/MIC vancomycin exposure breakpoints associated with optimal outcomes among patients with MRSA bloodstream infections in a multi-center, observational clinical trial.

To accomplish this, PROVIDE has been designed as a prospective, multi-center, observational study of patients with confirmed MRSA BSIs. Adult (≥18 years) patients admitted to a hospital with a MRSA positive blood culture who were initiated on vancomycin therapy ≤24 hours *prior to or* ≤48 hours *after* MRSA index blood culture collection and are being continued on vancomycin therapy for ≥ 72 hours *after* MRSA index culture collection can be included. Patients with an absolute neutrophil count <500 cells/mm or who are receiving renal replacement therapy will be excluded. Available standard of care vancomycin levels, as well as non-trough add-on tests on therapy days 1- 5, will provide critical vancomycin data. PROVIDE will seek to estimate the difference in failure rates among patients with AUCDAY2/MICBMD ratios ≥ 650 relative to those with AUCDAY2/MICBMD ratios < 650 and AUCDAY2/MICETEST ≥ 320 relative to those with AUCDAY2/MICETEST < 320.

Newly Initiated ARLG Projects

Name	Title	Principal Investigator
RADICAL	*A host-based mRNA classifier for differentiating viral and bacterial etiologies of acute respiratory tract infection*	Chris Woods
PROVIDE	*Prospective Validation of the Vancomycin Exposure Profile Associated with Optimal Outcomes among Patients with MRSA Bloodstream Infections*	Thomas Lodise
SCOUTCAP	*Short Course Outpatient Therapy for Community Acquired Pneumonia in Children Trial*	Charlie Huskins
CEPCRO	*Development of a Rapid Diagnostic Test to Detect Carbapenem-resistant Organisms Directly in Respiratory and Urine Samples*	Vance Fowler

Recent Publications

Ramirez MS, Xie G, Johnson S, Davenport K, van Duin D, Perez F, Bonomo RA, Chain P, Tolmasky ME. **Genome Sequences of Two Carbapenemase-Resistant Klebsiella pneumoniae ST258 Isolates.** Genome Announc. 2014 Jun 19;2(3). pii: e00558-14. doi: 10.1128/genomeA.00558-14. PubMed ID: 24948759 PMCID: PMC4064024.

Spellberg B **Antibiotic Judo: Working Gently with Prescriber Psychology to Overcome Inappropriate Use** JAMA Intern Med. 2014 Mar;174(3):432-3. doi: 10.1001/jamainternmed.2013.14019. PubMed ID: 24474306 PMCID: PMC4064591.

Hujer AM, Evans SR, Jiang H, Hujer KM, Hall T, Marzan C, Jacobs MR, Sampath R, Ecker DJ, Domitrovic TN, Chen L, Manca C, Chavda K, Zhang P, Fernandes H, Perez P, Kreiswirth BN, Fowler VG Jr, Chambers HF, Bonomo RA **Can Rapid Molecular Diagnostics Assist in the Choice of Beta-Lactam Antibiotics? An Analysis of Data from PRIMERS-I.** Presented on 5/12/2014, ECCMID 2014 Late Breaker

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