

FDA Physician Interviews – In-depth Interviews with Physicians on Clinical Trial Data in Professional Prescription Drug Promotion

IN-DEPTH INTERVIEW DISCUSSION GUIDE

Research Objective: Conduct in-depth interviews with primary care physicians and endocrinologists to understand their experience with and knowledge of clinical trial data (Section II), and assess their understanding and application of prescription drug promotional materials (Section III).

NOTES TO REVIEWER:

Question probes are *italicized*. These are suggestions for the interviewer to follow, and will be used or modified as deemed relevant and necessary in the natural flow of discussion.

Moderator instructions are highlighted in yellow.

Stimuli prompts are highlighted in blue.

Session Overview:

SECTION I: INTRODUCTION (5 min.)

The purpose in this section is for the moderator to explain the purpose of the research, lay down any ground rules or guidelines, and allow participants to ask any questions.

SECTION II: BACKGROUND INFORMATION (10 min.)

The purpose of this section is to ease into the conversation and gather background information including participants' experience with and understanding of clinical trial data, including any training.

SECTION III: STIMULI DISCUSSION (45 min.)

The purpose of this section is to provide a deep dive in participants' understanding of clinical trial data, particularly how they are interpreting data presented in the stimuli and how they would apply this information to their practice as well as their comprehension of specific areas of focus (e.g., non-inferiority, re-randomization).

CONCLUSION

If time permits, moderator will check with research team members and observers if they have additional questions (with participant on hold). If, yes moderator asks follow-up questions and then wraps up discussion and ensures that all of the participant's comments have been heard.

SECTION I: Introduction (5 minutes)

[Please refer to participant by FIRST NAME only.]

- My name is _____, and I'm part of an independent research company. This means that I'm here to listen to you and what you have to tell me, and I have no stake in how you respond.
- The purpose of today's interview is to get your thoughts and reactions about various topics we will be discussing. I also do not have a medical background so your feedback is extremely helpful.
- Your thoughts are very important to us, and your time today is appreciated.
- We will have about 60 minutes for our discussion.

As we begin, I want to review a few ground rules for our discussion.

- Your participation is voluntary and you have the right to withdraw from the study at any time.
- Most importantly, there are no 'right' or 'wrong' answers. We want to know your opinions and what you think about the things we will be discussing.
- Just a reminder, we are not selling anything, and I do not work for the people who are sponsoring this research, so don't hold back from giving me your honest opinions.
- As we move through our discussions, please make sure to refrain from providing any Protected Health Information to us. Please also refrain from providing any identifying information about your practice such as mentioning its name or names of your colleagues.
- Members of the research team are listening in to this interview and taking notes. This interview will also be audio recorded for data analysis and reporting. Only people who are involved in the project will have access to this data. **Is it ok if I start the audio recording now?** [START RECORDING]
- And just to confirm, can you see my screen on your computer? It should say "Participant [READ PARTICIPANT ID #]." OK great, we won't be using the computer just yet—I will let you know when we get to that part.

- Do you have any questions before we begin?

Okay, great. Let's get started.

SECTION II: Background Information (10 Minutes)

I'd like to start by talking a little bit about your background as a physician.

1. How long have you been practicing medicine?
2. Please describe your current practice setting.
 - a. *Do you currently have your own practice?*
 - b. *Do you partner with other physicians?*
 - c. *Are you or your practice associated with an academic institution or teaching hospital?*
3. What are some typical patient issues you treat?
4. What proportion of your patients is diabetic or pre-diabetic? [Probe for percentage]
5. What proportion of your patients is overweight? [Probe for percentage]

Now I'd like to shift the conversation to clinical trial design.

6. How often do you come across clinical trial data in your daily practice?
7. Where do you come across clinical trial data?
 - a. *Do you seek out clinical trial data? Explain (Why?).*
 - i. *If so, how?*
 - ii. *In what situations do you typically use clinical trial data?*
 - b. *Do you read any journals or publications that discuss clinical trials? If so, which ones?*
8. How comfortable are you in interpreting results from clinical drug trials?
 - a. *How often do you to interpret results from clinical drug trials?*
 - b. *In what situations do you typically need to interpret results from clinical drug trials?*
9. How comfortable are you applying results from clinical drug trials to patient care (or treatment)? Why is that?
 - a. *How do you decide what drugs/therapy to use for your patients with diabetes? With obesity?*

10. What type of formal training, if any, do you have on interpreting this type of data?
This might have been in medical school or after. [Probe on type of course–e.g., Biostatistics, Epidemiology]
 - a. *What about informal “on-the-job” training?* [Probe on type–e.g., CME training]
11. If you wanted to learn more about clinical trial design, how would you do that?
12. How frequently do you receive promotional materials about prescription drugs? [IF NEEDED: examples of these materials would be advertisements in a medical journal, a mailer, Pharm/Alert email, or a special brochure / pamphlet]
13. How frequently do the promotional materials that you receive include clinical trial data?

SECTION III: Stimuli Discussion (45 min.)

Now, I am going to ask that you use your computer. Are you looking at your computer now? OK, great. I am going to show you various prescription drug promotional materials on the screen and will be asking follow-up questions. Please keep in mind these drugs may or may not be applicable to your current practice or the patients you see; instead, we are using these promotional materials to facilitate discussion and gain a better understanding of how promotional items like these are typically utilized. We'll be looking at promotional materials for two different prescription drugs today.

[ORDER OF AFREZZA AND BELVIQ WILL BE RANDOMIZED (PLEASE SEE RANDOMIZATION TABLE). ONLY THE AD SHOWN FIRST WILL RECEIVE THE FULL QUESTIONNAIRE; THE SECOND AD WILL RECEIVE ONLY A CONDENSED QUESTIONNAIRE FEATURING ONLY CORE ITEMS. PLEASE ALLOCATE APPROXIMATELY 30 MINUTES FOR THE FIRST AD AND 15 MINUTES FOR THE SECOND AD. REFER TO APPENDICES FOR STIMULI QUESTIONS.]

RANDOMIZATION	Ad Shown First <i>Full Questionnaire</i>	Ad Shown Second <i>Condensed Questionnaire</i>
A	Afrezza (Appendix 1)	Belviq (Appendix 2; Q1-2, Q6-13)
B	Belviq (Appendix 2)	Afrezza (Appendix 1; Q1-2, Q6-15)

SECTION IV: Closing

[IF TIME PERMITS – PLEASE CHECK WITH RESEARCH TEAM/OBSERVERS FOR FOLLOW UP QUESTIONS.]

Thank you, this has been helpful. I am going to check quickly with my colleagues to see if there are any follow-up questions for you in the time we have remaining. I will be right back on the line.

[Put participant on hold]

MODERATOR TO ASK FOLLOW-UP QUESTIONS (if applicable)

[Thank participant]

Thank you very much for participating in this interview. I have enjoyed getting to know you, and appreciate your time and feedback. Is there anything that you would like to share that you didn't have the chance to share yet?

APPENDIX 1: Afrezza Questions

I am going to show you some prescription drug promotional material on Afrezza. Afrezza is rapid acting inhaled insulin that is used to control high blood sugar in adults with type 1 and type 2 diabetes.

1. Have you heard of Afrezza before? (Yes/No)
2. Have you ever prescribed Afrezza before? (Yes/No)

Now, I'd like you to take a few minutes to read through the promotional material on your screen. Please read as you typically would in order to evaluate the prescription drug being described. There are several pages and you can click through using your mouse. This is not the entire promotional piece. Let me know when you have finished reading and we will have some follow-up discussion.

[SHOW AFREZZA STIMULI SET]

[Allow participant to read for approx. 5 min (hard stop)]

3. Can you walk me through your process in evaluating this promotional material on Afrezza? Feel free to click through the materials again if there is anything specific you would like to refer to. [Allow participant to walk through process; use probes below as needed to ensure coverage.]
 - a. What sort of information were you looking for?
 - i. *What specific information in the Afrezza materials was most important to you?*
 - b. What items were unclear or confusing to you in going through the materials?
 - c. When reviewing this Afrezza piece, how much time did you spend looking specifically at the clinical trial data?
 - i. *How much time do you typically spend reviewing clinical trial data when you receive promotional materials like this?*

- d. *What additional information would you want to see about Afrezza to make a prescribing decision?*
 - i. *Where else would you go for more information?*
 - e. How would you explain the contents of the Afrezza piece to a patient?
 - f. *What sort of red flags did you look for?*
4. What factor(s) would go into your decision to prescribe or not prescribe Afrezza to a patient?
- a. *What role, if any, would the clinical trial data play in your decision?*
5. Imagine you were going to prescribe Afrezza to a patient—how would you explain the efficacy of Afrezza to them?

Now I'd like to ask you some specific questions about the information found in this promotional material. As I mentioned earlier, I do not have a medical background and your insight will help me understand these materials better.

[SHOW AFREZZA SLIDE 46]

6. How would you explain the concept of Randomized Controlled Trials (RCTs) for assessing drug efficacy to a medical student?
7. What about non-inferiority randomized clinical trials (RCTs)?
- a. *Have you encountered the term or concept of non-inferiority in your reading or practice? Please explain.*
8. Does the inclusion of non-inferiority impact your interpretation of clinical trial data? If so, how so? If not, why not?
9. How would you explain a non-inferiority margin of 10% in a clinical trial to a medical student?
10. How would you explain the concept of an adjusted mean to a medical student?
11. Footnote "A" below the graph details the use of the adjusted mean. How does the information in the footnote affect how you interpret the results of the graph?

[NOTE: RANDOMIZE ORDER OF STATEMENT Q & J]

12. Next I have a couple of statements about Afrezza I'd like you to put in layman's terms for me. In your own words, how would you explain what this statement means?

- [SHOW AFREZZA STATEMENT Q] [READ] "In adults with type 1 diabetes, the efficacy of Afrezza® inhaled insulin proved noninferior to that of insulin aspart within the pre-set noninferiority margin of 0.4%"
- [SHOW AFREZZA STATEMENT J] [READ] "Afrezza® provided less A1C reduction than insulin aspart, and the difference was statistically significant. More subjects in the insulin aspart group achieved the A1C target of $\leq 7\%$ "

13. [SHOW BOTH STATEMENTS] Looking at these statements together, are their conclusions similar or different? Please explain.

14. Could these two results come from the same study? Please explain.

[SHOW AFREZZA SLIDE 46]

15. Imagine you chose to prescribe Afrezza for a patient, how would you describe the efficacy of Afrezza as compared to the efficacy of insulin aspart to them?

APPENDIX 2: Belviq Questions

I am going to show you some prescription drug promotional material on Belviq. Belviq is a prescription weight-loss medication that, when used with diet and exercise, can help some overweight adults with a weight-related medical problem, or obese adults, lose weight and keep it off.

1. Have you heard of Belviq before? (Yes/No)
2. Have you ever prescribed Belviq before? (Yes/No)

Now, I'd like you to take a few minutes to read through the promotional material on your screen. It is not the entire Belviq piece. Please read as you typically would in order to evaluate the prescription drug being described. There are a several pages and you can click through using your mouse. Let me know when you have finished reading and we will have some follow-up discussion.

[SHOW BELVIQ STIMULI SET]

[Allow participant to read for approx. 5 min (hard stop)]

3. Can you walk me through your process in evaluating this promotional material on Belviq? Feel free to click through the materials again if there is anything specific you would like to refer to. [Allow participant to walk through process; use probes below as needed to ensure coverage.]
 - a. What sort of information were you looking for?
 - i. *What specific information in the Belviq materials was most important to you?*
 - b. What items were unclear or confusing to you in going through the materials?
 - c. When reviewing this Belviq piece, how much time did you spend looking specifically at the clinical trial data?
 - i. *How much time do you typically spend reviewing clinical trial data when you receive promotional materials like this?*

- d. *What additional information would you want to see about Belviq to make a prescribing decision?*
 - ii. *Where else would you go for more information?*
 - e. How would you explain the contents of the Belviq piece to a patient?
 - f. *What sort of red flags did you look for?*
4. What factor(s) would go into your decision to prescribe or not prescribe Belviq to a patient?
- a. *What role, if any, would the clinical trial data play in your decision?*
5. Imagine you were going to prescribe Belviq to a patient—how would you explain the efficacy of Belviq to them?

Now I'd like to ask you some specific questions about the information found in this promotional material. As I mentioned earlier, I do not have a medical background and your insight will help me understand these materials better.

6. How would you explain re-randomization in a clinical trial to a medical student?
- a. *Why would a research team decide to re-randomize participants?*
7. [SHOW BELVIQ PAGE 3] In this study, 3182 patients were randomly assigned to either Belviq with lifestyle modification or to placebo with lifestyle modification. At week 52, patients treated with Belviq were randomly reassigned to either Belviq with lifestyle modification or to placebo with lifestyle modification.

Why do you think re-randomization was done after year 1 in this trial?

- a. *How does re-randomization impact your interpretation (understanding) of the results?*
8. [SHOW BELVIQ PAGE 2] The footnote says "44% of Belviq patients and 51% of placebo patients withdrew prior to week 52." What are some implications of missing data like these?
- a. Did you notice this footnote previously? (Yes/No)

- i. *How does this footnote affect your interpretation of the results?*
 - b. Do you typically read footnotes when reviewing this type of information?
 - i. *How do footnotes typically affect your interpretation of any data being presented?*
- 9. [SHOW BELVIQ PAGE 3] Here, the title of the graph displaying the results is: “Mean weight change over time (all patients who completed the study).” Were you able to determine how many participants completed the study?
 - a. *If yes, how many?*
- 10. Given the previous information about patient withdrawal rates and the number of patients completing 104 weeks of treatment, what do you think the clinical implications of this missing data might be?
- 11. How would you explain Intent to Treat analysis to a medical student?
- 12. How would you explain per-protocol analysis to a medical student?
- 13. [SHOW BELVIQ PAGE 2] The impact on blood pressure and heart rate data was analyzed based on Modified Intent to Treat using Last Observation Carried Forward. How would you explain Modified Intent to Treat using Last Observation Carried Forward to a medical student?
 - c. *How does your understanding of Modified Intent to Treat using Last Observation Carried Forward impact your clinical interpretation of these results?*
 - d. *How do you think the results might be different if standard Intent to Treat analysis was done?*
 - e. *How do you think the results might be different if data was analyzed per-protocol?*