

ADC 101st Annual Conference

APRIL 19-21, 2024 | HERSHEY LODGE, HERSHEY, PA



Merkel Cell Carcinoma: Case-based Discussion on Management

H. William Higgins II, MD MBE

Associate Professor of Dermatology
University of Pennsylvania
Mohs Micrographic Surgery & Cutaneous Oncology
Lab Director, Pennsylvania Hospital Mohs Surgery Unit

Disclosures

- No relevant disclosures







National Comprehensive
Cancer Network®

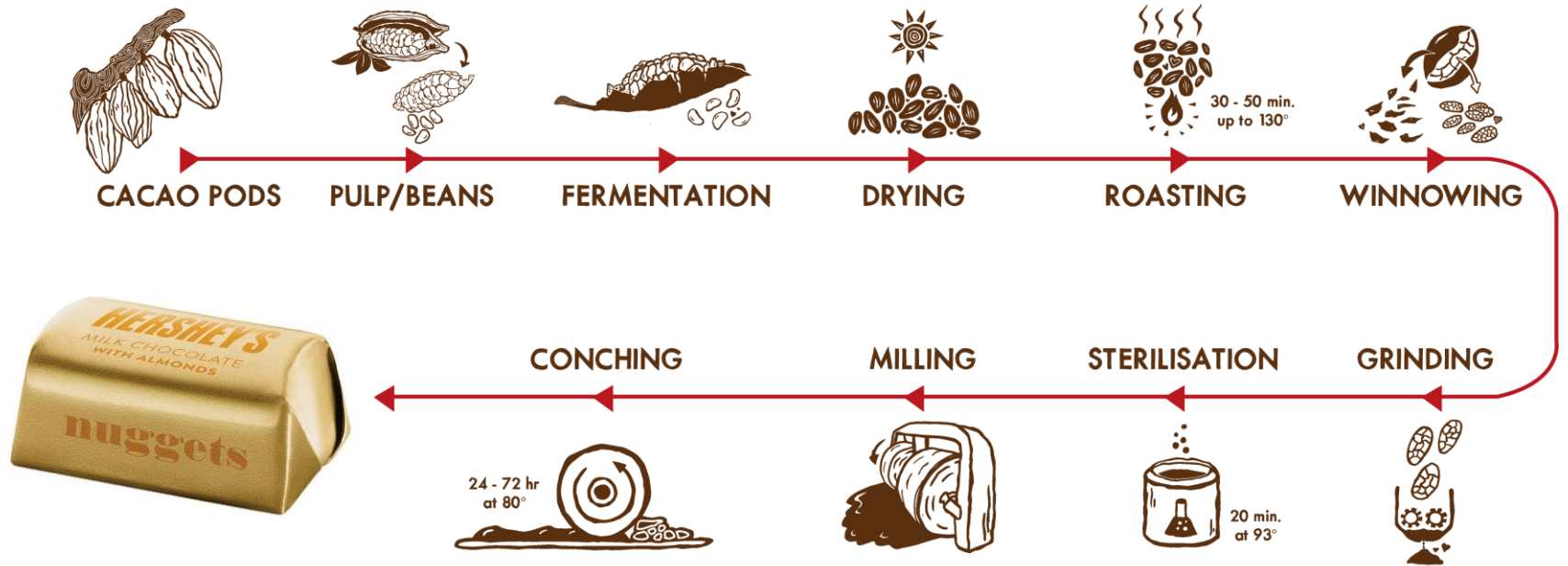
- Over 60 pages of material!
- Multiple versions that are updated regularly
- Brackets and more brackets!

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Merkel Cell Carcinoma

Version 1.2024 — November 22, 2023

Conventional Chocolate Process



Goals

- Walk through a case
- Highlight the most important management points (chocolate nuggets) for Dermatologists!

Case Description

- *88 year-old woman*
 - Initially presented with an 'abscess' of right ear, debrided by a plastic surgeon
 - 'Abscess' had improved initially but then returned to original size
 - No clinical lymphadenopathy
 - Presents for 2nd opinion



Audience Response Question

- *What's your next step?*
 - A. Warm compresses
 - B. Culture and start antibiotics
 - C. Biopsy
 - D. Debride again
 - E. Reassurance and monitor



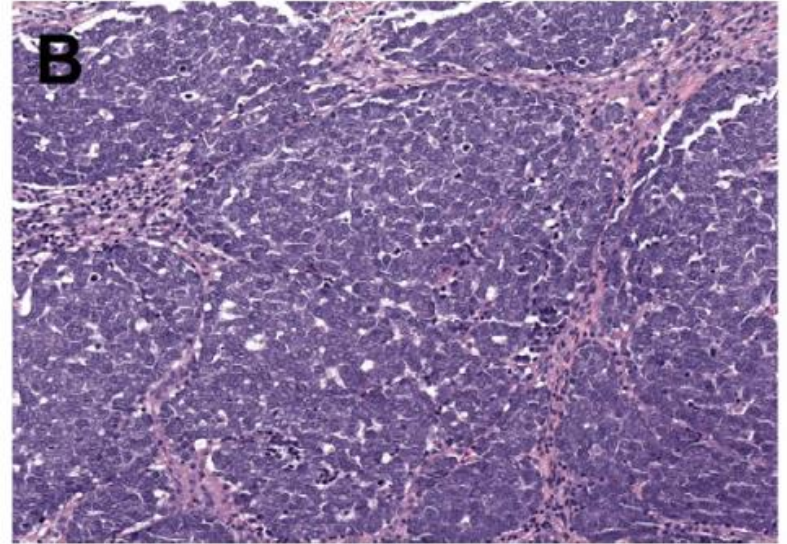
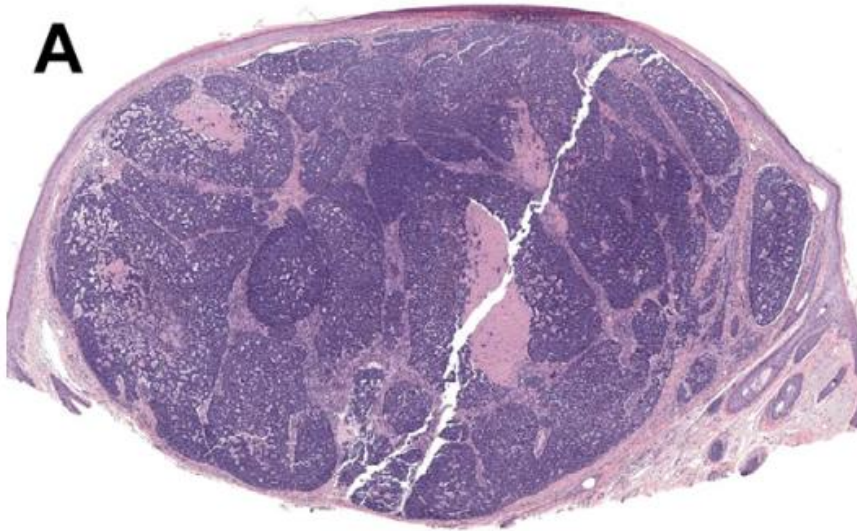
Audience Response Question

- *What's your next step?*
 - A. Warm compresses
 - B. Culture and start antibiotics
 - C. Biopsy**
 - D. Debride again
 - E. Reassurance and monitor



C. Biopsy

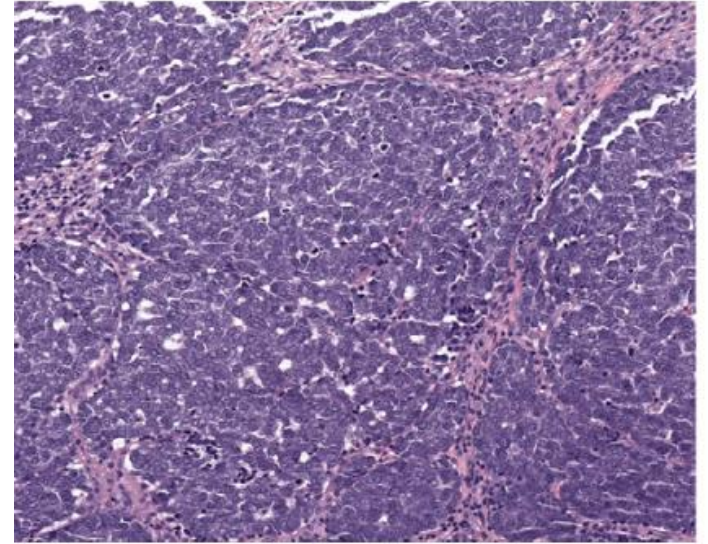
- *H& E stains at 25x and 150x*



Merkel Cell Carcinoma. Lewis DJ, Sobanko JF, Etkorn JR, Shin TM, Giordano CN, McMurray SL, Walker JL, Zhang J, Miller CJ, Higgins HW 2nd. *Dermatol Clin*. 2023 Jan;41(1):101-115.

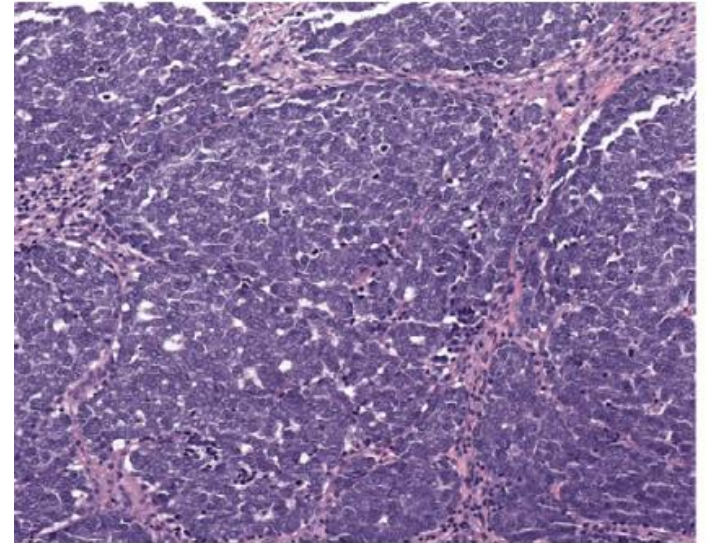
Audience Response Question

- *What stains would you order next?*
 - A. Smooth muscle actin
 - B. SOX-10
 - C. CK-20
 - D. Thyroid transcription factor-1
 - E. CD34
 - F. C and D



Audience Response Question

- *What stains would you order next?*
 - A. Smooth muscle actin
 - B. SOX-10
 - C. CK-20
 - D. Thyroid transcription factor-1
 - E. CD34
 - **F. C and D**



F. C and D

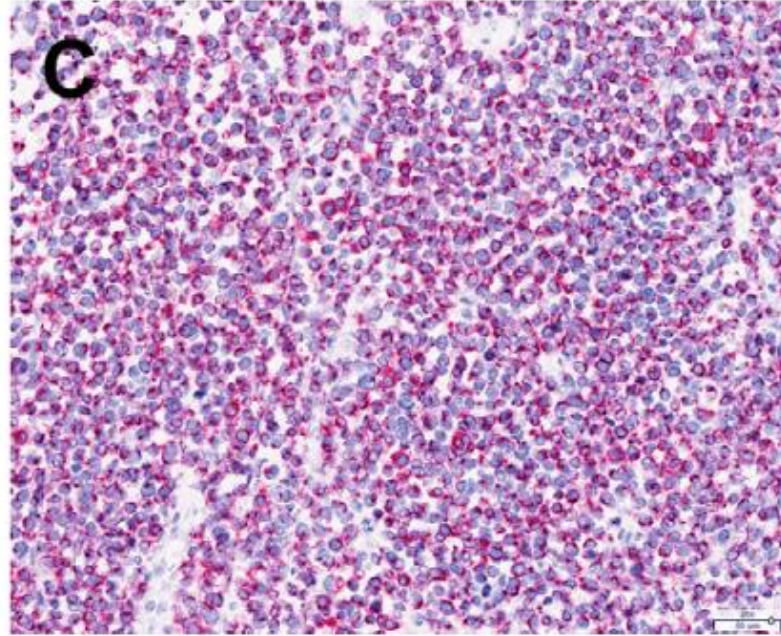


Table 1
Immunohistochemical staining of Merkel cell carcinoma and histopathologic mimics

| Stain | MCC | SCLC | Neuroblastoma | Ewing Sarcoma |
|--------------------------------|----------------|------|---------------|---------------|
| Cytokeratin-7 | — ^a | +/- | — | — |
| Cytokeratin-20 | + | — | — | — |
| Thyroid transcription factor-1 | — | + | — | — |
| Neuron-specific enolase | + | + | + | +/- |
| Chromogranin A | + | + | + | — |
| Synaptophysin | + | + | + | +/- |
| Neurofilament | + | — | + | + |
| CD56 | + | + | + | +/- |

Merkel Cell Carcinoma. Lewis DJ, Sobanko JF, Etkorn JR, Shin TM, Giordano CN, McMurray SL, Walker JL, Zhang J, Miller CJ, Higgins HW 2nd. *Dermatol Clin*. 2023 Jan;41(1):101-115.

Pathology – Bx showed Merkel cell carcinoma



CK-20 stain

Audience Response Question

- *A patient is referred for treatment of this 2cm Merkel cell carcinoma (MCC) on the ear. There is clinically no LAD. What is your next step?*
- Proceed with excision or Mohs alone
 - Schedule a sentinel lymph node biopsy preceding excision or Mohs
 - Refer patient for radiation (primary treatment)
 - Refer patient to medical oncology to start immunotherapy (primary treatment)

Audience Response Question

• *A patient is referred for treatment of this 2cm Merkel cell carcinoma (MCC) on the ear. There is clinically no LAD. What is your next step?*

A. Proceed with excision or Mohs alone

B. Schedule a sentinel lymph node biopsy preceding excision or Mohs

C. Refer patient for radiation (primary treatment)

D. Refer patient to medical oncology to start immunotherapy (primary treatment)

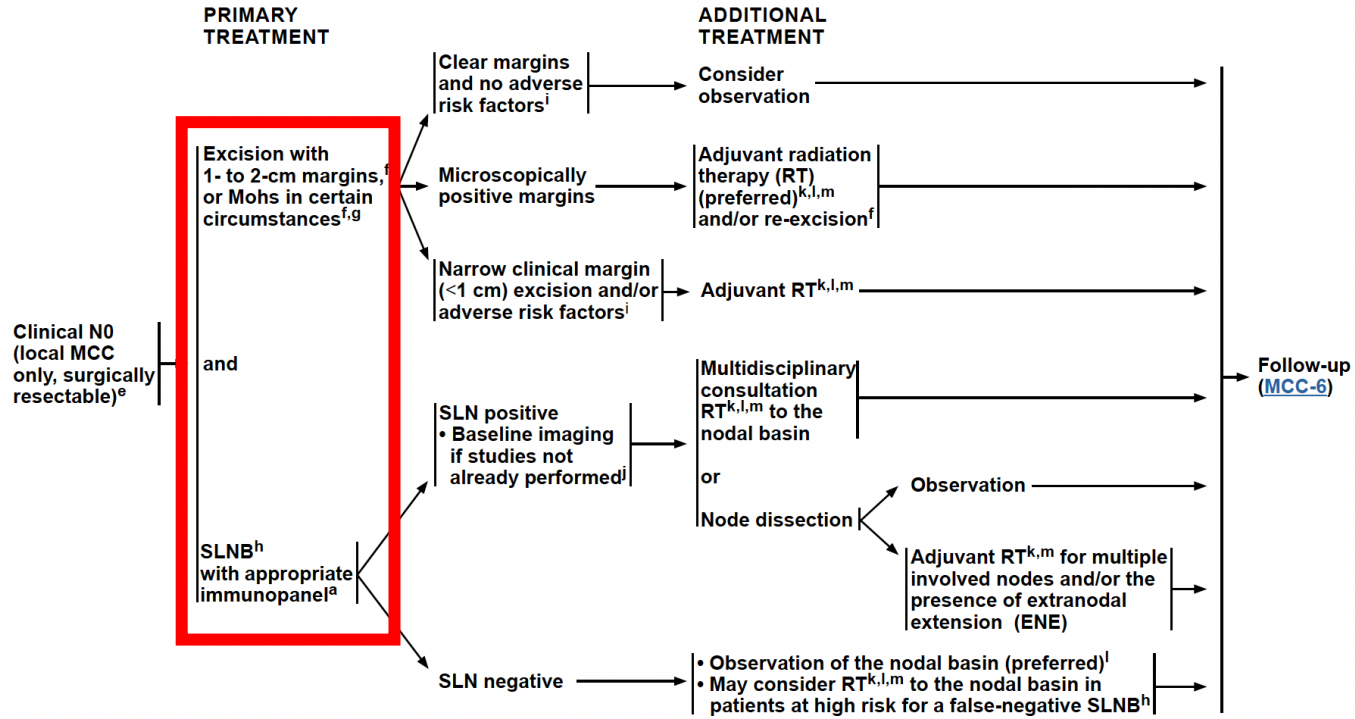


Nodal metastases occur in
25-30% of patients

**SLNB provides staging information
and aids in prognostication**

NCCN MCC Guidelines (Jan 2024)

CLINICAL N0 DISEASE, LOCAL MCC ONLY, SURGICALLY RESECTABLE



How often are SLNB performed with MCC?



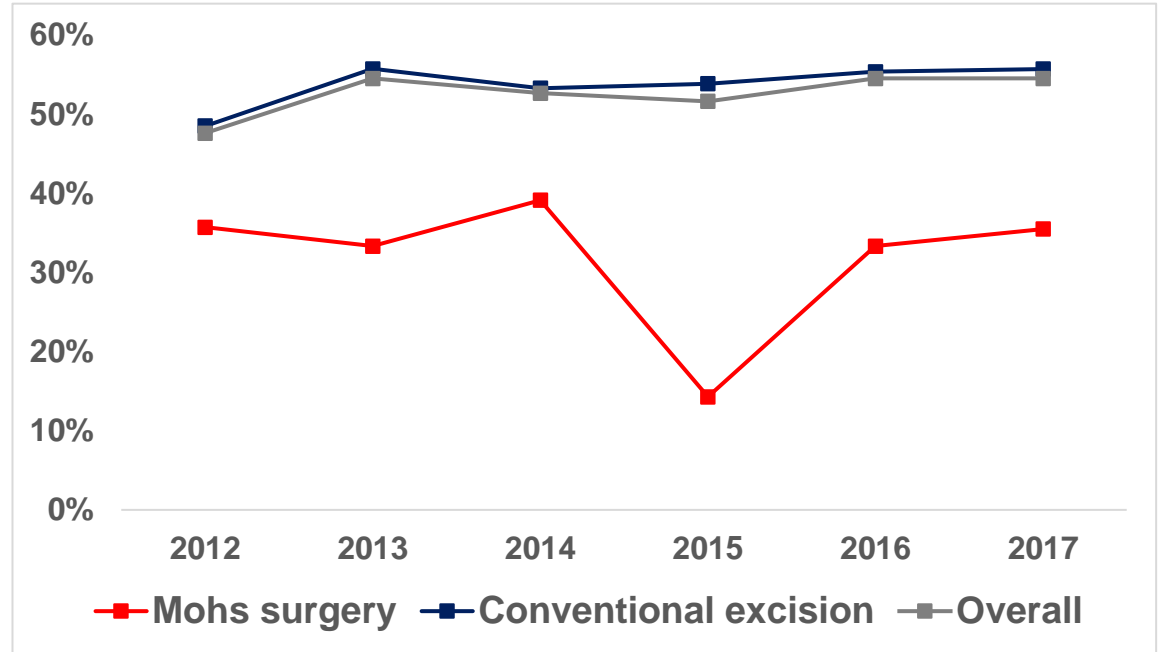
RESEARCH LETTER

Sentinel lymph node biopsy in Merkel cell carcinoma: Rates and predictors of compliance with the National Comprehensive Cancer Network guidelines

Sentinel lymph node biopsy in Merkel cell carcinoma: Rates and predictors of compliance with the National Comprehensive Cancer Network guidelines. Lewis DJ, Fathy RA, Nugent S, Etzkorn JR, Sobanko JF, Shin TM, Giordano CN, McMurray SL, Walker JL, Zhang J, Miller CJ, Higgins HW 2nd. *J Am Acad Dermatol.* 2023 Feb;88(2):448-450. doi: 10.1016/j.jaad.2022.05.054. Epub 2022 Jun 1. PMID: 35660413

Results: SLNB Compliance

| | |
|--------------------------------|------------|
| Overall compliance | 53% |
| Trend (2012-2017) | 48 → 55% |
| Conventional excision (n=2746) | 54% |
| Mohs surgery (n=155) | 32% |



Audience Response Question

- *A patient is referred for treatment of this 2cm Merkel cell carcinoma (MCC) on the ear. There is clinically no LAD. What is your next step?*

A. No imaging is needed

B. A PET scan should be ordered

C. Consider ordering serum Merkel cell polyomavirus (MCPyV) oncoprotein antibodies

D. B & C

Audience Response Question

- *A patient is referred for treatment of this 2cm Merkel cell carcinoma (MCC) on the ear. There is clinically no LAD. What is your next step?*

A. No imaging is needed

B. A PET scan should be ordered

C. Consider ordering serum Merkel cell polyomavirus (MCPyV) oncoprotein antibodies

D. B & C



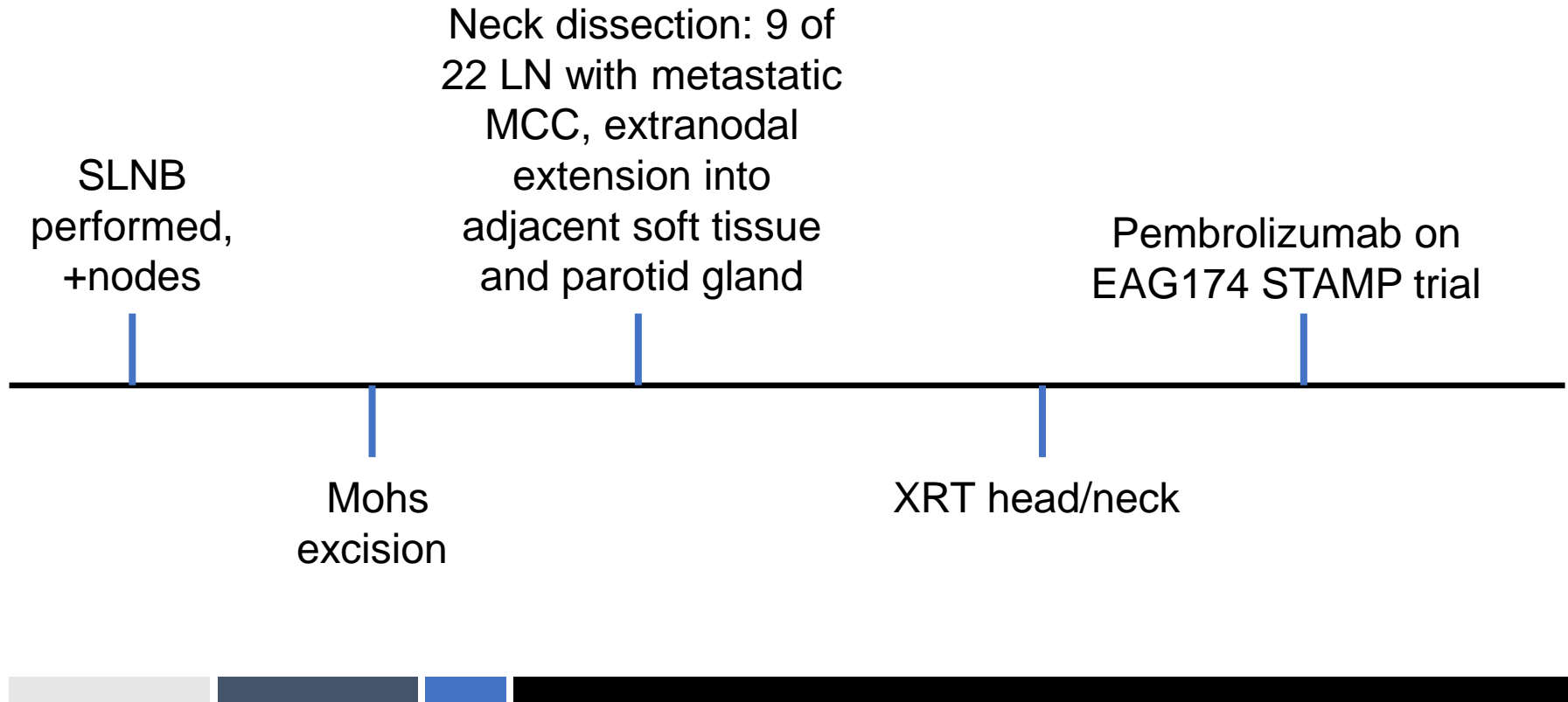
Whole-body FDG-PET

Occult metastatic disease detected in 12%–20% of patients presenting without suspicious H&P findings



Merkel cell polyomavirus (MCPyV) oncoprotein antibodies

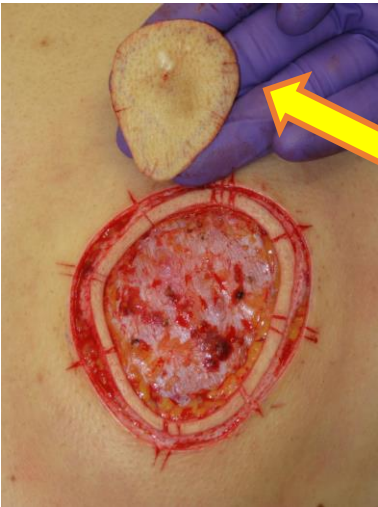
Baseline testing should be performed within 3 months of treatment, because titers are expected to decrease significantly after clinically evident disease is eliminated





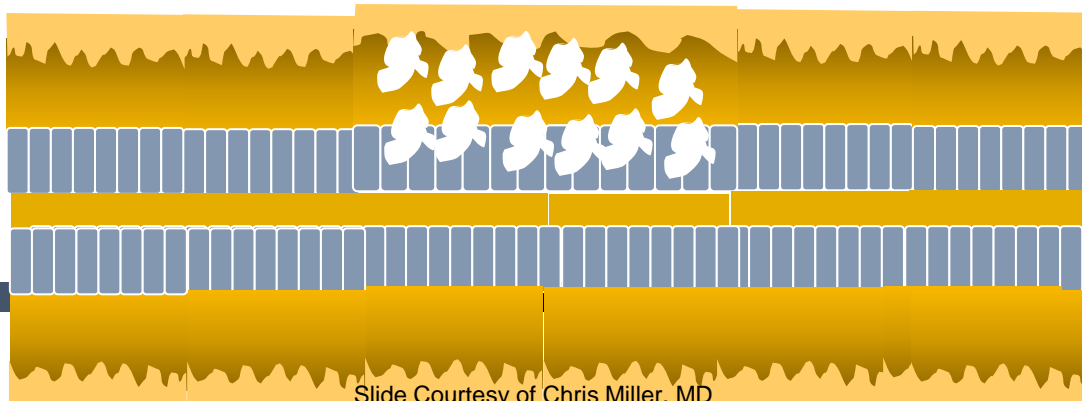
NCCN Guidelines for MCC

If MMS is performed, debulking excision with permanent vertical sections is recommended



Debulk Excision

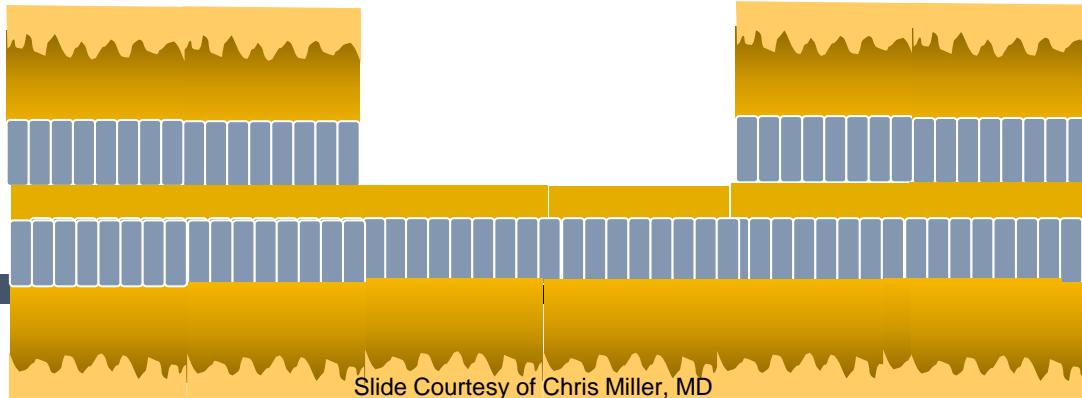
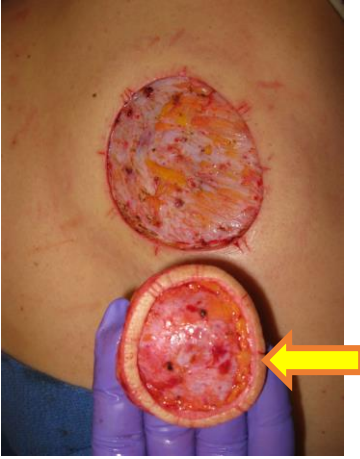
Sharply excise
to the perceived level of the tumor



Slide Courtesy of Chris Miller, MD

Mohs layer

Excise peripheral margin



Slide Courtesy of Chris Miller, MD

How do we stack up to NCCN guidelines?



High compliance with National Comprehensive Cancer Network guidelines and no local recurrences for patients receiving Mohs micrographic surgery for Merkel cell carcinoma: A single-center retrospective case series

Nugent ST, Lukowiak TM, Cheng B, Stull C, Miller CJ, Aizman L, Perz AM, Etkorn J, Sobanko JF, Shin TM, Giordano CN, Lukens JN, Miura JT, Modi MB, **Higgins HW 2nd**. *J Am Acad Dermatol*. 2022 Nov 4:S0190-9622(22)02981-4. doi: 10.1016

Methods

Retrospective case series of 30 tumors in 30 patients
Mohs micrographic surgery for stage I or II MCC

Outcome 1: Compliance with NCCN Guidelines



**Debulking excisions sent for
permanent sections in 100% of cases**



87% (26/30) received SLNB

2 declined SLNB

2 did not do SLNB due to medical comorbidities



Outcome 2: Recurrence after MMS

No local recurrences
mean follow-up of 3.3 yrs (SD: 3.2 yrs)



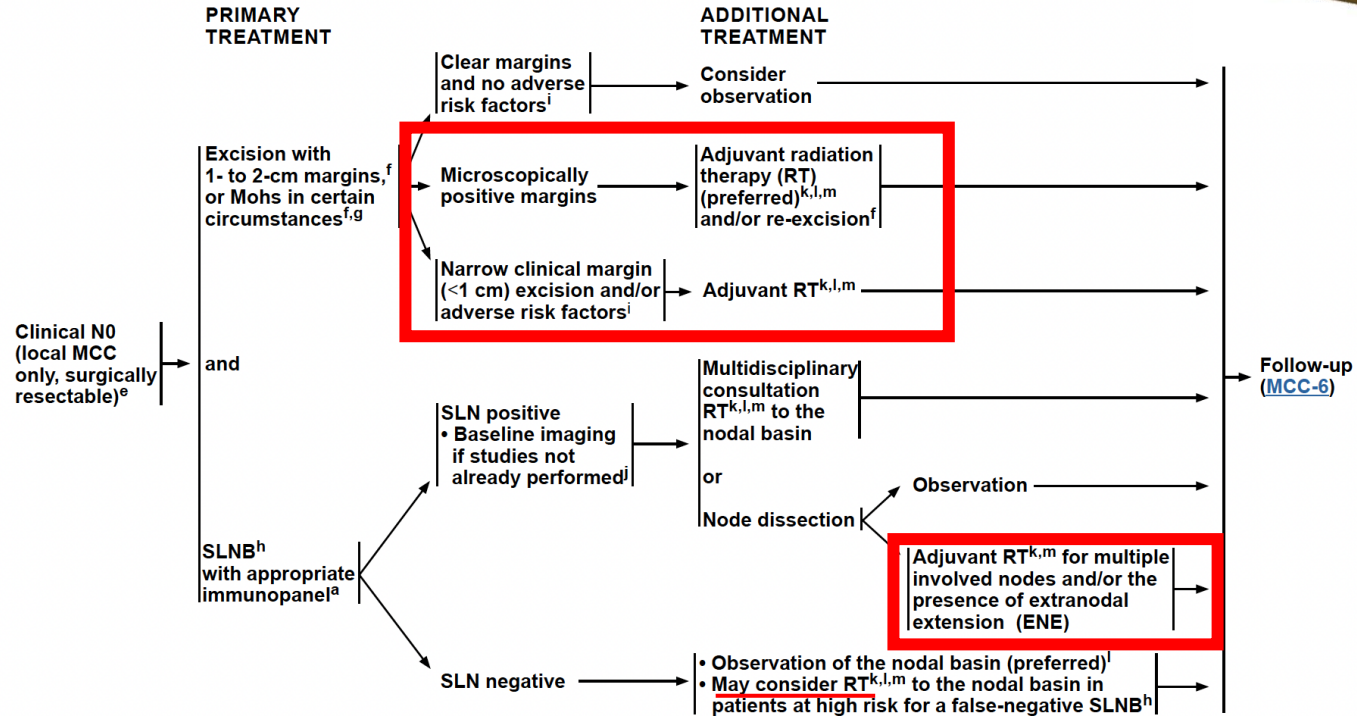
When do you refer for XRT?



NCCN MCC Guidelines (Jan 2024)



CLINICAL N0 DISEASE, LOCAL MCC ONLY, SURGICALLY RESECTABLE



Audience Response Question

- According to NCCN guidelines, which of the following is NOT an adverse risk factor for MCC?
 - A. Tumor >1cm
 - B. Perineural invasion
 - C. CLL
 - D. Head/neck primary site
 - E. Presence of lymphovascular invasion

Audience Response Question

- According to NCCN guidelines, which of the following is NOT a adverse risk factor for MCC?
 - A. Tumor >1cm
 - B. Perineural invasion**
 - C. CLL
 - D. Head/neck primary site
 - E. Presence of lymphovascular invasion

Adverse risk factors for MCC

- Tumor >1cm
- Chronic T-cell immunosuppression:
 - HIV, CLL, solid organ transplant
- Head/neck primary site
- Presence of lymphovascular invasion



Audience Response Question

- Which of the following features of a Merkel cell carcinoma indicates improved prognosis?
 - A. A patient that is seronegative for MCPyV oncoprotein antibody at diagnosis
 - B. A tumor that is CK20 negative
 - C. An unknown primary tumor
 - D. A tumor that is p63 positive

Audience Response Question

- Which of the following features of a Merkel cell carcinoma indicates improved prognosis?
 - A. A patient that is seronegative for MCPyV oncoprotein antibody at diagnosis
 - B. A tumor that is CK20 negative
 - C. **An unknown primary tumor**
 - D. A tumor that is p63 positive

Future Directions and Multidisciplinary Efforts

- Adjuvant immune checkpoint inhibitors
- Combination immune checkpoint inhibitors (such as anti-PD1 + anti-CTLA4)
- Adoptive T cell therapies
- Natural killer cell therapies
- Neoadjuvant therapy
- +/- Radiation

