

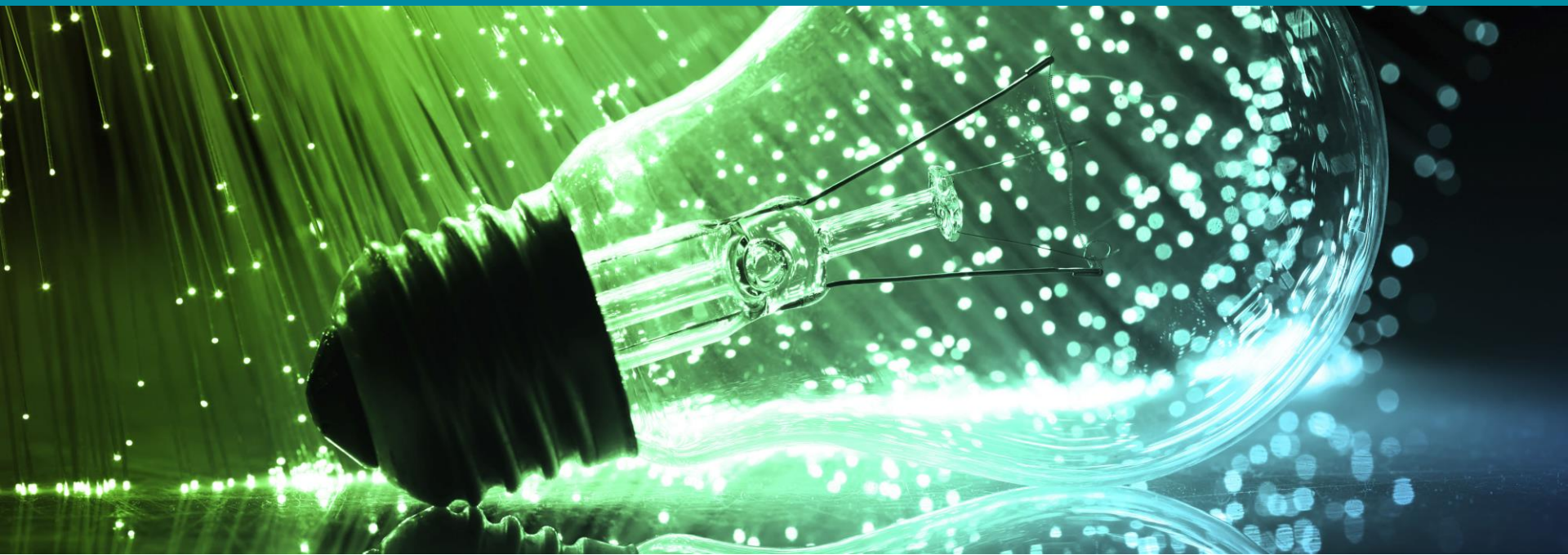
Session III: Perspectives of Providers and Investigators

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Disclaimer

The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

The presenter is an Employee of Duke University.

Background

➤ Main Objective:

- **Perspectives regarding risk and uncertainty**
- **Perspectives about using antibacterial drugs developed using these approaches**
- **Better understanding of how physicians make treatment decisions** for patients with complicated or resistant infections

➤ 23 Semi-Structured Interviews with Providers

- Academic and Community

Who Was Interviewed

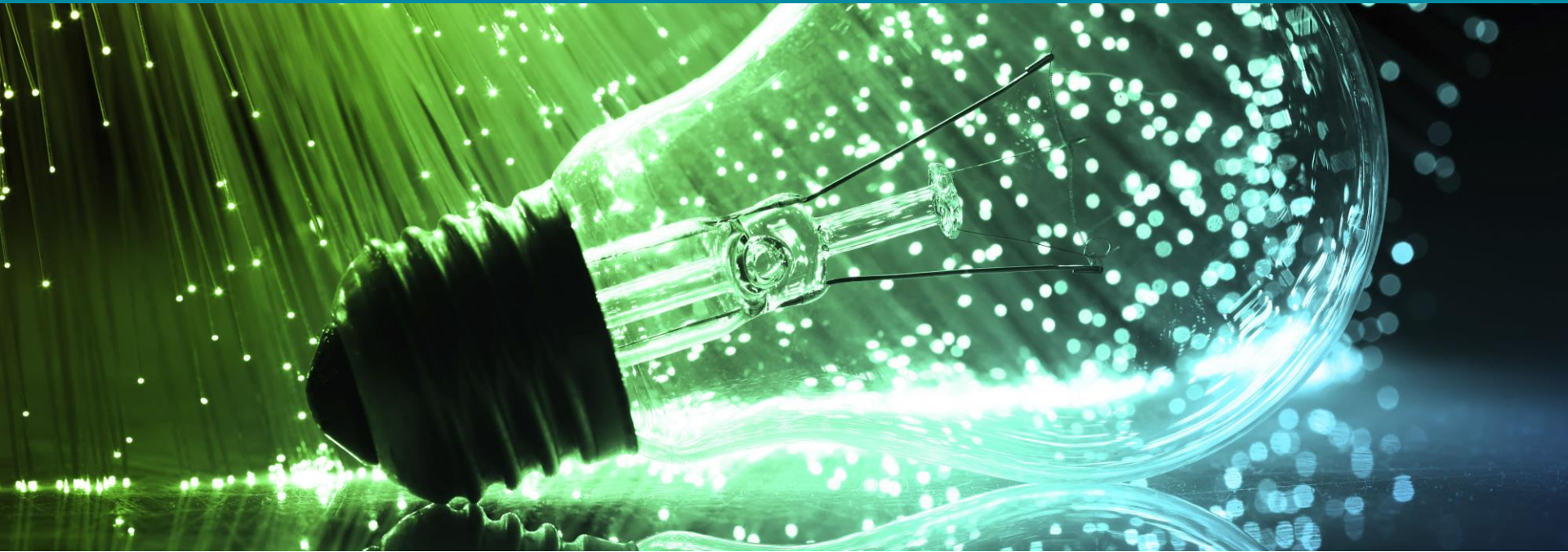
➤ Academic & Community Providers

- Internal Medicine
- Critical Care
- ID
- Pulmonology / Critical Care
- Hospitalists
- P & T Committee members

➤ Some overlap

- e.g., Academic P & T and Community Pulmonologist
- Total N=23 but appears larger due to overlap

Specialties	N=
P & T Committee	9 current + 2 former members
Infectious Disease	7
Critical Care/Intensivist	7
Community Only	11
Both	3



FINDINGS

Initial questions

- Think back to some of the patients you have seen who were seriously ill with a complicated (and possibly multi-drug resistant or hospital acquired infections). What have you found to be most challenging aspects of treating these patients?
- In those kinds of situations, how do you select the appropriate therapy? [Open-ended, then Probe]:

Greatest Challenges in Treating Patients with Complicated Infections

- ▶ Choosing appropriate antibiotic treatment before the pathogens are identified through cultures

- ▶ Treating medically complex and sick patients who require close monitoring, and whose ability to tolerate antibiotics with significant toxicity is unpredictable

Questions: streamlined development approaches

- ▶ Participants then given info about the FDA exploring streamlined development approaches, features of which may include:
 - Used to treat patients with limited or no alternative options
 - Clinical data more limited than what would be expected in a traditional development program

Reactions: streamlined development approaches

- All of the physicians interviewed **believe** that there is now a crisis with antibiotic-resistant infections and that **it is appropriate to be developing and reviewing new antibiotics through programs such as the streamlined development approaches**
- Benefits to pharmaceutical companies are reasonable if they incentivize development of new abx that will never be blockbusters

Perceptions: Excited but Cautious

*“It’s exciting in that it [streamlined development approaches] would give a pathway to get these drugs to patients who need them. It’s exciting in that we’d have access to life-saving meds earlier than we normally would in the ‘Phase I, II, III’ approach. **But I would want to have as much information as possible about the new drug and its sensitivities and in terms of how well it will work against different pathogens, as well as about its renal toxicity.**”*

“It would be good thing for FDA to put out information for clinicians to reassure them that prescribing drugs that have come through the streamlined process does not put them at risk for medical/legal problems.”

Plans: Use of abx developed via streamlined development approaches

- **None believed that antibiotics developed through this program should be used first line.**
- A few would rather use known drugs first due to limited available data on safety/efficacy, especially in critically ill
- **Use only for patients with true unmet need who have run out of viable options.**
 - Rationale: primarily to preserve the new drug so “it won’t become worthless in six months.”
- Tolerance of uncertainty about risks increases as patients get sicker and have fewer options

Concerns: Use of abx developed via streamlined development approaches

- **Most would not have concerns about using a new antibiotic developed through this shortened review process** in patients with unmet need, given that the available alternatives have serious and potentially life-altering toxicities, and that many other procedures and treatments used routinely in the ICU are also not well-supported by data.
- **A minority** of the physicians **expressed concern over using a drug developed through the streamlined development approach because of a lack of data both for efficacy and for side effects (especially renal effects)** when used in critically ill patients such as those in the ICU.

Confidence: Using Drugs Developed via streamlined development approaches

- ▶ Confidence **would be boosted by the fact that these new antibiotics are FDA approved and would have been scrutinized and vetted by their hospital's P&T committee** before being placed on the formulary.
 - If the new antibiotic contained a drug component the doctors have already used, it would further boost their confidence.

Need: Ongoing Clinical Use Data

- Some of the physicians said they would like **ongoing updates on the efficacy, side effects and toxicities of the streamlined development drugs as they are being used in real-life clinical settings**
- Some suggested that the **FDA require these data be continually submitted** as part of the approval process, and that the **FDA partner with a neutral and trusted third party** like the Infectious Disease Society of America (IDSA) **to inform physicians and establish treatment guidelines** for these new antibiotics

Perceptions: Need Real-World Data

*“I’m excited about having new products to use, because I face this problem a couple times a month when I have a patient who has a resistant infection, and it comes to having to use toxic medications. **But the Phase II trial data [of drugs developed under the streamlined program] doesn’t cover the kinds of patients I see. I want to know how it would do with real-world patients** who need this drug — the frail patients who may be on dialysis or on continual dialysis. How will they do?”*

Restrictions: Use of ABX Developed via streamlined development approaches

- Currently, **most ICU and ID physicians have very few restrictions on their authority to prescribe antibacterials.**
- **All thought that new antibiotics approved under this program should have mandatory ID consults with IDs who are on their hospital's antibiotic stewardship committee or who are certified experts in MDR infections** and the new antibiotics developed to treat them
- A few of the physicians said they wanted to **make sure that ID consults wouldn't interfere with critically ill patients getting lifesaving antibiotics in time to have the best outcomes.**

Need: Mandatory Bedside ID Consults

➤ **Almost all** said that new antibiotics developed under the streamlined development approach with limited safety data should have **mandatory ID consults every time they are initiated with patients**

*“Absolutely I would want to do this at my hospital. **It’s important to restrict or prevent overuse.**”*

However...

- All of the physicians said that patients' suggestion about having an **“A-Team”** review cases to decide whether patients are a good candidate for a newly developed antibiotic was **neither necessary or feasible**, because the time it would take to convene such a committee would delay life-saving treatment. They said that **a mandatory ID consult should suffice**

Patient Advanced Directive for SDP-Approved ABX Use

- **None** of the physicians interviewed **thought** having patients with chronic conditions necessitating frequent hospitalizations create an “advanced directive” about their wishes concerning drugs developed through a SDP was a good idea.
- They said that patients are not savvy when it comes to antibiotics in complicated infections, and the personal community physician never makes decisions for their patient in the ICU.

FDA News Release

Providers then given:

FDA approves new antibacterial drug Avycaz

- a press release announcing February 2015 approval of Avycaz

Note: This news release, issued on February 26, 2015, was modified on February 26, 2015, to correct the indication of avibactam (paragraph 2).

- An informational piece about Avycaz prescribing highlights and microbiology profile

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For Immediate

February 25, 2015

Release

Most had heard of Avycaz and presumably all were familiar with the cephalosporin component

Release

The U.S. Food and Drug Administration today approved Avycaz (ceftazidime-avibactam), a new antibacterial drug product, to treat adults with complicated intra-abdominal infections (cIAI), in combination with metronidazole, and complicated urinary tract infections (cUTI), including kidney infections (pyelonephritis), who have limited or no alternative treatment options.

Perceptions of AVYCAZ

- ▶ The vast majority said that they would be comfortable using a streamlined development drug like AVYCAZ with patients *with true unmet need*, and with no other viable options.
- ▶ Would not use AVYCAZ as first line therapy
 - None would use it if there were alternatives, even after cultures
 - Allows preservation of AVYCAZ for true unmet need
 - A few indicated discomfort using AVYCAZ in fragile pts due to rapidity of approval and limited data of the effect on the critically ill

Overall Perceptions & Limitations

- Crisis in ABDD
- Support need for streamlined approaches
- Providers more comfortable with current structures for internal review than patients
- Indicate they would not use these drugs as 1st line therapy or before culture results are known
- Would like real-time clinical use data provided
- Limitations: social desirability bias

Thank you.



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