EFFECT OF ADJUVANT IMMUNOTHERAPY ON RECURRENCE FREE SURVIVAL IN CUTANEOUS MELANOMA: A REAL-WORLD EXPERIENCE

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Background

The treatment for stage III cutaneous melanoma has changed significantly since 2017. Prospective randomized trials released that year showed completion lymphadenectomy (CLND) after a positive sentinel node biopsy (SLNB) did not improve melanoma specific survival[1] and that adjuvant immunotherapy in the form of PD1 inhibitors improved relapse free survival (RFS)[2]. However, these studies did not combine therapies – MSLT2 patients did not receive meaningful immunotherapy and patients in the adjuvant trials all had CLND following +SLNB. This single institution retrospective study evaluates the effect of receiving adjuvant immunotherapy on RFS for patients with stage III melanoma patients with a +SLNB and/or microsatellitosis that did not have CLND.

Methods

An IRB approved single institution cutaneous melanoma database was reviewed for patients treated with wide local excision and SLNB with clinical stage I or II disease between September 2016 and August 2021. Patients with a +SLNB and/or microsatellitosis were included. Patients who underwent CLND for a +SLNB were excluded. Stage III patients with microsatellites and a negative SLNB were included since this holds a worse prognosis than a single positive SLNB. The primary endpoint was melanoma RFS based on receipt of adjuvant PD1. Demographic, histopathologic, and clinical data was collected and compared by Chi-square, Fisher's exact test, or Two-way ANOVA. RFS between groups treated with adjuvant PD-1 immunotherapy or followed with observation alone was compared using Kaplan Meyer curves. Completion rates of adjuvant PD1 immunotherapy and adverse events were collected.

Results

43 patients were included in this study. 58.1% (n=25) were men with an average age of 61.0 years. Mean Breslow depth was 2.93 mm (±1.91) and 67.4% (n=29) had ulcerated tumors. The average number of +SLN was 1.19 nodes. 76.7% (n=33) of the patients had adjuvant treatment with a PD1 inhibitor. Patients receiving PD1 inhibitors had improved 3-year melanoma RFS compared to those who did not (74.4% vs. 53.6%, P=0.30, Fig. 1). Patients in the PD1 group were more likely to recur distantly (83.3%, n=5) while untreated patients were more likely to have a locoregional recurrence (100%, n=3). For patients treated adjuvantly with PD1, 69.7% (n=23) completed therapy. The most common side effects of PD1 were arthralgias (30.3%, n=10), weakness (24.4%, n=8), rash (24.4%, n=8), diarrhea (21.1%, n=7), and fatigue (21.1%, n=7). Reasons for stopping treatment were recurrence (20.0%, n=2), aseptic meningitis (10.0%, n=1), chronic diarrhea (10.0%, n=1), adrenal insufficiency (10.0%, n=1), arthralgia (10.0%, n=1), skin rash (10.0%, n=1), loss to follow up (10.0%, n=1), loss of funding for medications (10.0%, n=1), and patient choice (10.0%, n=1).

Table 1. Patient histopathologic and demographic comparison

	Immunotherapy	Observation	*P*-value
Total Patients			
	33 (76.7%)	10 (23.3%)	
Age (years)			
	61.2 (31-88)	60.5 (20-86)	0.96
Gender			
Male	20 (60.6%)	5 (50.0%)	0.72
Female	13 (39.4%)	5 (50.0%)	
Recurrence			
Yes	6 (18.2%)	3 (30.0%)	0.41
No	27 (81.8%)	7 (70.0%)	
Lesion Site			
Head/Neck	11 (33.3%)	3 (30.0%)	0.88
Trunk	15 (45.5%)	4 (40.0%)	
Extremity	7 (21.2%)	3 (30.0%)	
Breslow Thickness			
≤ 1 mm	6 (18.2%)	4 (40.0%)	0.22
1.1 - 4 mm	16 (48.5%)	5 (50.0%)	
≥ 4.1 mm	11 (33.3%)	1 (10.0%)	
Breslow Thickness			
Mean	3.17 mm (±1.77)	2.14 mm (±1.52)	0.13
Mitotic Rate			
0-5	12 (36.4%)	4 (40.0%)	0.44
5-10	11 (33.3%)	2 (20.0%)	
>10	7 (21.2%)	4 (40.0%)	
Unknown	3 (9.1%)	0	
No. Positive SLN			
0	2 (6.1%)	1 (10.0%)	0.80
1	25 (75.8%)	8 (80.0%)	
>/=2	6 (18.2%)	1 (10.0%)	
Microsatellitosis			
Present	2 (6.5%)	1 (10%)	0.56
Absent	31 (93.5%)	9 (90%)	
Ulceration			
Present	24 (72.7%)	5 (50%)	0.25
Absent	9 (27.3%)	5 (50%)	
Braf			
Mutant	3 (9.1%)	1 (10.0%)	0.44
Wild type	14 (42.4%)	3 (30.0%)	
Unknown	16 (48.5%)	6 (60.0%)	
Recurrence Type			
Local	1 (16.7%)	0	
Regional	0	3 (100%)	
Distant	5 (83.3%)	0	

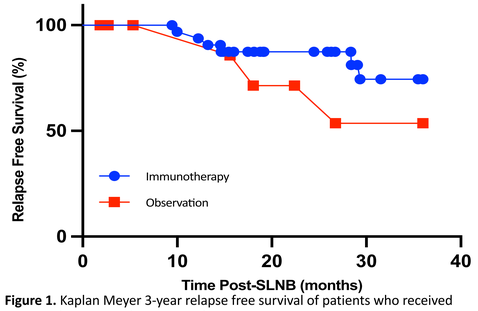

Figure 1. Kaplan Meyer 3-year relapse free survival of patients who received immunotherapy vs. observation alone post-SLNB

Table 2. Immunotherapy completion and complications.

Completed immunotherapy	**No. of Patients**
Completed	23 (69.7%)
Incomplete	10 (30.3%)
Immunotherapy complications	
Rash	8 (24.4%)
Diarrhea	7 (21.2%)
Arthralgia	10 (30.3%)
Weakness	8 (24.4%)
Fatigue	7 (21.2%)
None	10 (30.3%)
At least one symptom	23 (69.7%)
Reason for denying immunotherapy	
Patient Denied	7 (70.0%)
Recurrence before Immunotherapy	1 (10.0%)
Lost to follow up	2 (20.0%)
Reasons for not completing therapy	
Aseptic meningitis	1
Arthralgias	1
Adrenal insufficiency	1
Loss of funding	1
Recurrence	2
Chronic diarrhea	1
Tremor	1
Rash	1
Patient choice	1

Conclusions

Adjuvant treatment of patients with stage III cutaneous melanoma and deferred CLND with immunotherapy is associated with an improved RFS at 3 years. Our 3-year RFS of 74.4% compares favorably to other studies where 3-year RFS in treated patients is 63.7%[3]. This data suggests that the addition of adjuvant PD1 inhibition may reduce recurrence rates by 39% in the modern stage III cutaneous melanoma patient when compared to observation alone. This regimen was well tolerated with nearly 70% of patients completing therapy. This is valuable data for counselling patients on the benefits of adding PD1 inhibition to reduce recurrence rates.

References & Acknowledgements

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