Merkel Cell Carcinoma

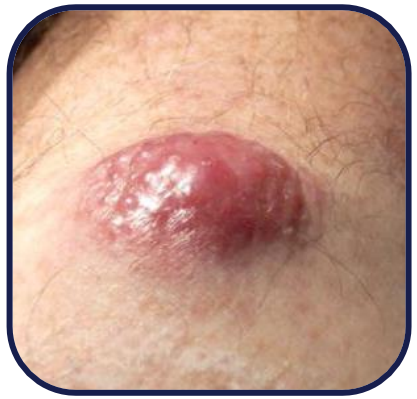
Disease State Overview

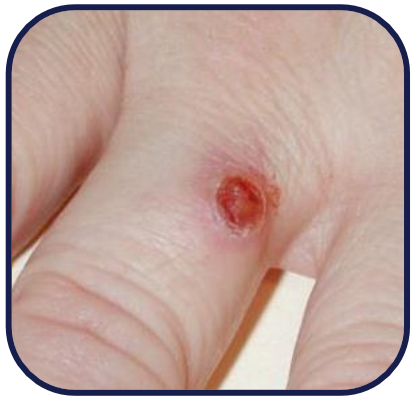
MI-DIS-US-0074 11/24

MCC is an Aggressive Cutaneous Malignancy

- MCC arises in the dermo-epidermal junction, and usually presents as a single, fast-growing, painless lump on sun-exposed skin, such as may be found on the head, neck, arms, legs, and trunk[1,2]
- Due to its nonspecific clinical appearance, MCC is rarely suspected before a biopsy is performed[1]

MCC nodule arising on a sun-exposed area of the arm[2]





MCC lesions are commonly misdiagnosed as cysts or other benign processes[2]

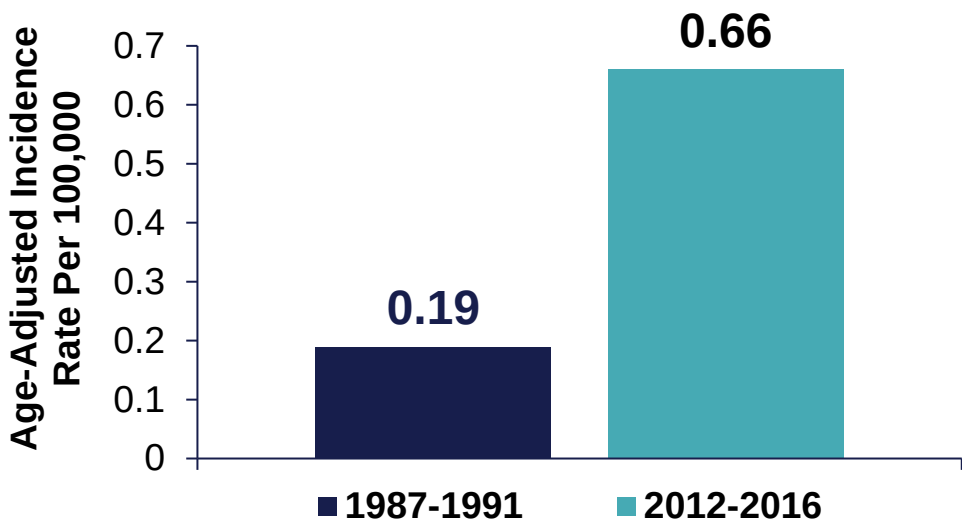
MCC develops rapidly with a strong tendency for local recurrence and distant spread.[2,3]
Mortality rate is high, exceeding that of melanoma.[4,5]

MCC, Merkel cell carcinoma.

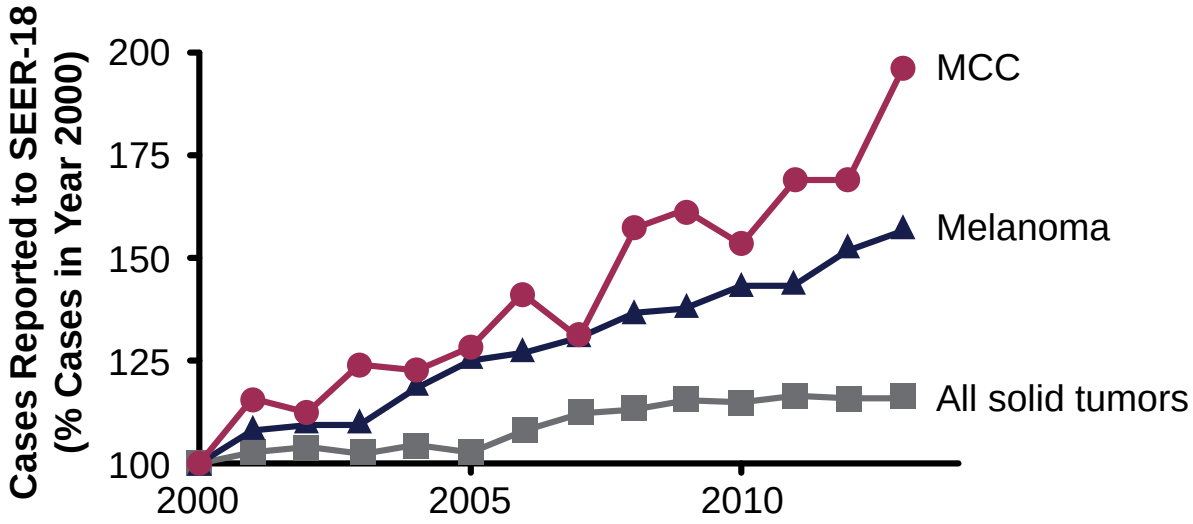
1. National Cancer Institute. Accessed November 2024. https://www.cancer.gov/types/skin/hp/merkel-cell-treatment-pdq#_242. 2. Heath M, et al. *J Am Acad Dermatol.* 2008;58:375-81. Pictures reprinted from *J Am Acad Dermatol*, Vol 58(3), .2 Heath M. et al, Clinical characteristics of Merkel cell carcinoma at diagnosis in 195 patients: the AEIOU features, Pages 375-81, 2008, with permission from the American Academy of Dermatology. 3. Medina-Franco H, et al. *Ann Surg Oncol.* 2001;8:204-8. 4. Grabowski J, et al. *Clin Med Oncol*. 2008;2:327-33. 5. Schadendorf D, et al. *Eur J Cancer.* 2017;71:53-69.

MCC is Rare, With a Rapidly Increasing Incidence

In the US from 2012 to 2016, the overall age-adjusted incidence rate for MCC **increased 3.5-fold** compared with 1987 to 1991[1]



MCC incidence in the U.S. has been **increasing by ≈6% per year** and is expected to continue at this rate as the population ages[1,2]



MCC incidence is increasing at a markedly higher rate than other skin cancers and solid tumors[2]

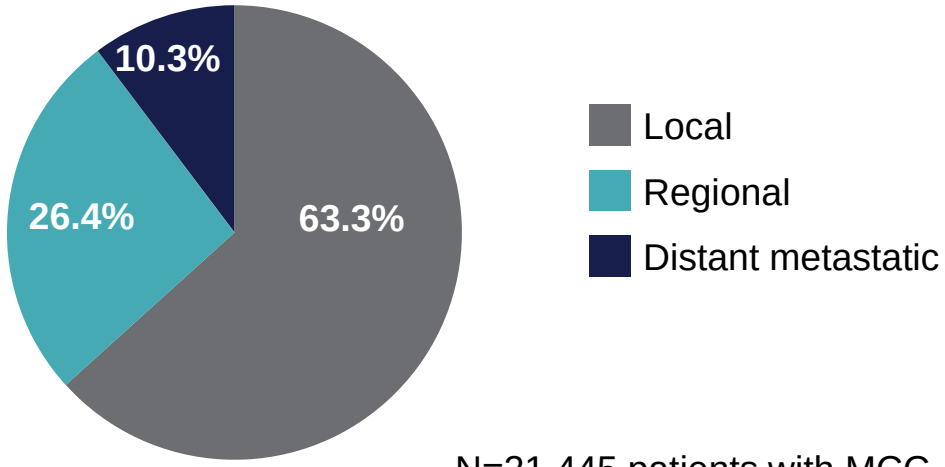
SEER, Surveillance, Epidemiology, and End Results; US, United States.

1. Jacobs D, et al. *JAMA Dermatol*. 2021;157:59-65. 2. Paulson KG, et al. *J Am Acad Dermatol*. 2018;78:457-463.e2. Figure reprinted from *J Am Acad Dermatol*. 78(3), Paulson KG et al, "Merkel Cell Carcinoma: Current United States Incidence and Projected Increases based on Changing Demographics", Pages 457-463, copyright (2018), with permission from the National Library of Medicine.

Metastasis and Disease Recurrence Are Frequent in MCC, and Prognosis Is Poor

More than one third of MCC patients present with regional or distant metastasis[1]

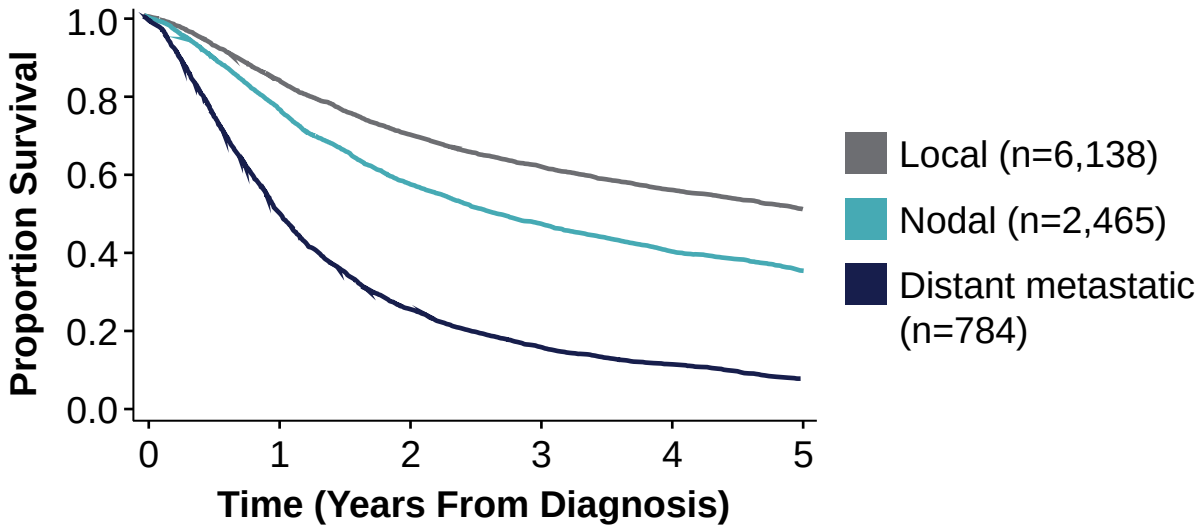
Extent of Disease at Presentation[1]



N=21,445 patients with MCC

Prognosis for metastatic or recurrent, locally advanced MCC is very poor

MCC 5-Year Survival by Disease Extent[3]



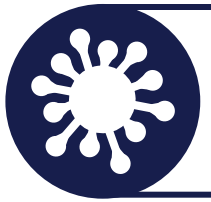
Recurrence is common (≈40%) and usually occurs within 3 years of diagnosis[2]

5-year OS of 51%, 35%, and 14% for local, nodal, and distant metastatic disease, respectively[3]

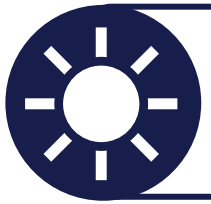
OS, overall survival.

1. Paulson KG, Bhatia S. *J Natl Compr Canc Netw*. 2018;16:782-90. 2. McEvoy AM, et al. *JAMA Dermatol*. 2022;158:382-389. 3. Harms KL, et al. *Ann Surg Oncol*. 2016;23:3564-3571.

Irrespective of the Underlying Cause, MCC Is a Highly Immunogenic Cancer



- Approximately 80% of MCCs are associated with MCPyV infection[1,2]
- Virus-positive MCCs elicit **oncoprotein-specific antibodies and a T-cell response**[3,4]



- MCC tumorigenesis can also be linked to UV exposure[3,4]
- UV exposure results in DNA damage and multiple oncogenic mutations that may generate **neoantigens for immune recognition**[3-6]

Both types of MCC show high expression of PD-L1, a marker of immune recognition[3,4]

DNA, deoxyribonucleic acid; MCPyV, Merkel cell polyomavirus; PD-L1, programmed cell death ligand 1; UV, ultraviolet.

1. Feng H, et al. *Science*. 2008;319:1096-1100. 2. Lipson EJ, et al. *Cancer Immunol Res*. 2013;1:54-63. 3. Vandeven NA, Nghiem P. *J Oncol Pract*. 2016;12:649-650. 4. Stachyra K, et al. *Int J Mol Sci*. 2021;22:6305. 5. Wong SQ, et al. *Cancer Res*. 2015;75:5228-5234. 6. Knepper TC, et al. *Clin Cancer Res*. 2019;25:5961-5971.

Summary

- MCC is an aggressive cutaneous malignancy that usually presents as a single, fast-growing, painless lump on sun-exposed skin, such as may be found on the head, neck, arms, legs, and trunk[1,2]
- MCC develops rapidly with a strong tendency for local recurrence and distant spread while having a high mortality rate[3,4]
- Recurrence is common, with a rate of ≈40%, and usually occurs within 3 years of diagnosis[5]
- Approximately 80% of MCCs are associated with MCPyV infection, although cases have also been linked to UV exposure[6-9]

1. National Cancer Institute. Accessed November 2024. https://www.cancer.gov/types/skin/hp/merkel-cell-treatment-pdq#_242. 2 Heath M. et al, Clinical characteristics of Merkel cell carcinoma at diagnosis in 195 patients: the AEIOU features, Pages 375-81, 2008, with permission from the American Academy of Dermatology. 3. Medina-Franco H, et al. *Ann Surg Oncol.* 2001;8:204-8. 4. Grabowski J, et al. *Clin Med Oncol*. 2008;2:327-33. 5. McEvoy AM, et al. *JAMA Dermatol*. 2022;158:382-389. 6. Feng H, et al. *Science*. 2008;319:1096-1100. 7. Lipson EJ, et al. *Cancer Immunol Res*. 2013;1:54-63. 8. Vandeven NA, Nghiem P. *J Oncol Pract*. 2016;12:649-650. 9. Stachyra K, et al. *Int J Mol Sci*. 2021;22:6305.