



Survival of patients with early invasive melanoma down-staged under the new eighth edition of the American Joint Committee on Cancer staging system

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1 **Article type:** Research letter

2 **Survival of patients with early invasive melanoma down-staged under the new 8th AJCC edition**

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33

34 **Abbreviations:**

35 AJCC- American Joint Committee on Cancer; DFS- disease-free survival;

36 SLNB- Sentinel lymph node biopsy; SSM- Superficial spreading melanoma

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49 The 8th edition of the American Joint Committee on Cancer (AJCC) melanoma staging took effect in
50 January 2018 (1). In this new edition, classification of T1 melanomas was modified, whereby mitotic
51 rate is no longer a staging criterion and 0.8mm not 1.0mm becomes the thickness boundary
52 between T1a and T1b (1). In order to better appreciate specific consequences of the new system for
53 patients with early melanoma, we assessed disease-free survival (DFS) as a surrogate of overall
54 survival in patients with early invasive melanoma who were down-staged from T1b to T1a under the
55 8th edition.

56 Study participants were enrolled in an ongoing follow-up study of high-risk primary melanoma at
57 time of their diagnosis with T1b-T4b cutaneous melanoma according to 7th edition AJCC staging,
58 from 2010 to 2014 in Queensland, Australia (2). Two institutional Human Ethics Committees
59 approved the study. Patients aged over 16 were recruited via public hospitals, private clinics and
60 pathology services. Clinical and patient information was collected at diagnosis via questionnaires and
61 histopathology reports provided information on tumour characteristics. Melanoma recurrences
62 were self-reported during 6-monthly follow-up questionnaires and confirmed by histopathology and
63 imaging.

64 T1b tumors were re-classified using the 8th AJCC edition and distributions of patient and tumor
65 characteristics were analysed according to AJCC edition. Three-year DFS was obtained by Kaplan–
66 Meier analysis for patients who remained T1b and those down-staged to T1a, and repeated whilst
67 stratifying by mitotic rate.

68 Of 208 patients with 7th edition T1b melanomas, 111 (53%) remained T1b and 97 (47%) decreased to
69 T1a under the 8th edition (Table 1). Patients down-staged to T1a were diagnosed with melanomas
70 <0.8mm thick, without ulceration and with mitotic rates 1-3/mm² (n=87) and >3/mm² (n=10). Five
71 recurrences occurred within 3 years of diagnosis in this down-staged subgroup, equating to an
72 overall DFS of 95%. When stratified by mitotic rate, patients with 1-3 mitoses/mm² and >3

73 mitoses/mm², had a 96% and 80% DFS respectively. The DFS of patients down-staged to T1a under
74 the 8th AJCC edition remains comparable to the 93% DFS of T1b melanomas.

75 Our early results suggest that mitoses remain an important prognostic feature of thin melanomas,
76 the majority of melanomas diagnosed today (3). Our results also estimate that nearly half of 7th
77 edition T1b tumors will be down-staged to T1a with the 8th edition, compared to a suggested 8% up-
78 staging of T1a to T1b (4). The main limitations of this study are short follow-up and a relatively small
79 study population. Although we do not know DFS for all T1a tumors, we do know 5-year cause-
80 specific survival for T1a melanoma is around 99% (5).

81 The subset of patients with 8th edition T1a melanomas with mitoses may not share the same
82 prognosis as those without mitoses. While the 8th edition AJCC classification brings new clarity to
83 melanoma staging overall, if our findings are corroborated in a larger patient cohort, clinicians will
84 need to be alerted to the higher risk of disease recurrence of this patient subgroup. Without specific
85 flagging of these higher-risk patients, their poorer outcomes will be indistinguishable, diluted by
86 better outcomes among the low-risk majority of patients with T1a melanomas without mitoses.

87

88 Table 1: Patient characteristics by AJCC edition and tumor stage

	7 th edition	8 th edition		p-value ³
	T1b N (%)	Down-staged to T1a N (%)	Remained T1b N (%)	
Total	208 (100)	97 (47)	111 (53)	
Age (years)				0.90
<65	117 (56)	55 (57)	62 (56)	
≥65	91 (44)	42 (43)	49 (44)	
Sex				0.83
Male	96 (46)	44 (45)	52 (47)	
Female	112 (54)	53 (55)	59 (53)	
Subtype				0.70
SSM ¹	126 (60)	66 (62)	66 (60)	
Nodular	14 (7)	5 (5)	9 (8)	
Other	68 (33)	32 (33)	36 (32)	
Body site				0.26
Head/neck	32 (15)	12 (12)	20 (18)	
Other	176 (85)	85 (88)	91 (82)	
Personal history				0.26
No	176 (85)	85 (88)	91 (82)	
Yes	32 (15)	12 (12)	20 (18)	
SLNB ²				0.0002
No	165 (82)	90 (93)	82 (74)	
Yes	36 (18)	7 (7)	29 (26)	
SLNB positivity				0.81 ⁴
No	35 (97)	7 (100)	28 (96)	
Yes	1 (3)	0 (0)	1 (4)	

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90 1- Superficial spreading melanoma

91 2- Sentinel lymph node biopsy

92 3- Chi-squared Test

93 4- Fisher's Exact Test

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96 REFERENCES

97

98 1. Gershenwald JE, Scolyer RA, Hess KR, Sondak VK, Long GV, Ross MI, et al. Melanoma staging:
99 Evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging
100 manual. *CA Cancer J Clin.* 2017;67(6):472-92.

101 2. Smithers BM, Hughes MCB, Beesley VL, Barbour AP, Malt MK, Weedon D, et al. Prospective
102 study of patterns of surgical management in adults with primary cutaneous melanoma at high risk of
103 spread, in Queensland, Australia. *J Surg Oncol.* 2015;112(4):359-65.

104 3. Glazer AM, Winkelmann RR, Farberg AS, Rigel DS. Analysis of trends in us melanoma
105 incidence and mortality. *JAMA Dermatology.* 2017;153(2):225-6.

106 4. Wilson JM, Rodriguez E, Kelly BC. Retrospective effects of the American Joint Committee on
107 Cancer's eighth edition guidelines for staging melanoma. *Journal of the American Academy of*
108 *Dermatology.*78(1):177-8.

109 5. Green AC, Baade P, Coory M, Aitken JF, Smithers M. Population-based 20-year survival
110 among people diagnosed with thin melanomas in Queensland, Australia. *J Clin Oncol.*
111 2012;30(13):1462-7.

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