Real-World Evidence on Treatment Patterns and Guidelines in Patients with Advanced Merkel Cell Carcinoma across the US and Europe

HSD94

Ankita Sood, Gagandeep Kaur, Barinder Singh
Pharmacoevidence Pvt. Ltd., Mohali, India

Science-led HEOR & Tech-driven AI

GET POSTER PDF

INTRODUCTION

- Advanced merkel cell carcinoma (aMCC) is a rare, aggressive neuroendocrine skin cancer that primarily affects older adults and people with sun-exposed skin[1]
- Key risk factors of the disease include advanced age, immunosuppression, ultraviolet (UV) exposure, and Merkel cell polyomavirus infection[2]
- Immune checkpoint inhibitors (ICIs) such as avelumab and pembrolizumab are recommended as first-line therapy for aMCC, but over 50% of patients fail to achieve sustained benefit, emphasizing the need for effective treatment strategies[3,4]

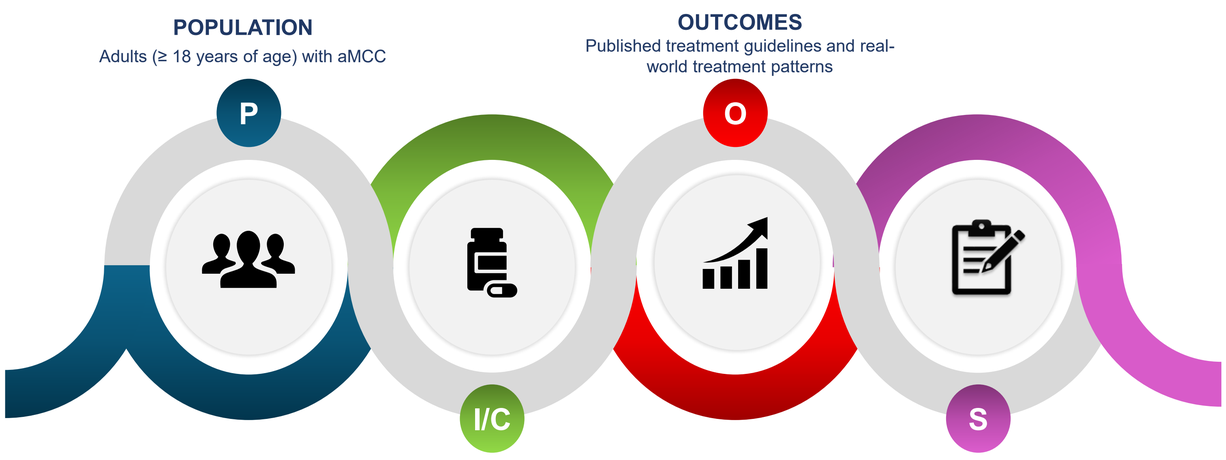
OBJECTIVE

- This systematic literature review (SLR) aimed to identify treatment recommendations based on guidelines and to examine real-world patterns of care for aMCC across the United States (US) and Europe

METHODS

- The current SLR adhered to National Institute for Health and Care Excellence (NICE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[5]
- Key biomedical databases, including Embase® and MEDLINE®, were searched for relevant English-language publications, focusing on guidelines and real-world treatment patterns in aMCC patients. The prespecified eligibility criteria are presented in **Figure 1**
- A transparent and unbiased approach was employed throughout the review process

Figure 1: Prespecified PICOS eligibility criteria for the selection of evidence

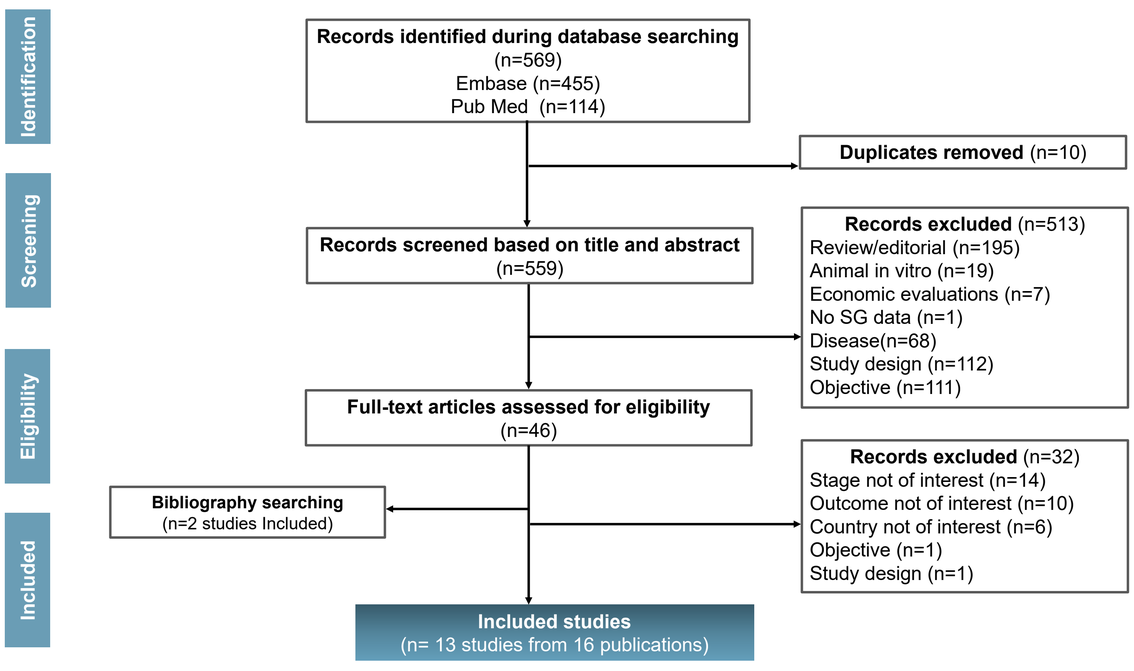


aMCC: Advanced Merkel Cell Carcinoma

RESULTS

- The SLR identified 13 studies reporting treatment patterns for aMCC in the US (n=10) and Europe (n=3) **(Figure 2)**
- The sample size across the included studies ranged from 14 to 648 patients
- The National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology/European Reference Network for Rare Adult Cancers (ESMO/EURACAN) guidelines recommend ICIs (avelumab, pembrolizumab, retifanlimab, and nivolumab) as first-line (1L) therapies for aMCC **(Table 1)**

Figure 2: PRISMA diagram for the screening process



Embase: Excerpta Medica database; PRISMA: Preferred Reporting Items for Systematic Reviews; SG: Subgroup

Table 1: Treatment approaches for inoperable or metastatic MCC[3,4]

LOT	NCCN	ESMO
Evaluation of Performance status and comorbidities		
First line	• **Preferred:** Clinical trial or PD-1/PD-L1 monotherapy (avelumab, nivolumab, pembrolizumab, retifanlimab) • **Also consider:** ipilimumab + nivolumab; BSC throughout care	• **Preferred:** clinical trial • **Alternative:** anti-PD-(L)1 ICI (avelumab, pembrolizumab, retifanlimab, nivolumab) + BSC; favor ICI over chemotherapy when feasible
Second line	• **If progression/contraindication after PD-1/PD-L1**: ipilimumab + nivolumab; chemotherapy options (platinum ± etoposide, CAV, single-agent platinum) • **Other options**: topotecan, pazopanib, octreotide LAR (if SSTR+), intralesional T-VEC (palliation)	• **Preferred:** clinical trial • **Alternative:** palliative RT and/or chemotherapy + BSC; chemotherapy options include platinum/etoposide, CAV, taxanes, or topotecan
Later line	• **Preferred**: Clinical trial. • **Otherwise**: Consider NGS-guided therapy if actionable	• **Preferred:** Clinical trial • **Alternative:** BSC

BSC: Best Supportive Care; CAV: Cyclophosphamide, Doxorubicin (Adriamycin), and Vincristine; ESMO: European Society for Medical Oncology; ICI: Immune Checkpoint Inhibitor; LAR: Long-Acting Release; LOT: Line of therapy; NCCN: National Comprehensive Cancer Network; NGS: Next-Generation Sequencing; PD-1: Programmed Death-1; PD-L1: Programmed Death-Ligand 1; RT: Radiotherapy; SSTR: Somatostatin Receptor; T-VEC: Talimogene Laherparepvec

- Both the guidelines recommend chemotherapy for patients who either have contraindications to ICIs or have experienced disease progression following immunotherapy[3,4]
- Across the US, immunotherapy was the most utilized 1L treatment option (27%-71%); whereas chemotherapy was utilized as 1L treatment option in 15-73% of the patients. Similar trends were observed across the Europe
- Across all the studies, the most utilized chemotherapy regimen was combination of platinum-based therapies (cisplatin/carboplatin) with etoposide, used in 11%-59.6% of patients
- **Table 2** depicts the patterns of systemic therapy use in aMCC patients across the US and Europe

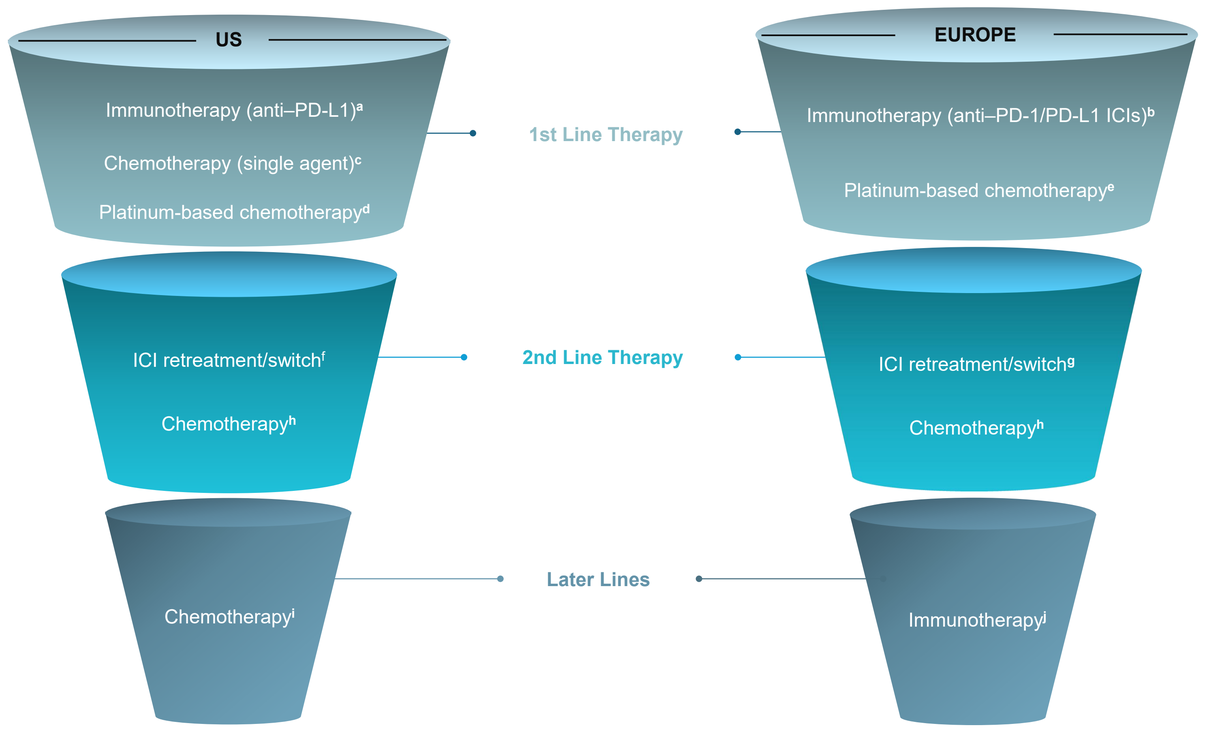
Table 2: Patterns for systemic therapy use in aMCC (US & Europe)

LOT	Treatment regimens	US (%)	Europe (%)
1L Immunotherapy	Avelumab, Pembrolizumab	27-71	89*
2L Immunotherapy	Avelumab, Ipilimumab/Nivolumab	15-71	7-11
2L+ Immunotherapy	Avelumab, Nivolumab	NR	21-100
1L Chemotherapy	Cisplatin ± Etoposide, Carboplatin ± Etoposide, Topotecan, Cyclophosphamide, Doxorubicin (or Epirubicin) and Vincristine	15-73	11-98
2L Chemotherapy	Carboplatin/Cisplatin + Etoposide	5-12	29*
2L+ Chemotherapy	Carboplatin, Carboplatin + Etoposide/Gemcitabine, Docetaxel, Etoposide, Irinotecan, Paclitaxel, Topotecan, Vincristine + Cyclophosphamide + Doxorubicin	8*	NR

1L, First-Line; 2L, Second-line; LOT, Line of therapy; NR, Not reported; US, United States, *Data available from a single study
Ranges represent variability across studies

- The major reasons for immunotherapy discontinuation involved disease progression, toxicity, or elective cessation after response. After discontinuation, patients often switched to alternate immunotherapy or chemotherapy regimens, including topotecan, vincristine, cyclophosphamide, doxorubicin, carboplatin, or local therapies such as surgery/radiotherapy
- Overall, real-world practice is consistent with guideline recommendations, wherein 1L ICIs are commonly administered, followed by palliative radiotherapy or platinum-etoposide chemotherapy in cases of ICIs contraindication or treatment failure **(Figure 3)**

Figure 3: Treatment Patterns by Line of Therapy (US & Europe)



a: Avelumab; **b**: Avelumab, Pembrolizumab; **c**: Etoposide; **d**: Carboplatin/Cisplatin + etoposide; **e**: Cisplatin + etoposide; **f**: Avelumab, Nivolumab; **g**: Avelumab, nivolumab, pembrolizumab; **h**: Carboplatin/Cisplatin + etoposide, Topotecan, Vincristine + Cyclophosphamide + Doxorubicin, Irinotecan, Gemcitabine, Docetaxel; **i**: Doxorubicin, Paclitaxel, Cisplatin + etoposide; **j**: Ipilimumab + Nivolumab; **1L**: First-Line; **2L**: Second-Line; **2L+**: Later lines; **PD-1**: Programmed Death-1; **PD-L1**: Programmed Death-Ligand 1; US: United States

CONCLUSIONS

- ❖ Real-world treatment patterns for aMCC are largely consistent with guidelines across the US and Europe
- ❖ Immunotherapies (avelumab, nivolumab, pembrolizumab) are the predominant first-line treatment option
- ❖ The findings of this SLR emphasize the importance of personalized treatment strategies and further research to optimize therapy sequencing in real-world settings

References

1. Nghiem P, et al. N Engl J Med. 2016;374:2542–2552.
2. Becker JC, et al. Nat Rev Dis Primers. 2017;3:17077.
3. NCCN. Merkel Cell Carcinoma. Version 2.2026.
4. ESMO. Merkel Cell Carcinoma. 2024.
5. Moher D et al., Systematic Reviews, 4(1): 1

Correspondence: Barinder Singh; barinder.singh@pharmacoevidence.com

Disclosure: AS, GK, and BS, the authors declare that they have no conflict of interest

ISPOR 2025; November 09-12; Glasgow, Scotland, UK