Patient preferences for treatment of metastatic melanoma

Carol Mansfield^{*1}, Briana Ndife², Joyce Chen², Kathleen Gallaher¹ & Sameer Ghate²¹RTI Health Solutions, Research Triangle Park, NC 27709, USA²Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936, USA*Author for correspondence: Tel.: +1 919 541 8053; carolm@rti.org**Aim:** To investigate patient preferences for clinical attributes of first-line metastatic melanoma treatments.**Materials & methods:** A discrete-choice experiment and best–worst scaling exercise were used to assess relative preferences for treatment attributes. **Results:** The 200 survey respondents had distinct preferences. Avoiding a 30% risk of colitis or hormone gland problems and avoiding severe fever were more important to respondents than avoiding a 20% risk of extreme sun sensitivity ($p < 0.05$). Patients preferred taking pills to receiving intravenous infusions in a clinic. When attributes were combined, approximately 85% of respondents preferred a risk profile similar to targeted therapy over a profile similar to immunotherapy, holding efficacy constant. **Conclusion:** Taking patient preferences into account can help patients get the full benefit from metastatic melanoma therapies.

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The introduction of targeted therapy and immune checkpoint inhibitors for metastatic melanoma has provided patients and physicians with unprecedented treatment options. In particular, patients whose tumors express mutant forms of the *BRAFV600* gene can choose from different agents that target their tumor's gene expression profile (i.e., targeted therapy) or immune checkpoint inhibitors that block certain proteins in the immune system and help restore T-cell function. The first available immune checkpoint inhibitor, ipilimumab (Bristol-Myers Squibb, NY, USA), introduced in 2011, was joined by targeted BRAF/MEK inhibitors such as dabrafenib and trametinib (Novartis Pharmaceuticals Corporation, Basel, Switzerland), cobimetinib and vemurafenib (Genentech, Inc. CA, USA), and additional immune checkpoint inhibitor agents nivolumab (Bristol-Myers Squibb) and pembrolizumab (Merck & Co., Inc., NJ, USA) [1]. Each of these treatment options presents trade-offs in terms of efficacy, adverse event (AE) profiles and administration mode and frequency [1,2]. Taken together, the choices now available to *BRAFV600*-positive metastatic melanoma patients present a complex set of decisions that must be weighed by physicians and patients as they choose a treatment regimen [3–9].

The American Society of Clinical Oncology recently issued consensus guidelines on physician–patient communication that stress physicians' responsibility to consider patient's goals for care [10]. Further, the US FDA's ongoing initiative aimed at patient-centered care is expected to increase the weight placed on patient preferences in regulatory decision making [11]. An FDA guidance document on incorporating patient preferences has been issued [12], and the agency has committed to increasing the patient voice in regulatory decision making.

As focus on the patient experience of treatment increases, a need arises for studies that address patient preferences in a systematic, reproducible way. One such method, the discrete-choice experiment (DCE), has emerged as an accepted methodology for gathering and analyzing quantitative data on the preferences of patients and caregivers in the healthcare setting [13]. Findings generated through DCE experiments have begun to be used to help guide regulatory decision making [14] and the development of tools that support shared decision making between patient and caregiver [15].

In the realm of metastatic melanoma care, few studies have been conducted to assess patient preferences in the targeted therapy era. Liu *et al.* conducted two studies that examined treatment preferences of patients with advanced

melanoma along with oncology nurses [16] and oncologists [17]. These studies revealed that patients placed more importance on overall survival (OS) compared with physicians [17]. Nurses and patients held similar views, with OS and reducing the risk of AEs being most important [16]. However, multiple outcome measures were used in these studies, and the risk of any serious AEs was presented as a single attribute. Among available treatments, serious AEs vary, and the risk of any single AE varies with individual medication or combination therapy [3,18]. Further, as these treatments and novel combination therapies are evolving, limited real-world data on OS and several of the other outcome measures are consistently available across existing treatments. To further elaborate the clinical attributes most important to advanced or metastatic melanoma patients, we designed a patient preference study that incorporated real-world clinical attributes among currently available first-line treatments.

Materials & methods

Study design

We conducted a cross-sectional study incorporating two types of patient preference methods, a DCE and a best–worst scaling (BWS) exercise.

The study examined the following end points:

- Patient preferences for metastatic melanoma treatments (overall, among respondents with an initial diagnosis of stage IV disease vs those with an earlier disease stage at diagnosis, and among respondents aged 47 years and older vs those younger than 47 years), given a choice among hypothetical treatment choices drawn from known clinical attributes of treatments approved for patients whose tumors express mutant *BRAFV600* protein, using a DCE exercise;
- Patient preferences for mode and frequency of treatment administration, using a BWS exercise.

Study population

Global Perspectives (Norwich, UK) recruited a convenience sample through patient associations, proprietary databases and opt-in online panels. Potential respondents were sent an email with a unique link to the survey. The first few questions in the survey screened potential respondents for eligibility.

To gain access to the survey, participants had to be 18 years or older, have a self-reported physician diagnosis of advanced or metastatic melanoma defined as diagnosis of stage III or stage IV melanoma or the melanoma had spread to other parts of the body since diagnosis, be able to read and understand English, and provide informed consent to participate in the survey. Respondents were compensated US\$75.

Survey instrument

Discrete-choice experiment

We developed and administered a DCE survey following guidelines for good research practices [19]. The survey methodology elicits patient preferences for clinical attributes that differ among treatments. Survey participants choose from a series of two presented hypothetical treatment profiles that combine attribute levels. Profiles are paired following a defined experimental design.

For this study, the DCE survey instrument was developed to elicit the relative importance of metastatic melanoma treatment attributes, using validated methods to measure preferences [20]. This study evaluated six attributes defined by three levels (Table 1). We chose the attributes based on available clinical literature for immunotherapies and targeted therapies used to treat *BRAFV600*-positive metastatic melanoma. The levels of the attributes were selected to span the range of outcomes observed in clinical data from previous studies with individual and combined therapies [21–31]. On the basis of limited availability of data on OS in some of the comparator treatments, we chose to present survey respondents with progression-free survival (PFS) data to best represent reported clinical outcomes [21–31]. For AEs, fever and the risk of extreme sun sensitivity were selected as representative of targeted therapies, and risk of colitis and hormone gland problems were selected as representative of immune checkpoint inhibitors. Oral administration was selected as representative for targeted therapies, and intravenous (IV) infusion was selected as representative for immune checkpoint inhibitors. The relevance of the attributes and levels was reviewed by clinical experts. The descriptions and levels were evaluated in 12 pretests with patients having a self-reported physician diagnosis of advanced or metastatic melanoma. Changes to the survey instrument were made based on participant feedback.

Table 1. Discrete-choice experiment attributes and levels and best–worst scaling items.

Discrete-choice experiment attributes	Levels
How long the medicine will keep the cancer stable (PFS)	13 months 7 months 4 months
How you take the medicine	Pills taken twice-a-day at home [†] IV infusion for 30 minutes every 3 weeks in the doctor's office [‡] IV infusion for 2.5 hours every 3 weeks in the doctor's office for four doses, then IV infusion for 60 minutes every 2 weeks [‡]
Fever for a few days each month [†]	None Mild to moderate Severe
Risk of tears or holes in your intestines (colitis) [‡]	0% 10% 30%
Risk of hormone gland problems [‡]	0% 10% 30%
Risk of extreme sensitivity to the sun [†]	0% 4% 20%
Best–worst scaling items	
One pill once-a-day at home [†]	
Two pills twice-a-day at home [†]	
Four pills twice-a-day at home [†]	
Two pills twice-a-day, plus one additional pill once-a-day at home [†]	
Three pills once-a-day for 21 days, then stop for 7 days (repeat) [†]	
Three pills once-a-day for 21 days, then stop for 7 days (repeat), plus four pills twice-a-day at home [†]	
IV for 30 minutes every 3 weeks in the doctor's office [‡]	
IV for 60 minutes every 2 weeks in the doctor's office [‡]	
IV for 2.5 hours every 3 weeks for four doses, then IV for 60 minutes every 2 weeks in the doctor's office [‡]	
[†] Associated with targeted therapies.	
[‡] Associated with immunotherapies.	
IV: Intravenous; PFS: Progression-free survival.	

The experimental design was created in Sawtooth Software (WA, USA) using a D-efficient algorithm to construct a fractional factorial experimental design [32–35]. The design was evaluated for level balance and correlation. The full design included 27 choice questions that were divided into three blocks of nine questions. Each respondent was randomly assigned to one block of nine DCE questions. [Figure 1A](#) presents an example DCE choice question.

Best–worst scaling

To further elucidate relative patient preferences for modes of administration, we developed a BWS study, which permits a ranking of the perceived burden of all items included in the exercise and a measure of relative magnitude of the burden of each item [36]. The study was designed using object-case BWS [37,38], which has been previously applied in healthcare settings [36,39–42]. The BWS included nine different modes and schedules of administration based on existing targeted therapy and immunotherapy. [Table 1](#) presents the BWS item levels evaluated in the study.

The BWS questions were created from an experimental design created in Sawtooth Software with one block of 12 questions. Each respondent was shown the same 12 questions in a random order. Each question contained a set of three items and asked to identify the highest- and lowest-ranked item in the set. [Figure 1B](#) presents an example BWS question.

Statistical analyses

Discrete-choice experiment

The DCE treatment choice questions were analyzed using a random-parameters logit (RPL) model estimated using NLOGIT version 5.0 (Econometric Software, Inc., NY, USA), which accounts for variations among individual

Figure 1. Example choice questions. (A) Example discrete-choice experiment question. **(B)** Example best–worst scaling question.
IV: Intravenous.

preferences in attribute levels across alternatives in each choice question and corrects for potential estimation bias [43,44]. The preference weights derived from the RPL analysis are a relative measure of the strength of preferences. More-preferred outcomes have higher preference weights, and a broader spread of preference weights within each attribute measure indicates stronger preferences for higher valued levels over lower valued levels.

Months of PFS, risk of colitis, risk of hormone gland problems and risk of extreme sensitivity to the sun were modeled as continuous linear variables after specification tests corroborated that the marginal effects of these attributes could be assumed to be constant within the range of levels shown to respondents. In other words, one-unit increases in the attributes were valued equally by respondents, regardless of the starting point for the increase. Mode of administration and fever were modeled as effects-coded variables. With effects coding, zero indicates the mean effect across all attribute levels rather than the omitted level, as in dummy coding [45]. Wald tests were used to identify differences between levels for each attribute at the 95% CI.

Treatment choices among patients who reported an initial diagnosis of stage IV cancer versus those with an earlier disease stage at initial diagnosis were analyzed using an RPL model with the same specification as the full-sample model. We created a dummy-coded variable that was equal to 1 if the respondent had stage IV cancer at diagnosis and interacted the dummy variable with each of the explanatory variables used in the main model. Each interaction variable was the product of the dummy-coded variable and one of the treatment attribute variables. The parameter on each of these interaction terms could be interpreted as the difference between the two subgroups for the preference weights for the corresponding attribute level. Differences in preferences were tested through a joint test of the significance of all the interaction terms (Wald test).

Preference shares

Results from the RPL model can be used to predict the probability that the average respondent would select one treatment profile over another. To calculate the probability that a respondent would select each profile if offered a choice between the two, we calculated a net clinical benefit score for each medication as the weighted sum of each medication profile's attribute levels, where the weights are the preference weights from the RPL model for the corresponding attribute level in the medication profile.

We used the results to explore preferences for treatments with typical AEs associated with different targeted therapy and immunotherapy options, assuming equal efficacy (holding PFS constant). We simulated a choice scenario comparing a targeted therapy profile that included a higher risk of fever, a higher risk of extreme sensitivity to the sun, and pills as the mode of administration with an immunotherapy profile that included risks of colitis and hormone gland problems, and administration by IV infusion for 2.5 h every 3 weeks in the doctor's office for four doses, then IV infusion for 60 min every 2 weeks. The coefficient for the higher risk of fever in the targeted therapy profile was calculated using a weighted average of the three levels of fever presented in the DCE questions and based on clinical data from the combination of dabrafenib and trametinib [21,26]. The coefficient for the risk of extreme sun sensitivity profile was based on clinical data from the combination of vemurafenib and cobimetinib [27]. The risk of colitis and hormone gland problems (hypothyroidism) for the immunotherapy profile were based on the treatment-related, all grades percentage risk for Opdivo (nivolumab) and Yervoy (ipilimumab) combination [31]. The preference share profiles and weighted average percentages used for the composite fever attribute are presented in Table 2.

Best–worst scaling

Importance weights were estimated using an RPL model that related respondents' choices for the most- and least-preferred items to the item-specific variables [36]. Larger coefficients indicate that the item was most preferred. Conversely, smaller coefficients indicate that the item was less preferred. Relative importance weights were created from the log-odds importance weights using a probability-based rescaling procedure [46].

Results

Study sample

Global Perspectives invited 23,157 individuals by e-mail to be screened for study eligibility. Of those invited, 455 individuals responded. Approximately half of these individuals (207) were eligible and consented to participate, and 200 (96.6%) completed the survey, which took respondents an average of 18.6 min to complete. Self-reported demographic and clinical characteristics of the respondents are shown in Table 3. The mean age of patients was 47 years (range: 20–76), and 111 (55.5%) were men. The stage of melanoma reported most commonly at diagnosis

Table 2. Preference share profiles for targeted therapy and immunotherapy, assuming same efficacy.		
Attribute	Targeted therapy	Immunotherapy
How long the medicine will keep the cancer stable (progression-free survival)	12 months	12 months
How you take the medicine	Pills taken twice-a-day at home	IV infusion for 2.5 h every 3 weeks in the doctor's office for 4 doses, then IV infusion for 60 min every 2 weeks
Risk of tears or holes in your intestines (colitis) [†]	0%	13%
Risk of hormone gland problems [‡]	0%	17%
Fever for a few days each month [§]	29% none, 66% mild-to-moderate, 5% severe	None
Risk of extreme sensitivity to the sun [¶]	2.36%	0%

[†]For the immunotherapy profile, the risk of colitis is based on the treatment related, all grades percentage risk for Opdivo (nivolumab) and Yervoy (ipilimumab) combination [31].

[‡]For the immunotherapy profile, the risk of hormone gland problems is based on hypothyroidism treatment related, all grades percentage risk for Opdivo (nivolumab) and Yervoy (ipilimumab) combination [31].

[§]For the fever attribute in the targeted therapy profile, a weighted average of the fever levels presented in the DCE questions was constructed by multiplying the preference weights for the three levels of the fever attribute by the probability of fever in Robert *et al.* [21]. For the survey, the description of mild-to-moderate fever corresponded to grade 1 or 2 and severe fever corresponded to grade 3 or 4. The weighted average was derived by the following equation: $FEV1 \times 0.29 + FEV2 \times 0.66 + FEV3 \times 0.05 = 0.97 \times 0.29 + 0.19 \times 0.66 + (-1.16) \times 0.05 = 0.35$.

[¶]For the targeted therapy, the risk of extreme sun sensitivity is based on the risk of grade 3 sun sensitivity in Larkin *et al.* [27].

DCE: Discrete-choice experiment.

Figure 2. Preference weights for each attribute level. The vertical bars around each mean preference weight represent the 95% CIs about the point estimate.
IV: Intravenous; PFS: Progression-free survival.

was stage III (n = 76 [38.0%]) or stage IV (n = 85 [42.5%]), and more than half of patients had been diagnosed at least 2 years prior to completing the survey.

Preference weights

Figure 2 presents the mean preference weight values for each attribute level. Overall, the preference weights were ordered as expected: respondents preferred longer PFS, no fever, no chance of colitis, no chance of hormone gland

Table 3. Patient characteristics.

Demographic characteristic	Statistic or category	Overall (N = 200)
Age (years)	Mean (SD)	47 (8.2)
	Minimum, maximum	20, 76
What is your gender?	Female	89 (44.5%)
	Male	111 (55.5%)
What is the highest level of education you have completed?	High school or equivalent (e.g., GED)	8 (4.0%)
	Some college but no degree	18 (9.0%)
	Technical school	4 (2.0%)
	Associate's degree (2-year college degree)	22 (11.0%)
	4-year college degree (e.g., BA, BS)	73 (36.5%)
	Some graduate school but no degree	10 (5.0%)
	Graduate or professional degree (e.g., MBA, MS, MD, PhD)	65 (32.5%)
Which of the following best describes your employment status?	Employed full-time	151 (75.5%)
	Employed part-time	7 (3.5%)
	Self-employed	6 (3.0%)
	Homemaker	6 (3.0%)
	Retired	9 (4.5%)
	Disabled/unable to work	19 (9.5%)
	Unemployed	2 (1.0%)
What type of health insurance do you have? (check all that apply)	I do not have health insurance	4 (2.0%)
	Private insurance that I pay for myself	87 (43.5%)
	Private insurance that my or my spouse's employer pays all or part of	48 (24.0%)
	Medicaid	56 (28.0%)
	Medicare	108 (54.0%)
	Veterans' health insurance	4 (2.0%)
	Other	4 (2.0%)
Disease characteristic		
When cancer is diagnosed, doctors will often describe the 'stage' of the cancer. The descriptions below match different stages of melanoma. Please pick the description below that best describes your category that describes the most severe diagnosis you received	Stage 0 [†]	1 (0.5%)
	Stage 1 [†]	2 (1.0%)
	Stage 2 [†]	36 (18.0%)
	Stage 3	76 (38.0%)
	Stage 4	85 (42.5%)
Time since diagnosis	Less than 6 months	5 (2.5%)
	6 months to less than 1 year	4 (2.0%)
	1 year to less than 2 years	41 (20.5%)
	2 years to less than 5 years	90 (45.0%)
	5 years to less than 10 years	46 (23.0%)
	10 years or more	14 (7.0%)
What types of treatments or medicines are you currently using to treat the melanoma, other than surgery? (Please check all that apply) (N = 157)	Targeted therapy	63 (40.1%)
	Immunotherapy	93 (59.2%)
	Chemotherapy	93 (59.2%)
	Radiation therapy	107 (68.2%)
	Other	3 (1.9%)
	Do not know/not sure of type of treatment	1 (0.6%)

[†] Follow-up question asked if melanoma had spread to other parts of the body of respondents who indicated stage 0, 1 or 2 at diagnosis.
 GED: General equivalency diploma; SD: Standard deviation.

Table 3. Patient characteristics (cont.).

Demographic characteristic	Statistic or category	Overall (N = 200)
What types of treatments or medicines have you used in the past to treat the melanoma (before your current treatment, if you are taking one)? (Please check all that apply; N = 186)	Targeted therapy	42 (22.6%)
	Immunotherapy	142 (76.3%)
	Chemotherapy	116 (62.4%)
	Radiation therapy	130 (69.9%)
	Other	7 (3.8%)
	Do not know/not sure of type of treatment	0
	None	0

† Follow-up question asked if melanoma had spread to other parts of the body of respondents who indicated stage 0, 1 or 2 at diagnosis.
GED: General equivalency diploma; SD: Standard deviation.

problems and no chance of extreme sensitivity to the sun. Statistical analysis of respondent choices within each attribute revealed that preferences for each attribute level were significantly different from each other, except pills taken twice-a-day at home and IV infusion for 30 min every 3 weeks in the doctor’s office. Respondents were indifferent between these two levels. When comparing the AEs presented in the study, respondents indicated that avoiding a 30% risk of colitis or hormone gland problems and avoiding a severe fever were more important than avoiding a 20% risk of extreme sun sensitivity ($p < 0.01$).

In the subgroup analysis, respondents with an initial diagnosis of stage IV melanoma had significantly different preferences from respondents initially diagnosed with an earlier stage ($p < 0.01$). Respondents diagnosed at stage IV placed relatively more weight on longer PFS and reducing the risks of colitis and hormone gland problems than respondents with an earlier disease stage at initial diagnosis (Figure 3). Patients aged 47 years and older also had significantly different preferences than younger patients ($p < 0.05$). Older respondents placed more emphasis on longer PFS than younger respondents, and they placed similar value on the increases in PFS and reductions the risk of colitis and hormone problems presented. Respondents younger than 47 years focused on avoiding treatment risks and were insensitive to the changes in PFS offered (Figure 4).

Preference shares

Approximately 85% of respondents preferred a treatment profile with AEs and mode of administration similar to a targeted therapy when compared with a treatment profile with AEs and mode of administration similar to an immunotherapy, based on the assumptions in Table 2 (Figure 5).

Best–worst scaling

Model results

To further assess patients’ preferences for mode of administration, we conducted a best–worst scaling experiment in which patients chose from multiple dosing options. In general, patients preferred oral dosing to an IV infusion. However, many respondents preferred a less burdensome IV infusion schedule to a complex dosing schedule that includes multiple pills several times a day in a regimen that includes drug holidays (Figure 6). Based on the CIs, the importance weights for the two most-preferred modes of administration, ‘one pill once-a-day at home’ and ‘two pills twice-a-day at home’, were not statistically significantly different from one another, nor were the three least-preferred items. The frequency and percentage of each item that was chosen as least and most preferred are presented in Supplementary Table 1.

Discussion

Prior to last decade, treatment options for patients diagnosed with advanced melanoma provided limited clinical benefit. The introduction of immune checkpoint inhibitors and molecularly targeted treatments offers physicians and their patients more choices and, for some patients, improved PFS and OS; however, each new therapy also presents a constellation of potential benefits and risks that must be weighed. In addition, the dosing method and frequency varies considerably among treatments.

We quantified patients’ preferences for treatment attributes and modes of administration found in commercially available treatments for metastatic melanoma. The range of PFS reported in clinical data for targeted and im-

Figure 3. Subgroup preference weights by stage at initial diagnosis. The vertical bars around each mean preference weight represent the 95% CIs about the point estimate.
IV: Intravenous; PFS: Progression-free survival.

munotherapies varies from about 4 to 13 months [5,8]. Our findings suggest that respondents value an increase in PFS from 4 to 13 months and are willing to trade the risk of AEs such as hormone gland problems, colitis and severe fever for a longer PFS benefit. In addition, patients with stage IV melanoma at diagnosis placed greater weight on increasing PFS and on lowering the risk of colitis and hormone gland problems than patients with an earlier stage of disease at diagnosis. Patients aged 47 years or older placed more emphasis on longer PFS than younger respondents, whereas younger respondents focused on avoiding treatment risks and were insensitive to changes in PFS.

Some monotherapies are administered as a continuous fixed regimen of a single pill once-a-day or two pills twice-a-day. Targeted therapy combinations typically range from twice-a-day oral administration to more complicated oral regimens, including those with a drug holiday (3 weeks on, 1 week off). Immune checkpoint inhibitors are typically administered as IV infusions with varying schedules. Our study respondents overall preferred taking pills to receiving IV administration; but, they preferred a less burdensome IV schedule to taking multiple pills several times a day (pill burden of ≥ 8 per day) or complicated dosing schedules.

Calculations of the probability that respondents would select therapies with characteristics (AEs and mode of administration) common to either targeted therapies or immunotherapies suggest that, on average, respondents preferred targeted therapy over immunotherapy treatments. The risks from fever and extreme sensitivity to the sun taken from clinical data on targeted therapies were preferred to the risks of colitis and hormone gland problems at the levels observed in data on immunotherapies.

The study has some limitations that should be considered when assessing the results. The diagnosis of advanced or metastatic melanoma was self-reported and the *BRAFV600* status of respondents was not assessed. Although some respondents were recruited through patient organizations and proprietary databases that screen respondents, other respondents were not independently screened. Patient-friendly descriptions of the attributes were presented,

Figure 4. Subgroup preference weights by age. The vertical bars around each mean preference weight represent the 95% CIs about the point estimate.

IV: Intravenous; PFS: Progression-free survival.

Figure 5. Preference shares for targeted therapy and immunotherapy with typical adverse events and modes of administration, assuming equal progression-free survival. The figure presents the percentage of respondents who prefer a treatment with an adverse event profile and mode of administration like those of targeted therapy versus the percentage of respondents who prefer a treatment with an adverse event profile and mode of administration like those of immunotherapy, assuming equal progression-free survival.

but not all patients may fully understand complex AEs such as endocrinopathies based on the description provided in the survey.

The attributes and levels were based on data from clinical trials for the therapies considered, but the sample was not selected to match the samples for the clinical trials. The sample may not match a nationally representative sample of patients with metastatic melanoma, so the preferences may not be generalizable to all patients.

The survey presents hypothetical scenarios to respondents. Decisions made in the survey may not fully predict decisions made in a clinical setting, where other considerations such as the physician's preferences, attributes such as duration of treatment and other AEs not included in the DCE may come into play. In addition, the final survey was administered online. The method of survey administration can influence respondents' responses, although

Figure 6. Best-worst scaling relative preference weights. The horizontal bars around each mean preference weight represent the 95% CIs about the point estimate.

IV: Intravenous.

previous research has shown in which direction responses might change and how to optimize the mode of survey administration for DCE surveys [47]. Some research has found that the results from online stated-preference surveys are not statistically different from those elicited through face-to-face interviews [48,49].

The PFS attribute was chosen due to the availability of patient data to support the attribute levels. Targeted agents have been associated with longer PFS [1,2,8,50], although comparable efficacy has been observed with a combination of immune checkpoint inhibitors [31]. At the time of the survey's design, data on OS were not available for every treatment. Therefore, conclusions are limited to patient choice based on PFS levels. The results may have differed if OS were included as an attribute. The preference share calculations held efficacy (PFS) constant and did not include the full range of administration modes for targeted and immunotherapies.

Conclusion

In this study, patients had distinct preferences for changes in attributes presented in the DCE, including PFS, the AE risks and the different modes and schedules of administration. Overall, patients preferred a treatment profile that included AEs and mode of administration associated with targeted therapies over immunotherapies. Taking

patient preferences into account may help patients find a treatment that fits their circumstances and tolerance for different types of AEs. A careful discussion of AEs may also help patients anticipate and manage AEs, leading to higher treatment satisfaction. Addressing patient preferences may help patients obtain the full benefit from the growing number of therapeutic options available for advanced and metastatic melanoma.

Summary points

- Recent advances in the treatment of metastatic melanoma, including the introduction of immune checkpoint inhibitors and molecularly targeted treatments, have resulted in more treatment choices and improved outcomes for many patients. Each of the available treatments for metastatic melanoma carries potential benefits and risks that must be weighed.
- The aim of this study was to investigate patient preferences for the clinical attributes that differ among first-line treatments for *BRAF*V600-positive metastatic melanoma.
- A discrete-choice experiment was conducted to elicit patients' relative preferences for treatment attributes including progression-free survival, mode and frequency of administration, and treatment-related adverse events.
- Analysis of the discrete-choice experiment data using a random-parameters logit model revealed distinct preferences among 200 survey respondents. Avoiding a 30% risk of colitis or hormone gland problems and avoiding severe fever were more important to patients than avoiding a 20% risk of extreme sun sensitivity ($p < 0.05$).
- A best–worst scaling exercise evaluating a range of treatment modes and administration schedules revealed that patients prefer taking pills at home rather than receiving intravenous infusions in a doctor's office, but they preferred a less burdensome intravenous schedule to a complicated pill dosing schedule.
- When attributes were combined in an analysis of preference, approximately 85% of respondents preferred the risk profile and mode of administration similar to a targeted therapy over a profile similar to an immunotherapy, holding efficacy constant.
- Overall, respondents in this study preferred a treatment profile that included adverse events and mode of administration associated with targeted therapies over immunotherapies.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at:
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Financial & competing interests disclosure

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Ethical conduct of research

The authors state that they obtained appropriate institutional review board approval and followed the principles outlined in the Declaration of Helsinki for this study. Informed consent was obtained from the survey respondents.

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