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ORIGINAL ARTICLE

A supportive care intervention for people with metastatic melanoma being treated with immunotherapy: a pilot study assessing feasibility, perceived benefit, and acceptability

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Abstract

Introduction Increasing numbers of metastatic melanoma (MM) patients are receiving immunotherapy treatment, including pembrolizumab, and the impact on their well-being is underexplored.

Objectives To assess the feasibility of a multimodal supportive care program to MM patients being treated with pembrolizumab.

Methods This pre-post-test feasibility cohort study recruited MM participants treated with pembrolizumab: (i) supportive care intervention with usual care and (ii) usual care. The intervention comprised comprehensive medical assessment by supportive care physician (SCP), exercise physiologist (EP), and dietitian then a tailored supportive care program. Programs included exercise, dietary advice, non-invasive complementary therapies, and psychology consultation. Outcome measures included adherence, patient-reported symptoms, anxiety and depression, and toxicity. Descriptive data are reported.

Results We recruited 28 participants: 13 intervention and 15 control; three did not complete the study. Most were male, with median age 66 (range 42–85) years. All intervention participants completed baseline assessments with SCP, EP, and dietitian. Two missed follow-up with EP or dietitian. Symptoms most troubling at baseline were as follows: fatigue ($n = 6$), sleep ($n = 6$), general aches and pains ($n = 5$), and memory ($n = 4$). All intervention participants were prescribed 16 exercise sessions; 8 (50%) completed all; overall exercise adherence was 85%. Integrative therapies were accessed by 85% (11) participants. Immunotherapy-related adverse event rates were low and SCP consultation identified symptoms not captured by CTCAE 4.0.

Conclusions A holistic supportive care intervention tailored to individual needs is feasible. The symptom burden in MM patients was low. Further investigation of the intervention is warranted, focused on populations with higher symptom burden to improve outcomes.

Keywords Metastatic melanoma · Immune checkpoint inhibitor · Immunotherapy · Oncology · Supportive care · Feasibility study · Pilot study

Introduction

Australia has the second highest incidence of melanoma in the world, and it is the fourth most common cause of cancer in Australia accounting for 3.8% of all cancer deaths in 2016. The incidence is rising globally [1]. Previously, diagnosis with stage IV metastatic melanoma meant incurable progressive disease and imminent death. With the introduction of checkpoint inhibitors, such as the programmed death-1 (PD-1) inhibitors (pembrolizumab and nivolumab) and anti-cytotoxic-T lymphocyte-associated antigen 4 antibody (ipilimumab), many patients experience improved survival. This has transformed advanced

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melanoma into a chronic disease for many patients with durable tumour responses and median overall survival exceeding 2 years [2–4]. In 2015 and 2016, pembrolizumab and nivolumab respectively were made available on the Pharmaceutical Benefits Scheme in Australia for patients with metastatic melanoma. [5] Checkpoint inhibitor usage (as monotherapy or in combination) in the general clinical community has increased rapidly with the potential to impact symptom burden in these patients [6].

As advanced melanoma patients are living longer, their well-being, functional status, and toxicity from treatment require monitoring and management. Early identification coupled with early intervention of immune-related adverse events (IrAEs) is critical to care in patients receiving pembrolizumab and similar immunotherapy agents [7]. In addition, novel supportive care interventions may play a role in minimising the impact of treatment, disease, and steroid-related symptoms.

Supportive cancer care aims to keep people living well while managing treatment-related toxicities. A whole person approach to well-being can improve patient quality of life (QoL) [8]. Exercise, nutrition, psychological support, and supportive medical care contribute to improved patient well-being and play an important role in fatigue management [9–13], with fatigue [14, 15] being the most common symptom experienced by patients receiving immunotherapy [15, 16]. Selected evidence-based, non-invasive complementary therapies have increasingly been found beneficial in the cancer supportive care setting [17].

Our unit has developed a model of supportive care aiming to ensure supportive care is accessed by those patients in need. Our model involves routine referral to supportive care services for a holistic assessment by a supportive care practitioner. Based on symptoms and patient preferences, tailored supportive care is available including exercise, nutritional support, psycho-oncology, and non-invasive complementary therapies [18]. Patients with metastatic melanoma were identified as a group who may benefit from this model of care, as they are predominantly treated with immunotherapy which is associated with novel toxicities. If the model of care was feasible in this population, it may prove useful in other cancer populations with higher symptom burden, such as lung or kidney cancer, for whom immunotherapy agents are emerging as standard of care.

This study aimed to assess the feasibility of providing a multimodal supportive care program to metastatic melanoma patients treated with pembrolizumab. In addition, we aimed to describe patients' self-rated QoL and well-being, disease and treatment-related symptoms, and any change in pembrolizumab treatment.

Method

Study design

We conducted a pre-/post-test cohort study including three patient cohorts: (1) patients established on treatment with pembrolizumab with responding or stable disease; (2) patients commencing immunotherapy (starting pembrolizumab within 1 month registration into study); and (3) control group: patients eligible for cohort 1 or 2 declining supportive care intervention. Due to a change in referral patterns, recruitment to cohort 2 was limited ($n = 1$), thus participants in cohorts 1 and 2 were combined into a single cohort, as all received the supportive care intervention, referred to as treatment group throughout the manuscript. See Fig. 1 for study design. Ethical approval for the study was provided by the Sydney Local Health District Concord zone Human Research Ethics Committee (HREC/15/CRGH/265).

Population

Patients with metastatic melanoma undergoing standard treatment with pembrolizumab were recruited from a single institution. Participants were required to be aged 18 years or older, diagnosed with advanced/metastatic melanoma, receiving or planned to start treatment with pembrolizumab, provide written informed consent, able to speak and read English sufficiently well to complete questionnaires, and take part in programs without an interpreter. Participants were excluded if they had medical, psychiatric, cognitive, or other conditions that may compromise ability to give informed consent, comply with the protocol, or complete the study, or other conditions that would contraindicate participation due to safety concerns or compliance with procedures. Patients with asymptomatic brain metastases were included in the study.

Procedure

Potentially eligible participants were referred to the study by their treating medical oncologist or cancer nurse. After consent, all baseline assessments, blood tests, and patient-reported outcome measures (PROMs) were completed. Validated instruments, including Functional Assessment of Cancer Therapy General (FACT-G) [15] and Fatigue (FACT-F) [19], Edmonton Symptom Assessment Scale (ESAS) [20], Hospital Anxiety and Depression Scale (HADS) [21], and PG-SGA, were used [22]. Adverse events were rated by clinicians using the NCI CTCAE 4.0 [23].

Treatment group participants were referred to the supportive care physician (SCP). All participants completed 3-weekly PROMs, until week 12, and all were invited to complete a

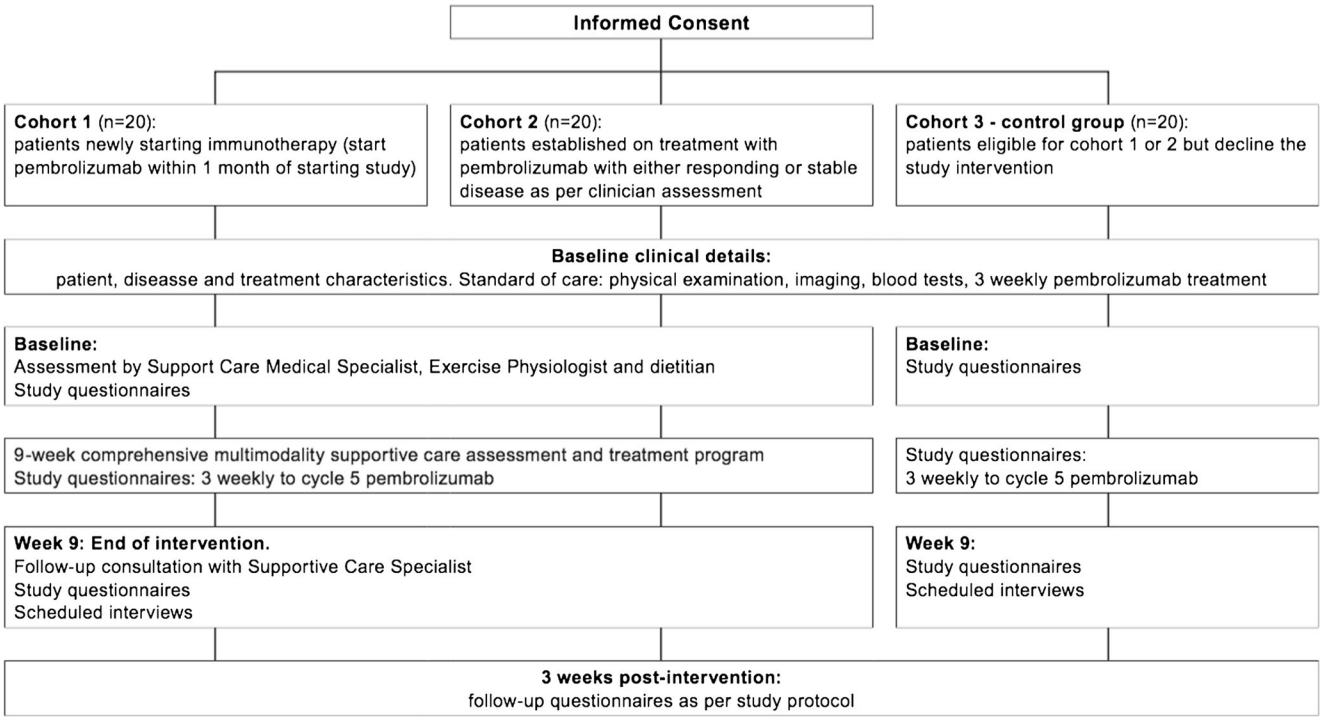

Fig. 1 Study schema

qualitative interview (reported elsewhere). During the 12-week study period adverse events, changes in pembrolizumab treatment and concomitant medications were recorded from medical records. Tumour response to pembrolizumab was determined by modified RECIST 1.1 [24]. Patients stopping immunotherapy continued in the study, completing study assessments as planned.

Control group patients were referred for supportive care interventions as per current standard practice (not following the holistic assessment intervention described below) (see Supplementary Table 1).

Pembrolizumab treatment

The 2 mg/kg delivered at 3-weekly intervals as per standard care. All participants were assessed at baseline by CT scan of the chest, abdomen, and pelvis within 2 weeks of commencing pembrolizumab and 12 weeks later. Control group: patients established on pembrolizumab treatment were assessed by CT scan of the chest, abdomen, and pelvis every 12 weeks.

Intervention—Living Well Program

Treatment group participants attended a 1-h holistic supportive care assessment with the SCP to identify supportive care needs and key patient concerns (see Supplementary Table 1 for details). Following this, all participants completed exercise and nutritional assessments, each 1 h in duration, with the exercise physiologist (EP) and dietitian. A tailored multimodal 8-week supportive care program was then devised to address each patient's individual supportive care needs in line with their preferences. Tailored programs all included an exercise program, the use of activity monitors (commercially available Misfit Shine™), home-based and exercise classes, as well as dietary changes, and complementary therapies (massage, reflexology yoga, qigong, mindfulness meditation, or acupuncture) provided by credentialed practitioners. Psycho-oncology services were offered to all patients. Participants were reviewed as required throughout the 9-week period by the SCP, EP, and dietitian. Follow-up consultations with the SCP, EP, and dietitian were completed at the end of the intervention.

Statistical considerations

The primary endpoint of feasibility was defined as completion of 75% of the recommended supportive care visits for each individual study participant. This was measured by assessing adherence to the recommended supportive care program (including refinements based on response to the individual program). Secondary endpoints of QoL, well-being, and disease- and treatment-related symptoms were descriptive across time-course of the study.

Descriptive data were reported to reflect number and severity of symptoms over time. Change in symptom scores were calculated using ESAS criteria for clinically

meaningful change, defined as change of 1 point on the symptom scale [20]. Change to immunotherapy treatment was reported descriptively. QoL scores were compared to Australian population normative data [25] using an online calculator [26] developed by the Quality of Life Office, University of Sydney.

Results

Between July 2016 and January 2017, 28 participants consented to take part. Most (57%) were male, born in Australia, and from major cities ($n = 22$, 78%). Their median age was 66 years (range 42–85). Complete demographic and disease details are provided in Table 1. Participants had a median time from first melanoma diagnosis of 8 years (range 0.17–30), and median time from diagnosis of metastatic disease of 2.75 years (range 0.17–11) given the duration they had lived with melanoma, they were a heavily pre-treated group, with 93% having had surgery, and 82% prior immunotherapy.

Living Well Program (intervention)

The Living Well Program (LWP) was feasible with adherence to program exceeding the pre-defined 75%. All intervention participants completed baseline assessments with SCP, EP, and DT. All completed end of intervention assessments with SCP, one participant did not complete this assessment with EP, and one with DT.

SCP holistic medical consultation

A total of 45 symptoms were recorded during the holistic supportive care assessment (see Table 2). Symptoms most frequently identified were fatigue and sleep disturbance. Symptoms identified in this assessment differed from those identified as part of adverse events reported by the medical oncology team.

Participants attending their second supportive care assessment were found to have improvement in 14 of their presenting symptoms, 4 were stable, 3 had deteriorated, and 22 were not noted in the follow-up assessment.

Dietitian assessments

At baseline, ten (77%) of intervention participants were classified as well-nourished or anabolic (SGA-A) and three (23%) as moderate or suspected malnutrition. The mean PGS-GA score was 3.77 (SD 2.242; range 1 to 8.12). The nutritional status of participants was stable over the intervention period, with 9-week mean PGS-GA score of 3.33 (SD 2.45). On the global assessment, 11 (85%) were classified as well-nourished or anabolic (SGA-A) and one moderate or suspected malnutrition.

Exercise physiology assessments

All participants in the intervention group were prescribed 16 sessions of exercise; recommended exercise programs were tailored to the preferences and capability of each participant. The mean number of sessions completed was 13.6 (range 5–16), achieving 85% (range 31–100%) adherence to prescribed exercise. Eight participants were prescribed a comprehensive program, including aerobic, resistance, and other classes; four were prescribed aerobic exercise only and one each resistance only, aerobic and yoga, and aerobic and qi gong. One did not complete any exercise sessions due to change in disease status and deterioration.

A home-based exercise program only was prescribed for eight participants, with the main reasons being: participant already exercising or logistical challenge of getting to hospital for classes. For the five who did take part in classes, one each attended 2, 3, 4, 5, and 6 classes.

End of intervention EP assessments were completed by 12/13 participants, reflecting 100 and 92% compliance with assessments pre- and post-intervention, respectively. Submaximal treadmill tests were not done on four occasions, due competing PET scan appointments, risk of falling, and active femoral metastases. The fitness parameters assessed were stable over the intervention and are reported in Table 2.

Complementary therapies

Use of recommended complementary therapies varied across the cohort, with 11/13 (85%) accessing between two and 18 sessions and two participants none. Massage was the most popular complementary therapy, used by nine participants (range one to six times each). Five participants received reflexology (range one to five sessions each) and mindfulness meditation and qigong classes were attended by two patients (one in each program). Two patients, 15% of the intervention group, accessed psychological services, with both these patients also accessing the touch therapies of massage or reflexology. Six patients missed scheduled appointments: two work-related, two due to scheduling problems, one was an inpatient, and one holiday-related.

Medical oncology assessment

Standard care continued throughout the study for both the intervention and control group.

Table 1 Participant characteristics and previous treatments

	Cohort 1 (intervention) $N = 13$ (%)	Cohort 2 (control) $N = 15$(%)	Total $N = 28$(%)
Sex			
Male	6 (21)	10 (36)	16 (57)
Female	7 (25)	5 (18)	12 (43)
Country of birth			
Australia	11 (39)	13 (46)	24 (86)
Other	2 (8)	2 (7)	5 (15)
English-speaking	13 (46)	15 (54)	28 (100)
Marital status			
Married/de facto	10 (36)	8 (29)	18 (64)
Separated/divorced	1 (4)	3 (11)	4 (14)
Single	0 (0)	2 (7)	2 (7)
Widowed	2 (7)	2 (7)	4 (14)
Work status			
Working (full-/part-time)	8 (28)	3 (11)	11 (39)
Retired	4 (14)	11 (39)	15 (54)
Home duties	1 (4)	0 (0)	1 (4)
Other	0 (0)	1 (4)	1 (4)
Smoking history			
Never	8 (29)	10 (36)	18 (64)
Previous	2 (7)	3 (11)	5 (18)
Current	1 (4)	1 (4)	2 (7)
Unknown	2 (7)	1 (4)	3 (11)
Median age (range)	61 (42–78)	72 (43–85)	66 (42–85)
Median years from diagnosis (range)	12.75 (0.33–24)	7 (0.17–30)	8 (0.17–30)
Median years from first metastatic disease (range)	3.3 years (0.17–11)	2.3 years (0.17–4)	2.75 (0.17–11)
Median months since starting pembrolizumab (range)	5 (0–22)	2 (0–32)	4 (0–32)
Prior surgery	12 (92)	14 (93)	26 (93)
Prior radiation therapy	6 (46)	5 (33)	11 (39)
Prior systemic therapy	12 (92)	11 (73)	23 (82)
Prior immunotherapy	12 (92)	11 (73)	23 (82)
Prior CAM	5 (38)	1 (7)	6 (22)
Current CAM	1 (8)	1 (7)	2 (8)
BRAF status			
Positive	4 (33)	7 (47)	11 (39)
Negative	8 (67)	8 (53)	16 (57)
Unknown	1 (8)	0 (0)	1 (3)

Pembrolizumab treatment

Pembrolizumab treatment was stopped or delayed in three participants during the study period. One due to symptomatic hypo-pituitary symptoms (pre-existing condition), two stopped soon after commencing due to disease progression, one of whom changed treatment, and the other had no further anti-cancer treatment.

Adverse events

Adverse event rates (related to both treatment and intervention) were low with the majority of participants at most time points not having a reported adverse event (see Table 3). There were two grade 3 adverse events (one jejunal stenosis, one low lymphocyte count). Supplementary Table 4 details adverse events at each time point.

Table 2 Results: supportive care physician symptom assessment and exercise physiologist fitness assessment pre- and post-intervention

Symptom	Initial SCP & EP assessment $N = 13$ (% of cohort reporting symptoms)	Follow-up SCP & EP assessment $N = 12$ (%of cohort)
Fatigue	6 (46%)	3 (25%)
Sleeping difficulties	6 (46%)	1 (8.3%)
Aches and pains generally	5 (38%)	NN
Cognitive issues	4 (31%)	1 (8.3%)
Anxiety	4(31%)	1 (8.3%)
Abdominal distension	3 (23%)	NN
Appetite changes	3 (23%)	1 (8.3%)
Joint/bone aches	3 (23%)	2 (17%)
Chest pain	1 (7.7%)	NN
Depression	1 (7.7%)	NN
Mouth dry & sore	1 (7.7%)	NN
Weight loss	1 (7.7%)	1 (8.3%)
Fitness assessment parameters		
Assessment component	Baseline $N = 13$	9 week $N = 12$
	Mean (SD)	Mean (SD)
Weight kg	83 (30)	82 (29)
Body fat %	32.0 (11.5)	32.61 (11.3)
Fat free mass kg	56.7 (19.7)	54.1 (18.6)
1RM strength (seated row)	32.1 (9.4)	37.9 (12.3)***
1RM strength (leg press)	67.1 (17.2)	57.9 (19.7)****
Number steps daily*	6842 (3758)	7147 (3037)*****
Hours of exercise	8.1 (0.75)	7.8 (0.7)******
VO2peak**	56 (30)	51 (34)

*From activity monitor

**Modified Balke Treadmill Test

***$N = 7$

****$N = 6$

*****$N = 10$

******$N = 9$

NN = not noted during assessment

A total of four patients died: one in the intervention and three in the control group; two patients died prior to completion of the study and a further two died after the 12-week assessment. All deaths were due to disease progression.

Patient reported outcome measures (PROMs)

Symptoms (ESAS)

At baseline, across both groups, sleep problems and fatigue were the most severe symptoms other than appetite, which was worse in the control group. Both groups reported memory problems. These symptoms remained moderate after completion of the intervention period, see Supplementary Table 2 for details.

There was little change in symptoms scores during the study. Figure 2 depicts the change in symptom scores for both cohorts. The intervention group demonstrated worsening dry mouth (1.47) and a slight improvement in memory (− 1.12). The control group did not report meaningful worsening in symptom scores, but did record slight improvement in numbness and tingling (− 1.07) and appetite (− 1.05) (Fig. 2).

Quality of life (FACT-G) Overall participants' general health-related QoL was comparable to normative data from the Australian population (see Supplementary Fig. 1) and remained stable over the duration of the study. Participants reported slightly poorer emotional well-being on the emotional well-being subscale of the FACT-G; this remained stable over the duration of the study.

Fatigue levels, generally, were good and participants were not reporting high levels of fatigue, nor did they report clinically meaningful change in either direction (see Supplementary Table 3).

Anxiety and depression (HADS) Most participants in the study were not anxious or depressed. Levels of clinical

Table 3 Results: number of adverse events at each time point by group

	None *N* (%)	1 *N* (%)	2 *N* (%)	3 *N* (%)	4 *N* (%)	5 *N* (%)	Missing
Group 2: intervention							
Baseline $n = 13$	9 (69)	1 (8)	2 (15)	0 (0)	0 (0)	0 (0)	1
Week 3 $n = 13$	7 (54)	2 (15)	2 (15)	1 (8)	0 (0)	0 (0)	1
Week 6 $n = 13$	6 (46)	1 (8)	2 (15)	1 (8)	0 (0)	0 (0)	3
Week 9 $n = 13$	7 (54)	1 (8)	2 (15)	1 (8)	1 (8)	0 (0)	2
Post-intervention $N = 13$	7 (54)	1 (8)	0 (0)	2 (15)	1 (8)	1 (8)	2
Group 3: usual care							
Baseline $n = 13$	11 (73)	3 (20)	1 (8)	0 (0)	0 (0)	0 (0)	0
Week 3 $n = 13$	8 (54)	2 (14)	1 (7)	1 (7)	1 (7)	0 (0)	2
Week 6 $n = 15$	8 (54)	1 (7)	2 (15)	1 (7)	0 (0)	0 (0)	3
Week 9 $n = 14$	8 (54)	1 (7)	2 (15)	1 (7)	1 (8)	0 (0)	2
Post-intervention $N = 13$	9 (69)	2 (15)	0 (0)	0 (0)	0 (0)	0 (0)	2

Adverse events were coding using the NCI Common Toxicity Criteria Terminology for adverse events v4.0

anxiety and depression were stable over the study in both groups (see Supplementary Table 4).

Discussion

Our LWP was feasible to deliver in practice, with participants completing assessments and adhering to their recommended supportive care program. Participants embraced the complementary therapies and exercise interventions available. Use of the ESAS identified additional symptoms, particularly related to mood, fatigue, and sleep, and facilitated discussion and tailoring of supportive care to patient need and preference. The intervention did not disrupt the work flow of the medical oncology team, making it feasible to implement in clinical practice. Ongoing correspondence and communication between the SCP and medical oncology team occurred as per standard practice.

Given the rapidly increasing number of patients receiving immunotherapy agents long-term and living with potential side effects, there is an imperative to develop effective supportive care strategies and clinical pathways to manage this population. The rapidity with which immunotherapy treatment has emerged as an effective therapy and been incorporated into clinical practice has not allowed time for supportive care interventions to develop alongside treatment. Early

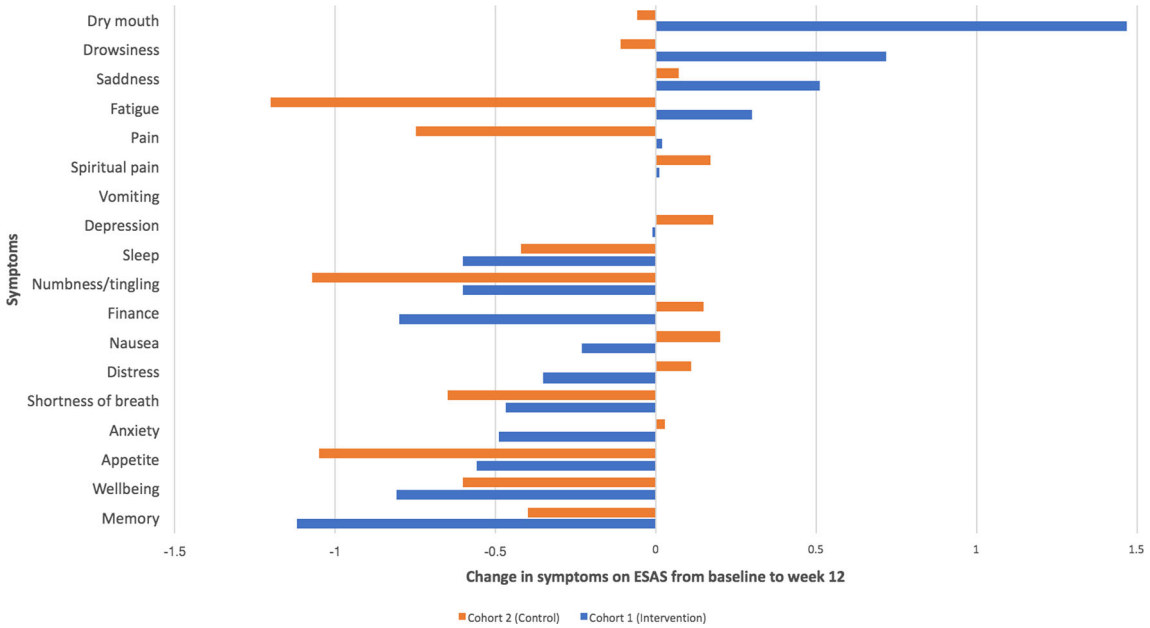

Fig. 2 ESAS score changes over time

detection of immunotherapy-related adverse-events is critical to maintaining the well-being of patients treated with these therapies [27] but needs to be integrated with comprehensive assessment of symptoms and their impact on patients' daily lives. Differences in symptoms detected as part of medical oncology and supportive care assessments support the need for multidisciplinary management.

A comprehensive medical assessment assists in personalising interventions to assist patients maintain and improve their well-being and coping. The supportive care medical consultation identified symptoms not previously identified by the medical oncology team using the CTCAE 4.0, suggesting that use of this tool alone may be insufficient to identify all symptoms patients' experience, missing symptoms that may be reduced if appropriate interventions are applied. The use of validated tools (PROMs) in clinical practice to screen, monitor, and follow patients' symptoms and QOL is increasingly common [28, 29]. The ESAS is a tool, validated in the cancer setting and used in many diverse populations including in the integrative oncology setting [20]. Although not used in this study, the Measure Yourself Concerns and Well-being (MYCAW) is another validated measure of patient concerns, unmet needs, and impact of therapy received. It has been applied in clinical practice particularly in the integrative oncology space [18], providing information to tailor supportive care to individual needs and to improve and monitor wellbeing [30, 31]. The coupling of patient reported outcomes to the CTCAE is not only acceptable but also may improve patient care by facilitating communication between patients and healthcare providers to discuss strategies to address symptoms of concern [32].

An integrative approach to caring for the whole person receiving immunotherapy relies on a comprehensive medical assessment by specialists with knowledge of the disease process, the potential toxicities of treatment, and of supportive therapies available to enhance and maintain well-being. It is also informed by a deeper understanding of the patient population and flexibility to personalise the approach to care.

With the growth of comprehensive cancer centres, there is capacity to provide multimodal supportive care interventions that include medical consultations, exercise therapy, and evidence-based complementary therapies [17]. Integrative oncology, exercise therapy, and SCP consultations and interventions focus on improving self-efficacy, assisting patients to develop skills to maintain their well-being [33]. In our model, the purpose of the initial SCP consultation was to engage the patient and evaluate their awareness and strategies of coping with their illness, and the limitations the disease and its treatment may have on them. Personalised interventions proposed by SCP or EP could assist patients to maintain and improve their well-being. The popularity of touch therapies (massage and reflexology) reflected participant preference as well the SCP perceiving the potential benefit for stress management, sleep disturbance, and musculoskeletal issues. Despite the assumption that a psychology intervention would be beneficial, the low uptake and lack of desire for talking therapies was similar to other studies in similar populations, requiring further evaluation regarding the reasons for this reticence [34–36].

Understanding the patient experience is essential to developing acceptable and holistic supportive care programs for patients living with metastatic cancer. Our study included semi-structured interviews of both intervention and control patients to explore their experience of living with melanoma, receiving immunotherapy, and the intervention more fully. Results of the qualitative analysis suggest coping and adjusting to living with uncertainty is a major concern for patients [37]. As our sample was small and the focus of the study on feasibility, QOL data was not assessed for statistical significance. Rather, this data along with qualitative and feasibility data from this study has informed service and intervention development.

While the study population was limited to people with stage IV melanoma, the intervention can be considered as a patient-tailored approach to providing holistic evidence-based interventions to address the patient's experience, symptoms, and supportive care needs. Using standardised measures inform our approach to individual patient care, including non-specific (anxiety, inactivity, stress management) and immunotherapy-specific symptoms. It would have potential to be generalisable to other populations.

Limitations

Although our study was small, with an insufficient number of participants to allow statistical comparison of group outcomes, our aim was to assess feasibility and determine potential value of further evaluation of this intervention. Screening logs were not kept, so we cannot report the number of patients approached and reasons for non-participation, and are unable to determine how representative our population is of all stage IV melanoma patients receiving immunotherapy treatment. Our population were, on average, long-term survivors of melanoma and most had lived a lengthy period with metastatic disease. Interestingly, patient symptom scores at baseline were low leaving little room for improvement; notably, most participants did not deteriorate.

This intervention requires a randomised controlled trial to determine effectiveness and cost-effectiveness in this and other populations treated with immunotherapy. Given the complex nature of the multi-modal intervention, incorporating a mixed method approach including objective measurement of intervention effect, PRO assessment, and qualitative exploration of patient experience and clinician perception would be optimal. Exploring the impact of this intervention in patients

who are receiving dual checkpoint inhibitor therapy would be a possible next step, where the rate of significant (grades 3–4) treatment toxicity can be as high as 59%, far higher than with anti-PD-1 monotherapy (21%) [38]. Patients receiving doublet therapy maybe at greater risk of needing steroids for prolonged periods to manage irAEs, with implications for further symptoms to address from steroid induced toxicity. Although the CheckMate 067 study reported equivalent QoL outcomes in patients receiving doublet ipilimumab and nivolumab compared to nivolumab alone [39].

Clinical implications

Patients living long-term with metastatic melanoma (or other cancers) receiving immunotherapy treatment are at risk of rapidly emerging symptoms and adverse events. Ensuring holistic assessment with a SCP and access to a comprehensive range of complementary supportive care interventions may reduce time to detection of clinically significant changes. People living longer with metastatic disease can benefit from interventions including exercise and evidence-based complementary therapies more commonly used in the survivorship space to maintain wellbeing and increase self-efficacy [13]. Services engaged in care of this population need to establish referral pathways to supportive care and actively evaluate their use and impact on patient outcomes. While this study was conducted in stage IV melanoma patients with a relatively low symptom burden, it may be of greater benefit in populations receiving immunotherapy with higher symptom burden (e.g. lung cancer). Integrating management of immunotherapy and its emerging side effects with integrative oncology and exercise interventions remains underexplored and requires rigorous evaluation.

Conclusion

Offering a holistic multimodal supportive care intervention to patients living with metastatic melanoma on immunotherapy was feasible and acceptable to them. Expanding supportive care by integrating complementary therapies was feasible and may enhance symptom control, coping, and well-being. Our population experienced low symptom burden and had good nutrition, fitness, and QoL, none of which changed over the course of the study. Supportive care consultations may be of greater benefit in populations with a higher symptom burden from disease (e.g. lung cancer) or treatment (e.g. patients receiving dual checkpoint inhibitor therapies), where toxicity rates are increased. The use of PROMs was feasible and may be helpful in identifying patients for timely referral to supportive care services. Furthermore, non-invasive complementary therapies and individualised exercise programs within a holistic supportive cancer care program were shown to be acceptable and feasible in a supportive care service suggesting further research is warranted.

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