Novel compound restores immune response in patients with melanoma

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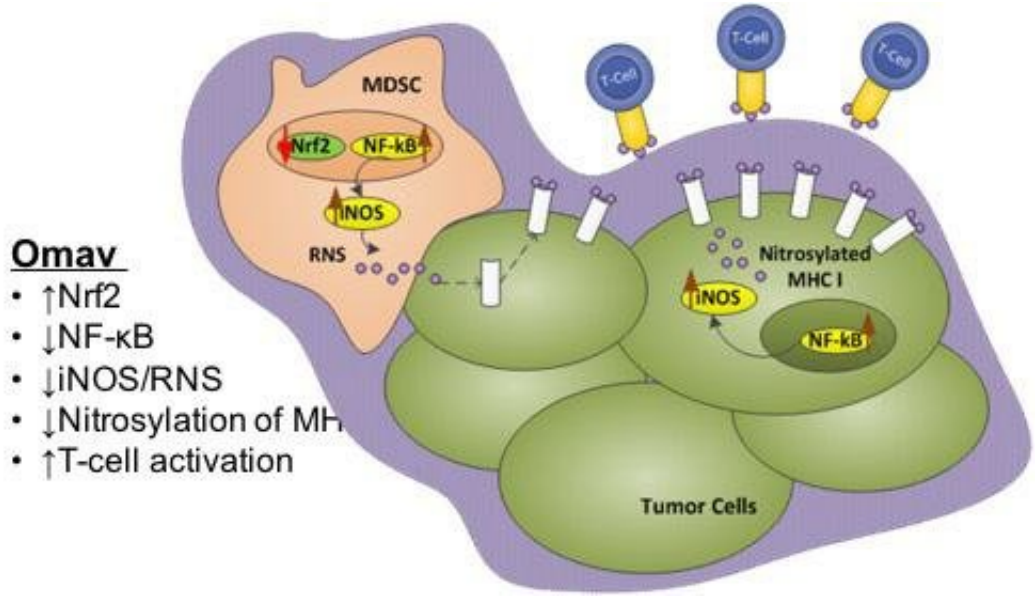

Credit: European Society for Medical Oncology

A novel compound may restore immune response in patients with melanoma, according to a study presented at the ESMO Immuno Oncology Congress 2017.

"Checkpoint inhibitors are a standard of care immunotherapy for metastatic melanoma," said lead author Dr Sapna Patel, Assistant Professor, Department of Melanoma Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, US. "However, many patients do not respond because myeloid derived suppressor cells

(MDSCs), a type of inhibitory cell, are present in the tumour microenvironment."

"In animal studies, omaveloxolone inhibited MDSCs and restored immune activity," she continued. "Myeloid-derived suppressor cells (MDSCs) produce reactive nitrogen radicals that alter the receptors on the surface of the tumour to hide it from cytotoxic lymphocytes that kill tumour cells. Omaveloxolone inhibits MDSC activity, suppresses reactive nitrogen radicals, and restores anti-tumour immune responses. Administering omaveloxolone with checkpoint inhibitors may improve the antitumour response of these immunotherapies."

This open label, multicentre, phase 1B trial investigated the safety and efficacy of omaveloxolone in combination with the checkpoint inhibitors ipilimumab or nivolumab. The study included 30 patients with unresectable or metastatic melanoma, of whom seven were naïve to checkpoint inhibitors and 23 had prior checkpoint inhibitor treatment.

The overall response rate was 57% in checkpoint inhibitor naïve patients and 17% in those with prior exposure. Median time to response was 19 weeks. There were no serious adverse events related to omaveloxolone and it was well tolerated in combination with ipilimumab or nivolumab.

Dr Patel said: "Our findings suggest that omaveloxolone may overcome resistance to checkpoint inhibitors. Omaveloxolone in combination with checkpoint blockade had activity in both naïve and checkpoint inhibitor refractory melanoma patients."

She added: "This is one of the first studies to demonstrate a meaningful response rate in the checkpoint inhibitor refractory melanoma population. Further dose escalation and dose expansion studies are underway as well as translational tissue-based experiments to clarify the impact of this treatment combination."

Commenting on the study for ESMO, Dr Olivier Michielin, head of Personalised Analytical Oncology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, said: "Omaveloxolone's novel mechanism of action is to block MDSCs, cells known to suppress the immune response. This study tested a new combination therapy in immuno oncology and found encouraging response rates with omaveloxolone plus ipilimumab or nivolumab in patients who were checkpoint inhibitor naïve or resistant. The combination was well tolerated and may address some of the immune escape mechanisms that limit the activity of current checkpoint blockade therapies."

Michielin added: "More data is needed before we can make a final call on whether there is a place, and where would the place be, for this combination in the current treatment portfolio. The next step should be a randomised trial to investigate whether omaveloxolone provides additional benefit when combined with the checkpoint blockade backbone, for example, comparing the efficacy of PD-1 blockade alone versus PD-1 blockade plus omaveloxolone."

More information: Abstract 5O_PR 'A phase 1b/2 study of omaveloxolone in combination with checkpoint inhibitors in patients with unresectable or metastatic melanoma' will be presented by Sapna Patel during a Proffered Paper Session on Friday 8 December, 08:30 to 10:30 CET in Room A. *Annals of Oncology*, Volume 28, 2017 Supplement 11. cslide.ctimeetingtech.com/esmo … nfcal/show/session/7

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