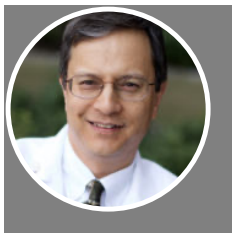
Recent from **EADO 2021**

Dr Ettore Minutilli



Dr Paul Nghiem

On 4 June 2021, Dr Ettore Minutilli attended (via zoom) the first International MCC Symposium organised by Prof Paul Nghiem and his collaborators. During this multicentre Merkel interest group (MMIG) meeting, Prof Nghiem introduced the scientific lectures of some American leaders on Merkel cell carcinoma (MCC), together with the most important European leaders, such as Prof Jurgen Becker (University of Duisburg-Essen, Germany). The most prestigious international leaders on MCC attended the meeting, which concluded with a brainstorm session on the second edition of the Symposium, due to take place in 2022.

The meeting proved to be a great occasion to confirm the strong scientific relationships between EADV and the American Academy of Dermatology (AAD).

The most important topics covered on MCC for future progress are summed up below.

There have been many exciting recent updates pertaining to the workup, initial management and indications for immunotherapy in MCC. In the past, National Comprehensive Cancer Network® (NCCN®) guidelines for MCC have been largely based on those for melanoma. However, studies have shown that there is a far higher chance (>13%) that MCC will have undergone clinically occult metastasis beyond the primary site than for melanoma (<1%). For this reason, it is now recommended that most MCC patients undergo a PET/CT scan as a part of their initial workup. PET/CT is more sensitive than CT in detecting baseline occult metastatic disease and in one in six cases this results in radical changes in initial management.

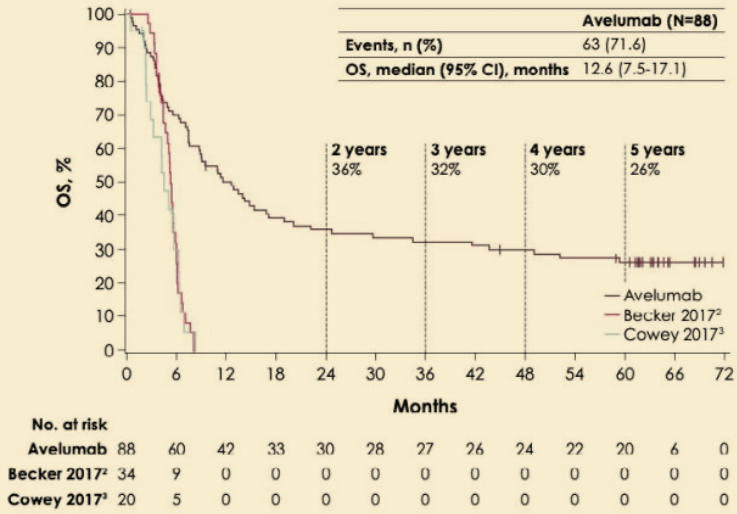
Vigorous controversy surrounds primary site treatment for patients whose disease has not spread: How wide should surgical margins be? Which patients need adjuvant radiation? In the past, most studies have only looked at margin

Overall survival in all paients compared with historical chemotherapy data

(from Nghiem P et al., ASCO 2021 Annual Meeting)

OS, overall survival.

This figure is for illustrative purpose only and is not a head-to-head comparison.



Merkel cell carcinoma (MCC) progress: to the **first International MCC Symposium 2021**

size and recurrence, without considering whether local radiation therapy was given. A recent study of 188 patients investigated the important interaction between surgery and radiation by comparing groups of patients who had narrow (≤1 cm) or wide (>1 cm) surgical margins, with or without subsequent radiation treatment. Among patients who received local radiation, the risk of recurrence did not differ between those with wide surgical margins vs. narrow surgical margins. For patients who did not undergo local radiation, recurrences were more likely in patients who had surgical margins ≤1 cm. This suggests that patients who are at risk (immune suppressed, larger primary tumour) will need adjuvant radiation and can avoid the potential morbidity of wide surgical margins. In contrast, patients who do not have elevated risk factors may benefit from wider surgical margins, as surgery alone will likely suffice. The final decision of whether a patient should receive adjuvant radiation should be made by considering potential risk factors including primary tumour size, tumour site, immune status, lymphovascular invasion and two factors that are only available after surgical excision: positive sentinel lymph node biopsy and positive surgical margins.

For MCC patients who have metastatic disease, there is ever-growing evidence to suggest that first-line immunotherapy is the best choice when possible. A recent study of chemo-refractory MCC patients compared immunotherapy (avelumab; anti-PDL1) to two cohorts of historical control subjects who received further chemotherapy. After one year, none of the 54 patients who received further chemotherapy were alive. In the avelumab treatment group, half of the 88 patients were alive at one year and ~33% were alive at five years. A separate study looked at patients who received first-line treatment with pembrolizumab. Remarkably, 60% of patients were still alive at three years. Taken together, these studies suggest that chemotherapy, which suppresses the immune system, is not preferred in the treatment of metastatic MCC and first-line immunotherapy should be prioritised. There remains the question of how long MCC patients should continue immunotherapy treatment. Recent data suggests that MCC has a higher risk of recurring after immunotherapy discontinuation than melanoma. Studies are still ongoing, but our suggested approach is to plan on treating with immunotherapy for several years and begin tapering treatment only after one to two years, by decreasing the frequency of infusions.

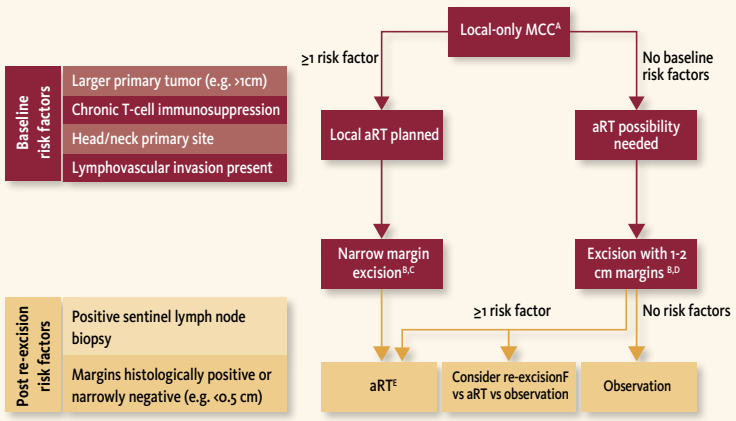
To obtain the recording of this first international meeting on MCC, please email Mrs Krista Lachance, Research Manager, Nghiem Lab – Division of Dermatology, University of Washington, Seattle, USA.

For further information on MMIG, visit merkelcell.org. ●

Ettore Minutilli, MD
Dermatology and Plastic Surgery, Catholic University of Sacred Heart, Rome, Italy

Paul Nghiem, MD PhD
Director of Dermatology, University of Washington, Seattle, USA

Local MCC treatment management (from Tarabadkar ES et al., JAAD 2021; 84:340-7)



This flowchart integrates treatment options with risk factors that are associated with local recurrence. Certain risk factors are available at the time of diagnosis (baseline), whereas others are available only after surgical excision (post re-excision). [A]Criteria for local-only MCC were as follows: clinically node negative, no in transit disease, and imaging negative for distant disease. [B]Sentinel lymph node biopsy was typically performed at this time. [C]Narrow excision margins minimize morbidity, and if aRT is performed microscopically positive margins are acceptable. [D]The goal should be primary tissue closure (ie, without a flap or graft) allowing aRT initiation within 3 to 4 weeks. [5, 19, 20] [E]If the sentinel lymph node biopsy result is positive, nodal aRT would typically be given in addition to primary site aRT. [F]The decision on re-excision is based on clinical setting (narrovv path margins, eg, <0.5 cm) and patient preference: re-excision versus aRT versus observation. aRT, Adjuvant radiation therapy; MCC, Merkel cell carcinoma.