# Quantifying Patient Preferences for Targeted Therapies in Metastatic Melanoma: A Discrete-Choice Experiment

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## Objective

**The aim of the study was to explore and quantify preferences of patients with BRAF V600E/K-mutant metastatic melanoma for treatment attributes that differentiate between currently approved BRAF-MEK targeted therapy combinations.**

## Conclusions

**Efficacy (progression-free survival [PFS]) was the most important driver of metastatic melanoma treatment choice.**

**However, safety and regimens were also found to influence treatment preferences, highlighting that treatment choices made by participants are based on trade-offs among multiple treatment attributes.**

**Choice share simulations estimated greater preference share for Profile 1 (comprised of 6 attributes, with levels corresponding to encorafenib + binimetinib).**

**This study contributes insights regarding treatment attribute preferences from the metastatic melanoma patient perspective, which may be valuable to inform individualized healthcare decisions regarding BRAF-MEK therapies and promote shared decision-making between patients and healthcare providers.**

## Considerations

**It should be noted that, findings reflect the attributes and levels tested in this current study, the specific scenarios constructed to simulate choice share, and the sample enrolled in this study.**

**Preference shares provide relative indicators of preference, thus may not truly reflect (or be able to account for all factors that may influence) market share.**

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**References:**

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## Background

- Targeted therapies (e.g., BRAF/MEK inhibitors) offer a personalized treatment approach for metastatic melanoma patients with a BRAF+ V600E/K mutation.
- Three BRAF-MEK targeted therapy combinations are currently approved in the US to treat BRAF V600E/K-mutant metastatic melanoma: dabrafenib + trametinib (D+T), vemurafenib + cobimetinib (V+C) and encorafenib + binimetinib (E+B). Available BRAF-MEK targeted therapies are differentiated by their dosing regimens, safety profiles, and efficacy.
- Previous studies have elicited general preference data regarding treatments for metastatic melanoma.[1,2] To date, however, no prior studies are known to have formally explored or quantified the patient preferences regarding safety (i.e., adverse events), dosing, and efficacy specifically in relation to attributes of available BRAF-MEK targeted therapies.

## Materials and Methods

### Study design:

- The study followed best practice guidelines for patient preference study design and analysis.[3-5] A two-phase study design was employed:

### Development and testing phase (N=12):

- A targeted review of existing peer-reviewed literature (pivotal clinical trial results, patient-focused qualitative research, and prior patient preference studies) and FDA-approved drug labels for BRAF-MEK therapies ([V+C, D+T, E+B]; June 2021) identified differentiating attributes and levels.
- Direct feedback from the target patient population was sought; qualitative interviews (combined concept elicitation and in-depth cognitive debriefing) were conducted with N=12 participants with a self-reported diagnosis of metastatic melanoma.
  - Interviews confirmed comprehension and importance/relevance of the attributes/levels identified and supported content validity of the draft attributes and levels (A&L) grid.
- Final selection of attributes/levels was based on perceived importance to participants with metastatic melanoma and evidence of clinically meaningful differentiation across BRAF-MEK therapies (e.g., reported rates of incidence of AEs) in consultation with an expert oncologist.

### Discrete choice experiment (N=142)

- Participants (with a self-reported diagnosis of metastatic melanoma) were recruited via patient advocacy groups to participate in a cross-sectional online survey (including a discrete choice experiment [DCE]).
- Participants completed 12 choice tasks in the DCE (presented as two alternative treatment profiles) and selected the profile they preferred as a melanoma treatment (forced choice).
  - Choice tasks were based on an A&L grid, comprising 6 attributes in total: 5 attributes with 3 levels each, and 1 attribute with 2 levels (Table 2).

### Statistical analysis:

- Analysis of DCE data utilized Hierarchical Bayesian (HB) estimation to calculate preference weights at the individual level.[6] From this, mean preference weights were calculated at the sample level and reported for each attribute level.
- Relative attribute importance (RAI) was calculated using the mean preference weights; the range of preference weights was taken for each attribute, then re-proportioned to a percentage.
  - RAI is ratio-scaled, enabling proportionate comparison between attributes (e.g., RAI 20% is twice as important than RAI 10%).
  - The higher the RAI, the more influential an attribute was to treatment choice.
- A simulator (in Excel) was used to calculate the sum of the corresponding level preference weights across all attributes for categorical variables, or the sum of the multiple of the value and the weight for continuous variables.
  - Summed preference weights were subjected to exponential transformation, then re-scaled to 100 to derive a percentage preference share (or choice probability) for each profile.
- Preference shares were estimated for the base-case scenario (Table 3).
  - Three profiles, each comprising 6 attributes, with levels corresponding to BRAF-MEK therapies: Profile 1 with E+B; Profile 2 with V+C; Profile 3 with D+T. Where percentage (continuous) levels do not match the exact level tested in the A&L grid, the preference weights are interpolated between the relevant levels tested in the DCE.
  - Levels selected in profiles were devised in accordance with clinical literature (i.e., safety data) and FDA-approved product labels.

**Table 1. Participant demographic and clinical characteristics (N=142)**

| Description | Total Sample (N=142) |
|---|---|
| Age (years) | |
| Median | 49 |
| Min/Max | 22–74 |
| Gender, n (%) | |
| Male | 31 (21.8) |
| Female | 111 (78.2) |
| Ethnic origin, n (%) | |
| Caucasian | 138 (97.2) |
| Hispanic or Latino | 2 (1.4) |
| Black/African American | 1 (0.7) |
| Native American or American Indian | 1 (0.7) |
| Geographical region, n (%) | |
| Midwest | 41 (28.9) |
| Northeast | 23 (16.2) |
| South | 42 (29.6) |
| West | 36 (25.4) |

**Table 1. Continued (1)**

| Description | Total Sample (N=142) |
|---|---|
| Health literacy Status, n (%) | |
| High likelihood of limited literacy | 5 (3.5) |
| Possibility of limited literacy | 9 (6.3) |
| Adequate literacy | 128 (90.1) |
| Employment status, n (%) | |
| Currently working (full time / part time) | 59 (41.5) / 23 (16.2) |
| Not currently working | 52 (36.6) |
| Other | 8 (5.6) |
| Skin type (Fitzpatrick scale adaptation), n (%) | |
| I tan regularly | 5 (3.5) |
| I am capable of tanning | 72 (50.7) |
| I rarely tan | 60 (42.3) |
| I never tan | 5 (3.5) |
| Time since diagnosis of metastatic melanoma, n (%) | |
| ≤1 year | 52 (36.6) |
| >1-3 years | 45 (31.7) |
| > 3 years | 45 (31.7) |

**Table 1. Continued (2)**

| Description | Total Sample (N=142) |
|---|---|
| BRAF mutation status, n (%) | |
| BRAF positive | 63 (57.3) |
| BRAF negative | 38 (34.5) |
| Unknown | 9 (8.2) |
| Stage of melanoma, n (%) | |
| Stage III | 56 (39.4) |
| Stage IV | 83 (58.5) |
| Unknown | 3 (2.1) |
| Exposure to BRAF-MEK therapies, n (%) | |
| Never received BRAF-MEK therapy | 104 (73.2) |
| Yes | 38 (26.8) |
| *Encorafenib + binimetinib* | 21 (55.3) |
| *Dabrafenib + trametinib* | 21 (55.3) |
| *Vemurafenib + cobimetnib* | 3 (7.9) |

**Table 2. Attributes and levels (A&L) grid**

| Attribute | Level 1 | Level 2 | Level 3 |
|---|---|---|---|
| Dosing requirements | 9 pills in the morning<br>3 pills in the evening | 7 pills in the morning<br>1 pill in the evening | 2 or 3 pills in the morning<br>2 or 3 pills in the evening |
| Food requirements | Taken on an empty stomach (1 hour before or at least 2 hours after a meal) | Taken with or without food | – |
| Efficacy (PFS) | 11 months | 13 months | 15 months |
| Fever* | 55% of patients | 30% of patients | 10% of patients |
| Photosensitivity* | 45% of patients | 25% of patients | 5% of patients |
| Diarrhea* | 30% of patients | 45% of patients | 60% of patients |

*Levels for AEs reflect Grade 1 and 2 incidence rates and were framed in the survey as such

## Results

### Study sample

- 142 participants participated in a cross-sectional online survey (including a DCE). Descriptive statistics for sample sociodemographic and clinical characteristics are presented in Table 1.

### Preference weights

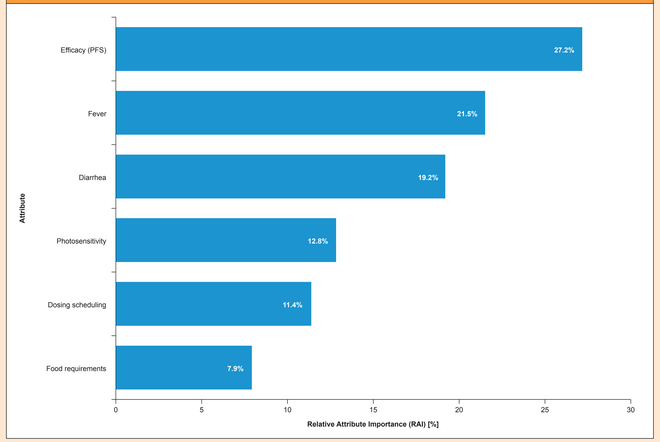
- Preference weights were consistent with the natural and logical ordering of levels, with better safety/survival outcomes or less burdensome regimens being preferred to worse safety/survival outcomes or more burdensome regimens.
- The range in preference weights within attributes is shown in Figure 1:
  - Efficacy (PFS) was associated with the largest range: (2.83 – [-2.73] = 5.56).
  - Fever was associated with largest range among safety attributes (2.11 – [-2.47] = 4.58), with greater weight placed between 30% and 55% incidence (0.36 – [-2.47] = 2.83).
  - The range of preference weights was lowest for the food requirements attribute: (0.72 – [-0.72] = 1.44).

Figure 1. Mean preference weights for each attribute


### Relative attribute importance

- Efficacy (PFS) had the highest RAI (27.2%) relative to other attributes in this study (Figure 2).
  - Safety attributes had relatively lower RAI than PFS. Fever (RAI: 21.5%) and diarrhea (RAI: 19.2%) had higher RAI values than photosensitivity (RAI: 12.8%). Fever and diarrhea were 1.7 and 1.5 times more important than photosensitivity, respectively.
  - Regimen attributes (dose scheduling [RAI: 11.4%] and food requirements [RAI: 7.9%]) had the lowest RAI; being 2.4 and 3.4 times less important than PFS, respectively.
- Ordering of RAIs was consistent when stratified by clinical and demographic subgroups.

Figure 2. Relative Attribute Importance (%)




### Preference share

*Preference share findings are presented in Table 4.*

- Findings estimated 90.1% preference share for Profile 1 (E+B), relative to Profile 2 (V+C) (1.3%) and Profile 3 (D+T) (8.6%).
  - Findings suggest that greater efficacy (PFS), lower incidence rates for safety attributes (i.e., diarrhea [33.5%]; photosensitivity [5.0%]) and fever [14.0%]), as well as the comparatively less-burdensome regimens, contributed to preference share for Profile 1.

**Table 3. Simulation base-case scenario for BRAF-MEK therapies**

| Attribute | Profile 1: E+B | Profile 2: V+C | Profile 3: D+T |
|---|---|---|---|
| Dosing requirements | 9 pills in the morning<br>3 pills in the evening | 7 pills in the morning<br>1 pill in the evening | 2 or 3 pills in the morning<br>2 or 3 pills in the evening |
| Efficacy (PFS) | 14.9 months | 12.3 months | 11.4 months |
| Food requirements | Taken with or without food | Taken with or without food | Taken on an empty stomach (1 hour before at least 2 hours after a meal) |
| Fever | 14% | 24% | 49% |
| Photosensitivity | 45% | 25% | 5% |
| Diarrhea | 33.5% | 50% | 33.23% |

- A sensitivity analysis was conducted to estimate preference shares for an alternative scenario in which efficacy was held constant across profiles (PFS levels in Profiles 2 and 3 increased to 14.3 to match Profile 1).
  - Marginal differences in preferences shares for this alternative scenario (compared to the base case scenario) were observed (Profile 1: -7.1%; Profile 2: +1.5%, Profile 3: +5.6%) (Table 4).

**Table 4. Preference shares for simulated base-case and alternative scenarios**

| | Profile 1: E+B | Profile 2: V+C | Profile 3: D+T |
|---|---|---|---|
| Base-case scenario | 90.1% | 1.3% | 8.6% |
| Alternative scenario* | 83.0% | 2.8% | 14.2% |

*The alternative case assumes efficacy (PFS) is held constant across profiles.