

Provider perceptions of antibacterial drug development and the streamlined approval process for situations of immediate unmet medical need

A telephone in-depth interview topic guide

I. Introduction

Hello Dr. _____ this is Diane Bloom, and I'm calling to conduct the telephone interview we have scheduled. I want to first thank you for taking time out of your busy schedule to share your ideas and opinions.

This interview study is being conducted on behalf of Duke University and Clinical Trials Transformation Initiative (CTTI), a public-private partnership funded, in large part, by the FDA, to explore various aspects of clinical trials with the goal of identifying practices to increase their quality and efficiency.

One of their ongoing projects is trying to gain a better understanding of how physicians make treatment decisions about very ill patients with complicated or antibiotic resistant infections. We want to better understand provider perspectives about using antibacterial drugs approved using an FDA streamlined development and approval process. We have asked you to participate in this interview because your point of view and insights will be extremely valuable to this effort.

I am looking forward to hearing your ideas on the topics we will be discussing. I am audio recording our discussion today just to make sure I get all of your ideas and comments. I would like to assure you, however, that the discussion will be confidential, and that nothing you say will be associated in any way with your name, so please feel free to talk candidly.

The audio files will be kept safely in a locked facility until they are transcribed, then they will be destroyed. The transcribed notes of the focus group will contain no information that would allow you to be linked to specific statements. (If there are any questions or discussions that you do not wish to answer or participate in, you do not have to do so.)

II. Interview Guide

1. I'd like to begin by asking you to tell me a little about your area of expertise and your practice setting.
 - Academic or community?
 - Urban or rural?
 - How many physicians?

2. **(If they practice in a community setting)** If you have admitted one of your patients to the hospital and, while there, that patient contracts a hospital acquired or resistant infection, who treats that patient? (open-ended) then probe:
 - Do you continue to treat the patient, or do you hand them off to specialists?
 - Is there more than one physician who weighs in on the treatment decisions in this case? If so, who?

3. 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?

4. In those kinds of situations, how do you select the appropriate therapy? [Open-ended, then Probe]:
 - Do you typically consult with others about potential treatment options before making a decision? If yes: Who? Which specialties?
 - How much, if at all, does the patient or the family generally weigh in on the treatment decision in these kinds of cases?

5. The FDA is exploring potential solutions for streamlining the drug development process for antibacterials for patients with potentially life-threatening or multi-drug resistant infections where there is **“unmet medical need.”**

- If I were from Mars, visiting Earth for the first time and never heard of the phrase “**unmet medical need**” before, how would you describe it to me?
6. In particular, The FDA is exploring drug development programs which will enable clinicians to prescribe potentially lifesaving antibiotics earlier in their development cycle to patients with limited to no alternative treatment options, with the understanding that the usual, clinical development program has been streamlined, with respect to focusing on the unmet need population, for these drugs. The FDA still requires and reviews data that is adequate to characterize the safety and effectiveness of the product in the unmet need population in addition to other supportive information. However, this clinical data would be more limited compared to what would be expected for drugs approved using a traditional development program.

Now, I'd like to take out handout #1 about these types of streamlined development programs and take a couple of minutes to read it:

- a. What are your general reactions to the piece you just read?
- b. What would you say makes this development process different from the traditional drug development process?
- c. What do you see as the pros and cons/tradeoffs of new antibacterials developed under this type of review program?

7. Please look at Handout # 2. This is the press release which describes the 2015 approval of AVYCAZ (Ceftazidime-Avibactam) which is an antibacterial drug which was recently approved under this kind of streamlined process to treat serious intra-abdominal and UTI infections in very ill patients who have an unmet medical need with limited or no other options. I'd like to take a moment to have you read about the approval of AVYCAZ. [HANDOUT # 2: Press release]

- a. What is your reaction to the piece you just read?

8. Now I'd like you to look at Handout #3: The product profile/highlights of AVYCAZ

- a. What are your general reactions to AVYCAZ?
- b. Under what circumstances would you feel comfortable using it?
- c. Under what circumstances would you not feel comfortable using it?
- d. What questions would you want answered before you decided whether to use it in a particular patient?
- e. What would you think about a hospital policy that would insist on an ID consult prior to using a new drug with limited safety data such as AVYCAZ?
- f. What would you think about hospitals having a pre-designated “A-team” that would meet and discuss all cases like this and make a joint decision about whether to give a patient one of the new antibacterials approved under a faster review process but with limited safety information? [Pros and cons?]

9. Now I'd like you to read handout #4 which is a scenario about a patient you are evaluating in the ICU. I'd like to hear your thoughts about treatment options and recommendations. [HANDOUT #4: SCENARIO OF PATIENT WITH INTRA ABDOMINAL INFECTION]

- a. Think out loud for a moment. What would your immediate thoughts be about this patient?
- b. What options would you consider for this patient? [open-ended]
- c. How likely would you be to prescribe AVYCAZ for this patient given its limited safety profile? Why do you say that?
- d. How would you weigh the risks and benefits?
- e. What concerns or questions would you have?
- f. What additional information would you want to know about this drug before prescribing it?
- g. Would you be comfortable making the decision to use a new antibacterial drug such as AVYCAZ with this patient or would you want to consult with someone else about it? [If they would consult]: Who, would you call or

consult with? (probe: the Pharm D on call? or the consult ID doc? Other?)

- If you consulted with experts the first few times you prescribed AVYCAZ to a patient, would you want to consult on all subsequent cases as well, or would you feel comfortable after a certain number of times (how many?) making the decision on your own? Why?

i. If you don't know for sure what the bug is, would you use it before getting the culture comes back from the lab? Why?

j. If you decided AVYCAZ should be used in this case, would you have a conversation with the patient or their family? If so: what would you say to them? If not: Why not?

10. Let's imagine that this same patient presents with **HABP or VABP**, would you use AVYCAZ or another option for this patient. Why?

11. If you see patients in your practice who have underlying conditions which put them at greater risk for frequent hospitalizations and serious infections, would you have a discussion with them at a time when they are not acutely ill, about the option of using this kind of new antibiotic should the situation arise in the future? Why or why not? How would such a conversation go?

12. Do you have anything else you would like to add that we haven't talked about so far?

Thank you for taking part in this discussion. Your ideas and insights will be extremely valuable to the researchers working on these issues.