Main Survey—Part I

INTRO1 Thank you for agreeing to participate in this study today.

Make sure you are comfortable and can read the screen from where you sit.

This study aims to understand how medical providers interpret promotional materials from pharmaceutical companies such as sales aids or brochures. We are not connected with the drug being promoted.

The survey will take about **20 minutes** to complete. We ask you to complete the survey in one sitting (without taking any breaks) to avoid distractions. Your input is extremely valuable.

[----------NEXT SCREEN----------]

INTRO2 On the next screen, you will be shown two pages of a sales aid for a new prescription drug. **In the interest of time, you will see only a specific portion of the sales aid and not the full material.**

Imagine that this sales aid is for a medication that you might be interested in prescribing to your patients.

Even though the sales aid is on a computer screen, please review it as if you received it from a pharmaceutical representative.

The sales aid has two pages. You can flip between the pages by clicking on the "**View Page 1**" and "**View Page 2**" buttons at the bottom of each page. Once you finish viewing the sales aid, please click "**Start Next Part of Survey**" to move to the next part of the survey.

We will then ask you some questions about the sales aid. These questions focus on the content of the sales aid and are not a test of intelligence.

[----------NEXT SCREEN----------]

[PRESENT SALES AID]

[DO NOT ALLOW RESPONDENTS TO GO BACK TO PREVIOUS PAGES IN THE SURVEY]

[ON TOP OF SALES AID INCLUDE THE FOLLOWING TEXT]

Even though the sales aid is on a computer screen, please review it as if you received it from a pharmaceutical representative.

[----------NEXT SCREEN----------]

PRETEST Were you able to view the image?

1. Yes
2. No [TERMINATE]

[----------NEXT SCREEN----------]

SCRIPT1 We would now like to ask you a series of questions based on the portion of the sales aid you saw.

[----------NEXT SCREEN----------]

ENDPOINT [IF CONDITION=1-10] What clinical endpoint did the chart in the sales aid focus on?

[RANDOMIZE RESPONSE OPTIONS]
3. Overall survival **[Correct for DRUGY]**
4. Progression-free survival **[Correct for DRUGX]**
5. Time to progression
6. Objective response rate

[IF CONDITION=11-15] Which one of the following choices is the surrogate endpoint that the chart in the sales aid focused on?

[RANDOMIZE RESPONSE OPTIONS]
7. Decrease in iron load **[Correct]**
8. Reduction in side effects
9. Improvement in symptoms
10. Increase in objective response rate

[----------NEXT SCREEN----------]

INDICATION According to the sales aid, [IF CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI in combination with Rd (lenalidomide + dexamethasone); IF CONDITION=11-15: FEXXOPER] is approved to treat patients with which medical condition?

[RANDOMIZE RESPONSE OPTIONS]

[IF CONDITION=1-5]
11. Unresectable or metastatic melanoma patients with a BRAF V600E/V600K mutation **[Correct]**
12. Refractory BRAF V600E mutation positive-hairy cell leukemia
13. Multiple myeloma patients who have received one to three prior therapies

[IF CONDITION=6-10]
14. Multiple myeloma patients who have received one to three prior therapies **[Correct]**
15. Treatment-naïve multiple myeloma patients

16. Non-Hodgkin lymphoma patients

[IF CONDITION=11-15]

17. Transfusional iron overload due to thalassemia syndrome **[Correct]**
18. Transfusional iron overload due to myelodysplastic syndrome
19. Transfusional iron overload due to hereditary hemochromatosis

[----------NEXT SCREEN----------]

REVIEW The following information **may or may not** have been in the portion of the sales aid you just viewed. Please indicate whether you noticed the following types of information in the sales aid you viewed.

[RANDOMIZE ORDER]	**No, I did not notice it** 1	**Yes, I skimmed it** 2	**Yes, I read most or all of it** 3
REVIEW1A [IF CONDITION=1-5: Limitations of subgroup analysis; IF CONDITION=6-15: Discussion of statistical significance of results]			
REVIEW1B Visual display of the data (e.g., chart or graph)			
REVIEW1C List of potential side effects			
REVIEW1D Complete prescribing information			

[----------NEXT SCREEN----------]

ATTEN_DISC The image below has been blurred for the purpose of this question.

[DISPLAY SCREENSHOT OF SECOND PAGE OF SALES AID WITH A BLACK BOX OVER WHERE THE SPECIFIC DISCLOSURE WOULD BE]

Here is an edited portion of the sales aid you just saw. Was there text in the area shaded in black, or was there no text?

20. There was text
21. There was no text

[----------NEXT SCREEN----------]

DISC_FU [DISPLAY SCREENSHOT OF SECOND PAGE OF SALES AID WITH A BLACK BOX WHERE THE SPECIFIC DISCLOSURE WOULD BE] [IF ATTEN_DISC= yes] How closely did you read the information in the black box?

22. I saw it but did not read it
23. I skimmed it

24. I read most or all of it

[----------NEXT SCREEN----------]

DISC_OE [IF DISC_FU = 2 or 3] Please enter anything that you recall reading in the text included in the black box. We understand that it may be difficult to remember details even if you read the information closely. This is not a test. Please just do your best to note what you recall.

[----------NEXT SCREEN----------]

RECOGNITION The following statements **may or may not** have been in the portion of the sales aid you just viewed. Please indicate whether you recall **seeing** the following statements in the sales aid, regardless of whether you believe they are true.

[DISPLAY IF CONDITION=1-5. RANDOMIZE ORDER OF SUBITEMS]	**Do Not Recall Seeing** 1	**Recall Seeing** 2
RECOGX1 This presentation includes information of uncertain clinical utility and should be interpreted cautiously in making treatment decisions.		
RECOGX2 [IF CONDITION= 2 OR 4] In the figure above, a Cox model was used to estimate hazard ratios. [IF CONDITION=3 OR 5] The figure above presents the observed treatment effects in various subgroups by baseline characteristics in the study. [IF CONDITION=1: Randomly assign people to either see the technical or nontechnical sentence]		
RECOGX3 A multicenter, randomized, double-blind, placebo-controlled study evaluated the efficacy and safety of XEDALITI + VULPAFEN.		
RECOGX4 XEDALITI + VULPAFEN can cause fetal harm when administered to a pregnant woman.		

[DISPLAY IF CONDITION=6-10. RANDOMIZE ORDER OF SUBITEMS]	**Do Not Recall Seeing** 1	**Recall Seeing** 2
RECOGY1 This presentation includes information of uncertain clinical utility and should be interpreted cautiously in making treatment decisions.		
RECOGY2 [IF CONDITION=7 OR 9] Overall survival (OS) was tested hierarchically after the co-primary endpoints. [IF CONDITION=8 OR 10] Overall survival (OS) was a		

secondary endpoint of this study. [IF CONDITION=6: Randomly assign people to either see the technical or nontechnical sentence]		
RECOGY3 A Phase 3, randomized, open-label study evaluated the efficacy and safety of XEDALITI in combination with Rd.		
RECOGY4 XEDALITI + Rd demonstrated a similar incidence of adverse events vs Rd alone.		

[DISPLAY IF CONDITION=11-15. RANDOMIZE ORDER OF SUBITEMS]	**Do Not Recall Seeing** **1**	**Recall Seeing** **2**
RECOGZ1 This presentation includes information of uncertain clinical utility and should be interpreted cautiously in making treatment decisions.		
RECOGZ2 [IF CONDITION= 12 OR 14] These data are derived from an open label, uncontrolled, nonrandomized analysis of preexisting clinical data from 12 studies. [IF CONDITION=13 OR 15] These data are derived from a retrospective analysis of patients from 12 previous studies. [IF CONDITION=11: Randomly assign people to either see the technical or nontechnical sentence]		
RECOGZ3 There are no controlled trials demonstrating a direct treatment benefit, such as improvement in functioning or increased survival.		
RECOGZ4 There are no studies with FEXXOPER with pregnant women to inform any drug-associated risks.		

[----------NEXT SCREEN----------]

[RANDOMIZE PRESENTATION ORDER OF BENEFICIAL AND IMPROVE]

BENEFICIAL Based on the sales aid you saw, how beneficial do you think [CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER] might be for treating [IF CONDITION=1-5: unresectable or metastatic melanoma patients with a BRAF V600E/V600K mutation, IF CONDITION=6-10: multiple myeloma patients, IF CONDITION=11-15: patients with transfusional overload]?

25. Not at all beneficial
26. Somewhat beneficial
27. Moderately beneficial
28. Very beneficial
29. Extremely beneficial

IMPROVE Based on the sales aid, to what extent do you agree or disagree with the following statement:

I believe [CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER] improves [IF CONDITION=1-5, progression-free survival of patients. IF CONDITION=6-10, overall survival of patients. IF CONDITION=11-15, a patient's iron load.]

30. Completely disagree
31. Disagree
32. Somewhat disagree
33. Somewhat agree
34. Agree
35. Completely agree

[----------NEXT SCREEN----------]

EVIDENCE1 Based on the sales aid, to what extent do you agree or disagree with the following statement:

I believe there is strong evidence of [IF CONDITION=1-5: XEDALITI + VULPAFEN'S; CONDITION=6-10: XEDALITI + Rd's; IF CONDITION=11-15: FEXXOPER'S] benefit to patients.

36. Completely disagree
37. Disagree
38. Somewhat disagree
39. Somewhat agree
40. Agree
41. Completely agree

[----------NEXT SCREEN----------]

EVIDENCE2 How much evidence does the sales aid provide that [IF CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER] is appropriate to treat [IF CONDITION=1-5: unresectable or metastatic melanoma patients with a BRAF V600E/V600K mutation? IF CONDITION=6-10: multiple myeloma patients? CONDITION=11-15: patients with transfusional overload?]

42. Insufficient evidence
43. Preliminary evidence
44. Strong evidence

[----------NEXT SCREEN----------]

DECISIONS Which one of the following statements best summarizes how you feel about the **data** presented in this sales aid?

45. The data would not be useful in making prescribing decisions.
46. I would consider the data when making prescribing decisions.
47. I would change my prescribing decisions based on the data.

[----------NEXT SCREEN----------]

[RANDOMIZE PRESENTATION ORDER OF COMPLEX AND CONFUSING1]

COMPLEX How **complex** was the information presented in the portion of the sales aid you saw?

48. Not at all complex
49. Somewhat complex
50. Moderately complex
51. Very complex
52. Extremely complex

CONFUSING1 How **confusing** was the information presented in the portion of the sales aid you saw?

53. Not at all confusing
54. Somewhat confusing
55. Moderately confusing
56. Very confusing
57. Extremely confusing

[----------NEXT SCREEN----------]

CONFUSING2 Please think about the average [IF SPECIALTY=1: primary care physician, IF SPECIALTY=2, 3 , 4, or 5: oncologist] in your field. How confusing would he or she find the information in the sales aid you saw?

58. Not at all confusing
59. Somewhat confusing
60. Moderately confusing
61. Very confusing
62. Extremely confusing

[----------NEXT SCREEN----------]

[RANDOMIZE PRESENTATION ORDER OF BELIEVABLE, CREDIBLE, AND BIASED]

BELIEVABLE How **believable** was the information presented in the portion of the sales aid you saw?

63. Not at all believable
64. Somewhat believable
65. Moderately believable
66. Very believable
67. Extremely believable

CREDIBLE How **credible** was the information presented in the portion of the sales aid you saw?

68. Not at all credible
69. Somewhat credible

70. Moderately credible
71. Very credible
72. Extremely credible

BIASED How **biased** was the information presented in the portion of the sales aid you saw?

73. Not at all biased
74. Somewhat biased
75. Moderately biased
76. Very biased
77. Extremely biased

[----------NEXT SCREEN----------]

Main Survey—Part II

[PUT LINK TO SALES AID ON THE TOP OF EACH SCREEN. CAPTURE PARADATA ON WHETHER RESPONDENT CLICKS ON LINK FOR EACH SCREEN.]

SCRIPT2 When answering the remaining questions, click on the link at the top of the page above the question to view the same sales aid you saw earlier.

[----------NEXT SCREEN----------]

P_VIGNETTE Sarah has been diagnosed with [IF CONDITION=1-5: metastatic melanoma with a BRAF V600 mutation. IF CONDITION=6-10: multiple myeloma. She has received three previous therapies and has documented disease progression. IF CONDITION=11-15: thalassemia and has developed iron-overload due to her transfusions. Chelation therapy did not sufficiently reduce her iron levels.]

Based on the information presented in the sales aid, Sarah is a good candidate for [CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER].

78. Completely disagree
79. Disagree
80. Somewhat disagree
81. Somewhat agree
82. Agree
83. Completely agree

[----------NEXT SCREEN----------]

N_VIGNETTE John was newly diagnosed with [IF CONDITION=1-5: wild-type BRAF melanoma; IF CONDITION=6-10: myelodysplastic syndrome; IF CONDITION=11-15: iron-overload due to myelodysplastic syndrome].

Based on the information presented in the sales aid, John is a good candidate for [CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER].

84. Completely disagree
85. Disagree
86. Somewhat disagree
87. Somewhat agree
88. Agree
89. Completely agree

[----------NEXT SCREEN----------]

MOREINFO If you had patients with [IF CONDITION=1-5: unresectable or metastatic melanoma with a BRAF V600E/V600K mutation, IF CONDITION=6-10: multiple myeloma who have received one to three prior therapies, IF CONDITION=11-15: transfusional iron overload due to thalassemia syndromes,] how interested would you be in finding more information about [IF CONDITION=1-5: the use of XEDALITI in combination with VULPAFEN; IF CONDITION=6-10: the use of XEDALITI in combination with Rd; IF CONDITION=11-15: FEXXOPER]?

90. Not at all interested
91. Somewhat interested
92. Moderately interested
93. Very interested
94. Extremely interested

[----------NEXT SCREEN----------]

SCRIPT4 For the following questions, if you don't know the answer or aren't sure, just take your best guess.

[RANDOMIZE ORDER OF ALL COMPREHENSION ITEMS: THERAPY—PRELIM. PRESENT EACH QUESTION ON A SEPARATE SCREEN]

[----------NEXT SCREEN----------]

THERAPY According to the sales aid, [CONDITION=1-5: XEDALITI + VULPAFEN; IF CONDITION=6-10: XEDALITI + Rd; IF CONDITION=11-15: FEXXOPER] is considered a…

95. First-line therapy **[Correct for DRUGX]**
96. Second-line therapy **[Correct for DRUGY and DRUGZ]**

[----------NEXT SCREEN----------]

ANALYSIS_C [IF CONDITION=1-5] According to the sales aid, is this statement true or false?

The subgroup analysis assessed the consistency of the results according to prognostic factors as well as age and geographical location.

97. True **[Correct]**
98. False

ANALYSIS_E [IF CONDITION=6-10] According to the sales aid, which statement best describes the analysis in the sales aid you saw?

[RANDOMIZE RESPONSE ORDER]

99. Overall survival analysis was conducted at the completion of the clinical trial.
100. Overall survival analysis was conducted before the completion of the clinical trial. **[Correct]**

ANALYSIS_F [IF CONDITION=11-15] According to the sales aid, which statement best describes the analysis in the sales aid you saw?

[RANDOMIZE RESPONSE ORDER]

101. This analysis used data from other clinical trials that were previously conducted. **[Correct]**
102. A new randomized controlled clinical trial was conducted to identify patients for this study.

[----------NEXT SCREEN----------]

RESULTS1_C [IF CONDITION=1-5] According to the sales aid, which one of the following statements is true?

[RANDOMIZE OPTIONS 1-3]

103. The benefit for progression-free survival was evident in only a few patient subgroups.
104. Some subgroups significantly deviated from the overall effect.
105. The sales aid reported a statistically significant subgroup–treatment interaction effect.
106. None of the above. **[Correct]**

RESULTS1_E [IF CONDITION=6-10] According to the sales aid, which one of the following statements is true?

[RANDOMIZE OPTIONS 1 & 2]

107. The interim analysis for overall survival found a positive (but nonsignificant) trend favoring XEDALITI in combination with Rd versus Rd alone. **[Correct]**
108. The interim analysis for overall survival found a positive and statistically significant trend favoring XEDALITI in combination with Rd versus Rd alone.
109. None of the above.

RESULTS1_F [IF CONDITION=11-15] According the sales aid, which one of the following statements is true?

[RANDOMIZE OPTIONS 1-3]

110. The success rate was achieved for the three indicators of iron overload.
111. For each efficacy measure, in order for the FEXXOPER therapy to be considered successful, the lower limit of the 95% confidence interval had to be greater than 20%.
112. There is a 95% likelihood that the true success rate for reduction in liver iron concentrate (LIC) falls between 33 and 51%.
113. All of the above. **[Correct]**

[----------NEXT SCREEN----------]

RESULTS2_C [IF CONDITION=1-5] According to the sales aid, is this statement true or false?

A plot of the hazard ratios summarizing exploratory subgroup analyses suggested treatment benefit for all evaluated subgroups.

114. True **[Correct]**
115. False

RESULTS2_E [IF CONDITION=6-10] According to the sales aid, is this statement true or false?

Although not statistically significant, patients taking XEDALITI in combination with Rd had a 23% lower risk of death than those taking Rd alone.

116. True **[Correct]**
117. False

RESULTS2_F [IF CONDITION = 11-15] According the sales aid, is this statement true or false?

Serum ferritin was reduced by more than 20% in 50% of patients treated.

118. True **[Correct]**
119. False

[----------NEXT SCREEN----------]

RESULTS3_C [IF CONDITION=1-5] According to the sales aid, is this statement true or false?

The benefit of XEDALITI + VULPAFEN was seen whether or not the patient was male or female.

120. True **[Correct]**
121. False

RESULTS3_E [IF CONDITION=6-10] At the time of the interim analysis, what was the survival probability of patients taking XEDALITI in combination with Rd?

122. 100%
123. 77%
124. 60% **[Correct]**
125. 53%
126. 23%

RESULTS3_F [IF CONDITION=11-15] What percentage of patients achieved sponsor-defined treatment success for liver iron concentrate (LIC)?

127. 100%
128. 62%
129. 42% **[Correct]**
130. 50%
131. 20%

[----------NEXT SCREEN----------]

LIMITS_C [IF CONDITION=1-5] Which, if any, of the following limitations are limitations of the analyses presented in the sales aid?

[RANDOMIZE OPTIONS 1-3]

132. The analysis did not appropriately control the false-positive rate in conducting multiple subgroup analyses.
133. There may be an imbalance between the two treatment groups in baseline characteristics.
134. The analysis did not account for the effects of the other subgroup factors.
135. All of the above. **[Correct]**
136. None of the above.

LIMITS_E [IF CONDITION=6-10] Which, if any, of the following limitations are limitations of the analyses presented in the sales aid?

[RANDOMIZE OPTIONS 1-3]

137. The analyses were conducted before the conclusion of the study. **[Correct]**
138. The study did not have a control group.
139. There was a high rate of missing data.
140. All of the above.
141. None of the above.

LIMITS_F [IF CONDITION=11-15] Which, if any, of the following limitations are limitations of the analyses presented in the sales aid?

[RANDOMIZE OPTIONS 1-3]

142. There was a high rate of missing data.
143. The study did not have a control group.

144. There was wide variability of results among the included studies.
145. All of the above. **[Correct]**
146. None of the above.

[----------NEXT SCREEN----------]

PRELIM Is this statement true or false?

The data presented in the sales aid clearly translates into clinical benefit.

147. True
148. False **[Correct]**

[----------NEXT SCREEN----------]

[SALES AID LINK NO LONGER AVAILABLE ON SCREEN]

TECHNICAL To what extent do you agree or disagree with the following statement:

Overall, the sales aid used a lot of technical language such as complex terminology, statistical terms, or jargon.

149. Completely disagree
150. Disagree
151. Somewhat disagree
152. Somewhat agree
153. Agree
154. Completely agree

[----------NEXT SCREEN----------]

PREFERENCE Below are two versions of a disclosure statement that could appear in the sales aid for [IF CONDITION=1-10: XEDALITI; IF CONDITION=11-15: FEXXOPER].

[RANDOMIZE ORDER]

Option A. [IF CONDITION=1-5, FILL DRUGX_TECHNICAL, IF CONDITION=6-10, FILL DRUGY_TECHNICAL, IF CONDITION=11-15, FILL DRUGZ_TECHNICAL]

Option B. [IF CONDITION=1-5, FILL DRUGX_NONTECHNICAL, IF CONDITION=6-10, FILL DRUGY_NONTECHNICAL, IF CONDITION=11-15, FILL DRUGZ_NONTECHNICAL]

Which one of the disclosure statements do you **prefer**?

155. Option A
156. Option B

157. No preference

Conditional text	Display
{DRUGX_TECHNICAL}	In the figure above a Cox model was used to estimate hazard ratios and corresponding 95% confidence intervals for observed treatment effects in various subgroups by baseline characteristics in the study. The subgroup analyses were pre-specified in the statistical analysis plan, but there was no statistical procedure pre-specified in the statistical analysis plan to appropriately control the overall Type 1 error rate at a significance level of two-sided 0.05. The 95% confidence limits shown also do not reflect the effect of a particular factor after adjustment for all other factors. In addition, because the randomization was not stratified by the factor that defines the subgroup, it could cause imbalance between the two treatment groups in baseline characteristics or other known or unknown factors within the subgroup. Therefore, apparent homogeneity or heterogeneity among groups should not be over interpreted.
{DRUGX_NONTECHNICAL}	The figure above presents the observed treatment effects in various subgroups by baseline characteristics in the study. The subgroup results (e.g., disease state, age, sex) are considered exploratory. There was no procedure in place to appropriately control the false positive rate in conducting multiple analyses or to adjust each subgroup analysis to account for the effects of the other subgroup factors. In addition, there may be imbalance in baseline characteristics among the compared subgroups. Therefore, it may not be appropriate to draw conclusions regarding the efficacy of the combination of Xedaliti and Vulpafen for patients with unresectable or metastatic melanoma with BRAF V600E or V600E mutations in these particular subgroups.
{DRUGY_TECHNICAL}	Overall survival (OS) was tested hierarchically after the co-primary endpoints of overall response rate (ORR) and progression free survival (PFS) to preserve the experiment-wise type-I error at the 5% level. No alpha was allocated to OS rate comparisons at specific time points (such as 36 months). The nominal alpha level for OS at interim analysis was calculated using a separate O'Brien Fleming spending function, based on the actual number of deaths observed at the time of analysis (295 deaths). The alpha level for the interim OS analysis (0.014) was calculated as an adjustment to the 295/427 (69%) of data maturity. The p-value of 0.0257 from the interim OS analysis was larger than the threshold of 0.014. Thus, a conclusion that Xedaliti confers a benefit in terms of OS cannot be made at this time.
{DRUGY_NONTECHNICAL}	Overall survival (OS) was a secondary endpoint of this study (progression free survival and overall response rate were the co-primary endpoints). The analysis of overall survival (OS) was conducted before data collection was complete. OS rate comparisons at specific time points (such as 36 months) were exploratory. The p value threshold for the interim OS analysis was adjusted because only 69% of the study had been completed at the time of analysis. The interim analysis was not statistically significant. Thus, a conclusion that Xedaliti confers a benefit in terms of OS cannot be made at this time.

Conditional text	Display
{DRUGZ_TECHNICAL}	These data are derived from an open label, uncontrolled, non-randomized analysis of pre-existing clinical data from 12 studies. The primary endpoint was the change in serum ferritin from baseline within one year of treatment with Fexxoper. Success was calculated as the proportion of patients with a ≥20% decline in serum ferritin from baseline within one year of treatment. Secondary endpoints included change in cardiac MRI T2 and Liver Iron Concentration (LIC) within one year of treatment with Fexxoper. Fexxoper therapy was considered successful in individual patients who experienced a ≥20% increase in cardiac MRI T2* or a ≥20% decline in LIC within one year of therapy. Success rates by study overall and their 95% CIs were calculated based on Clopper-Pearson exact confidence interval. Data were pooled from heterogeneous studies. There were several limitations to these studies; for example, retrospective designs, small sample sizes, lack of control groups, missing data, and missing treatment compliance assessments. There was a high rate of missing data among the pooled studies and significant variations in results among the evaluated studies. These limitations raise an issue of data integrity and heterogeneity that can potentially cause biased results. For serum ferritin, in 33% (4/12) of the studies, the lower bound of the 95% confidence interval was less than the pre-specified target of 20%. For LIC, in 50% (3/6) of the studies, the lower bound of the 95% confidence interval was less than the pre-specified target of 20%. A total of 20 (7.6%), 79 (29.9%), 94 (35.6%) and 127 (48.1%) subjects dropped out of the studies by month 3, 6, 9 and 12, respectively. High dropout rate could make the results unreliable and misleading.
{DRUGZ_NONTECHNICAL}	These data are derived from a retrospective analysis of patients from 12 previous studies. No control group or randomization was used and the drug name was not disguised. The primary endpoint was the change in serum ferritin from baseline within one year of treatment with Fexxoper. Success was calculated as the proportion of patients with a ≥20% decline in serum ferritin from baseline within one year of treatment. Secondary endpoints included change in cardiac MRI T2 and Liver Iron Concentration (LIC) within one year of treatment with Fexxoper. Fexxoper therapy was considered successful in individual patients who experienced a ≥20% increase in cardiac MRI T2* or a ≥20% decline in LIC within one year of therapy. The characteristics (e.g., study design, treatment duration, patient selection criteria, exferperone doses) of the studies from which the patients were selected varied significantly. This pooled analysis has several serious limitations including lack of randomization, lack of control group, high rate of missing data, and ignoring the variation between studies by simple pooling, all of which can potentially cause biased results. For each endpoint, there was a wide variability of success rates among the individual studies that were pooled in the analysis. This was particularly true for serum ferritin and LIC. The number of subjects that dropped out of the studies continued to increase over 12 months. High dropout rates could also make the results unreliable and misleading.

[----------NEXT SCREEN----------]

PREFERWHY [PRETEST ONLY. IF PREFERENCE ≠ 3] Please tell us why you prefer Option [IF PREFERENCE=1: A, IF PREFERENCE=2: B].

[----------NEXT SCREEN----------]

SCRIPT5 FDA designates some new prescription drugs it reviews and approves as "breakthrough drugs" or "breakthrough therapies".

FAMILIAR How familiar are you with the "breakthrough therapy" designation?

158. Not at all familiar
159. A little familiar
160. Familiar
161. Very familiar

[----------NEXT SCREEN----------]

[IF FAMILIAR = 1, SKIP to BTDV1/BTDV2]
[RANDOMIZE ORDER OF BTKNOW1 AND ACCEL. PRESENT EACH QUESTION ON A SEPARATE SCREEN]

BTKNOW1 For drugs that are intended to treat serious conditions, what is the minimum level of evidence that the FDA requires manufacturers to gather for the FDA to label a drug as a breakthrough?

162. Strong evidence (e.g., randomized trials evaluating clinical outcomes)
163. Preliminary evidence (e.g., uncontrolled studies or studies testing surrogate outcomes) **[Correct]**
164. Very preliminary evidence (e.g., *in vitro* lab or animal studies)

[----------NEXT SCREEN----------]

ACCEL Is this statement true or false?

FDA's breakthrough therapy designation pathway automatically qualifies a drug to receive accelerated approval.

165. True
166. False **[Correct]**

[----------NEXT SCREEN----------]

[RANDOMIZE WHETHER PARTICIPANT SEES BTDV1 OR BTDV2]

BTDV1 Imagine your patient has a serious medical condition for which there has been no effective treatment. The FDA recently approved 2 new drugs to treat this condition.

Both drugs are oral tablets to be taken once a day, have similar adverse effect profiles, and are equally covered by the patient's insurance.

Which would you choose first?

[RANDOMIZE OPTIONS 1-2]

167. Axabex, an FDA-designated breakthrough drug
168. Zykanta, a drug with early promising study results showing that the drug may demonstrate substantial improvement over available therapies

BTDV2 Imagine your patient has a serious medical condition for which there has been no effective treatment. The FDA recently approved 2 new drugs to treat this condition. Both drugs are oral tablets to be taken once a day, have similar adverse effect profiles, and are equally covered by the patient's insurance.

Which would you choose first?

[RANDOMIZE OPTIONS 1-2]

169. Zykanta, an FDA-designated breakthrough drug
170. Axabex, a drug with early promising study results showing that the drug may demonstrate substantial improvement over available therapies

[----------NEXT SCREEN----------]

SCRIPT6 We now have just a few more questions about your background and professional experience.

YEARS Since you received your license to treat patients, how many years have you been practicing in your primary specialty?

_____ years [RANGE: 0 to 80]

RX [IF NOT ONCOLOGIST] On average, how many prescriptions for oncology medications do you write **each month**?

____ prescriptions

SETTING In the past 12 months, in which of the following practice settings have you seen patients for treatment or evaluation? *Select <u>all</u> that apply*.

[Programmer: Multi-punch response items should be saved to dataset as binary variables with response options: 1='Selected' OR 0='Not selected'.]

SETT1 Academic medical center or medical school
SETT2 Medical center not affiliated with a medical school
SETT3 Community hospital
SETT4 Office-based practice
SETT5 HMO or integrated health care system
SETT6 Other (please specify) _____

NCI_CENTER Are any of the practice locations where you have seen patients in the past 12 months National Cancer Institute (NCI) cancer centers or NCI cancer center affiliates?

		Yes 1	No 2
NCI_CENTER1	NCI cancer center		
NCI_CENTER2	NCI cancer center affiliate		

CLINTRIAL In the past 5 years, have you served in any of these roles in a randomized controlled trial (RCT)?

		Yes 1	No 2
CLINTRIAL1	Primary investigator		
CLINTRIAL2	Site investigator		
CLINTRIAL3	Enrolled patients in an RCT		
CLINTRIAL4	Author on a paper reporting findings from an RCT		

DRUGREP Do you or your primary practice have any restrictions in place that reduce pharmaceutical sales representatives' access to you?

171. No restrictions in place
172. Some restrictions (e.g., appointments are required or preferred)
173. Representatives are not granted access

[----------NEXT SCREEN----------]

TRUST In general, how credible do you find prescription drug promotion materials that are marketed to health care providers?

174. Not at all credible
175. Somewhat credible
176. Moderately credible
177. Very credible
178. Completely credible

[----------NEXT SCREEN----------]

[RANDOMIZE ORDER OF POWER AND STATTEST]

POWER How comfortable are you interpreting factors that influence a study's statistical power?

179. Not at all comfortable
180. Somewhat comfortable
181. Moderately comfortable
182. Very comfortable
183. Extremely comfortable

STATTEST How comfortable are you assessing if the correct statistical tests were used in a study to answer the study's research question?

184. Not at all comfortable
185. Somewhat comfortable
186. Moderately comfortable
187. Very comfortable
188. Extremely comfortable

[----------NEXT SCREEN----------]

STATLIT I understood all of the statistical terms presented in the sales aid I saw.

189. Completely disagree
190. Disagree
191. Somewhat disagree
192. Somewhat agree
193. Agree
194. Completely agree

[----------NEXT SCREEN----------]

SALESAID In the past 12 months, from which of the following sources have you received sales aids for prescription drugs? *Select all that apply*.

[RANDOMIZE RESPONSE OPTIONS EXCEPT FOR "NONE" and "OTHER"] **[Programmer:** Multi-punch response items should be saved to dataset as binary variables with response options: 1='Selected' OR 0='Not selected'.]

SALESAID1 Medical conference or seminar
SALESAID2 Pharmaceutical representative
SALESAID3 Colleague
SALESAID4 Pharmaceutical company webpage
SALESAID5 Medical app (e.g., Epocrates)
SALESAID6 Other (please specify) _____
SALESAID7 None [IF SELECTED, NO OTHER OPTIONS CAN BE SELECTED]

[----------NEXT SCREEN----------]

FDA Was the drug in the sales aid FDA-approved or not FDA-approved?

195. The drug was FDA-approved
196. The drug was not FDA-approved

[----------NEXT SCREEN----------]

DEBRIEF Your responses have been very helpful. Thank you very much for taking part in this survey! The purpose of this study is to learn about how providers feel about scientific data in prescription drug promotions and how they use this information in clinical practice. [IF CONDITION=1-10: **XEDALITI**; IF CONDITION=11-15: **FEXXOPER**] **is a fictitious drug and is not a product currently for sale.**