

## Can adapalene be repurposed for melanoma?

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*Madam*, Melanoma, the most lethal skin cancer, accounts for 75% of deaths by skin cancer in the US.<sup>1</sup> Nivolumab, Pembrolizumab, and a combination of Nivolumab and ipilimumab are used in adjuvant therapy for distant metastatic melanoma.<sup>2</sup>

The combination therapy of ipilimumab and nivolumab for melanoma per patient per month was estimated to be USD 71,689.<sup>3</sup> Nevertheless, the efficiency of these treatments is limited.<sup>4</sup> Furthermore, metastasis can reduce the effectiveness of cancer treatment. With time, cancer cells can also develop resistance to drugs. Hence alternative treatment regimens should be identified.<sup>5</sup> The development of new therapies requires a vast amount of time, research, and investment. Drug repurposing provides an alternate approach to this passage. It refers to the new application of previously approved drugs. This process is rapid, potentially safer, and cost-effective.<sup>5</sup>

Adapalene, a third-generation retinoid, is an FDA-approved drug used topically to treat acne vulgaris. Adapalene has also demonstrated powerful inhibitory effects on colony formation in melanoma cells. It has already been used in the treatment of colon cancer and hepatoma. Hence urgent development of novel treatment options is needed. Adapalene simultaneously induces S-phase cell arrest and apoptosis. It prompted S-phase arrest as a short-term response by downregulating S-phase-related proteins: CDK2, cyclin A2, and cyclin D1. It also increased the protein level of the DNA damage marker,  $\gamma$ -H2AX, and decreased levels of BRCA-1 and RAD51, thus suppressing the DNA repairing system. Thus, it activates the DNA damaging system and inhibits the DNA repairing system in melanoma

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cells. This further amplifies the induction of S-phase arrest and apoptosis.<sup>4</sup>

Clinical trials should be conducted to establish the role of adapalene in treating distant metastatic melanoma. As Adapalene is already an FDA-approved drug,<sup>4</sup> this approach to researching would save time, and investments and would be potentially safer.

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