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Nivolumab shows signs of superior response rate compared to standard chemo in advanced melanoma

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The monoclonal antibody nivolumab achieves superior response rates and a longer duration of response than standard chemotherapy[1] in patients whose melanoma has progressed after treatment with ipilimumab, according to phase III data presented at the ESMO 2014 Congress in Madrid, Spain.

"Previously-treated advanced melanoma patients have limited options," says the study's principal investigator, Professor Jeffrey Weber, Director of the Donald A. Adam Comprehensive Melanoma Research Center of Excellence at the Moffitt Cancer Centre, Tampa, Florida.

Nivolumab is an antibody in a class of drugs called 'checkpoint inhibitors', that act to relieve a critical brake placed on the immune system by the tumour itself. The drug then reinvigorates patients' anti-tumour immune response and promotes shrinkage of the tumour.

In this first phase III trial of nivolumab among melanoma patients whose disease has progressed even after treatment with ipilimumab, 405 patients with unresectable metastatic melanoma were randomized in a ratio of 2:1 either to intravenous nivolumab (3 mg/kg) or the investigator's choice of chemotherapy regimens: dacarbazine (1000 mg/m2), or carboplatin AUC6 plus paclitaxel (175 mg/m2).

The primary endpoints of the study were objective response rate to

treatment and overall survival, but researchers are also looking at the impact of treatment on secondary objectives of safety, progression-free survival, health-related quality of life and expression of the programmed death-1 ligand (PD-L1), which is the ligand of PD-1 targeted by nivolumab.

Preliminary data from a sub-group of the nivolumab-treated patients in the open-label trial show that nivolumab has markedly higher clinical activity with a 32% response rate, as well as lower toxicity compared to the chemotherapy reference arm, with a 11% response rate.

Treatment responses were also longer-lasting in the nivolumab group compared to the chemotherapy group, and there was a 31% incidence of higher-grade treatment-related side effects in the chemotherapy group compared to only 9% incidence in the nivolumab group.

"The impressive data on duration of response suggest that there will be significant prolongation of progression-free and overall survival when the analysis of those data is mature," says Weber.

In summary, Weber says, "The differences in response rate and toxicity markedly favour the use of the PD-1 blocking antibody nivolumab compared to results seen with chemotherapy in patients that have failed ipilimumab."

Commenting on the findings, Professor Olivier Michielin of the Department of Oncology, University of Lausanne, Switzerland, says, "These results add another piece of evidence that PD blockade is rapidly becoming a central part in our armamentarium against melanoma, progressively replacing chemotherapy with more effective and less toxic options."

"These results demonstrate that PD blockade, contrary to a common and

old dogma of immunotherapy, can produce rapid and deep responses even in advanced and bulky disease. This opens exciting new opportunities to widen the scope of application of immuno-oncology for the treatment of stage IV melanoma," says Michielin.

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