Patient and Oncology Nurse Preferences for the Treatment Options in Advanced Melanoma

A Discrete Choice Experiment

**Background:** Understanding the perceptions of patients and oncology nurses about the relative importance of benefits and risks associated with newer treatments of advanced melanoma can help to inform clinical decision-making.

**Objectives:** The aims of this study were to quantify and compare the views of patients and oncology nurses regarding the importance of attributes of treatments of advanced melanoma. **Methods:** A discrete choice experiment (DCE) was conducted in US-based oncology nurses and patients diagnosed with advanced melanoma. Patients and nurses were enlisted through online panels. In a series of scenarios, respondents had to choose between 2 hypothetical treatments, each with 7 attributes: mode of administration (MoA), dosing schedule (DS), median duration of therapy (DoT), objective response rate (ORR), progression-free survival (PFS), overall survival (OS), and grade 3 or 4 adverse events (AEs). Hierarchical Bayesian logistic regression models were used to estimate preference weights. **Results:** A total of 200 patients with advanced melanoma and 150 oncology nurses participated. The relative importance estimates of attributes by patients and nurses, respectively, were as follows: OS, 33% and 28%; AEs, 29% and 26%; ORR, 25% and 27%; PFS, 12% and 15%; DS, 2% and 3%; DoT, 0% and 0%; and MoA, 0% and 0%.
Conclusion: Both patients and oncology nurses valued OS, ORR, and AEs as the most important treatment attributes for advanced melanoma, followed by PFS, whereas DS, DoT, and MoA were given less value in their treatment decisions.

Implications for Practice: Oncology nurses and patients have similar views on important treatment considerations for advanced melanoma, which can help build trust in shared decision-making.

According to the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute, there will be an estimated 76,380 new cases of skin melanoma in the United States in 2016, and an estimated 10,130 people will die as a result of the disease.1 Patients with unresectable or metastatic (advanced) melanoma clinically have the most advanced form and are often difficult to cure because the cancer has spread to the lymph nodes or other locations in the body. The 5-year survival rates for skin melanoma dramatically differ depending on whether it is localized (98.4%), regional (62.9%), or distant (17.9%).

After years of limited treatment options for advanced melanoma, newer forms of immunotherapy and targeted drugs have emerged as being more effective than chemotherapy.2 Immunotherapy drugs include pembrolizumab (Keytruda), nivolumab (Opdivo), and ipilimumab (Yervoy), whereas targeted therapy drugs include cobimetinib (Cotellic), vemurafenib (Zelboraf), dabrafenib (Tafinlar), and trametinib (Mekinist). These drugs can be prescribed as monotherapy or combination therapy, which offer potential benefits over monotherapy but may place patients at risk for more frequent or more severe adverse effects.3 In addition, there are other important characteristics associated with treatment regimens such as complexity of dosing schedule, mode of administration (ie, oral vs intravenous), and frequency of infusion.

As new treatment options become available, assessing the value patients and healthcare providers place on key attributes of treatment can ultimately lead to better clinical decisions and outcomes for advanced melanoma patients. The American Cancer Society emphasizes that it is “important to carefully consider the possible benefits and side effects of any recommended treatment before starting it.”2 Engagement of patients is consistent with the movement toward patient-centered care introduced by the 2010 Affordable Care Act that seeks to improve the evidence and trust in shared decision-making.

The aims of this study were to quantify and compare the views of patients and oncology nurses in the United States regarding key attributes associated with treatments of advanced melanoma using a derived preference-based approach, the DCE. These aspects of medication treatment included positive and negative outcomes such as overall survival (OS) and severe, life-threatening, and/or disabling adverse effects, as well as the patient treatment experience, such as length of infusion time and dosing schedule.

Objectives

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Methods

Respondents

Patients and nurses were enlisted through online panels. The database for patients was established by the Endeavour network through relationships with advocacy groups and direct relationships/previous work with advanced melanoma patients. Nurses were recruited from US-based nurses in the All Global commercial panel or All Global panel partners who are fellow Trust Alliance Members. The US-based panel of nurses is 10% male and 90% female, ages 29 to 39 years (20%), 40 to 55 years (65%), and 56 to 75 years (15%); regional representation is as follows: midwest, 19%; west, 21%; south, 31%; and northeast, 29%. To participate, advanced melanoma patients had to meet all of the following criteria: 18 years or older, diagnosed with advanced melanoma, had an Eastern Cooperative Oncology Group performance status rating between 0 and 3, were able to operate a computer with Internet access, were able to read and understand English, and provided informed consent to participate. For oncology nurses to participate, they had to meet all of the following criteria: practiced nursing between 3 and 30 years, worked in an oncology service, involved in assisting physicians with advanced melanoma patients/prescribing treatment or in administering

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systemic treatments to advanced melanoma patients, spent at least 75% of their time on direct patient care, saw/treated a minimum number of cancer (~80 monthly) and advanced melanoma (~4 monthly) patients, had access to and knowledge of how to operate a computer with access to a Web site during the interview, were able to read and understand English, and provided informed consent to participate.

**Study Design**

In this study, respondents were asked to choose between 2 hypothetical treatment profiles for advanced melanoma (no real treatments or treatment names were mentioned), where each scenario is presented in the form of a paired comparison (as illustrated in Figure 1). A preference weight for each attribute level is derived by modeling, which quantifies the willingness to accept trade-offs related to outcomes (eg, survival), adverse effects, and other important nonclinical treatment characteristics (eg, dosing schedule). Discrete choice experiment has been applied in various disease areas, including oncology, and offers stakeholders a mechanism to participate in decision-making. Before the main study, qualitative pilot interviews were conducted to assess task comprehension, key attributes of treatment, and other elements in the survey. Pilot interviews were conducted in a total of 28 people (12 oncologists, 8 patients, and 8 nurses). Participants were asked about their experience with advanced melanoma and its treatment and to identify the aspects of treatment they felt were most important considerations for the patient. The interviews were conducted by an experienced moderator through telephone for approximately 60 minutes. All stimuli materials (questionnaire/DCE tasks) were shown via desktop sharing. All interviews were anonymous, and the respondents were not identifiable to the moderator.

Attribute levels were chosen to encompass a range salient to respondents, even if those levels were hypothetical or not feasible given currently available therapies. The DCE tasks were evaluated with each of the stakeholder groups to ensure that the stakeholders understand the preference decisions and would be able to make these choices with the information at hand. In addition to the DCE tasks, all other questions were also reviewed to ensure that these were clear and understood and that response categories encompassed the range of possible responses. The refined survey included 7 attributes: mode of administration, dosing schedule, median duration of therapy, objective response rate (ORR), progression free survival (PFS), overall survival (OS), and grade 3/4 toxicities.

| ATTRIBUTE                        | MEDICINE A | MEDICINE B |
|---------------------------------|------------|------------|
| Mode of administration          | IV         | IV         |
| Dosing Schedule                 | One medicine taken by 30 minute infusion every 3 weeks | One medicine taken by 60 minute infusion every 2 weeks |
| Median Duration of Therapy      | 3 months   | 8 months   |
| Objective Response Rate (ORR)   | 15%        | 33%        |
| Progression Free Survival (PFS) | 3 months   | 5 months   |
| Overall Survival (OS)           | 45% of patients survive to 12 months | 55% of patients survive to 12 months |
| Grade 3/4 Toxicities            | 10%        | 55%        |

*Figure 1* Example of a paired comparison in a discrete choice experiment for nurses.
(3, 8, and 12 months), objective response rate (ORR) (15%, 33%, and 65% chance of response), progression-free survival (PFS) (3, 5, and 11.5 months), OS (45%, 55%, and 75% survival to 12 months), and grade 3 or 4 adverse events (AEs) (10%, 32%, and 55% likelihood of occurrence) (Table 1). Each attribute had 3 levels except dosing schedule (8 levels). Each hypothetical treatment profile was created by varying the levels of each of the 7 attributes, for example, OS being an attribute, and the level referring to the percentage of patients who survived to 12 months. Following guidelines issued by the International Society of Pharmacoeconomics and Outcomes Research,7 the experimental design (ie, the combination of attributes and levels presented to respondents) was developed using the D-efficiency algorithm available in SAS version 9.3. This method ensured that a sufficient number of respondents were presented with sufficient combinations of attributes and levels to estimate a preference function. Restrictions were imposed in the various designs to prevent respondents from seeing combinations that may be either unrealistic or illogical (eg, oral and infusion every 3 weeks). Each respondent was presented with 11 choice-based scenarios. Sample sizes were determined by 2 separate considerations: attaining an acceptable expected margin of error given the DCE design (88 scenarios, 8 blocks) and obtaining a large enough sample for each stakeholder group to reflect the likely diversity of responses within that group. An a priori power analysis suggested that a sample of 150 would be necessary to obtain an expected margin of error of ±5% to 9% given the DCE design.

Because we expected preferences to vary more for patients than for nurses, a larger patient sample size was targeted (N =200). The survey also included several non-DCE-related questions that asked the respondents directly about the importance of the medication attributes by asking them to select the 3 most important attributes to them. All study materials and procedures were reviewed and approved before study execution by Pearl Institutional Review Board (Indianapolis, Indiana).

**Analysis**

First, the levels of stability and consistency of responses were examined to identify those whose response patterns suggested a lack of attention in completing the task. Respondents were excluded from analysis if they failed basic validity checks, such as providing clearly inconsistent selections by choosing profiles containing less desirable characteristics, providing responses with little variability, completing the survey much faster than expected, and/or providing numeric values that were disproportionately higher compared with the average (outliers).

Relative preference weights for each attribute level were estimated using a hierarchical Bayesian logistic regression model with effect coding parameterization. The reference “level” in effect coding parameterization is the average across the levels tested in each attribute rather than a specific level itself (as in

| Attribute                        | # | Levels                                                                 |
|----------------------------------|---|------------------------------------------------------------------------|
| Mode of administration           | 1 | Oral: a medication taken by mouth for a period                        |
| Dosing schedule                  | 2 | IV: an infusion given into the vein for a period                      |
|                                  | 3 | Subcutaneous: shot given under the skin using a short needle to inject |
|                                  |   | a drug into the tissue layer between the skin and the muscle          |
| Median duration of therapy       | 1 | 3 mo                                                                  |
|                                  | 2 | 8 mo                                                                   |
|                                  | 3 | 12 mo                                                                  |
| Objective response rate          | 1 | 15/100 patients (15% chance of responding)                            |
|                                  | 2 | 33/100 patients (33% chance of responding)                            |
|                                  | 3 | 65/100 patients (65% chance of responding)                            |
| Progress-free survival           | 1 | 3 mo                                                                  |
|                                  | 2 | 5 mo                                                                   |
|                                  | 3 | 11.5 mo                                                                |
| Overall survival                 | 1 | 45/100 patients (45% of patients survive to 12 mo)                    |
|                                  | 2 | 55/100 patients (55% of patients survive to 12 mo)                    |
|                                  | 3 | 75/100 patients (75% of patients survive to 12 mo)                    |
| Grade 3 or 4 adverse events      | 1 | 10/100 patients (10% likelihood of experiencing a serious adverse    |
|                                  |   | effect)                                                               |
|                                  | 2 | 32/100 patients (32% likelihood of experiencing a serious adverse    |
|                                  |   | effect)                                                               |
|                                  | 3 | 55/100 patients (55% likelihood of experiencing a serious adverse    |
|                                  |   | effect)                                                               |

**Table 1 • Description of Attributes and Levels in the Discrete Choice Experiment**
Results

Respondents

A total of 935 advanced melanoma patients were invited to participate, and 273 (29.2%) responded to the invitation. Of these, 11 (1.2%) had to be replaced for failing validity tests. The final sample consisted of a total of 200 patients (21.4%) who met screening criteria and completed the study. Most patients were female (60.5%), married (68.5%), and white (83.5%); had at least a college degree (73.0%); were employed (95.5%); and had an annual household income of equal to or greater than USD 50,000 (82.0%). The age distributions in years were 3% (≤30), 26% (31–40), 37% (41–50), 26% (51–60), and 8% (61 or older). Most patients had used or were currently using 1 to 2 different treatments (76.5%). Among patients currently receiving treatment, the most common medications were Opdivo (20.0%), Keytruda (18.5%), and Yervoy (13.5%). Medications used most commonly in the past included Yervoy (28.0%), followed by chemotherapy and Proleukin (both 11.0%).

A total of 13,544 nurses nonspecific to oncology were invited to participate with the proviso that we were interested in oncology nurses. Among them, 1,546 (11.4%) responded to the invitation, and 4 initial participants (0.3%) had to be removed and replaced for failing validity tests. In total, 150 nurses (1.1%) met screening criteria and completed the study (78.7% nurses, 21.3% nurse practitioners). The vast majority spent most of their time in patient-related care tasks (95.5%) and had practiced for an average of 16.7 years (SD, 8.7). They saw an average of 192.7 cancer patients per month, with an average of 28.5 of those patients described as “advanced melanoma.”

Preferences for Treatment Attributes

The most important treatment attributes for patients were OS, AEs, ORR, and, to a lesser extent, PFS (Table 2 and Figures 2 and 3). Overall survival was the most important attribute, having the largest vertical distance between regression coefficients (Figure 2) and the longest bar (Figure 3). In terms of interpretation, similar levels of importance of levels of attributes can be determined from differences in $\beta$ coefficients. For instance, in Table 2 under the patient column, increasing the ORR from 33% to 65% (a difference in coefficients of 2.49) is approximately similar in importance to decreasing the likelihood of experiencing a serious AE from 32% to 10% (Table 3). Dosing schedule, mode of administration, and median duration of therapy were considered relatively unimportant compared with efficacy and safety.

The main difference in DCE results between patients and nurses was that nurses assigned greater importance to ORR than AEs, whereas patients assigned greater importance to risk of AEs than ORR (Table 3). However, these differences in the relative importance were not statistically significant (all $p$ values > .05). Exploratory subgroup analyses in patients and nurses revealed no statistically significant differences based on age, income, education, and location for patients and years in practice, type of practitioner, and practice location for nurses (all $p$ values > .01).

When patients were directly asked to select the 3 most important attributes from the full list of 7 attributes (non-DCE approach), OS was most often chosen (61.5%), followed by ORR (49.5%), PFS (43.0%), and AEs (32.5%); the remaining attributes ranged from 15 to 18% (Table 3). When oncology nurses were asked to choose the 3 most important of the 7 attributes, 74.7% selected OS, 58.0% selected PFS, 58.0% selected AEs, and 36.7% selected ORR, with less than 15% having selected the other attributes.

Discussion

By using DCE-based approach, we found that both patients and oncology nurses considered OS, AEs, and ORR as the most
important attributes of medication therapy of advanced melanoma. To a lesser extent, PFS was also an important attribute. Although the order of importance of AEs and ORRs was switched, the importance weights were not significantly different, indicating that the perceptions of oncology nurses and patients were well aligned. Similarly, DCE results revealed

| Attribute                          | Level                                                                 | Patients (N = 200) | Nurses (N = 150) |
|------------------------------------|-----------------------------------------------------------------------|-------------------|-----------------|
| Mode of administration             | Oral                                                                  | 0.049             | -0.343          |
|                                    | Intravenous                                                           | -0.075            | 0.334           |
|                                    | Subcutaneous                                                          | 0.026             | 0.008           |
| Dosing schedule                    | Two medicines where 1 medicine is taken twice daily and the other medicine is taken once daily | 0.308             | 0.237           |
|                                    | One medicine taken daily                                             | 0.308             | 0.112           |
|                                    | One medicine taken twice daily                                       | 0.308             | 0.011           |
|                                    | One medicine taken by a 30-min infusion every 3 wk                   | 0.228             | 0.013           |
|                                    | One medicine taken by a 60-min infusion every 2 wk                   | 0.223             | 0.013           |
|                                    | One medicine taken by a 90-min infusion every 3 wk                   | -0.604            | 0.030           |
|                                    | Two medicines both are given as a 150-min infusion every 3 wk for 3 mo (plus/minus: 1 of the 2 medicines is continued as a 60-min infusion every 2 wk for 5 mo or more) | -0.702            | -0.849          |
|                                    | One medicine given by 1 injection every 3 wk                          | -0.069            | -0.278           |
|                                    | 3 mo                                                                  | 0.095             | 0.077           |
|                                    | 8 mo                                                                  | -0.044            | 0.046           |
|                                    | 12 mo                                                                 | -0.054            | -0.103           |
| Objective response rate            | 15/100 patients (15% chance of responding)                           | -2.494            | -3.641           |
|                                    | 33/100 patients (33% chance of responding)                           | 0.001             | -0.301           |
|                                    | 65/100 patients (65% chance of responding)                           | 2.494             | 3.942            |
| Progression-free survival          | 3 mo                                                                  | -0.915            | -1.809           |
|                                    | 5 mo                                                                  | -0.573            | -0.035           |
|                                    | 11.5 mo                                                               | 1.487             | 1.844            |
| Overall survival                   | 45/100 patients (45% of patients survive to 12 mo)                    | -2.367            | -4.283           |
|                                    | 55/100 patients (55% of patients survive to 12 mo)                    | -0.382            | -0.339           |
|                                    | 75/100 patients (75% of patients survive to 12 mo)                    | 4.049             | 4.622            |
| Grade 3 or 4 adverse events       | 10/100 patients (10% likelihood of experiencing a serious adverse effect) | 3.107             | 3.488            |
|                                    | 32/100 patients (32% likelihood of experiencing a serious adverse effect) | -0.309            | 0.175            |
|                                    | 55/100 patients (55% likelihood of experiencing a serious adverse effect) | -2.798            | -3.663           |

Figure 2 Preference weights for melanoma treatment attributes and levels for patients (N = 200) and nurses (N = 150).

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that both patients and oncology nurses considered dosing schedule, mode of administration, and median duration of therapy much less important compared with OS, AEs, and ORR.

In addition to the implicit DCE approach, a direct (non-DCE) approach was also used. It corroborated the DCE results in terms of the most important attributes but also indicated that a subset of patients (15%–18%) ranked dosing schedule, duration, and mode of administration among the 3 most important. This contrasted with DCE results, which marginalized the latter attributes, and suggests that it is still informative to directly ask patients about important medication therapy considerations using varying formats.

The DCE provides an implicit, structured approach that is more informative than other methods in terms of providing preference weights specific to each level defined within an attribute and its contribution to an overall preference function. However, by construction, the DCE juxtaposes attributes that relate to the experience of patient care, such as duration of therapy, with outcomes of care, such as survival. Perhaps not surprisingly, the results showed that much greater importance is placed on clinical outcomes of treatment relative to the patient experience with care, such as dosing schedule. The decision to prioritize health outcomes ahead of experience with care is generally observed in practice across many settings in healthcare. For example, patients with end-stage renal disease on dialysis are willing to undergo the unpleasant and inconvenient experience of dialysis several times a week to live longer. Although the DCE results showed that, compared with efficacy and safety, patient experience or convenience is less important, they should not be interpreted as implying that patients or nurses consider the experience of care as unimportant. The patient experience is one of the main goals in the provision of healthcare, which is a balance of cost, outcomes, and patient experience, referred to as the “triple aim” of the healthcare system.10 In that context, the

**Table 3** Importance of Attributes: Patients Compared With Nurses

| Attribute                                | Patients (N = 200) | Relative Importance of Attribute Through DCE Approach | Frequency Attribute Selected in Top 3 Through Non-DCE Approach, % | Nurses (N = 150) | Relative Importance of Attribute Through DCE Approach | Frequency Attribute Selected in Top 3 Through Non-DCE Approach, % |
|------------------------------------------|--------------------|-------------------------------------------------------|---------------------------------------------------------------|------------------|-------------------------------------------------------|---------------------------------------------------------------|
| Overall survival                         | 32.7               | 61.5                                                  |                                                               | 28.0             | 74.7                                                  |                                                               |
| Objective response rate                  | 25.3               | 49.5                                                  |                                                               | 27.0             | 36.7                                                  |                                                               |
| Progression-free survival                | 11.6               | 43.0                                                  |                                                               | 15.0             | 58.0                                                  |                                                               |
| Grade 3 or 4 adverse events              | 28.8               | 32.5                                                  |                                                               | 26.0             | 58.0                                                  |                                                               |
| Dosing schedule                          | 1.5                | 17.5                                                  |                                                               | 3.0              | 12.0                                                  |                                                               |
| Mode of administration                   | 0                  | 15.0                                                  |                                                               | 1.0              | 12.7                                                  |                                                               |
| Median duration of therapy               | 0.1                | 15.0                                                  |                                                               | 0.0              | 6.0                                                   |                                                               |
| Varied with medication                   | 20.0               |                                                       |                                                               |                  | 11.3                                                  |                                                               |
| Do not know/not sure                     | 1.0                |                                                       |                                                               | 1.0              | 2.7                                                   |                                                               |
| Prefer not to answer                     | 1.0                |                                                       |                                                               |                  | 0.0                                                   |                                                               |

Abbreviation: DCE, discrete choice experiment.

All p values > .05 (not significant) comparing relative importance of attribute between patients and nurses for the DCE results.
patients' perspectives about treatment attributes are generally aligned is valuable to families and patients seeking input on treatment selection in the shared decision-making process. Notably, studies applying DCE to melanoma are beginning to emerge, with several studies reporting study designs, but have yet to publish the results. They examined judgments about the benefits of new treatments of melanoma among physicians, patients, and healthy controls and found that patients were most willing to accept adverse effects to extend survival, whereas physicians were the most unwilling. The finding that oncology nurses and patients' perspectives about treatment attributes are generally aligned is valuable to families and patients seeking input on treatment selection in the shared decision-making process. Notably, studies applying DCE to melanoma are beginning to emerge, with several studies reporting study designs, but have yet to publish the results.12,13

This study had several limitations. Discrete choice experiment is a stated preference method where patients evaluate hypothetical medication choices, which simulate possible clinical decisions, but it may not resonate with the same clinical or emotional consequences as real-life decision-making. The patients who participated in this study were relatively younger and thus healthier and more likely to be employed than the patient population in the United States, likely because the survey was Web based so the results may not generalize to all advanced melanoma patients or patients outside the United States. Similarly, all nurses were from an online panel, so there may be limitations to the generalizability of results if they are systematically different from the broader national pool of oncology nurses. Future research could consider examining the values of patients and nurses in other countries, conduct qualitative interviews to further probe the reasons that respondents prefer certain choices, and examine the role of age, spirituality, and psychosocial constructs such as personality in choosing among treatment attributes.

In summary, DCE revealed that OS, AEIs, and ORR were the most important considerations in selecting among advanced melanoma treatments for both patients and nurses, whereas dosing schedule, mode of administration, and median duration of therapy were relatively less important compared with efficacy and safety. Patients and oncology nurses' views on the importance of characteristics of drug treatments of advanced melanoma are well aligned, which can help to build trust in shared decision-making situations.

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