Oncologist preferences for attributes of CDK4/6i treatments in advanced/metastatic breast cancer: Discrete choice experiment and best-worst scaling

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INTRODUCTION

Among women in the United States (US), breast cancer is the most prevalent type of malignancy and is one of the main causes of cancer-related mortality [1]. Up to 10% of patients are diagnosed with de novo metastatic breast cancer (mBC), and nearly a third of patients who are treated at an earlier disease stage with endocrine therapy will eventually develop mBC [2].

Endocrine therapy, such as tamoxifen and aromatase inhibitors (AIs), continues to be a mainstay of treatment for mBC. However, a new class of drugs with a selective inhibitor of the cydin-dependent kinases (CDK4/6i), including palbociclib, ribociclib, and abemaciclib, is available for treatment of hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative mBC [3].

While there have been no head-to-head comparisons to date, all 3 CDK4/6i have demonstrated to be effective for mBC with respect to increases in overall response rates and progression-free survival, relative to endocrine therapy. However, treatment-related toxicities, as well as recommended dosing frequency and requisite monitoring, vary depending upon the specific CDK4/6i [3].

Given the relatively recent approval of these agents, little is known about how oncologists perceive them in terms of toxicities and other characteristics or what trade-offs oncologists would potentially make in choosing among currently available CDK4/6i. A greater understanding of these issues is thus warranted.

OBJECTIVE

- This study examined oncologists' preferences for CDK4/6i for the treatment of HR+/HER2- mBC, with a specific focus on dosing and toxicities.

METHODS

Study participants

- This quantitative study was conducted via an online survey administered to oncologists in the US who treat patients with mBC. All data were self-reported. A convenience sample of oncologists were recruited via the Lightspeed Health Panel and other affiliated commercial healthcare panels.
- Oncologists must have met all the following inclusion criteria to participate:
  - Board-certified oncologist
  - In oncology practice between 2 and 35 years
  - Must have spent at least 75% of time dedicated to direct patient care
  - Managed approximately five patients with mBC using systemic treatments at the time of study participation
  - Must have had experience using CDK4/6i
- Oncologists who were unwilling or unable to comply with study procedures were excluded.

Study design and data collection

- This cross-sectional study was conducted in two phases with oncologists who treat patients with mBC patients.
- A discrete-choice experiment (DCE) method was used [4]. The DCE modeling approach is designed to assess respondents' willingness to accept tradeoffs among hypothetical treatment profiles providing information on key factors (e.g. side effects, dosing schedule, etc.) that drive an individual's choice.

Measures

- Practice characteristics (e.g., practice setting, number of patients with mBC seen each month, etc.) were assessed for each participant.
- The primary outcome variable in this study was treatment choice.
- The DCE is based on a strong foundation in psychology and economics [5,6]. The approach used in this study was consistent with best practice guidelines published by the International Society of Pharmacoeconomic and Outcomes Research (ISPOR) [4].
- In the DCE, the participants were asked to consider two hypothetical treatment profiles shown side-by-side and were asked to choose the one that was preferable to them (Figure 1). Each hypothetical treatment profile consisted of combinations of values ("levels") for characteristics ("attributes") that define the profile. The final list of attributes and levels included in this study are shown in Figure 2.
- Respondents also participated in a separate best-worst scaling exercise [7], which enabled the ranking of a larger set of 16 attributes in order of importance. These attributes were presented to the respondent four items at a time; the participant was then asked to choose the most important and least important item from the four presented.
- In Phase 1, the survey was developed based on a review of the relevant literature and clinical trial data. It was then piloted with N=8 oncologists using qualitative interviews via telephone and a desktop sharing platform to ensure the DCE exercise and survey items were clear and easy to understand.
- In Phase 2, the final quantitative survey was self-administered online.
- Prior to any data collection, the study protocol was granted exemption from a central institutional review board. All participants provided their informed consent electronically.

Figure 1. Example preference elicitation task

Treatment A	Treatment B
• 43% risk of lowering treatment dose due to side effects • 81% risk of diarrhea with a 9% chance of severe diarrhea (increase of seven or more loose or watery stools per day which requires hospitalization) • 17% risk of abdominal (belly) pain with a 1% chance of severe abdominal pain • Requires electrocardiogram (ECG) testing to assess heart function 3 times within the first 3 months of treatment to monitor the 6% risk of arrhythmia • 66% chance you will develop low white blood cell counts during treatment that may not cause symptoms but may result in a 5% risk of a serious infection. • 2 pills taken every day with food • Stop taking 1 pill for 7 days per month	• 40% risk of lowering treatment dose due to side effects • 81% risk of diarrhea with a 9% chance of severe diarrhea (increase of seven or more loose or watery stools per day which requires hospitalization) • 11% risk of abdominal (belly) pain with a 1% chance of severe abdominal pain • Does not require electrocardiogram (ECG) testing to assess heart function • 22% chance you will develop low white blood cell counts during treatment that may not cause symptoms, but may result in a 4% risk of a serious infection • 4 pills per day taken with or without food • Stop taking 3 pills for 7 days per month

Statistical Analyses

- Descriptive statistics were reported for all study variables, including means and standard deviations (SDs; continuous variables) and frequencies and percentages (categorical variables).
- A hierarchical Bayesian logistic regression model with effects coding was used to estimate preference weights.
- The relative importance of each attribute was calculated for the attributes included in the DCE based on the summed preference weights. The relative importance was computed for the larger set of attributes used in the best-worst scaling exercise based on the rate that an attribute was selected as most important or least important in prescribing a new treatment.

RESULTS

Practice characteristics

- A total of 209 oncologists participated in this study and had been in practice for an average of 15.8 years (Table 1).

Figure 2. Attributes and levels included in the study

	Attributes	Levels
Non-clinical attributes	Dosing Regimen	• 2 pills per day taken with food • 3 pills per day taken with or without food • 4 pills per day taken with or without food
	Dosing Schedule	• Pills taken everyday • Stop taking 1 pill for 7 days per month • Stop taking 3 pills for 7 days per month
Safety	Risk of dose reduction due to AE	• 36% risk of lowering treatment dose due to side effects • 43% risk of lowering treatment dose due to side effects • 45% risk of lowering treatment dose due to side effects
	Risk of all grades and grade 3/4 diarrhea	• 81% risk of diarrhea with a 9% chance of severe diarrhea (increase of seven or more loose or watery stools per day which requires hospitalization) • 35% risk of diarrhea with a 1% chance of severe diarrhea (increase of seven or more loose or watery stools per day which requires hospitalization) • 26% risk of diarrhea with a 1% chance of severe diarrhea (increase of seven or more loose or watery stools per day which requires hospitalization)
	Risk of abdominal (belly) pain	• 29% risk of abdominal (belly) pain, with 1% chance of severe abdominal pain • 17% risk of abdominal (belly) pain, with 1% chance of severe abdominal pain • 11% risk of abdominal (belly) pain, with 1% chance of severe abdominal pain
	Need for ECG monitoring to assess heart function	• Requires electrocardiogram (ECG) testing to assess heart function 3 times within the first 3 months of treatment to monitor the 6% risk of arrhythmia • Does not require electrocardiogram (ECG) testing to assess heart function
	Risk of Grade 3/4 neutropenia	• 22% chance you will develop low white blood cell counts during treatment that may not cause symptoms, but may result in a 4% risk of a serious infection • 60% chance you will develop low white blood cell counts during treatment that may not cause symptoms, but may result in a 1% risk of a serious infection • 66% chance you will develop low white blood cell counts during treatment that may not cause symptoms, but may result in a 5% risk of a serious infection

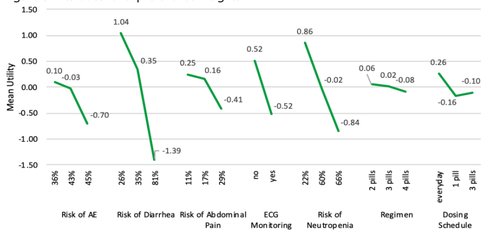
Attribute-level preference weights

- Utilities for the risk of diarrhea and risk of neutropenia show the widest variation (Figure 3).
- The difference between level estimates allows us to evaluate the effect of a change within an attribute. For example, the change from a 36% chance to an 81% chance of diarrhea (0.35-[-1.39]=1.74) far outweighed the change in risk from 17% to 29% in abdominal pain (0.25-[-0.41]=0.66).

Table 1. Practice characteristics

	Variable	N	%
Practice Location	Major metropolitan/urban area	132	63.2
	Suburb/small city	70	33.5
	Rural/small town	7	3.3
Primary Specialty	Medical oncology	172	82.3
	Hematology oncology	37	17.7
	Variable	**Mean**	**SD**
Years in Practice		15.75	6.67
Percent of Time Spent in Direct Patient Care		93.33	6.78
Percent of Time in Practice Setting	Community-based solo or group practice	44.95	44.73
	Out-patient oncology center or clinic	22.39	36.81
	Academically-based practice	23.06	38.69
	NCCN designated cancer center	9.17	27.08
	Other setting	0.43	2.78
Number of Patients with mBC Seen/Treated in Past 3 Months		71.24	24.83
Percent of Time Treating Patients with mBC		57.76	28.60
Number of Patients with HR+/HER2- mBC		41.64	21.79
Number of Patients with HR+/HER2- mBC on Systemic Treatment		36.53	19.83

Figure 3. Attribute-level preference weights

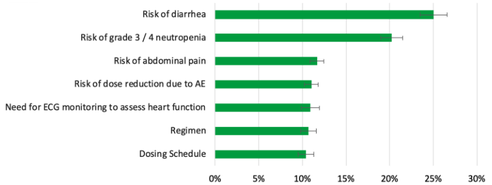


Note. Utilities reflect the strength of preference for an attribute level. The mean utilities represent the average preferences for the population. Utility weights should not be interpreted by themselves. Instead, the magnitude of change within one attribute should be compared to a change within another attribute. AE: Adverse event; ECG: Electrocardiogram.

Relative importance of treatment attributes

- The relative importance of improving from the perceived least favorable level to the most favorable level for each attribute are shown in (Figure 4).
- Risk of diarrhea and risk of neutropenia were the most important for choosing a treatment. Each of these two attributes was about twice as important as the other attributes.

Figure 4. Attribute relative importance

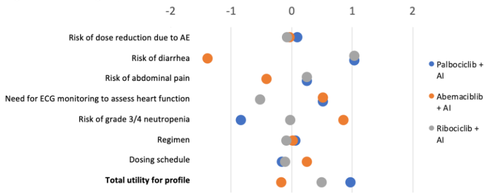


Note. Relative importance estimates are ratio-scaled. 95% confidence intervals are shown for each estimate of relative importance. AE: Adverse event.

CDK4/6i profile preferences

- Abemaciclib + AI fared poorly on the risk of diarrhea, and Palbociclib + AI and Ribociclib + AI fared poorly on the risk of grade 3/4 neutropenia (Figure 5). Oncologists preferred the overall combination of safety and non-clinical attributes associated with Palbociclib + AI.

Figure 5. Oncologist preferences for selected treatment profiles

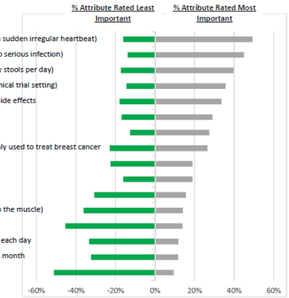


Note. AE: Adverse event; AI: Aromatase Inhibitor.

Best-worst attribute ratings

- When examining the larger set of attributes in the best-worst scaling exercise, the attributes rated as most important by oncologists were consistent with the results from the DCE (Figure 6).
- Risk of grade 3/4 neutropenia and the risk of diarrhea were in the top 3 most important attributes; a lower risk of heart dysfunction was rated as most important, overall.

Figure 6. Attribute relative importance



- Preferences expressed by participants in this study may not generalize to all oncologists, and other factors that may influence treatment decisions, such as costs, risk-benefit profile, and patient characteristics, were not included in the study. The influence of every possible adverse event on treatment preferences could not be determined.
- While the DCE was designed to simulate real-world treatment choices and to align with clinical evidence, it cannot fully represent the clinical, emotional, and financial consequences involved in treatment decision-making. Thus, stated preferences may differ from actual choices.

CONCLUSIONS

- Oncologists most preferred the Palbociclib + AI profile due to its association with a lower risk of diarrhea and no ECG monitoring, compared with Abemaciclib + AI and Ribociclib + AI, respectively.
- For oncologists, the risk of diarrhea and the risk of grade 3/4 neutropenia were most important to treatment choice, and they valued these attributes similarly. Oncologists also perceived the risk of heart dysfunction to be of high importance. Hence, oncologists may prefer those treatment regimens that have a lower risk for these adverse events.

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