Merkel cell carcinoma (MCC) is a rare neuroendocrine cutaneous tumour with high metastatic potential and mortality. MCC carcinogenesis can be initiated by DNA damage caused by chronic ultraviolet light (UV) exposure or by Merkel cell polyomavirus (MCPyV) infection.

MCC presents as a rapidly growing cutaneous or subcutaneous nodule, most often on sun-exposed areas such as the face and neck. Owing to this non-specific presentation, diagnosis cannot be based on clinical examination alone. The analysis of the immunohistological markers of a biopsy specimen of the primary lesion can confirm the diagnosis, as MCC has a characteristic antigenic expression profile. However, none of these markers can prognosticate patients or predict their response to therapy.

Wide surgical excision of the primary MCC tumour and adjuvant radiotherapy to the tumour bed are the standard of care. If the patient is ineligible or the procedure has functional implications, radiotherapy is a valid alternative. Adjuvant radiotherapy to the lymph nodes of the draining basin could also contribute to local disease control. Both monochemotherapy and polychemotherapy regimens for metastatic or refractory MCC have low response rates.

Identification of the cell of origin of MCC, together with an improved understanding of the mechanism of viral carcinogenesis, might enable the identification of susceptibility factors for MCPyV-driven carcinogenesis. Immune-checkpoint blockade therapy could greatly benefit patients with advanced-stage MCC. However, only around half of these patients respond to this treatment and a substantial number develop secondary resistance. Thus, an understanding of the mechanisms of primary and secondary immune escape is necessary to overcome these issues.