

# Merkel Cell Carcinoma

A Rare but Aggressive Skin Cancer

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# Learning objectives

- Role of Immunotherapy in Merkel cell carcinoma
- Common side effects of Immunotherapy
- Other potential therapies

# Definition

- **Merkel cell carcinoma (MCC)** is named after **Friedrich Sigmund Merkel**, a German anatomist who first described **Merkel cells** in 1875
- **Merkel cells** are specialized **neuroendocrine cells** found in the **basal layer of the epidermis** .
- They function as **mechanoreceptors** — helping with the sense of **touch**.
- Merkel cells share characteristics with both **nerve cells** and **hormone-secreting cells**.
- In **Merkel cell carcinoma**, these cells (or related progenitors) undergo **malignant transformation** into a rare but aggressive cancer.
- Typically presents as a **painless, rapidly growing nodule** on sun-exposed skin
- Associated with: Merkel cell polyomavirus (MCPyV), chronic UV exposure and immunosuppression

# Staging

## Clinical (cTNM)

- **T N M**
- **Stage 0** Tis N0 M0
- **Stage I** T1 N0 M0
- **Stage IIA** T2-T3 N0 M0
- **Stage IIB** T4 N0 M0
- **Stage III** T0-T4 N1-3 M0
- **Stage IV** T0-T4 Any N M1

## Pathological (pTNM)

- **T N M**
- **Stage 0** Tis N0 M0
- **Stage I** T1 N0 M0
- **Stage IIA** T2-T3 N0 M0
- **Stage IIB** T4 N0 M0
- **Stage IIIA** T1-T4 N1a(sn)  
or N1a M0
- T0 N1b M0
- **Stage IIIB** T1-T4 N1b-3  
M0
- **Stage IV** T0-T4 Any N M1

# Treatment per Stage

1

## Stage I–II (Localized):

- **Wide local excision** with clear margins
- **Sentinel lymph node biopsy**
- Consider **adjuvant radiotherapy** to surgical bed

2

## Stage III (Nodal):

- Surgery ± **lymph node dissection**
- **Radiotherapy to nodal basin**
- Consider **immunotherapy** (especially if high risk)

3

## Stage IV (Metastatic):

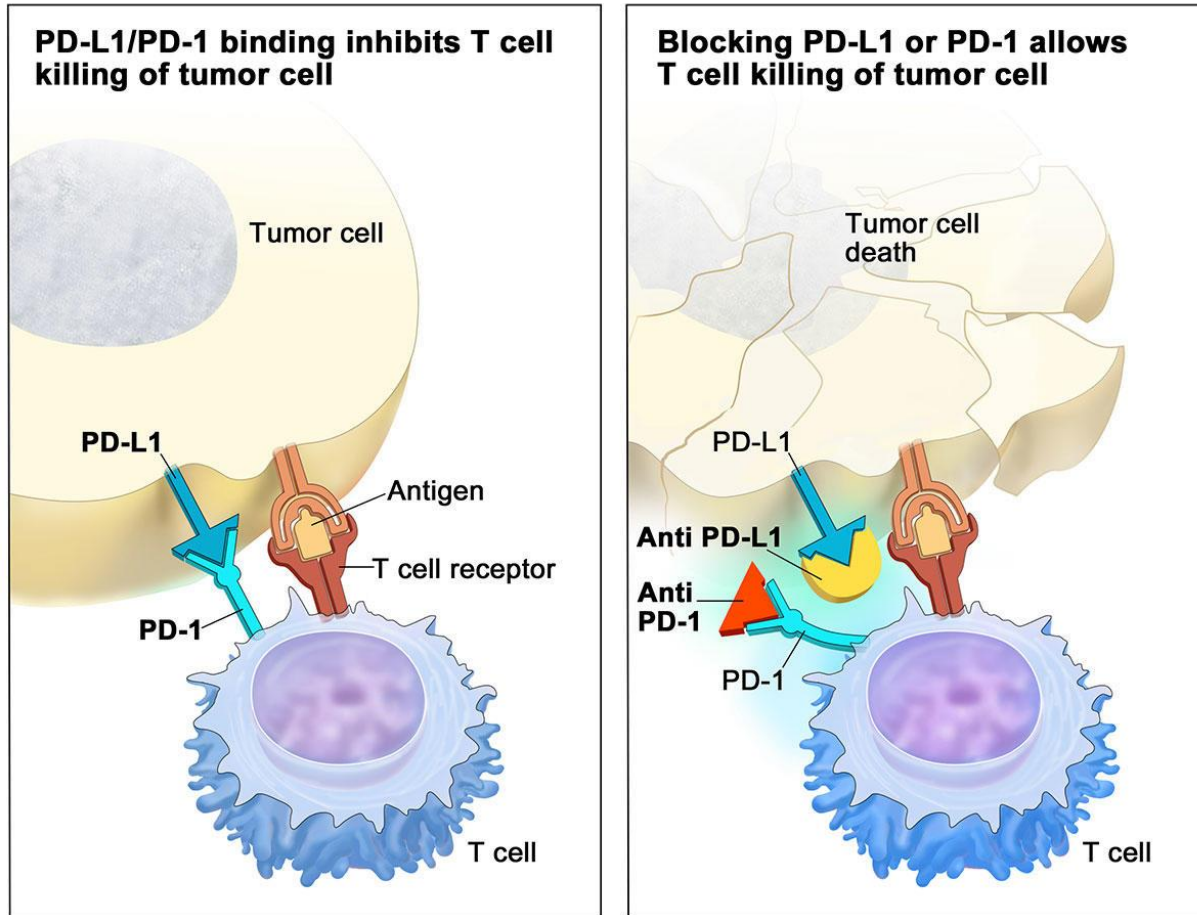
- Systemic therapy: **immunotherapy is first-line**
- Palliative radiotherapy for symptom control
- Chemotherapy if immunotherapy fails or is contraindicated
- Systemic chemotherapy (platinum-based regimen) with was the mainstay of treatment of metastatic Merkel cell carcinoma pre-2016
  - High initial response rates (~55–60%)
  - But short-lived responses (median duration: 3–5 months), median overall survival: 9–12 months, high toxicity especially in elderly patients, and no long-term survival benefit



# Role of Immune Therapy

- **Checkpoint inhibitors** are now standard for advanced MCC:
  - **Avelumab** (PD-L1 inhibitor)
  - **Pembrolizumab, Nivolumab** (PD-1 inhibitors)
- High response rates and durable remissions
- Used in:
  - Metastatic disease (first-line)
  - Adjuvant therapy in some high-risk Stage III cases
- Better tolerated than chemotherapy

# Checkpoint Proteins Inhibitors



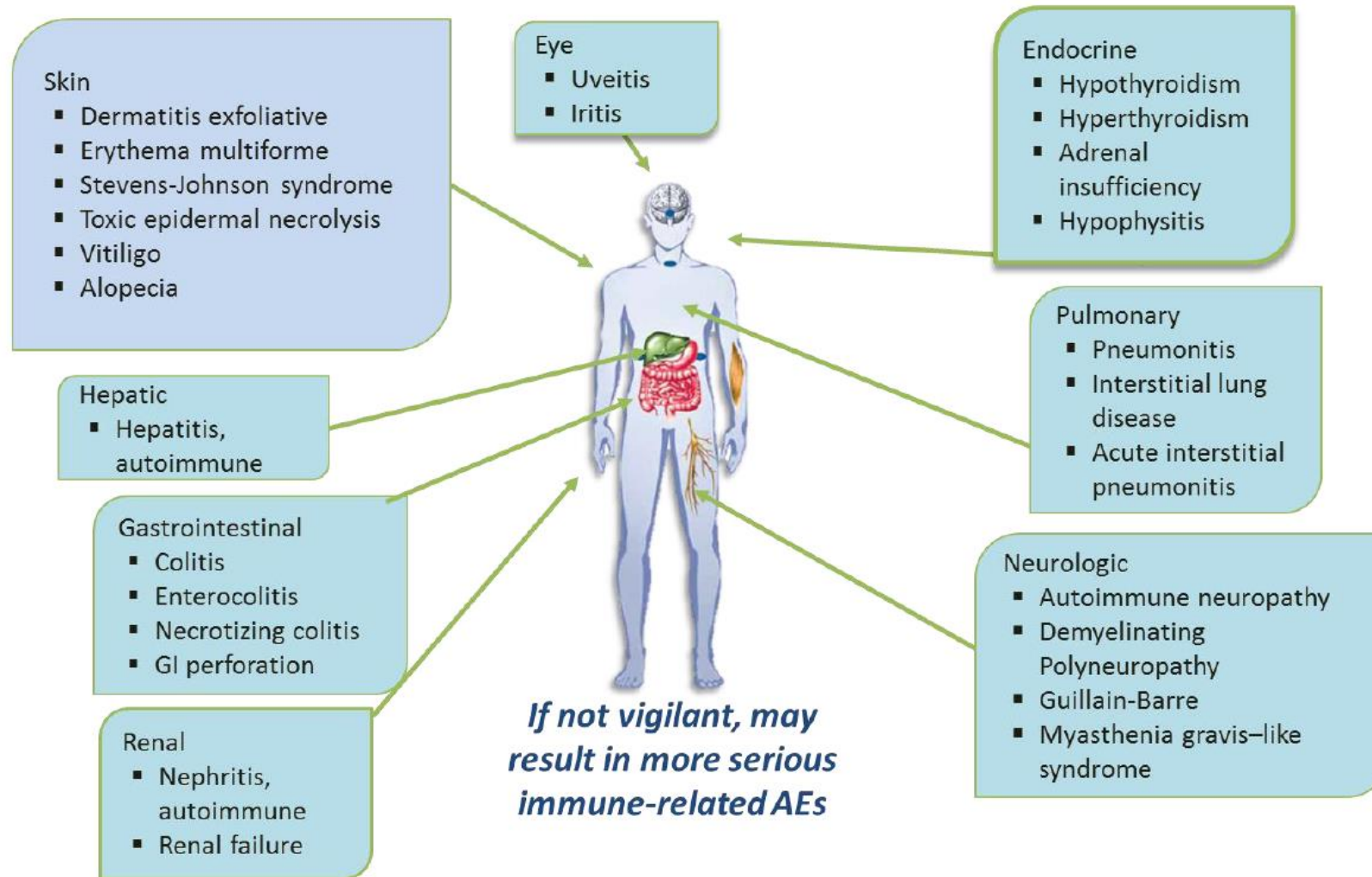
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# Systemic treatment available under PBS

- Avelumab 10mg/kg Q2w ongoing
- Costs around \$ 5000 per cycle
- Chemotherapy Carbo/etoposide
- Costs \$ 420 per cycle

# Side effects of Immunotherapy



# Recent Advances in Merkel Cell Carcinoma (2024–2025)

## Immunotherapy & Trials

- **Nivolumab ± Ipilimumab:** Combination checkpoint blockade in advanced MCC under investigation (Phase I/II)
- **Neoadjuvant pembrolizumab + lenvatinib:** 58% pathological complete response pre-surgery (ASCO 2025)
- **Retifanlimab (PD-1):** FDA accelerated approval for recurrent/metastatic MCC (POD1UM-201)

## Survival Impact

- **US registry study:** Immunotherapy doubled 2-year survival in advanced MCC since 2010
- **Real-world avelumab:** 57% response rate, durable outcomes in metastatic MCC

## Targeted & Novel Therapies

- **225Ac-Satoreotide:** Alpha-emitter radiotherapy + checkpoint inhibitors (Phase I/II launch 2025)
- **Virus-targeted strategies:** MCPyV vaccines and adoptive T cells in development

## Biomarkers & Monitoring

- **Circulating tumor DNA (ctDNA):** NCCN 2025 recommends for relapse surveillance
- **Hypofractionated radiotherapy:** New guideline option for non-surgical cases

## Special Populations

- **Immunosuppressed patients:** Lower response (~50%) to PD-1/PD-L1 inhibitors; ongoing trials exploring safer options

# Novel Treatments

- **Virus-targeted therapies** (MCPyV vaccine research ongoing)
- **Combination immunotherapy** (dual checkpoint blockade)
- **Oncolytic viruses**, adoptive T cell therapies (experimental)
- **Biomarker studies** to predict immunotherapy response
- Trials exploring neoadjuvant immunotherapy before surgery

**Thank You**

# References

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