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DOI: 10.1159/000321177**No Role for Melanoma Treatment in the Association between Melanoma and Amyotrophic Lateral Sclerosis or Parkinson's Disease**Peter D. Baade^{a, b}, Elena Herrero Hernández^g, D. Michal Freedman^f, B. Mark Smithers^{c, d}, Lin Fritsch^e^aViertel Centre for Research in Cancer Control, Cancer Council Queensland, ^bSchool of Public Health, Queensland University of Technology, and ^cDepartment of Surgery and ^dQueensland Melanoma Project, Princess Alexandra Hospital, University of Queensland, Brisbane, Qld., and ^eWestern Australian Institute for Medical Research, University of Western Australia, Perth, W.A., Australia; ^fDivision of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, Md., and ^gCenter for Research on Occupational and Environmental Toxicology, Oregon Health and Science University, Portland, Oreg., USA

In 2007 we published the results of our study of all people diagnosed as having melanoma in Australia between 1982 and 2001, and compared their mortality risk of amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD) to the general population [1]. Although the absolute risk was small, the melanoma cohort had a 70% higher risk of death due to ALS and a nearly 3-fold higher risk of death due to PD than the general population, consistent with a US study [2], strengthening the evidence for an association between melanoma and each of the 2 neurodegenerative diseases.

In Australia, surgical excision is the preferred treatment for melanoma, with no patient receiving adjuvant therapy after resection of a primary lesion. Patients with stage III disease rarely receive interferon, with most being watched or treated in clinical trials. The only melanoma patients who receive chemotherapy are those diagnosed as having a stage IV melanoma.

We suggested that it was unlikely that treatment was an explanation for the observed association [3]. However, in the absence of definitive data about the thickness of melanomas in the study cohort, it was possible that a large proportion of melanoma patients who died of either ALS or PD had thicker melanomas. Thus this treatment hypothesis remained a possibility, particularly when several chemotherapeutics that could be used in the treatment of more advanced melanoma have neurotoxic effects [4, 5].

While specific treatment data are not available, we sought additional information about the thickness of the melanoma among our original melanoma cohort. In the absence of stage information, thickness is the strongest predictor of survival [6]. This information was provided by the Australian Institute of Health and Welfare, who matched the melanoma cohort information with the

Table 1. Melanoma thickness for persons diagnosed as having melanoma in Australia between 1982 and 2001

Melanoma thickness	Melanoma patients who died from ALS ¹	Melanoma patients who died from PD ^{2, 3}	All melanoma patients
<i>Diagnoses in 1982–2001</i>			
≤ 1.00 mm	28 (53)	59 (46)	73,819 (58)
1.01–2.00 mm	8 (15)	16 (13)	17,429 (14)
2.01–4.00 mm	6 (11)	19 (15)	10,889 (9)
> 4.00 mm	1 (2)	16 (13)	6,035 (5)
Unknown	10 (19)	18 (14)	18,086 (14)
Total	53 (100)	128 (100)	126,258 (100)
<i>Diagnoses in 1990–2001</i>			
≤ 1.00 mm	13 (57)	29 (47)	56,246 (63)
1.01–2.00 mm	6 (26)	10 (16)	12,398 (14)
2.01–4.00 mm	3 (13)	9 (15)	7,658 (9)
> 4.00 mm	1 (4)	7 (11)	4,389 (5)
Unknown	0 (0)	7 (11)	8,058 (9)
Total	23 (100)	62 (100)	88,749 (100)

Melanoma includes cancers coded in ICD-10 as C43. Source: Australian Cancer Database, AIHW. Figures in parentheses are percentages.

¹ Indicates those who died >12 months after their diagnosis of melanoma, up to the end of 2001, with the underlying cause of death coded as 335.2 (ICD-9) or G12.2 (ICD-10).

² Indicates those who died >12 months after their diagnosis of melanoma, up to the end of 2001, with the underlying cause of death coded as 332 (ICD-9) or G20 (ICD-10).

³ Of the original case group of 129 melanoma patients who died of PD, 1 patient could not be matched and has been excluded from this analysis.

melanoma thickness details collected by each of the state and territory cancer registries. Before 1990 there was a relatively large proportion of melanoma cases with missing thickness data (~27%), so we have presented thickness data for the full period and the restricted 1990–2001 period (~9% missing thickness).

These results (table 1) show that of the 53 melanoma patients who died of ALS, only 1 (2%) was known to have melanoma diagnosed >4 mm thickness. The corresponding percentage among the 128 melanoma patients who died of PD was 13% (n = 16).

While not definitive, the thickness distribution for the melanoma patients who died of ALS or PD provides greater weight to

the hypothesis that chemotherapeutics have played minimal or no role in the previously reported association. As such we felt it was important to disseminate this information in order to more appropriately focus future research efforts in understanding the biological bases of the co-occurrence of both diseases. Alternative mechanisms to explain the co-occurrence could include genetic variants and gene expression changes in pigmentation genes occurring in PD [7] and in ALS [8]; shared embryological origin for melanocytes and neurons, commonalities between melanin and dopamine synthesis and variants of melastatins (TRPMs) [9, 10], due to the involvement of selected TRPMs in this cancer and in neuronal cell death.

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A/Prof. Peter D. Baade, Senior Research Fellow
 Viertel Centre for Research in Cancer Control
 Cancer Council Queensland, PO Box 201
 Spring Hill, QLD 4001 (Australia)
 Tel. +61 73 634 5317, Fax +61 73 259 8257
 E-Mail peterbaade@cancerqld.org.au