

## Supplementary Online Content

Thomas NE, Krickler A, Waxweiler WT; Genes, Environment, and Melanoma (GEM) Study Group. Comparison of clinicopathologic features and survival of histopathologically amelanotic and pigmented melanomas: a population-based study. *JAMA Dermatol*. Published online August 27, 2014. doi:10.1001/jamadermatol.2014.1348.

**eMethods.** Methods of Follow at Individual Study Centers

**eTable 1.** Relationship Between Histopathologically Amelanotic and Pigmented Melanoma and Age and Breslow Thickness Stratified by Sex for 3207 Primary Melanomas From 2761 Patients

**eTable 2.** Hazard Ratios for Overall Death According to Histopathologic Pigmentation Among 2736 Patients With Primary Melanomas

This supplementary material has been provided by the authors to give readers additional information about their work.

## eMethods

### Methods of follow at individual study centers

Within the United States, all registries had individual and state follow up, with identification of individuals whose status was unknown sent for identification to the National Death Index "Plus". In Canada, subjects were linked with the Cancer Registry using their unique ID number. Those GEM subjects for whom vital status was unknown were manually linked with the National Mortality Database in Ottawa where cause of death and date of death are determined from death certificates. In Italy, a record linkage was performed for each municipality. Death certificates were then obtained. In Australia, the cancer registry receives lists of newly registered deaths in NSW every two weeks and then registry records are also matched with the National Death Index of the Australian Institute of Health and Welfare.

**eTable 1. Relationship Between Histopathologically Amelanotic and Pigmented Melanoma and Age and Breslow Thickness Stratified by Sex for 3,207 Primary Melanomas from 2,761 Patients<sup>a</sup>**

Characteristic	Males			Females		
	No. (%) of Patients		P Value <sup>b</sup>	No. (%) of Patients		P Value <sup>b</sup>
	Pigmented (n=1,728)	Amelanotic (n=134)		Pigmented (n=1,234)	Amelanotic (n=111)	
Age at diagnosis, yr						
<50	334 (96)	15 (4)	.007	517 (92)	42 (8)	.55
50-69	816 (93)	58 (7)		456 (92)	41 (8)	
>70	578 (90)	61 (10)		261 (90)	28 (10)	
Breslow thickness, mm						
≤2.00	1,505 (96)	70 (4)	<.001	1,121 (94)	72 (6)	<.001
>2.00	223 (78)	64 (22)		113 (74)	39 (26)	

<sup>a</sup>Included invasive single melanomas and multiple melanomas (index and previous).

<sup>b</sup>P values are from Pearson's chi-square tests.

**eTable 2. Hazard Ratios for Overall Death According to Histopathologic Pigmentation Among 2,736 Patients with Primary Melanomas<sup>a</sup>**

Characteristic	No. (%) of Patients		Fully Adjusted <sup>b</sup>	
	Censored (n=2,276)	Overall Deaths (n=460)	HR (95% CI)	P Value
Histopathologically amelanotic				
No	2,102 (84)	395 (16)	1 [Reference]	.44
Yes	174 (73)	65 (27)	0.9 (0.7-1.2)	
Age, y				
Increase in 10-y increments	–	–	1.6 (1.5-1.8)	<.001
Sex				
Male	1,200 (78)	339 (22)	1 [Reference]	.01
Female	1,076 (90)	121 (10)	0.8 (0.6-0.9)	
Anatomic site				
Trunk	317 (72)	124 (28)	1 [Reference]	
Head, neck	1,010 (83)	212 (17)	1.1 (0.9-1.4)	.002
Upper extremities	430 (86)	70 (14)	0.8 (0.6-1.0)	
Lower extremities	519 (91)	54 (9)	0.6 (0.5-0.9)	
AJCC tumor stage <sup>c</sup>				
T1a	1,181 (90)	130 (10)	1 [Reference]	
T1b	351 (91)	35 (9)	1.0 (0.7-1.4)	
T2a	420 (81)	98 (19)	1.8 (1.4-2.4)	
T2b	46 (65)	25 (35)	3.6 (2.3-5.5)	<.001
T3a	141 (70)	61 (30)	2.8 (2.1-3.9)	
T3b	61 (57)	46 (43)	4.1 (2.9-5.7)	
T4a	48 (62)	29 (38)	3.4 (2.3-5.3)	
T4b	28 (44)	36 (56)	5.3 (3.5-7.9)	

Abbreviations: AJCC, American Joint Committee on Cancer; HR, hazard ratio; CI, confidence interval.

<sup>a</sup>Of the 2,995 participants in this study, multiple primary melanomas patients (MPMs) who were missing histopathologic pigmentation (n = 141) or AJCC tumor stage (n = 32) for their selected (usually thicker) melanoma and single primary melanoma patients (SPMs) missing AJCC tumor stage (n = 86) were excluded. Patients who entered the study as SPMs who developed a subsequent melanoma were treated as time-dependent.

<sup>b</sup>This Cox model also included study center and whether SPM or MPM.

<sup>c</sup>T1a, Breslow thickness ≤1.0 mm and absence of ulceration or mitoses; T1b, Breslow thickness ≤ 1.0 mm and presence of ulceration or mitoses; T2a, Breslow thickness 1.01-2.0 mm without ulceration; T2b, Breslow thickness 1.01-2.0 mm with ulceration; T3a, Breslow thickness 2.01-4.0 mm without ulceration; T3b, Breslow thickness 2.01-4.0 mm with ulceration; T4a, Breslow thickness > 4.0 mm without ulceration; T4b, Breslow thickness > 4.0 mm with ulceration.