Immunotherapy Should Be First Line in Merkel Cell Carcinoma

Roxanne Nelson, RN, BSN

March 18, 2019

2 Read Comments

Upfront immunotherapy with pembrolizumab (*Keytruda*, Merck & Co) in patients with advanced Merkel cell carcinoma (aMCC) shows an improved overall survival and response rate when compared with historical controls, and has a generally manageable safety profile, according to new findings.

The results are from the longest follow-up for any programmed cell death (PD) inhibitor administered first-line for MCC and have led the researchers to say that these immunotherapies should be used upfront in the treatment of this disease.

MCC is a rare and aggressive neuroendocrine skin cancer that is often fatal. It is diagnosed in approximately 1600 people each year in the United States.

However, the annual incidence of new MCC diagnoses has risen by 95% between 2000 and 2013.

The new results follow up on the expanded phase 2 Cancer Immunotherapy Trials Network-09/Keynote-017 trial of pembrolizumab. The findings represent the longest follow-up for any anti–PD-1/PD-L1 drug administered in the first-line treatment setting for aMCC.

The cohort included 50 treatment naïve adults with aMCC who received a median of 10.5 doses of pembrolizumab, with a median treatment duration of 6.6 months. The median follow-up time at database cutoff was 14.9 months.

The 24-month overall survival rate was 68.7%, and the median was not reached among patients who responded, the researchers report.

The study was published online ahead of print February 6, 2019, in the *Journal of Clinical Oncology.*

"Although the present study is the farthest along in the first line, there are highly consistent data from several studies of MCC now," commented lead author Paul Nghiem, MD, PhD, professor and head of the division of dermatology at the University of Washington, Seattle.

Other studies include a trial in 88 patients with avelumab (*Bavencio*, EMD Serono), which led to approval from the US Food and Drug Administration for metastatic MCC in 2017, when it became the first approved treatment for this disease. In December 2018, pembrolizumab was approved for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic MCC.

"It appears that the consensus in the field, and as noted in the National Comprehensive Cancer Network guidelines for MCC, is that unless a patient has contraindications to PD-1 pathway blockade, these agents should be the first line of therapy for advanced MCC," Nghiem told *Medscape Medical News.*

Some studies have also looked at the use of PD-1 pathway inhibitors in the second or third line for MCC patients, primarily with avelumab, explained Nghiem.

"These studies showed a far better response for this agent than historical chemotherapy data," he said.

"However, the chance of benefiting from immune checkpoint therapy is nearly twice as high if MCC patients do not first get chemotherapy," he added.

Immunotherapy Promising

The authors point out that growing evidence supports the hypothesis that MCC is an immunogenic cancer, considering that the incidence is greater than 10-fold higher in people who are chronically immunosuppressed.

Cite this: Roxanne Nelson. Immunotherapy Should Be First Line in Merkel Cell Carcinoma - Medscape - Mar 18, 2019.

Immunotherapy Should Be First Line in Merkel Cell Carcinoma

Roxanne Nelson, RN, BSN

March 18, 2019

2 Read Comments

Merkel cell polyomavirus (MCPyV) occurs in the majority (~80%) of MCC tumors, and the persistent expression of MCPyV T-antigen oncoproteins is required for virus-positive (VP) tumor cells to proliferate.

The other 20% of MCC cases are believed to result from DNA damage caused by ultraviolet light, and the virus-negative (VN) MCC subset has a tumor mutational burden that is about 100-fold greater than the low mutational burden observed with VP-MCC.

It has also been clarified that "non–self-antigens" are present in both types of MCC tumors, the researchers comment.

Until the advent of immunotherapy, cytotoxic chemotherapy was the only systemic treatment option available for patients with aMCC, but the benefit was modest with a median progression-free survival of approximately 90 days.

However, recent clinical trials of PD-1 pathway inhibitors in this population, either used as first-line or later therapy, have shown increased progression-free and overall survival compared with historical data from patients treated with chemotherapy.

Study Details

In this Keynote-017 study, patients received pembrolizumab (2 mg/kg every 3 weeks) for up to 2 years. The median age was 70.5 years, and nearly two-thirds (64%) had MCPyV tumors.

The objective response rate to treatment with pembrolizumab was 56%, with 28 responses (12 complete responses and 16 partial responses). In addition, five patients (10%) achieved stable disease, and 16 patients (32%) had progressive disease.

No significant differences were observed between the response rates in patients with VP-MCC (19/32; 59%) versus those with VN-MCC (9/17; 53%; $P = .765$).

Among the 28 patients who responded to therapy, the median response duration was not reached (range, 5.9 to 34.5+ months).

At 24 months, progression-free survival was 48.3%, with a median duration of 16.8 months. There were also no significant difference in survival outcomes between patients with VP-MCC and those with VN-MCC ($P = .48$ and $P = .77$, respectively).

Treatment-related adverse events of any grade occurred in almost every patient (n = 48, 96%), and grade 3 or greater treatment-related adverse events occurred in 14 (28%) of patients. A total of 7 (14%)

of patients discontinued treatment due to adverse events, and there was one treatment-related death.

New Biomarkers Needed

Not all patients respond to immunotherapy, as witnessed in this study, and there is a need for identifying biomarkers other than PD-1/L1, the researchers comment.

Nghiem notes that his group published a 2018 study along these lines based on patients in this same clinical trial.

"It found that the distance between PD-1–positive and PD-L1–positive cells within the tumor was predictive of response to pembrolizumab, where higher numbers of nearby cells suggested response was more likely," he said. "While there are tantalizing hints of better biomarkers, it appears we do not yet have anything that is so predictive that it could provide real confidence as to whether an immune checkpoint inhibitor will work."

The study was supported by the National Cancer Institute and the National Institutes of Health/NCI Cancer Center Support Grant in Seattle. The authors also acknowledge support from the Merkel cell carcinoma patient gift fund at University of Washington; the Kelsey Dickson MCC Challenge Grant from the Prostate Cancer Foundation; and Merck, which provided pembrolizumab and partial funding for this study. Nghiem has disclosed relationships with EMD Serono, Merck Sharp & Dohme, Sanofi/Regeneron, Pfizer, and Bristol-Myers Squibb. He also has a patent pending for high-affinity T-cell receptors that target the Merkel polyomavirus. Other co-authors have disclosed multiple relationships with industry.

J Clin Oncol. 2019;37:693-702. Abstract

For more Medscape Oncology news, join us on Facebook and Twitter .

2 Read Comments

Cite this: Roxanne Nelson. Immunotherapy Should Be First Line in Merkel Cell Carcinoma - Medscape - Mar 18, 2019.

What to Read Next on Medscape

BUSINESS OF MEDICINE

Diagnosis and Management of Malignant Tumors of the Eyelid, Conjunctiva, and Orbit

Highlights of the 66th Annual Meeting of the American Academy of Dermatology

Persistent, Friable Nodule of the Scalp