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De novo versus nevus-associated melanomas: differences in associations with prognostic indicators and survival

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Background/Objectives: Although 20%-30% of melanomas are histopathologically 'nevus-associated', the majority of melanomas arise *de novo*, i.e. in clinically normal skin with no associated nevus. We examined whether these forms of melanoma differed in their associations with clinical and histopathologic features, and patient survival.

Methods: We analyzed 2 prospective cohorts from our institution with protocol-driven follow up information (NYU1, n=1048; NYU2, n=1202). We used univariate and multivariate analyses to examine associations between *de novo* versus nevus-associated melanoma classification and age, anatomic site, tumor thickness, tumor ulceration, mitotic index, histological subtype, clinical stage, and survival. We tested the associations identified in NYU1 using NYU2 as a replication cohort.

Results: In NYU1, *de novo* melanomas were associated with tumor thickness > 1.0mm (p<0.0001), ulceration (p=.024), nodular subtype (p=.009), stage > 1 (p<0.0001), older age (p<0.0001), and shorter overall survival (p=.0007). In NYU2, *de novo* melanoma was again significantly associated with tumor thickness > 1.0mm (p<0.0001), ulceration (p<0.0001), nodular subtype (p<0.0001), stage > 1 (p<0.0001), older age (p<0.0001),

and shorter overall survival (p<0.0001). In multivariate analysis, *de novo* classification was an independent, poor prognostic indicator. Male patients had a statistically significantly worse survival than female patients if their melanoma was *de novo* (NYU1, p<0.0001; NYU2, p=0.0004); unexpectedly, there was no gender difference in survival among patients with nevus-associated tumors.

Conclusion: These data suggest that *de novo* melanomas are more aggressive than nevus-associated melanomas. This classification scheme may also provide a useful framework for investigations into gender differences in melanoma outcomes. Recognizing these trends may have implications for screening.