

2022

Cancer Patient Beliefs and Attitudes Regarding Immune Checkpoint Inhibitor Therapy

Nedal Darwish

Arnot Ogden Medical Center, darwish.nedal@gmail.com

Delaney C. Stuhr

Lake Erie College of Osteopathic Medicine, delaney.stuhr@gmail.com

Haily M. Datz

Lake Erie College of Osteopathic Medicine, hailydatz@gmail.com

Halima Bakillah

Arnot Ogden Medical Center, halima.bakillah@arnohealth.org

Tenzin Tseky

Arnot Ogden Medical Center, tenzin.tseky@arnohealth.org

Mohamed Manaa

Arnot Ogden Medical Center, Mohamed.manaa@arnohealth.org

Serge Dauphin

University of Rochester Medical Center, serge.dauphin@arnohealth.org

Follow this and additional works at: <https://scholar.rochesterregional.org/advances>



Part of the [Oncology Commons](#)



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](#)

Recommended Citation

Darwish N, Stuhr DC, Datz HM, Bakillah H, Tseky T, Manaa M, Dauphin S. Cancer Patient Beliefs and Attitudes Regarding Immune Checkpoint Inhibitor Therapy. *Advances in Clinical Medical Research and Healthcare Delivery*. 2022; 2(3). doi: 10.53785/2769-2779.1110.

ISSN: 2769-2779

This Observational Study is brought to you for free and open access by RocScholar. It has been accepted for inclusion in *Advances in Clinical Medical Research and Healthcare Delivery* by an authorized editor of RocScholar. For more information, please contact Advances@rochesterregional.org.

Cancer Patient Beliefs and Attitudes Regarding Immune Checkpoint Inhibitor Therapy

Author ORCID ID:
0000-0003-1877-8921

Abstract

The development and widespread use of immune checkpoint inhibitors (ICIs) have advanced the field of oncology in a short period of time. Despite this, patient perception regarding this new medication class has not been adequately assessed, which may affect treatment decisions and adherence. The Belief about Medicines Questionnaire (BMQ) is a validated survey composed of 18 questions which analyzes patient's beliefs about the necessity of prescribed medication and concern about the potential adverse events caused by the medication. General medication overuse and harm are also determined. This is the first study to utilize the BMQ for patients on ICI therapy.

Keywords

Immune checkpoint inhibitors, Oncology, Cancer, Quality care, Patient beliefs

Creative Commons License



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/)

Conflict of Interest Statement

There are no conflicts of interests to declare.

Cover Page Footnote

We would like to acknowledge the continued efforts and support of Angela Black in academics and research at Arnot Ogden Medical Center

OBSERVATIONAL STUDY

Cancer Patient Beliefs and Attitudes Regarding Immune Checkpoint Inhibitor Therapy

Nedal Darwish ^{a,*}, Delaney C. Stuhr ^b, Haily M. Datz ^b, Halima Bakillah ^a, Tenzin Tseky ^a, Mohamed Manaa ^a, Serge Dauphin ^c

^a Arnot Ogden Medical Center, United States

^b Lake Erie College of Osteopathic Medicine, United States

^c University of Rochester Medical Center, United States

Abstract

The development and widespread use of immune checkpoint inhibitors (ICIs) have advanced the field of oncology in a short period of time. Despite this, patient perception regarding this new medication class has not been adequately assessed, which may affect treatment decisions and adherence. The Belief about Medicines Questionnaire (BMQ) is a validated survey composed of 18 questions which analyzes patient's beliefs about the necessity of prescribed medication and concern about the potential adverse events caused by the medication. General medication overuse and harm are also determined. This is the first study to utilize the BMQ for patients on ICI therapy.

Keywords: Immune checkpoint inhibitors, Oncology, Cancer, Quality care, Patient beliefs

1. Introduction

Cancer remains the second leading cause of death in the United States and is associated with an increase in morbidity.¹ The rapid development and use of immune checkpoint inhibitors (ICIs) is argued to have revolutionized the field of oncology.² A study in 2014 of metastatic melanoma estimated a median overall survival of 5.3 months (95% CI = 4.3–6.3 months). The Checkmate 067 trial published a mere 7 years later demonstrated a survival benefit in unresectable melanoma of with median overall survival of 72.1 months of patients on ICI combination therapy of nivolumab and ipilimumab.^{3,4} On the other hand, patients with advanced malignancy may have no response to therapy, while suffering the huge financial burden of the drugs cost. Also, adverse effects of ICIs can include a spectrum of autoimmune response that may occur as a result of attenuation of essential immune mechanisms. Commonly there is loss of naive T cells that result in

invasion of organs causing inflammatory damage, hypothyroidism, hepatotoxicity, and pneumonitis.

Currently, clinical trials involving ICIs number around 3000 or around 2/3s of all active oncologic trials. Despite this, there are few studies determining the beliefs and attitudes regarding these medicines in the oncologic patient population. Beliefs about medications and perception of disease have the potential to affect a patient's compliance and adherence of medications and their decisions regarding treatment.⁵ In the case of ICIs, compliance can be considered congruent to participating or continuing recommended treatment. This is especially important in oncologic care where choice of therapy is ultimately the patient's decision, usually in the context of financial cost and medical risk vs benefit. A patient's perception of their disease and subsequent management was identified and is emphasized by the National Institute for Clinical Excellence (NICE) as a factor for medication adherence. The three variables NICE considers

Received 15 June 2022; revised 13 July 2022; accepted 13 July 2022.
Available online 12 September 2022

* Corresponding author.

E-mail addresses: darwish.nedal@gmail.com (N. Darwish), delaney.stuhr@gmail.com (D.C. Stuhr), hailydatz@gmail.com (H.M. Datz), halima.bakillah@arnohealth.org (H. Bakillah), tenzin.tseky@arnohealth.org (T. Tseky), Mohamed.manaa@arnohealth.org (M. Manaa), serge.dauphin@arnohealth.org (S. Dauphin).

<https://doi.org/10.53785/2769-2779.1110>

2769-2779/© 2022 Rochester Regional Health.



most important for patient adherence are patients' beliefs and concerns, satisfaction with involvement in the treatment decision, and "practice" support (e.g., written and verbal medication instruction, simplified regimens, reminders) using the medication.⁶ The BMQ is a validated questionnaire designed to determine a patient's cognitive representation about medication addressing necessity, concerns, general overuse, and general harm.⁷ This study aims to begin to address the pressing need for a more comprehensive analysis of patients' beliefs and concerns regarding ICI therapy in the face of a novel and highly publicized and promoted product.

2. Methods

This cross-sectional study was approved by the Institutional Review Board of Lake Erie College of Osteopathic Medicine. Men and women over the age of 18 who are actively being treated for any malignancy on immune checkpoint inhibitor therapy were consented to participate in the study. The treatment team was independent of the research team and were not involved in data collection or analysis. Patients were allowed to be on combination chemotherapy and immunotherapy agents. Data was collected between March and May of 2022 by members of the research team using an interviewer administered BMQ, a validated 18 question survey (Supplemental material 1) which assesses a patients' beliefs and attitudes in three different sections: BMQ-Necessity (5 items, score range 5–25) and BMQ-Concern (5 items, score range 5–25), which describe a patients' beliefs of the necessity and the concern of potential adverse effects of the medication respectively. BMQ-Overuse (4 items, score range 4–20) and BMQ-Harm (4 items, score range 4–20), which describe a patients' general beliefs about medical care and medicine. The BMQ utilizes a Likert response scale of five points including 1 = Strongly disagree; 2 = Disagree; 3 = Neutral; 4 = Agree; 5 = Strongly agree. It was stressed to the patients that the results would be anonymous and that their providers would not be informed of their individual responses. Patient identifying information including name and medical record number was removed. The research staff was not blinded from other patient demographic information or results of the BMQ. Four scores were calculated from the BMQ (harm, overuse, necessity, concern). The patients were then organized into 4 groups based on their scores: Accepting if necessity was ≥ 15 and concern < 15 . Ambivalent if necessity ≥ 15 and concern ≥ 15 . Indifferent if necessity < 15 and concern < 15 . Skeptical if necessity < 15 and concern ≥ 15 . A Necessity-

Concern differential was calculated by obtaining the difference between the Necessity and Concern score. Statistical analysis was performed using SPSS 22. Statistical significance was defined as a $p \leq 0.05$.

3. Results

Twenty-six patients on ICI therapy were recruited for the study from a single center out of 46-screened patients, thus a satisfactory response rate was achieved (56%). Full patient demographics are included in Table 1. The mean age was 65.0 (SD = 13.98). Patient ICI therapy mostly consisted of pembrolizumab (85.6%) but also included nivolumab and durvalumab treatments. Patients were taking ICI monotherapy (61.5%) or with concurrent chemotherapy (34.6%). Patient malignancies included non-small cell lung cancer (NSCLC) squamous cell subtype, NSCLC adenocarcinoma subtype, small cell lung carcinoma, renal cell carcinoma, breast cancer, melanoma, colorectal carcinoma, uterine carcinoma, esophageal cancer, and endometrial carcinoma. Patient BMQ responses are shown in Table 2.

There was a significant difference between the BMQ Necessity and Concern score ($n = 26$, mean difference = 6.85, $p = 0.0001$) as determined by paired t-test. The overall mean BMQ Necessity score was 19.5 (SD = 3.10) demonstrating patients felt strongly about their personal need of ICIs. The overall mean BMQ Concern score was 12.65 (SD = 2.69), demonstrating that patients were not concerned of the range of potential adverse consequences of ICIs. BMQ Necessity and Concern scores were combined into an attitudinal analysis (Fig. 1), with a dramatic majority categorized as "accepting" of their condition (77%, $n = 20$), just under a fifth were "ambivalent" (19%, $n = 5$), only one was "indifferent" (4%, $n = 1$) and none were skeptical

Table 1. Patient demographic characteristics.

Demographic Characteristics		N = 26 n (%)
Gender	Female	15 (57.7%)
	Male	11 (42.3%)
Medication	Pembrolizumab	22 (84.6%)
	Nivolumab	2 (7.7%)
	Durvalumab	2 (7.7%)
Therapy	Monotherapy	16 (61.5%)
	Concurrent Chemotherapy	10 (38.5%)
Malignancy	NSCLC squamous cell subtype	7 (26.9%)
	NSCLC adenocarcinoma subtype	5 (19.2%)
	Small cell lung carcinoma	1 (3.8%)
	Renal cell carcinoma	4 (15.3%)
	Breast cancer	3 (11.5%)
	Colorectal carcinoma	1 (3.8%)
	Uterine carcinoma	1 (3.8%)
	Endometrial carcinoma	1 (3.8%)

Table 2. BMQ responses and scoring.

	Strongly Disagree %	Disagree %	Neutral %	Agree %	Strongly Agree %
Necessity (5 items, score range 5–25)					
My health, at present, depends on my immunotherapy medication	0	7.7	7.7	53.8	30.8
My life would be impossible without my immunotherapy medication	0	11.5	30.8	42.3	15.4
Without my immunotherapy medication, I would be very ill	0	7.7	34.6	42.3	15.4
My health in the future will depend on my immunotherapy medication	0	3.8	26.9	34.6	34.6
My immunotherapy medication protects me from becoming worse	0	0	19.2	46.2	34.6
Concern (5 items, score range 5–25)					
Having to take immunotherapy medication worries me	7.7	69.2	7.7	15.4	0
I sometimes worry about the long term effects of my immunotherapy medication	3.8	42.3	11.5	42.3	0
My immunotherapy medication is a mystery to me	3.8	42.3	3.8	50	0
My immunotherapy medication disrupts my life	11.5	65.4	7.7	15.4	0
I sometimes worry about becoming too dependent on my immunotherapy medication	3.8	84.6	3.8	7.7	0
Overuse (4 items, score range 4–20)					
If doctors had more time with patients they would prescribe fewer medications	3.8	42.3	23.1	30.8	0
Doctors use too many medications	7.7	57.7	19.2	15.4	0
Doctors place too much trust on medicines	3.8	61.5	19.2	15.4	0
Natural remedies are safer than medicines	3.8	46.2	26.9	23.1	0
Harm (4 items, score range 4–20)					
Most medicines are addictive	3.8	73.1	15.4	7.7	0
Medicines do more harm than good	7.7	65.4	11.5	15.4	0
People who take medicines should stop their treatment for a while every now and again	11.5	57.7	26.9	3.8	0
All medicines are poisons	11.5	73.1	3.8	11.5	0

(n = 0, 0%). The Necessity-Concern differential was 6.85, again revealing a high level of judgement that the personal need for ICI's outweighed the potential harm. Overall mean BMQ Overuse score and BMQ Harm scores were 10.4 (SD = 2.90) and 9.0

(SD = 1.09) respectively, demonstrating that some patients were wary of medication overuse and harm in general, however the majority exhibited trust in medication use by physicians and trust in medications. BMQ scoring was assessed by key patient

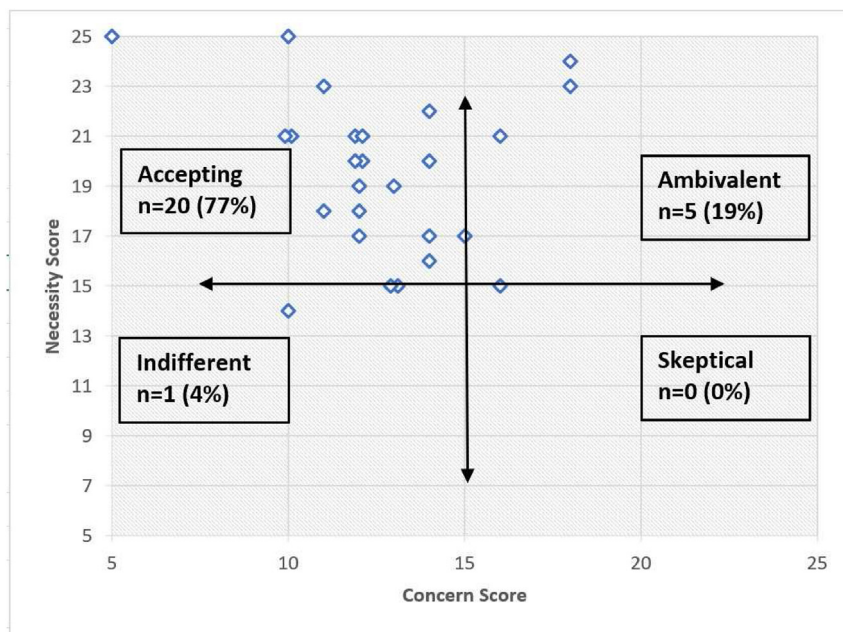


Fig. 1. Attitudinal Analysis scatterplot. Accepting: necessity ≥15 and concern <15. Ambivalent: necessity ≥15 and concern ≥15 Indifferent: necessity <15 and concern <15 Skeptical: necessity <15 and concern ≥15.

Table 3. Variable analysis.

	Variable	Mean	Mean difference	SD	SEM	p	CI
Necessity	Adjunctive therapy (n = 10)	19.06	1.14	3.26	0.81	0.384	-3.78 to 1.51
	Monotherapy n = 16	20.2	-1.14	3.05	0.96		
	Stage IV CA (n = 20)	19.35	0.65	2.83	0.63	0.6667	-3.74 to 2.44
	Stage II-III CA (n = 6)	20	-0.65	4.38	1.79		
	Male (n = 11)	19.82	0.55	3.65	0.94	0.667	-3.19 to 2.09
Concern	Female (n = 15)	19.27	-0.55	2.48	0.75		
	Adjunctive therapy (n = 10)	12.31	0.89	2.87	0.72	0.433	-3.19 to 1.41
	Monotherapy n = 16	13.2	-0.89	2.57	0.81		
	Stage IV CA (n = 20)	13.3	-2.8	2.32	0.52	0.025	0.38 to 5.22
	Stage II-III CA (n = 6)	10.5	2.8	3.15	1.28		
Overuse	Male (n = 11)	13.27	-1.07	2.41	0.73	0.334	-3.32 to 1.17
	Female (n = 15)	12.2	1.07	2.96	0.76		
	Adjunctive therapy (n = 10)	10.56	-0.46	3.39	0.85	0.706	-2.04 to 2.96
	Monotherapy n = 16	10.1	0.46	2.23	0.71		
	Stage IV CA (n = 20)	10.55	-0.72	2.19	0.49	0.612	-2.16 to 3.60
Harm	Stage II-III CA (n = 6)	9.83	0.72	5	2.04		
	Male (n = 11)	10.36	0.4	2.58	0.78	0.976	-2.43 to 2.51
	Female (n = 15)	10.4	-0.4	3.29	0.85		
	Adjunctive therapy (n = 10)	9.19	-0.49	2.23	0.56	0.544	-1.15 to 2.12
	Monotherapy n = 16	8.7	0.49	1.42	0.45		
Harm	Stage IV CA (n = 20)	9.15	-0.65	1.73	0.39	0.483	-1.23 to 2.53
	Stage II-III CA (n = 6)	8.5	0.65	2.66	1.09		
	Male (n = 11)	9.27	-0.47	1.95	0.59	0.55	-2.08 to 1.14
	Female (n = 15)	8.8	0.47	1.97	0.51		

There was no significant difference between BMQ scoring based on patient demographics except for BMQ Concern in patients with Stage IV (mean = 13.3, n = 20) vs Stage II-III cancer (mean = 10.5, n = 6) (mean difference = 2.8, p = 0.025) demonstrating patients were indeed more concerned about the harm of their medications in more advanced disease.

demographics including gender, presence of adjunctive therapy, and stage of cancer (Table 3).

4. Discussion

This is an exploratory post hoc analysis using survey questionnaire data from people with cancer on novel ICI therapy to understand their beliefs and attitudes regarding the medication class. Despite being a preliminary study with a small size (N = 26), statistical significance was achieved. Overall, this study demonstrates that patients on ICIs strongly believe that both their medication are necessary and safe. The attitudinal analysis results were dramatic in this study. When differentiated into groups based on BMQ Necessity and Concern scoring, the vast majority of patients were placed into the “accepting” subtype. This was characterized by a Necessity score >15 and Concern score <15; this is substantial when juxtaposed to the zero patients placed in the “skeptical” subtype characterized by a Necessity score of <15 and concern score >15.

While this pattern has been shown to be positively correlated to medication compliance and adherence, this may not be necessarily beneficial for every patient. As stated previously, ICIs are novel

medications in the treatment of cancer, and have revolutionized the field in a short period since their discovery. However, like any other medication, there exists potential for adverse events, and in as much as half of patients with advanced disease, there may be no effect of the medication on morbidity and mortality. A study recently published by Glisch et al. demonstrated an association of ICI use with poor performance status, lower hospice enrollment in the last 30 days of life, and dying in the hospital.⁸ Another study by Winquist et al. reveals that there is a subpopulation of patients on ICIs for solid tumors, a primary indication for their use, who may suffer early mortality, despite overall benefit in median survival time.⁹ Our study does show that patient Concern scoring significantly is higher in patients with more advanced disease. One plausible explanation is that their oncologists have conveyed and subscribed to these patients a more pragmatic approach to their disease with a more realistic prognostic outlook. Further investigation is needed on patient sentiment on ICIs to understand their impact on treatment. According to the National Institute of Clinical Excellence, patient perception of their medication guides treatment decisions, as well as how and whether they take

prescribed medication. The BMQ is a validated survey which quantifies patient sentiment regarding medication. We have established a framework to use the BMQ questionnaire in patients on ICI therapy for malignancy, and this should be validated and applied in a larger scale multi-center study.

There are limitations to our study. First the sample size was small (N = 26), despite reaching most of our target population. Patient rationale behind opting out of participation were not recorded. Second, different ICIs were included in the study; therefore, these outcomes cannot be attributed to one ICI. Third, not all ICIS were studied thus the study cannot be representative to all in the medication class. Fourth, patients were recruited from a single center and were categorized into stages of cancers that were not necessarily congruent. Fifth, only patients actively on ICIs were surveyed, and patients' beliefs and attitudes about the medication in patients who refused treatment were not surveyed. Sixth, the ability of the patients on combination therapy to distinguish between immunotherapy and chemotherapy was not assessed, and the beliefs and attitudes regarding chemotherapy versus immunotherapy should be investigated in future studies. Finally, appropriateness and rationale of treatment were not analyzed, and adverse effects of treatment were not detailed.

5. Conclusions

We have established a framework to use the BMQ to analyze patient beliefs and attitudes of ICI therapy in patients with malignancy. We have demonstrated that our patients on ICI therapy were resolutely "accepting" that their medication is necessary and are satisfied with their potential for adverse effects. We also have demonstrated that concern does increase with more advanced disease.

Conflict of Interest

There are no conflicts of interests to declare.

Acknowledgement

We would like to acknowledge the continued efforts and support of Angela Black in academics and research at Arnot Ogden Medical Center.

References

1. Vaddepally RK, Kharel P, Pandey R, Garje R, Chandra AB. Review of indications of FDA-approved immune checkpoint inhibitors per NCCN guidelines with the level of evidence. *Cancers*. 2020;12(3):738. Published 2020 Mar 20. <https://doi.org/10.3390/cancers12030738>.
2. Robert C. A decade of immune-checkpoint inhibitors in cancer therapy. *Nat Commun*. 2020;11(1):3801. Published 2020 Jul 30. <https://doi.org/10.1038/s41467-020-17670-y>.
3. Sandru A, Voinea S, Panaitescu E, Blidaru A. Survival rates of patients with metastatic malignant melanoma. *J Med Life*. 2014; 7(4):572–576.
4. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Long-Term outcomes with nivolumab plus ipilimumab or nivolumab alone versus ipilimumab in patients with advanced melanoma. *J Clin Oncol*. 2022;40(2):127–137. <https://doi.org/10.1200/JCO.21.02229>.
5. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res*. 1999;47(6):555–567. [https://doi.org/10.1016/s0022-3999\(99\)00057-4](https://doi.org/10.1016/s0022-3999(99)00057-4).
6. Chapman SC, Horne R, Eade R, Balestrini S, Rush J, Sisodiya SM. Applying a perceptions and practicalities approach to understanding nonadherence to antiepileptic drugs. *Epilepsia*. 2015; 56(9):1398–1407. <https://doi.org/10.1111/epi.13097>.
7. Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns Framework. *PLoS One*. 2013;8(12), e80633. <https://doi.org/10.1371/journal.pone.0080633>.
8. Glich C, Hagiwara Y, Gilbertson-White S, Gao Y, Lyckholm L. Immune checkpoint inhibitor use near the end of life is associated with poor performance status, lower hospice enrollment, and dying in the hospital. *Am J Hosp Palliat Care*. 2020; 37(3):179–184. <https://doi.org/10.1177/1049909119862785>.
9. Winquist E, Kuruvilla S, Nichols AC, Lenehan JG, Macneil SD, Palma DA. Early mortality with immune checkpoint inhibitors (IOs) in solid tumors: an inconvenient truth? *J Clin Oncol*. 2018; 36(15) suppl:12121.