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Brief Communication

Melanoma-Specific Clinical Outcomes of Inpatient Immune Checkpoint Blockade Treatment

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Abstract

Background: Little is known about patient outcomes with advanced melanoma following inpatient initiation or continuation of immune checkpoint blockade (ICB).

Methods and Results: We conducted a single institution retrospective case series of advanced melanoma patients who initiated ICB as an inpatient (initial inpatient cohort, $n = 9$), or continued ICB as an inpatient after previously starting as an outpatient (outpatient then inpatient cohort, $n = 5$). One patient had a partial response to ICB initiated as an inpatient, but ultimately died of melanoma after 13.5 months. Median overall survival for initial inpatient cohort was 1.0 month (95% CI: 0.2-11.2), and 1.4 months (95% CI: 0.4-58.0) for the outpatient then inpatient cohort. Three patients were alive >6 months after inpatient ICB administration.

Conclusion: Despite overall poor outcomes, some patients may benefit from inpatient ICB. This study provides additional information for clinicians to appropriately counsel patients on expectations following inpatient ICB.

Key words: melanoma; immunotherapy; inpatient treatment.

Introduction

Little is known about the benefit of immune checkpoint blockade (ICB) administration in the inpatient setting for patients with advanced melanoma. One prior single-center study of patients with a variety of solid tumors reported that while overall efficacy from inpatient ICB was poor, some patients with advanced melanoma had prolonged overall survival.[1] This raises the possibility that a subset of patients with advanced melanoma may benefit from inpatient ICB administration. We sought to further investigate this population. Our goal was to provide additional data on ICB outcomes for patients with advanced melanoma that will help practicing oncologists appropriately set expectations when considering inpatient ICB administration.

Methods

After obtaining institutional review board approval, we conducted a single institution retrospective case series of patients treated with inpatient ICB at Memorial Sloan Kettering Cancer Center between 2011-2021. Pharmacy records were reviewed to identify patients with unresectable stage III/IV melanoma who received a dose of inpatient ICB. Follow-up continued until November 9, 2021. Patients were divided into two cohorts: an "initial inpatient" cohort if they received their first dose of ICB as an inpatient, and an "outpatient then inpatient" cohort if they received ICB as an outpatient and subsequently received at least one dose of the same ICB regimen while inpatient. Eastern Cooperative Oncology Group (ECOG) performance status was determined by the treating oncologist at the time of inpatient ICB administration. Lactate dehydrogenase (LDH) levels were reported within 30 days prior to inpatient ICB. Tumor responses for response were assessed based on clinician subjective determination of response and review of imaging. Toxicity was assessed through chart review. Median overall survival was calculated using Kaplan-Meier methodology from the date of initial inpatient ICB administration for both cohorts.

Results

Patients and Treatment

Fourteen patients in total ($n = 9$ initial inpatient; $n = 5$ outpatient then inpatient), all hospitalized for complications of advanced melanoma, received inpatient ICB. Patient details, including ICB toxicities, are shown in Table 1.

Initial Inpatient Cohort

One patient had a clinician assessed partial response (PR) (11%, 1/9), two had stable disease (SD) (22%, 2/9), and six had progressive disease (67%, 6/9). The one patient with tumor shrinkage had a response which lasted 83 days. Among the two patients with SD, time from SD to progression was 42 and 161 days. No patients remained progression free during the follow-up

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Table 1. Patient demographics, baseline characteristics, and inpatient ICB regimens.

Cohort	Age	Sex	Melanoma Subtype	Inpt ICB	Stage	*BRAF* Mutation	ECOG	LDH> 2x ULN	Response Inpt ICB	Admission Reason	Inpt ICB Regimen Discontinuation Reason	Toxicity Event (if any)	Discharge Location	Hosp Readmit Within 30 Days	Doses Before Inpt ICB	Doses During Inpt ICB	Doses During Output ICB	Time to Death (Months)
Initial inpatient																		
1	62	M	Cutaneous	Ipi	M1c	WT	1	N/A	SD	Pain control*	Progression		SAR	No	-	1	3	5.9
2[a]	79	M	Cutaneous	Ipi+Nivo	M1d	WT	3	N/A	SD	Symptomatic	Toxicity	Diarrhea	SAR	No	-	1	0	11.2
3[a]	50	M	Cutaneous	Ipi+Nivo	M1d	WT	2	N/A	PR	Symptomatic brain	Progression	Rash, fatigue	SAR	No	-	2	1	13.5
4	27	M	Cutaneous	Ipi+Nivo	M1c	WT	1	Yes	PD	Pain control*	Death		Home hospice	No	–	1	N/A	0.3
5	71	F	Mucosal	Ipi+Nivo	III	WT	1	N/A	PD	GIB	Toxicity	Colitis, hyponatremia	Home	Yes	–	1	0	2.9
6	66	F	Unknown	Ipi+Nivo	M1c	Not described or tested	2	N/A	PD	Liver failure	Death		Home hospice	No	–	1	N/A	0.2
7	56	M	Cutaneous	Ipi+Nivo	M1d	V600E/K	2	Yes	PD	Pain control*	Progression		Home	Yes	–	1	1	1.0
8	62	F	Cutaneous	Pembro	M1d	WT	2	Yes	PD	Pain control*	Death		Home hospice	No	–	1	N/A	0.2
	79	M	Cutaneous	Nivo	M1d	WT	3	N/A	PD	Symptomatic brain	Death		SAR	No	–	1	0	0.9
Outpatient then inpatient																		
10	62	F	Cutaneous	Ipi+Nivo	M1d	V600E/K	1	Yes	PD	Pain control, FTT	Toxicity	Renal failure	Inpatient rehab	No	1	1	0	0.5
11	69	M	Cutaneous	Ipi+Nivo	M1c	Not or tested	Missing	Yes	PD	Symptomatic	Death	Pneumonitis	Home	No	1	2	N/A	1.4
12[a]	64	F	Acral	Pembro	M1a	Not described or tested	1	No	PD	Symptomatic cutaneous	Progression		SAR	No	4	1	3	58.0
13	35	M	Cutaneous	Pembro	M1d	V600E/K	3	Yes	PD	Pain control*	Death		Home hospice	No	1	1	N/A	0.4
14	52	F	Unknown	Pembro	M1d	V600E/K	3	N/A	PD	Symptomatic brain	Progression		SAR	Yes	2	1	3	5.6

All patients died; time to death calculated from date of first inpatient ICB treatment.
[a]Patients who lived >6 months from inpatient ICB administration.
*Bone metastases.
Abbreviations: BOR, best overall response; ECOG, Eastern Cooperative Oncology Group performance score; F, female; FTT, failure to thrive; GIB, gastrointestinal bleed; Hosp, hospital; ICB, immune checkpoint blockade; Inpt, inpatient; Ipi, ipilimumab; LDH, lactate dehydrogenase (2× ULN = two times the upper limit of normal, MSKCC ULN 246 U/L), M, male; Mets, metastasis; N/A, not available; Nivo, nivolumab; Outpt, outpatient; PD, progressive disease; Pembro, pembrolizumab; PR, partial response; Readmit, readmission; SAR, subacute rehab; SD, stable disease; WT, wild type.

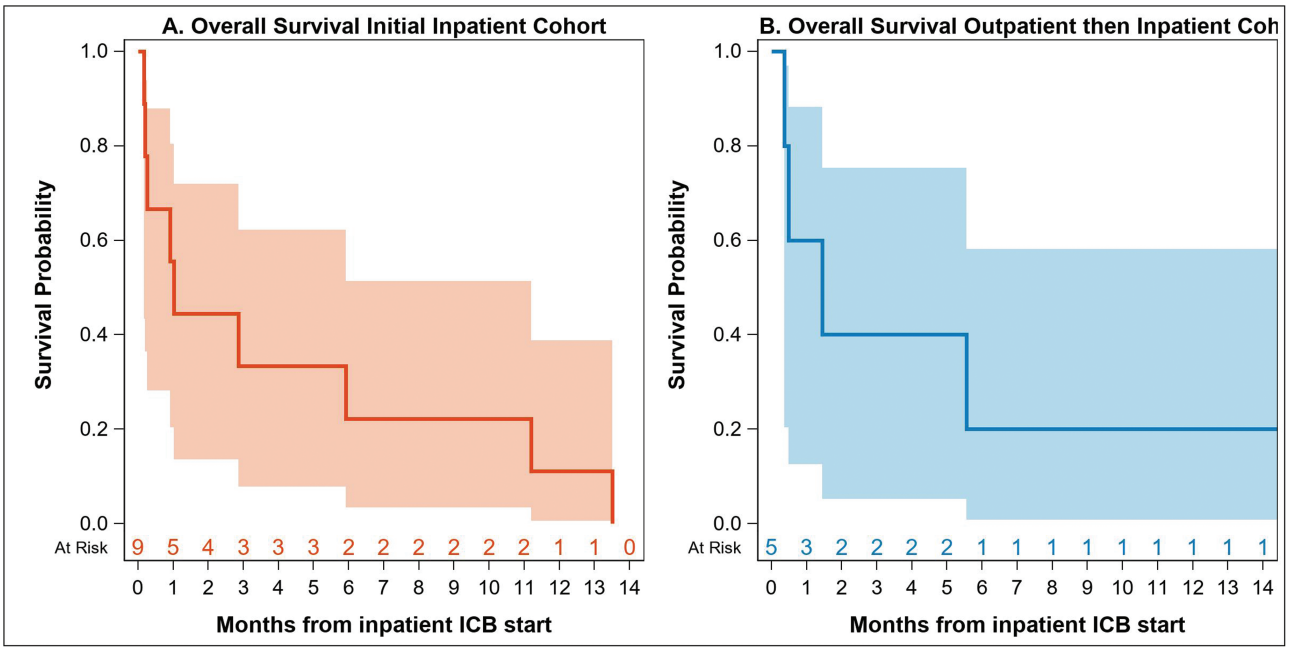

Figure 1. Overall survival of initial inpatient and outpatient then inpatient cohorts. (**A**) Overall survival of initial inpatient cohort. Median overall survival of initial inpatient cohort was 1.0 month. Tick marks indicate censored patients. Shaded areas represent 95% CI. **(B)** Overall survival of outpatient then inpatient cohort. Median overall survival of this cohort was 1.4 months. Tick marks indicate censored patients. Shaded areas represent 95% CI.

period. Two patients discontinued ICB due to toxicity. Three patients died during the hospitalization where they received ICB. Two patients were alive >6 months from ICB administration. Median overall survival for patients in this cohort was 1.0 month (95%CI: 0.2-11.2) following inpatient ICB administration, Figure 1A. All deaths in this cohort were due to melanoma.

Outpatient Then Inpatient Cohort

Median time from ICB regimen start to hospital admission was 63 days. All patients (n = 5) had primary progressive disease to the inpatient ICB regimen. The median time from inpatient ICB administration to disease progression was 44 days. One patient discontinued ICB due to toxicity. Two patients died during the hospitalization where they received ICB. Median overall survival for patients in this cohort was 1.4 months (95%CI: 0.4-58.0) following inpatient ICB administration, Figure 1B. The majority of deaths were due to melanoma related complications (80%, 4/5). One death was due to serous uterine cancer without evidence of melanoma (described below); this patient lived >6 months from inpatient ICB administration.

Description of Three Patients Alive >6 Months from Inpatient ICB Administration

Table ID#2 (Initial Inpatient Cohort)

This patient was admitted with new brain metastases and received whole brain radiotherapy and one dose of inpatient ipilimumab + nivolumab with stable disease. This patient did not receive additional treatment following discharge given poor performance status but lived 11.2 months after inpatient ICB administration.

Table ID#3 (Initial Inpatient Cohort)

This patient was admitted with new brain metastases and received stereotactic radiation and two doses of inpatient ipilimumab + nivolumab with shrinking melanoma in the brain and mediastinal lymph nodes. They eventually received outpatient ipilimumab + nivolumab and died of worsening brain metastases 13.5 months following inpatient ICB administration.

Table ID#12 (Outpatient then Inpatient Cohort)

This patient received four doses of outpatient pembrolizumab prior to their hospitalization for infective cellulitis of progressing cutaneous melanoma. They received one dose of inpatient pembrolizumab and continued pembrolizumab as an outpatient with ongoing disease progression. Cisplatin, vinblastine, and temozolomide (CVT) chemotherapy were subsequently given 4.1 months following hospital discharge, resulting in a complete response to melanoma for 50.9 months. This patient ultimately died from unrelated serous uterine cancer.

Discussion

While patients with advanced melanoma receiving ICB during inpatient hospitalizations generally have poor outcomes, some patients may still have some benefit from ICB; two patients hospitalized with symptomatic brain metastases lived >11 months after inpatient ICB. To our knowledge, this is the first study to specifically report outcomes among patients with advanced melanoma who initiated ICB as an inpatient and provide details about patients who survived >6 months. Our results are consistent with a previous study across several tumor types.[1] However, we extend these observations by providing more data among patients who initiated ICB as an inpatient and more fully characterize the clinical courses of the few patients who had prolonged overall survival.

Our work adds to the growing body of evidence showing ICB near the end of life and in patients with poor performance statuses has low, but still possibly some efficacy.[2,3] We acknowledge our small, single institution sample size, but any data on this

understudied topic is important to aid complex goals of care conversations that arise in this population. Whether these patients would have had worse outcomes without inpatient ICB is unclear, but since some patients had ICB toxicity resulting in ICB discontinuation, the potential harms of ICB in this vulnerable patient population are important considerations. Additionally, inpatient administration of ICB is incredibly expensive for hospitals paying for inpatient treatment, including costly ICB.[4] Consideration of inpatient ICB administration should be made on a case-by-case basis while balancing financial burdens and end-of-life care. To ensure representativeness of our findings, future multicenter studies in larger cohorts are needed.

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Conflict of Interest

Katherine Panageas: Catalyst Biotech, Dynavax Tech, Sunesis Pharmaceuticals, Viking Therapeutics (OI); **Michael Postow:** BMS, Merck, Array BioPharma, Novartis, Incyte, NewLink Genetics, Aduro, Eisai, Pfizer (C/A), RGenix, Infinity, BMS, Merck, Array BioPharma, Novartis, AstraZeneca (RF). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

Author Contributions

Conception/design: K.L., M.P. Provision of study material or patients: V.P. Collection and/or assembly of data: K.L. Data analysis and interpretation: K.L., H.K., K.P., M.P. Manuscript writing: K.L., H.K., K.P., M.P. Final approval of manuscript: All authors.

Data Availability

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

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