Abstract #331391

Management of resected stage III/IV melanoma with adjuvant immunotherapy

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Background

Adjuvant therapy with anti-PD1 reduces the risk of recurrence in resected stage III/IV melanoma[1,2]. It has been well tolerated in trials, with discontinuation rates of less than 10% for toxicity[2].

The timing, nature and management of recurrences is being explored, with recent findings describing different management strategies for recurrences developing ON and OFF adjuvant treatment[4]. No comparative data exist regarding imaging surveillance strategies for patients receiving adjuvant treatment. The aim of this study was to describe the use of adjuvant nivolumab as it entered routine clinical practice in Australia for resected stage III and IV melanoma between August 2018 and March 2020.

Methods

Retrospective analysis of patients from 11 Australian centres who received adjuvant nivolumab for resected stage III/IV melanoma were included in this study. Efficacy, toxicity, surveillance, patterns of recurrence, management and further treatment outcomes were examined.

Results

Table 1: Patient and disease characteristics

	N = 471, (%)
Age (years)	
Median (range)	64.0 (17.0, 94.0)
Sex	
Female	153 (32.5)
Male	318 (67.5)
AJCC8th ed Stage	
IIIA	28 (5.9)
IIIB	194 (41.2)
IIIC	175 (37.2)
*Intransit only	* 64 (13.6)
IIID	11 (2.3)
IV	63 (13.4)
Molecular status	
BRAF Mutant	128 (27.2)
Wildtype	278 (59.0)
Unknown	65 (13.8)
Melanoma Subtype	
Cutaneous	387 (82.2)
Occult Primary	72 (15.3)
Acral	10 (2.1)
Mucosal	2 (0.4)

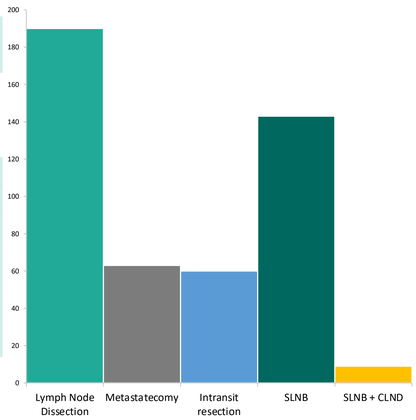

Figure 1: Types of surgical resection

152 patients had a positive sentinel lymph node biopsy (SLNB), of which only 6% went on to have a completion lymph node dissection (CLND) (figure 1).

Treatment Discontinuation and Surveillance

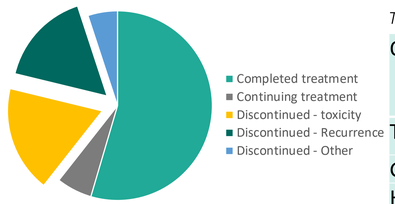

Figure 2: Reasons for treatment discontinuation

Median duration of treatment was 10.4 months. **18% of patients discontinued treatment early for toxicity.**

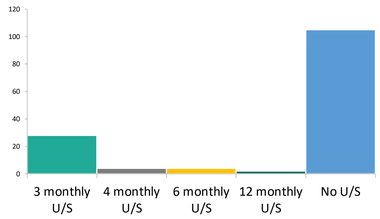

Figure 3: Frequency of ultrasound surveillance, SLNB+

Only 25% of SLNB without CLND patients had routine surveillance of the lymph node basin. Most patients had systemic surveillance every 3 months. 15% of patients had scans every 6 months.

Table 2: Toxicities leading to discontinuation

Organ System	Total, n= 87 (%)	Grade 1/2 (n)	Grade 3/5 (n)
Total		28 (32%)	59 (68%)
Gastrointestinal	28	6	22
Hepatic	13	3	10
Respiratory	6	3	3
Neurological	9	3	6
Skin	7	3	4
Rheumatological	9	6	3
Ocular	3	2	1
Endocrine	6	1	5
Renal	4	1	3
Myocarditis	2	0	2

Figure 4: Systemic scan frequency

Timing and Pattern of Recurrence

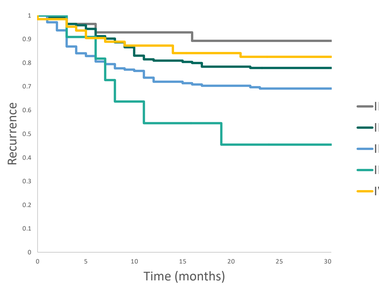

Figure 5: Kaplan Meier RFS by AJCCv8 Substage

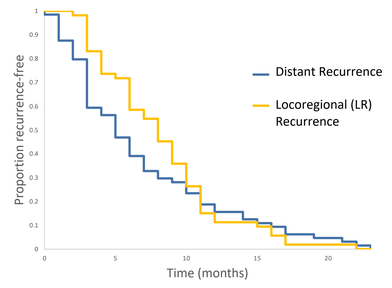

Figure 6: Recurrence-free survival by site (LR v Distant)

117 (25%) patients had disease recurrence. 65% recurred while ON treatment and 35% OFF treatment (>1 month after last treatment dose). 24-month RFS was 69%. Median time to recurrence was 6 months..

Management of Recurrence

Of those who recurred with LR disease only, most (46/56, 82%) underwent surgery. 18% (10/56) patients who recurred with LR disease subsequently recurred distantly.

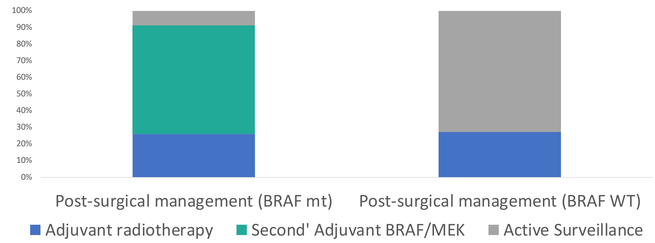

Figure 7: Management post resection of LR recurrence

58 patients received systemic therapy for unresectable or distant recurrence. No responses were observed for CTLA-4 or PD1 monotherapy for patients recurring ON or OFF adjuvant treatment. 2-year OS was 92%.

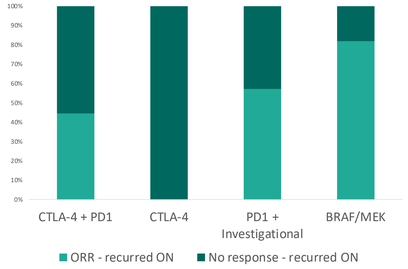

Figure 8: Management of distant recurrence: recurrence ON adjuvant PD1

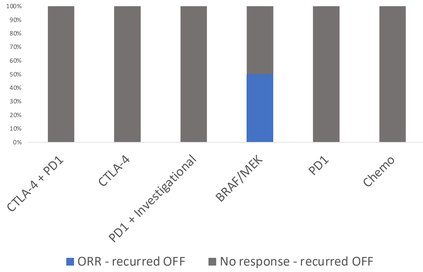

Figure 9: Management of distant recurrence: recurrence OFF adjuvant PD1

Conclusion

- Despite higher rates of discontinuation due to toxicity (18%) compared with clinical trial cohorts, the efficacy data appear similar.
- Most early recurrences are distant
- Many with LR recurrence soon recur distantly thereafter.
- Second line adjuvant BRAF/MEK inhibitors are frequently used for resected LR recurrence.
- Both CTLA-4+PD-1 and BRAF/MEK inhibitors appear to have activity after distant recurrence. CTLA-4 monotherapy had no response in this data set.

References

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