

IDSA

Infectious Diseases Society of America

Novel Agents for Antimicrobial Resistant Bacteria: The Role of uUTI Studies

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Key Points

- Urgent need for novel agents to treat antibiotic resistant bacterial infections
- Feasibility of uUTI studies provides a path forward
- Clinically meaningful endpoints
- Role of stewardship and guidelines
- Economic incentives are necessary

Need for Novel Agents — UTIs

- Emergence and spread of multidrug resistant ESBL producing *Enterobacteriaceae* significantly restricts therapeutic options; **50% increase in ESBLs from 2013 to 2019.**
- Repurposing older drugs such as pivmecillinam (not available in US), fosfomicin, and nitrofurantoin buys some time while we await new agents, but resistance is likely to develop to these agents too.
- Increasing numbers of patients admitted to hospital, receiving PICC lines for UTI treatment, leading to complications with PICC lines, risk of HAIs higher costs, disruption to patients' lives.

Sources

<https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>

<https://www.sciencedirect.com/science/article/pii/S1876034119301807>

Urgent Need for Novel Agents — Other Indications

- Last FDA antibiotic approval November 2019
- In 2019, 4.95 million people died with drug-resistant bacterial infections. Of these, 1.27 million deaths were directly caused by AMR
- Lack of antibiotic options continues to worsen outcomes for patients with a wide array of needs—cancer chemotherapy, transplantation, COVID-19, hip/knee replacements, opioid use, etc.
- We desperately need novel agents for several Gram-negative infections—HABP/VABP, bacteremia, sepsis, etc.

Because uUTI studies are relatively feasible to do, they are a crucial gateway to developing agents that can be used for indications with greater unmet need.

Tebipenem Example

- Clarity on potential data inadequacies would be helpful to inform future efforts
- Spero to reduce its workforce by 75%
- Potential downstream impact on other developers considering possible oral agents for Gram negatives

Clinically Meaningful Endpoints

- For uUTI and cUTI, endpoints should focus on clinical improvement, not microbiological eradication in the urine
 - Asymptomatic bacteriuria

Optimal Use of New Agents

- Novel agents for Gram-negative UTIs will be clinically useful for other Gram-negative infections with limited or no treatment options. **To support optimal use:**
 - Fund **post-approval studies** to gather additional clinically relevant data, particularly in other infections for which there is not enough data to support an indication.
 - Rely upon **stewardship programs** (increase their funding & staffing; expand stewardship to all health care settings); **PASTEUR Act** will help.
 - Utilize **professional society clinical guidelines**: IDSA now regularly updates guidance on treatment of MDR gram negative infections (most recent March 2022) to guide optimal use and rapid appropriate uptake of new agents.

Source:

<https://www.idsociety.org/practice-guideline/amr-guidance-2.0/>

Economic Incentives Remain Necessary

- PASTEUR Act gaining momentum 40 bipartisan cosponsors in the House
- President's FY2023 Budget Request language aligns with PASTEUR: *“proposal designed to combat antibiotic-resistant bacteria by encouraging the development of innovative antimicrobial drugs. This proposal would provide annual payments from a contract valued between \$750 million and \$3 billion to the developers of newly approved antimicrobial drugs. By delinking revenue from the volume of sales, these advance market commitments properly incentivize the market entry of new antimicrobials and ensure that the American people are armed with an adequate supply of properly stewarded antimicrobial products against highly dangerous drug-resistant microbes.”*
- **Everyone should press Congress to pass PASTEUR this year.**