

SKIN CANCER

Propranolol limits melanoma recurrence

Drug repurposing offers the potential to identify effective, inexpensive anticancer therapies. The possible use of the β -blocker propranolol for the treatment of melanoma exemplifies this concept.

Stress has been implicated as a driver of melanoma progression, and propranolol has antiangiogenic and anti-migratory effects on cancer cells through inhibition of noradrenaline signalling via β -adrenoceptors. Correspondingly, retrospective clinical studies have revealed that the use of this drug is associated with favourable melanoma outcomes. Hence, De Giorgi *et al.* carried out a small clinical trial to prospectively evaluate the anti-melanoma effects of propranolol.

Of 53 patients with thick cutaneous melanoma (stage IB–IIIA) enrolled, 19 consented at the time of diagnosis to take off-label propranolol (80 mg daily) as an adjuvant therapy, and the 34 patients who were unwilling to receive propranolol formed the control group. Notably, ulcerated melanoma was more prevalent in the propranolol group (63% versus 35%; $P = 0.05$); the two treatment groups were

otherwise well-balanced for baseline clinical characteristics and prognostic factors.

At 3 years, disease-free survival was 84.2% and 58.8% in the propranolol and control arms, respectively, equating to an 80% risk reduction from propranolol (HR 0.18; 95% CI 0.04–0.89; $P = 0.03$) after multivariate Cox modelling. The short follow-up duration limited the power to demonstrate a significant effect on mortality, although a trend towards improved overall survival was observed with propranolol (HR 0.64; 95% CI 0.10–3.96; $P = 0.63$). Importantly, no adverse effects of propranolol were reported.

These results are striking, particularly considering the significant imbalance in ulceration — a risk factor for disease progression — disfavoring the propranolol group. A larger, randomized controlled trial is now warranted to clarify the role of propranolol in the treatment of melanoma.

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ORIGINAL ARTICLE De Giorgi, V. *et al.* Propranolol for off-label treatment of patients with melanoma: results from a cohort study. *JAMA Oncol.* <http://dx.doi.org/10.1001/jamaoncol.2017.2908> (2017)

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