Dual checkpoint inhibitor blockade shows promise as first-line and salvage therapy for Merkel cell carcinoma patients

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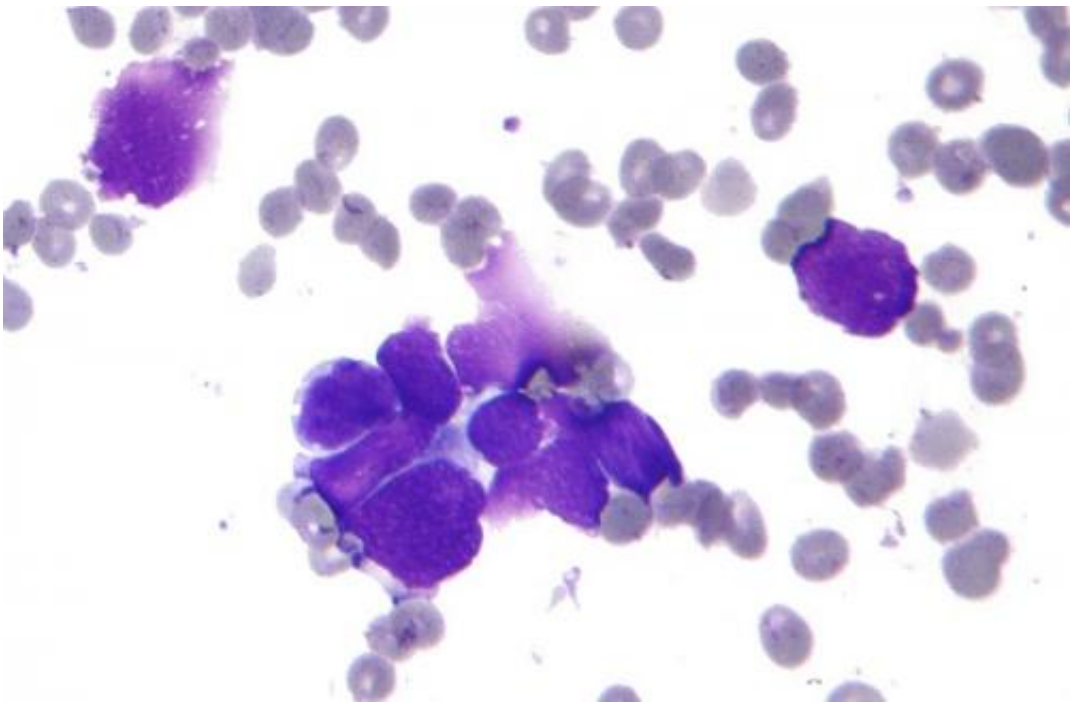

Micrograph of a lung primary small cell carcinoma, a type of carcinoma. Credit: Wikipedia

Merkel cell carcinoma is a rare but aggressive form of skin cancer that has a high rate of metastasis and poor patient outcomes. The current standard of care for patients with recurrent, unresectable or metastatic disease is immune checkpoint inhibitor monotherapy targeting anti-

programmed death receptor 1 (anti-PD-1) and programmed death ligand 1 (PD-L1), but only about half of patients respond to this therapy. Moffitt Cancer Center is one of two institutions in the U.S. investigating a new dual checkpoint inhibitor therapy with or without stereotactic body radiation therapy. Results from the phase 2 clinical trial were published in *The Lancet*, in conjunction with a presentation at the European Society for Medical Oncology Congress.

Fifty patients with unresectable, recurrent or stage 4 Merkel cell carcinoma were randomly assigned to two treatment groups. One group received ipilimumab, a checkpoint inhibitor targeting cytotoxic T lymphocyte-associated antigen 4 (CTLA4), and nivolumab, an anti-PD-1/ PD-L1 inhibitor. The other group was treated with the ipilimumab and nivolumab combination along with stereotactic body radiation therapy. Both groups had a mix of patients who had previously been treated with immune checkpoint inhibitor therapy targeting anti-PD-1/ PD-L1 and some who had not received that type of therapy. The primary endpoint for this phase of the trial was objective response rate, defined as the percentage of patients whose tumors decreased or disappeared after receiving the therapy.

After an average 14.6 months of follow-up, 100% of patients who had not received previous immune checkpoint inhibitor therapy, regardless of the treatment group, responded to the investigational combination therapy, with 41% of patients having a complete response. Of the 26 patients who had received prior anti-PD-1/PD-L1 therapy, eight responded to therapy with four having a complete response.

"Our results show that first-line combination therapy with nivolumab and ipilimumab has a high overall response rate with durable responses for patients with advanced Merkel cell carcinoma," said Sungjune Kim, M.D., Ph.D., principal investigator of the trial and associate member of the Radiation Oncology Department at Moffitt. "This presents a new

option for patients who may not respond to the current standard of care therapy for this disease."

Kim added that the addition of stereotactic body radiation therapy did not improve efficacy of the nivolumab and ipilimumab combination therapy.

More information: Sungjune Kim et al, Combined nivolumab and ipilimumab with or without stereotactic body radiation therapy for advanced Merkel cell carcinoma: a randomised, open label, phase 2 trial, *The Lancet* (2022). DOI: 10.1016/S0140-6736(22)01659-2

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