Patient Preferences for Treatment Options in Advanced Melanoma

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Background

- Multiple treatment options exist for patients with metastatic melanoma[1]
- 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]
- It is unclear what factors of individual therapies are most important to patients
- Engagement of patients is consistent with the movement towards patient-centered care introduced by the Affordable Care Act that seeks to improve the evidence for treatment decisions by engaging key stakeholders in health care[3]
- We conducted a discrete choice experiment (DCE) to better understand aspects of therapy most important to US-based patients

Methods

Patients

- In order to participate, advanced melanoma patients had to meet all of the following criteria: aged 18 years or older, diagnosed with advanced melanoma (defined as unresectable or metastatic melanoma), had an Eastern Cooperative Oncology Group performance status rating between 0-3, were able to operate a computer with Internet access, were able to read and understand English, and provided informed consent

Study design and analysis

- In Phase 1 (qualitative), the treatment attributes and levels were identified through literature review and conducting qualitative interviews with a total of 28 people (12 oncologists, 8 patients, and 8 nurses)
- In Phase 2 (quantitative, the DCE study was conducted where scenarios were presented in which respondents had to choose between two hypothetical profiles of different treatment options, in patient-friendly language
- A D-efficient algorithm (SAS 9.3) was used to ensure a sufficient number of respondents were allocated evenly across orthogonal combinations of attributes and levels[4]
- The survey also included several non-DCE related questions that asked the respondent about importance of the medication attributes by asking them to select the three most important attributes to them, and then to rank those attributes
- Relative preference weights for medication features were estimated using a hierarchical Bayesian logistic regression model with effects coding parameterization[5]

Results

- Of 935 invitees, 273 (29%) responded, and 200 (21%) completed the study. The majority of respondents were female (61%), white (84%), diagnosed in past five years (80%), and currently undergoing treatment (60%)
- 98% had medical insurance, typically through an employer (46.0%) or Medicaid plus a private insurance (19.5%)
- Most patients had used 1-2 different treatments (76.5%)
- Among patients currently receiving treatment, the most common medications were nivolumab (20.0%), pembrolizumab (18.5%), and ipilimumab (13.5%)
- When patients were directly asked to select the 3 most important attributes from the full list of 7 attributes (non-DCE approach), overall survival (OS) was most often chosen (61.5%), followed by objective response rate (ORR) (49.5%), progression-free survival (PFS) (43.0%), adverse events (AE) (32.5%), dosing schedule (18%), mode of administration (15%), and duration of therapy (15%)
- The classifier system for the DCE based on Phase 1 had 7 attributes and 3 levels for most attributes (**Table 1**)

Table 1. Attributes and levels for the DCE

Attribute	#	Levels
Mode of Administration	1	Oral – A medication taken by mouth for a period of time
	2	IV - An infusion given into the vein for a period of time
	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
Dosing Schedule	1	Two medicines; one medicine is taken twice daily, the other once daily
	2	One medicine taken once daily
	3	One medicine taken twice daily
	4	One medicine taken by 30 minute infusion every 3 weeks
	5	One medicine taken by 60 minute infusion every 2 weeks
	6	One medicine taken by 90 minute infusion every 3 weeks
	7	Two medicines, both are given as a 150-minute infusion every 3 weeks for 3 months (plus/minus: one of the two medicines is continued as 60 minute infusion every 2 weeks for 5 or more months)
	8	One medicine given by one injection every 3 weeks
Median Duration of Therapy	1	3 months
	2	8 months
	3	12 months
Objective Response Rate (ORR)	1	15 out of 100 patients (15% chance of responding)
	2	33 out of 100 patients (33% chance of responding)
	3	65 out of 100 patients (65% chance of responding)
Progression-Free Survival (PFS)	1	3 months
	2	5 months
	3	11.5 months
Overall Survival (OS)	1	45 out of 100 patients (45% of patients survive to 12 months)
	2	55 out of 100 patients (55% of patients survive to 12 months)
	3	75 out of 100 patients (75% of patients survive to 12 months)
Grade 3/4 Toxicities/Adverse Events	1	10 out of 100 patients (10% likelihood of experiencing a serious side effect)
	2	32 out of 100 patients (32% likelihood of experiencing a serious side effect)
	3	55 out of 100 patients (55% likelihood of experiencing a serious side effect)

Results (continued)

- An example of a DCE choice-based task between 2 hypothetical medications is shown (**Figure 1**); each patient had to complete 11 tasks
- Patients valued OS, AE, and ORR as most important when making a treatment decision, and to a lesser extent PFS (**Figure 2**)
- Compared to efficacy and safety, dosing schedule, duration of therapy, and mode of administration were relatively unimportant
- Comparable differences between coefficients in can be used to interpret similarities in importance
  - ie, a decrease in likelihood of serious side effects from 32% to 10% (β=3.4) is comparable in importance to an increase in OS from 45% to 55%

Figure 1. Example of choice-based scenario

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/Adverse Events	 10%	 55%
SELECT ONLY ONE	**MEDICINE A**	**MEDICINE B**
If these were the only medications available to you for first-line treatment of a patient with advanced (unresectable/metastatic) melanoma, which one would you choose?	❑	❑

Figure 2. DCE-based relative importance of attributes to oncologists

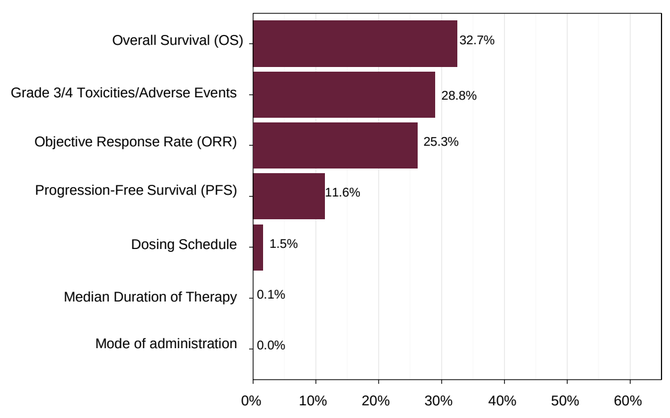
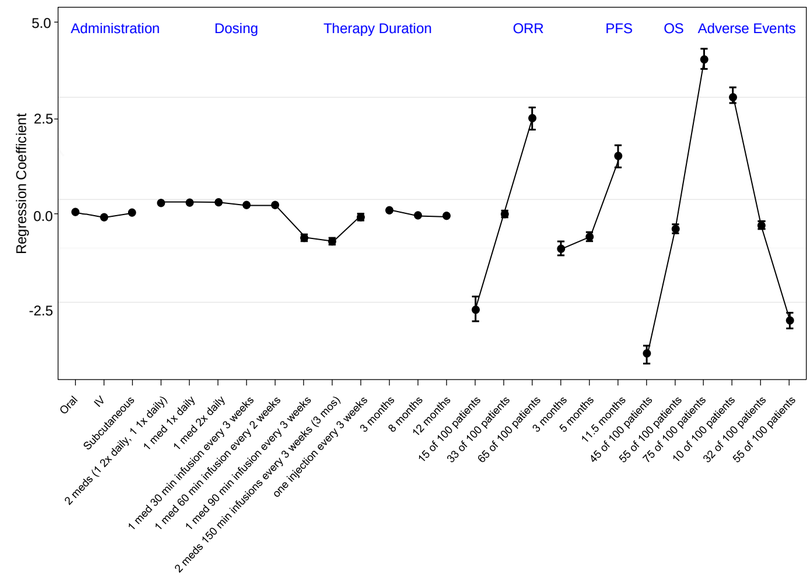


Figure 3. Oncologists' preference weights for melanoma treatment attributes and levels (n=226)



Discussion/Conclusion

- OS, AEs, and ORR were the most important considerations to patients in selecting among advanced melanoma treatments
- Dosing schedule, mode of administration, and median duration of therapy were relatively less important to patients compared with OS, AEs, and ORR
- This was one of the first DCE-based studies in advanced melanoma, an indirect approach to identifying treatment preferences that allows for a preference weight to be assigned to each level of each attribute and a value of relative importance of each attribute in stating preferences for treatment
- The direct (non-DCE) approach indicated a subset of patients (15%-18%) had dosing schedule, duration, and mode of administration among the top 3 most important, which contrasts with DCE and suggests it is still informative to directly ask patients.
- A limitation of the study is generalizability, as patients in this study were relatively younger, and thus healthier and more likely to be employed, than the advanced melanoma patient population in the United States,[2] likely because the survey was Web based
- Understanding the relative importance of aspects of medication therapy to patients can to help inform the shared decision making with oncologists

References

1. Atkins MB, Larkin J. *J Natl Cancer Inst*. 2016;108(6):djv414.
2. American Cancer Society. Treatment of melanoma skin cancer, by stage. Retrieved from: http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/melanoma-skin-cancer-treating-by-stage.
3. Selby JV, Beal AC, Frank L. *JAMA*. 2012;307(15):1583-1584.
4. Reed Johnson F, Lancsar E, Marshall D, et al. *Value Health*. 2013;16(1):3-13.
5. Hauber AB, Gonzalez JM, Groothuis-Oudshoorn CG, et al. *Value Health*. 2016;19(4):300-315.
6. Krammer R, Heinzerling L. *PLoS One*. 2014;9(11):e111237.
7. National Cancer Institute. SEER stat fact sheets: melanoma of the skin. Retrieved from http://seer.cancer.gov/statfacts/html/melan.html.
8. Stenehjem D, Korytowsky B, Oderda G, Wanishayakorn T, Bauer H, Brixner D. *Value Health*. 2015;18(7):A469-A470.

Disclosures

FXL, SE and RS are employees of Merck & Co. Inc. Kenilworth, NJ, USA, a manufacturer of medication therapy used to treat melanoma. GDB, EW, and EB are employees of Kantar Health, which was retained as paid consultants by Merck & Co. Inc. Kenilworth, NJ, USA, to conduct this research. RJ served as a paid advisor to the study, but received no compensation for the development of this poster.