The Oncologist, 2023, **28**, 351–357
https://doi.org/10.1093/oncolo/oyac266
Advance access publication 6 February 2023
Original Article

Decision-Making and Health-Related Quality of Life in Patients with Melanoma Considering Adjuvant Immunotherapy

Thomas M. Atkinson[1], Jennifer L. Hay[1,3], Soo Young Kim[1], Elizabeth Schofield[1], Michael A. Postow[2,3], Parisa Momtaz[2,3], Allison Betof Warner[2,3], Alexander N. Shoushtari[2,3], Margaret K. Callahan[2,3], Jedd D. Wolchok[2,3,4], Yuelin Li[1], Paul B. Chapman[*,2,3]

[1]Department of Psychiatry & Behavior Sciences, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[2]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[3]Weill Cornell Medical College, New York, NY, USA
[4]Ludwig Institute for Cancer Research, New York, NY, USA

*Corresponding author: Paul B. Chapman, MD, Memorial Sloan Kettering Cancer Center, 300 East 66th Street, New York, NY 10065, USA. Tel: +1 646 888 4162; Fax: +1 646 888 4253; Email: chapmanp@mskcc.org

Abstract

Background: Adjuvant anti-PD1 treatment improves relapse-free survival (RFS) but has not been shown to improve overall survival (OS) in melanoma and is associated with risks of immune-related adverse events (irAEs), some permanent. We identified factors patients consider in deciding whether to undergo adjuvant anti-PD1 treatment and assessed prospective health-related quality of life (HRQoL), treatment satisfaction, and decisional regret.

Patients and Methods: Patients with stage IIIB-IV cutaneous melanoma and free of disease, were candidates for adjuvant anti-PD1 immunotherapy, and had not yet discussed adjuvant treatment options with their oncologist were eligible. Participants viewed a 4-minute informational video tailored to their disease stage which communicated comprehensive, quantitative information about the risk of relapse both with and without adjuvant treatment, and risks of each irAE before deciding whether or not to opt for adjuvant therapy. We collected data on demographics, HRQoL, and attitudes toward adjuvant treatment over 1 year.

Results: 14/34 patients (41%) opted for adjuvant anti-PD1 immunotherapy, 20/34 (59%) opted for observation. Patients choosing adjuvant immunotherapy scored higher on HRQoL social well-being at pre-treatment, were more likely to endorse positive statements about adjuvant immunotherapy, and to perceive that their physician preferred adjuvant therapy. They had lower decisional regret and higher satisfaction, even if they experienced toxicity or recurrence.

Conclusions: When provided with comprehensive quantitative information about risks and benefits of adjuvant anti-PD1 immunotherapy, 20/34 (59%) of patients opted for observation. Patients choosing adjuvant immunotherapy had lower decisional regret and higher satisfaction over time even if they had poorer outcomes in treatment.

Implications for Practice

When patients are provided quantitative information about their risk of relapse (eg, the magnitude of improved RFS with adjuvant therapy, the fact that adjuvant therapy is not known to improve OS since treatment can be effective at relapse if needed, the specific risk of irAEs with the understanding that some are permanent), a substantial proportion prefer observation only. Their decision is influenced by friends and family, perceived physician preference, and other personal factors. Patients opting for adjuvant treatment have less decisional regret, even if they experience irAEs or recurrence.

Introduction

In stage III melanoma patients who are free of disease after surgical resection of involved lymph nodes, a year of adjuvant treatment with PD1-blocking antibodies (nivolumab or pembrolizumab) is an FDA-approved treatment option. Approval was based on randomized clinical trials of nivolumab versus ipilimumab[1] and pembrolizumab versus placebo,[2] which showed improved relapse-free survival (RFS) in patients receiving adjuvant anti-PD1 immunotherapy. It remains unknown whether adjuvant immunotherapy is associated with improved overall survival (OS) compared to immunotherapy at the time of relapse. On the other hand, adjuvant immunotherapy is associated with frequent immune-related adverse events (irAEs),[3,4] some of which are serious and likely

Received: 11 October 2022; Accepted: 30 November 2022.

permanent. irAEs that are acceptable when treating patients with metastatic disease may be less acceptable in the adjuvant setting when there is a substantial possibility of disease-free survival with surgery alone and effective treatment options in the event of metastatic recurrence.

As a result, full patient discussions of the risks and benefits of adjuvant anti-PD1 immunotherapy are complicated. In this pilot study, we produced 4 short videos (1 each for stage IIIB, IIIC, IIID, and IV patients) quantifying the risks of relapse, the benefits of adjuvant anti-PD1 therapy, and the risks of toxicities. Patients viewed the video prior to discussion with their oncologist. We examined how patients make the decision of whether or not to undergo adjuvant anti-PD1 immunotherapy when they are made aware of the magnitude of improvement in RFS, the incidence and potential consequences of irAEs, the lack of demonstrated OS improvement compared to treatment at the time of relapse, and that observation without adjuvant immunotherapy is a reasonable option. We also examined factors that influenced patient decisions, their satisfaction with their decision prospectively, health-related quality of life (HRQoL), and regret related to that decision at multiple time points over the subsequent year after they made their treatment decision.

Methods

Patients and Trial Design

In this prospective cohort pilot study, adults (ie, age ≥18) were eligible if they had stage IIIB, IIIC, IIID, or IV cutaneous melanoma, were free of disease after surgical resection, were being offered adjuvant immunotherapy (ie, nivolumab or pembrolizumab), had not yet formally discussed their treatment options with their medical oncologist and could provide written informed consent. Patients were ineligible if they had received prior checkpoint inhibitor therapy or were candidates for adjuvant dabrafenib/trametinib therapy. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline and was approved by the Memorial Sloan Kettering Cancer Center (MSK) Institutional Review Board.

After enrollment, patients viewed a 4-min informational video developed for this study that featured an actor delivering a script developed by the MSK Melanoma Disease Management Team to communicate comprehensive information about the risks and benefits of adjuvant anti-PD1 immunotherapy given their specific melanoma stage (video for stage IIIB patients https://youtu.be/3AW4H2WaAIw; video for stage IIIC patients https://youtu.be/qi6kbf1xuuE; video for stage IIID patients https://youtu.be/5IUP95glzc0; video for stage IV patients https://youtu.be/ipg8EqdhzKQ). The videos made 3 major points. First, the risk of relapse for the patient's specific stage and substage was communicated. This was based on published data from the placebo group of the adjuvant dabrafenib/trametinib COMBI-AD trial[5] because, at the time, this was the most comprehensive source of RFS data available by stage III substage. Risk of relapse for stage IV patients was based on large retrospective data.[6,7] Second, the benefits of adjuvant anti-PD1 were stated as improved 18-month RFS by 20%-25% based on published data available at the time.[1,4] The video expressly stated there were no data indicating improved OS compared to treatment at the time of relapse. Third, a comprehensive list of irAEs was provided along with the likelihood of each one, based on published data.[1] The video also indicated which irAE would likely be permanent. By using these videos, we ensured that all patients received the same comprehensive, quantitative information on the risks and benefits. Patients could watch the video as many times as they wished. Since the videos were only available in English, patients had to speak English to participate in this study.

Patients then continued their visit with the medical oncologist who conducted their usual visit and was available to answer any questions. The patient completed a demographics questionnaire, the Functional Assessment of Cancer Therapy-General (FACT-G) and the melanoma module (FACT-M),[8] and an adapted version of the Adjuvant Treatment Beliefs Scale (ATBS)[9] (see Supplementary Materials), which asks patients to indicate the likelihood of positive and negative outcomes related to treatment with adjuvant immunotherapy. This measure differed from the original ATBS in that the term "adjuvant nivolumab or pembrolizumab" was substituted for the term "chemotherapy" in the stem "If I am treated with chemotherapy, then." Patients then met with their oncologist to discuss treatment options further and make their treatment decision. Prior to being made aware of their patient's decision, the medical oncologist completed a single-item assessment to indicate their preference regarding the patient's treatment (preferred adjuvant anti-PD1 treatment, preferred observation, no preference). This was not shared with the patient.

At 3 months, patients completed a face-valid internally developed brief questionnaire and reported which factors (eg, perceived physician recommendation, speaking with family/loved ones, the provided informational video) affected their decision. Patients also completed the FACT-M, along with measures of treatment satisfaction (ie, Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-General; FACIT-TS-G)[10] and decisional regret (ie, Decisional Regret Scale; DRS).[11] FACT-M, FACIT-TS-G, and DRS were assessed again at 6-, 9-, and 12-months post-enrollment (see Supplementary Material). Patients underwent cross-sectional imaging every 3 months. Relapse and irAE data were extracted from the electronic medical record.

Statistical Analysis

This was an observational pilot trial with no formal hypothesis testing. Assuming there would be an equal distribution of adjuvant therapy acceptors and rejectors, a sample size of $N = 50$ provided 80% power to detect a moderate effect size, with a standardized difference of at least $d = 0.81$ using an independent samples t-test.

Baseline participant characteristics, disease, HRQoL, and PRO measures are reported overall and by treatment decision. Group comparisons were based on statistical methods appropriate for the variable types, including X^2, Fisher's exact, independent samples t, and Wilcoxon median tests. HRQoL and PRO measures were scored according to published scoring rules, and the average subscale scores between the treatment decisions (immunotherapy vs. observation groups) were compared primarily by CIs, across time points at baseline, 3-, 6-, 9-, and 12-months post-enrollment. Among these outcomes, higher scores represented better outcomes generally, except in the decisional regret scale, where lower scores represented fewer regrets and thus better outcomes. Individual items from the adapted ATBS prior to patient decision were compared between groups using independent samples t-tests. All analyses were done using R statistical software 4.2.0.[12]

Results

Between February 2019 and September 2020, 39 patients from the practices of 6 MSK clinicians were enrolled in the study. Although our accrual target was 50, we had to close accrual prematurely due to the COVID-19 pandemic. Five patients were deemed ineligible or inevaluable (2 elected to start adjuvant dabrafenib/trametinib before patients with BRAF V600 mutated tumors were excluded from the study, 2 were found to have metastatic disease, and 1 withdrew consent). Thirty-four patients completed at least the baseline surveys (Table 1). The median age was 60.5 (range 26-88). Participants were mostly male (65%), White (94%), non-Hispanic (88%), and had a college degree or higher (74%). Most patients had either stage IIIB (38%) or IIIC (44%). Nine patients (27%) had undergone a lymph node dissection (LND) prior to enrollment.

Factors Associated with Patient Decisions

Of the 34 participants, 14 (41%; 95%CI, 25-58) elected to start adjuvant anti-PD1 therapy—all received nivolumab. Three of these patients experienced irAEs (1 patient with colitis, 1 patient with hypothyroidism, and 1 patient with a combination of hypothyroidism, hepatitis, and vitiligo). Twenty patients (59%; 95%CI, 42-75) chose observation. During the year on-study, melanoma relapse was seen in 6/14 (43%) of patients on adjuvant nivolumab and 10/20 (50%) of patients on observation.

Patients who chose adjuvant nivolumab scored higher on baseline FACT-G social well-being (P = .03) compared to those who chose observation and continued to score higher throughout the year of follow-up but did not differ on any other facets of HRQoL (Fig. 1). There were no other differences in the FACT-G subtests (physical, emotional, or functional well-being) or in the FACT-M (Supplementary Fig. S1).

Adjuvant treatment beliefs differed by treatment decision (Table 2). Those who chose observation had significantly higher scores on negative beliefs about treatment, such as concerns about length of time to get back to normal daily life (mean difference = 0.73, P = .047), looking awful (mean difference = 0.77, P = .01), or being worn out by frequent hospital visits, even though there were no extra visits scheduled for patients on adjuvant therapy (mean difference = 0.73, P = .03), and significantly lower scores on positive aspects of treatment, such as "life will be prolonged" (mean difference = −0.76, P = .016). The pattern was reversed for those who chose adjuvant treatment.

Table 1. Patient characteristics.

	Patients opting for adjuvant treatment (n = 14)	Patients opting for observation (n = 20)	Total (N = 34)	P-value
Age				.40
Mean (SD)	57.79 (9.32)	61.35 (13.41)	59.88 (11.87)	
Median (range)	57 (45-75)	63.5 (26-88)	60.5 (26-88)	
Gender—*n* (%)				.44
Women	6 (42.9%)	6 (30.0%)	12 (35.3%)	
Men	8 (57.1%)	14 (70.0%)	22 (64.7%)	
Race—*n* (%)				.99
White	13 (92.9%)	19 (95%)	32 (94.1%)	
Black or African American	1 (7.1%)	0 (0%)	1 (2.9%)	
Asian/Pacific Islander	0 (0%)	1 (5.0%)	1 (2.9%)	
Ethnicity—*n* (%)				.20
Non-Hispanic	14 (100%)	16 (80.0%)	30 (88.2%)	
Hispanic	0 (0%)	2 (10.0%)	2 (5.9%)	
Not reported	0 (0%)	2 (10.0%)	2 (5.9%)	
Education—*n* (%)				.16
12 Years/completed high school	0 (0.0%)	4 (20.0%)	4 (11.8%)	
Some college	2 (14.3%)	3 (15.0%)	5 (14.7%)	
College graduate	7 (50.0%)	6 (30.0%)	13 (38.2%)	
Postgraduate	5 (35.7%)	7 (35.0%)	12 (35.3%)	
Cancer stage—*n* (%)				.24
IIIB	4 (28.6%)	9 (45.0%)	13 (38.2%)	
IIIC	6 (42.9%)	9 (45.0%)	15 (44.1%)	
IIID	2 (14.3%)	0 (0%)	2 (5.9%)	
IV	2 (14.3%)	2 (10.0%)	4 (11.8%)	
Lymph node dissection—*n* (%)				.31
Yes	4 (28.6%)	5 (25.0%)	9 (26.5%)	

Race tested via Fisher's Exact test with White versus all others. Education and cancer stage tested using Mantel-Haenszel X^2 test. FACT-M subscales tested using 2-sample Wilcoxon test. FACT-G indicates functional assessment of cancer therapy—general.

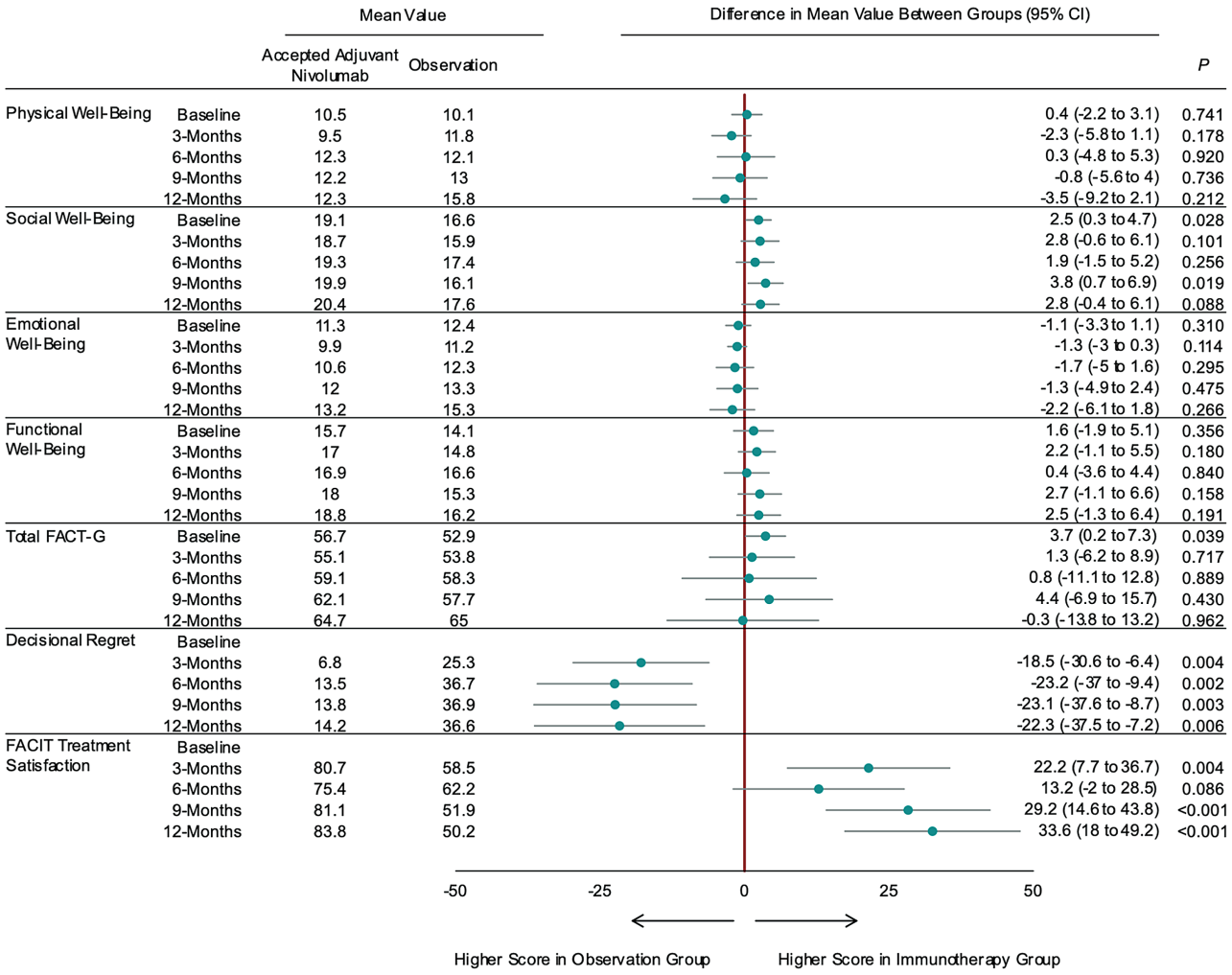

Figure 1. Mean values for each subtest for treated and observation groups are shown. There were no baseline scores for decisional regret and FACIT treatment satisfaction. For each subtest, lower scores indicate lower levels of well-being, more regret, and less satisfaction. Subtest scores ranged from 0 to 28 for physical well-being, social well-being, and functional well-being. Emotional well-being ranged from 0 to 24; total FACT-G ranged from 0 to 108; decisional regret and FACIT treatment satisfaction ranged from 0 to 100. Differences in mean scores between the 2 cohorts are shown with 95% CIs. *P* values were calculated using independent t tests.

These patients were more likely to feel that treatment would reduce the risk of recurrence (mean difference = −0.68, $P = .006$), and would increase their confidence that they had contributed toward their cure (mean difference = −0.79, $P = .02$). There were no significant differences between treatment groups on expectations of toxicities or recovery after surgery (all *P*-values > .05).

Physicians favored adjuvant therapy for their patients in 35% of cases, favored observation in 35% of cases, and had no preference in 29% of cases. Although these preferences were not shared with the patients, patient choice regarding adjuvant therapy (accept vs. observation) significantly correlated with the physician's preference (accept vs. observation/no preference) ($r = 0.31$, $P = .013$). Perceived physician preference, along with speaking with family and loved ones, the informational video, and patient personal reasons were all factors that influenced most patients' decisions (Table 3). Patients who opted for adjuvant therapy were more likely than patients opting for observation to be influenced by what they perceived to be their oncologist's preference ($P = .021$).

HRQoL, Satisfaction, and Decisional Regret Post-Decision

There was generally very low decisional regret for all patients but those who chose adjuvant immunotherapy had significantly lower decisional regret compared to those who opted for observation (Fig. 1). There was a small, significant increase in decisional regret over time for all patients, most noticeably between the 3-month and 6-month follow-ups. Patients who opted for adjuvant therapy also had greater treatment satisfaction (Fig. 1). We assessed a variety of variates for association with decisional regret, including development of toxicity or relapse, (Table 4). There was no association between any of the variables; one exception was that patients who had undergone an LND had less decisional regret compared to those without LND.

Discussion

Adjuvant anti-PD1 immunotherapy is FDA-approved for stage III (and recently, stage IIB and IIC)[13] melanoma patients, and while it has been shown to improve RFS, there is no

Table 2. Adjuvant treatment beliefs assessed prior to patient decision.

Adjuvant treatment beliefs scale item and direction of statistical difference	Overall mean (SD) $n = 34$	Patients opting for adjuvant treatment mean (SD) $n = 14$	Patients opting for observation mean (SD) $n = 20$	*P*-value
Beliefs more frequent in patients who opted for adjuvant treatment				
I will have done everything I can to be cured.	3.82 (1.27)	4.29 (1.27)	3.50 (1.19)	**.021**
My life will be prolonged.	3.91 (0.90)	4.36 (0.84)	3.60 (0.82)	**.016**
The risk of the disease coming back will be less.	4.03 (0.72)	4.43 (0.65)	3.75 (0.64)	**.006**
I will be actively contributing something toward my cure.	4.18 (0.81)	4.64 (0.63)	3.84 (0.76)	**.004**
My chance of being cured will be greater.	3.94 (0.83)	4.29 (0.91)	3.68 (0.67)	**.044**
I will be less worried about the disease recurring.	3.59 (1.10)	4.29 (0.91)	3.10 (0.97)	**.002**
Beliefs more frequent in patients who opted for observation				
I will take longer before I can get on with my normal daily life.	2.50 (1.08)	2.07 (1.07)	2.80 (1.01)	**.047**
I will think I am in a bad state of health.	2.27 (0.88)	1.86 (0.86)	2.58 (0.77)	**.026**
I will look awful.	1.88 (0.88)	1.43 (0.65)	2.20 (0.89)	**.009**
I will be worn out by frequent visits to the hospital.	2.50 (1.24)	2.07 (1.38)	2.80 (1.06)	**.032**
Beliefs equally prevalent in both groups				
I will experience side effects such as nausea, fatigue, and hair loss.	3.00 (0.74)	2.86 (0.77)	3.10 (0.72)	.370
I will recover more slowly, physically, after surgery	2.35 (0.99)	2.25 (1.04)	2.42 (1.00)	.716

Note: Items are coded 1 = definitely not, to 5 = definitely. Differences between patients opting for adjuvant treatment and patients opting for observation were tested via 2-sample Wilcoxon test.
Values in bold indicate statistical significance.

Table 3. Self-reported factors that influenced patient decisions.

	Accepted adjuvant nivolumab, $n = 12$	Observation, $n = 17$	*P*-value
Perceived physician recommendation	12 (100%)	11 (64.7%)	.028
Speaking with family/loved ones	10 (83.3%)	13 (76.4%)	1.0
Informational video	10 (83.3%)	13 (76.4%)	1.0
Personal reasons	11 (91.7%)	15 (88.2%)	1.0

Data from 5 patients were missing due to patient withdrawal from study (2), patient failed to complete the month 3 questionnaire (2), or patient died (1).

evidence to date that it improves OS compared to treatment at the time of relapse. After our study was in progress, 3-year follow-up data from Keynote 054 (adjuvant pembrolizumab vs. placebo) was published.[2] The RFS data from the placebo group and the magnitude of RFS improvement with pembrolizumab were consistent with the data stated in our videos. Adjuvant anti-PD1 immunotherapy is associated with irAEs, some of which are serious and potentially permanent. Since many of these patients would not have relapsed after surgery, the risk/benefit analysis is complex and patients often struggle in deciding whether or not to undergo adjuvant anti-PD1 immunotherapy. In this study, we provided patients with clear and quantitative information on the risks and benefits of anti-PD1 adjuvant immunotherapy using standardized informational videos in an attempt to ensure that each study participant received the same comprehensive information about the risks and benefits of adjuvant immunotherapy. We studied predictors and prospective outcomes of treatment decisions. In this setting, the majority of our patients (20/34) opted for observation.

Treatment choices reflected distinct beliefs about adjuvant therapy. Patients who chose observation were more influenced by the burdens of treatment, such as a time associated with continued clinic visits, and the longer trajectory to feeling better, whereas those who opted for adjuvant treatment were more influenced by the belief that they would be actively contributing to an improved outcome. Patients who opted for treatment were more likely to believe that treatment may prolong their lives even though the informational video stated that we do not have evidence that this is true. Patients reported that the video helped them make a decision about adjuvant therapy. Other factors that influenced decision-making were speaking with family or friends, personal reasons, and the patient's perception of what they thought their oncologist preferred, although perception of physician preference contributed more strongly to the decision for treatment rather than observation.

Most of the HRQoL metrics (eg, physical, emotional, or functional well-being) were no different between the patients

Table 4. Predictors of decisional regret at 12-months.

Predictors	Beta coefficients	95% CI	*P*-value
Age	0.58	–0.17-1.32	.12
Male vs. female	2.37	–15.63-20.37	.79
White vs. non-White	7.04	–26.66-40.74	.67
Non-Hispanic vs. Hispanic	–19.81	–52.71-13.08	.23
College graduate/more vs. some college/less	–17.13	–50.26-16.00	.30
Relapsed vs. did not relapse	3.75	–13.58-21.08	.66
Stage IIIB vs. stage (IIIC, IIID, IV)	–6.16	–23.65-11.33	.48
CLND vs. no CLND	–19.82	–39.47-0.17	**.05**
irAEs	–5.45	–33.50-22.60	.69
Colitis	–17.14	–63.61-29.33	.46
Hypothyroid	1.02	–32.79-34.83	.95
Vitligo	–27.5	–73.19-18.19	.23

*Tested using univariate linear regression.
Abbreviations: CLND, complete lymph node dissection; irAE; immune-related adverse event.

opting for adjuvant therapy and those who chose observation. However, patients opting for treatment had less decisional regret and higher social well-being over the subsequent year compared to those who chose observation. Of note, social well-being was also higher at baseline among those who chose treatment over observation, possibly reflecting enhanced social support that contributed to opting for a treatment associated with increased medical burdens or toxicities.

Overall, decisional regret was low in all patients although decisional regret was lower in patients who chose adjuvant therapy compared to those who chose observation. This may have an impact on patient-physician discussions and patient reflection at the time of treatment choice. Decisional regret was also lower in patients who had undergone LND consistent with the idea that more aggressive treatment may be associated with less decisional regret. Surprisingly, decisional regret was not affected by whether or not the patient recurred or had an irAE.

One obvious limitation of the study is that the cohort size is relatively small and the study was conducted at a single tertiary cancer center in New York City among participants who had high levels of formal education. Another limitation was that we had to limit participation to English-speaking patients because resources did not allow us to produce informational videos in different languages. These factors may limit the generalizability of the results. However, the methods used in this study, including the informational video, can be applied to other populations of patients considering adjuvant anti-PD1 immunotherapy. It will be of interest to determine if the findings in this study are also seen in cohorts in different geographical, social, and cultural settings as well as different types of cancers. We believe that instructional videos may be useful in other clinical situations to explain risks and benefits to patients.

Conclusion

The decision whether to undergo adjuvant anti-PD1 immunotherapy is a complex one that is affected by the patient's pre-treatment sense of well-being and attitudes about the value of adjuvant therapy and the potential disadvantages and toxicities. The decision is influenced by providing objective information on risks and benefits, by speaking with family and friends, and by what the patient perceived to be the physician's preference. In this context, when patients were provided quantitative information on the risks and benefits of adjuvant anti-PD1 therapy and offered a choice between adjuvant therapy and observation, a minority of patients opted for adjuvant therapy, although given the small sample size, the 95% confidence limits ranged from 25%-58%). These patients experienced less decisional regret over the year of observation than patients who opted for observation.

Funding

This study was supported by grants from the NCI (P30 CA08748) and the Parker Institute for Cancer Immunotherapy.

Conflict of Interest

Michael A. Postow reported receiving consulting fees from BMS, Merck, Novartis, Eisai, Pfizer, and Chugai and support to institutions from RGenix, Infinity, BMS, Merck, and Novartis. Allison Betof Warner reported a consulting relationship with BMS. Alexander N. Shoushtari reported serving on advisory boards for Bristol-Myers Squibb, Immunocore, and Novartis and trial support from Bristol- Myers Squibb, Immunocore, Novartis, Tagovax, Polaris, Pfizer, Checkmate Pharmaceuticals, Foghorn Therapeutics, Linnaeus Therapeutics, and Prelude Therapeutics. Margaret K. Callahan reported research support (institutional) from Bristol-Myers Squibb and consulting fees from Merck, InCyte, Moderna, ImmunoCore, and AstraZeneca. Jedd D. Wolchok reported being a consultant for Apricity, CellCarta, Ascentage Pharma, AstraZeneca, Astellas, Bicara Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Dragonfly, Georgiamune, Imvaq, Larkspur, Maverick Therapeutics, Psioxus, Recepta, Tizona, and Sellas; grant/research support from Bristol Myers Squibb and Sephora; and equity in Apricity, Arsenal IO, Ascentage, Beigene, Imvaq, Linneaus, Georgiamune, Maverick, Tizona Pharmaceuticals, and Trieza. Paul B. Chapman disclosed consulting for Merck, Immunocore, AstraZeneca, and Pfizer and equity interest in Rgenix. The other authors indicated no financial relationships.

Author Contributions

Conception/design: T.M.A., J.L.H., P.B. C. Provision of study material or patients: M.A.P., P.M., A.B.W., A.N.S., M.K.C., J.D.W., P.B.C. Collection and/or assembly of data: S.Y.K., E.S. Data analysis and interpretation: T.M.A., J.L.H., S.Y.K., E.S., Y.L., P.B.C. Manuscript writing: T.M.A., J.L.H., S.Y.K., M.A.P., P.M., A.B.W., A.N.S., M.K.C., J.D.W., P.B.C. Final approval of manuscript: All authors.

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary Material

Supplementary material is available at *The Oncologist* online.

References

1. Weber J, Mandala M, Del Vecchio M, et al. Adjuvant nivolumab versus ipilimumab in resected stage III or IV melanoma. *N Engl J Med*. 2017;377:1824-1835. https://doi.org/10.1056/nejmoa1709030.
2. Eggermont AMM, Blank CU, Mandala M, et al. Longer follow-up confirms recurrence-free survival benefit of adjuvant pembrolizumab in high-risk stage III melanoma: updated results from the EORTC 1325-MG/KEYNOTE-054 trial. *J Clin Oncol*. 2020;38:3925-3936. https://doi.org/10.1200/jco.20.02110.
3. Mandala M, Larkin J, Ascierto PA, et al. Adjuvant nivolumab for stage III/IV melanoma: evaluation of safety outcomes and association with recurrence-free survival. *J ImmunoTher Cancer*. 2021;9(8):e003188. https://doi.org/10.1136/jitc-2021-003188.
4. Eggermont AMM, Blank CU, Mandala M, et al. Adjuvant pembrolizumab versus placebo in resected stage III melanoma. *N Engl J Med*. 2018;378:1789-1801.
5. Long GV, Stroyakovskiy D, Gogas H, et al. Combined BRAF and MEK inhibition versus BRAF inhibition alone in melanoma. *N Engl J Med*. 2014;371(20):1877-1888.
6. Ollila DW, Morton DL. Surgical resection as the treatment of choice for melanoma metastatic to the lung. *Chest Surg Clin N Am*. 1998;8:183-196.
7. Ollila DW, Hsueh EC, Stern SL, Morton DL. Metastasectomy for recurrent stage IV melanoma. *J Surg Oncol*. 1999;71:209-213. https://doi.org/10.1002/(sici)1096-9098(199908)71:4<209::aid-jso1>3.0.co;2-2.
8. Cormier JN, Ross MI, Gershenwald JE, et al. Prospective assessment of the reliability, validity, and sensitivity to change of the functional assessment of cancer therapy-melanoma questionnaire. *Cancer*. 2008;112:2249-2257. https://doi.org/10.1002/cncr.23424.
9. Jansen SJ, Otten W, Baas-Thijssen MC, et al. Explaining differences in attitude toward adjuvant chemotherapy between experienced and inexperienced breast cancer patients. *J Clin Oncol*. 2005;23:6623-6630. https://doi.org/10.1200/jco.2005.07.171.
10. Peipert JD, Beaumont JL, Bode R, et al. Development and validation of the functional assessment of chronic illness therapy treatment satisfaction (FACIT TS) measures. *Qual Life Res*. 2014;23:815-824.
11. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. *Med Decis Making*. 2003;23:281-292. https://doi.org/10.1177/0272989x03256005.
12. Team RC. *R: A Language and Environment for Statistical Computing*. Vienna, Austria, R Foundation for Statistical Computing; 2022. Retrieved from http://www.R-project.org
13. Luke JJ, Rutkowski P, Queirolo P, et al. Pembrolizumab versus placebo as adjuvant therapy in completely resected stage IIB or IIC melanoma (KEYNOTE-716): a randomised, double-blind, phase 3 trial. *Lancet*. 2022;399:1718-1729. https://doi.org/10.1016/s0140-6736(22)00562-1.