# Summary of 11th Annual MMIG Meeting

**(Merkel cell carcinoma Multi-center Interest Group)**

## Friday March 4, 2016
## American Academy of Dermatology Annual Meeting
## Washington D.C.
## Prepared by Drs. Erica Shantha Tarabadkar & Paul Nghiem

## Announcements:

1) If you are interested in presenting at next year's MMIG meeting in Orlando, Florida on March 3rd, 2017 (Friday 5 – 7 pm), please send Paul an email (pnghiem@uw.edu) with a proposed topic that is relevant to MCC patient care or translational research.

## Speakers/Topics (detailed in following pages):

1. **Update on MCC staging—New national data & planned 8th Edition AJCC staging system**
   Chris Bichakjian (Michigan)

2. **Exploring the role of Hedgehog signaling in Merkel cell carcinoma**
   Isaac Brownell (NCI)

3. **Response rate & durability of chemotherapy in 62 MCC cases: How good is the standard of care?**
   Erica Shantha Tarabadkar (UW)

4. **Clinical trials in MCC: Update on pembrolizumab (anti-PD1) and overview of current clinical trials**
   Paul Nghiem (UW)

5. **MCC incidence is increasing in Sweden: An epidemiologic analysis**
   John Paoli (Sahlgrenska University Hospital, Sweden)

1. **Update on MCC staging—New national data & planned 8th Edition AJCC staging system**
   Chris Bichakjian (Michigan)

   Dr. Bichakjian's team at UM used the NCDB database to evaluate over 14,000 MCC cases as the basis of the new staging system. Dr. Bichakjian reviewed the major considerations and changes for the AJCC 8th Edition staging system which now includes separate clinical and pathological staging that is more consistent with general AJCC staging. The new system is thus more similar to that for melanoma, eliminating A/B substages that indicated nodal status (pathological vs. clinical) in stage I and II. (Of note, using the new system, it will be important to mention whether a patient with 'Stage I MCC' had 'clinical or 'pathologic' staging or it will be unclear if nodal evaluation was performed by clinical exam or pathologic/microscopic study.)

   The new system separates nodal disease based on whether the primary tumor was present or "unknown", because the latter category has strikingly improved survival. The 8th Edition staging system was recently published in Annals of Surgical Oncology:

   http://www.ncbi.nlm.nih.gov/pubmed/27198511

2. **Exploring the role of Hedgehog signaling in Merkel cell carcinoma**
   Isaac Brownell (NCI)

   Dr. Brownell reviewed the hedgehog (Hh) signaling pathway and earlier data (from other groups) that implied the Hh pathway is active in MCC tumors. Dr. Brownell's team carried out more extensive genetic studies and concluded that gene expression studies showed no evidence of Hh activation in MCC, that MCC cell lines did not respond to Hh pathway inhibitors, and thus that the Hh signaling pathway does not appear to be active in MCC.

   Dr. Brownell also presented a relevant, provocative case: A 73 yo man with history of multiple SCC and BCC tumors who was started on vismodegib 150 mg daily for advanced BCC. After 2 months on vismodegib, he developed an axillary MCC with no apparent primary lesion. The vismodegib was stopped and the MCC tumor regressed within two months of stopping vismodegib. Dr. Brownell and team questioned if the remarkable timing of MCC onset/regression was associated with vismodegib and Hh signaling acting as a tumor suppressor or if these events were coincidental. In aggregate, Dr. Brownell concluded there was no credible evidence that Hh pathway signaling *promotes* MCC growth or development.

3. **Response rate & durability of chemotherapy in 62 MCC cases: How good is the standard of care?**
   Erica Shantha Tarabadkar (UW)

   Dr. Shantha (who just got married & is now Dr Tarabadkar!) reviewed the efficacy of chemotherapy in MCC, as cytotoxic chemotherapy is commonly used to treat advanced Merkel cell carcinoma (MCC). She reviewed data from the Seattle repository. Among 62 patients, the response rate (RR) to first-line chemotherapy was 55% (34/62), with complete responses (CR) in 13% (8/62), and partial responses (PR) in 42% (26/62). 39% (24/62) had progressive disease. Median progression free survival (PFS) was 94 days and median overall survival was 9.5 months from start of chemotherapy. Among 30 of the 62 patients who received second-line chemotherapy, RR was 23% (7/30; 1 CR, 6 PR), and median PFS was 61 days.

   In summary, first-line chemotherapy is associated with a high RR in metastatic MCC, but responses are typically not durable, and the median PFS is only 3 months. Indeed, at 1 year, only 5% of patients had not developed progressive disease. These data should serve as a useful comparator for immunotherapies currently being explored for metastatic MCC.

   **Publication:**
   http://www.ncbi.nlm.nih.gov/pubmed/27431483

4. **Clinical trials in MCC: Update on pembrolizumab (anti-PD1) and overview of current clinical trials**
   Paul Nghiem (UW)

   Dr. Nghiem reviewed the results of the Cancer Immunotherapy Trials Network (CITN) pembrolizumab in MCC clinical trial. A total of 26 patients received at least one dose of pembrolizumab. The objective response rate among the 25 patients with at least one evaluation during treatment was 56%; 4 patients had a complete response, and 10 had a partial response. Relapses occurred in 2 of the 14 patients who had an initial response (14%). The response duration ranged from 2.2 months (and ongoing) to 9.7 months (and ongoing). The rate of progression-free survival at 6 months was 67% (95% CI, 49 to 86). A total of 17 of the 26 patients (65%) had virus-positive tumors. The response rate was 62% among patients with MCPyV-positive tumors (10 of 16 patients) and 44% among those with virus-negative tumors (4 of 9 patients). Drug-related grade 3 or 4 adverse events occurred in 15% of the patients.

   These data were presented at the 2016 American Association for Cancer Research meeting in April 2016 and were published in the NEJM (see link below).

   **Publication**: http://www.nejm.org/doi/full/10.1056/NEJMoa1603702

   The Atlantic article: http://www.theatlantic.com/politics/archive/2016/04/cancer-the-final-frontier/478962/
   Washington Post article: https://www.washingtonpost.com/news/to-your-health/wp/2016/04/19/breakthrough-cancer-therapy-shows-growing-promise/

## Clinical Trials in MCC:

**Anti-PD-L1**: https://clinicaltrials.gov/ct2/show/NCT02155647?term=Merkel+cell+carcinoma&rank=9

**Anti-PD-1:**
https://clinicaltrials.gov/ct2/show/NCT02267603?term=Merkel+cell+carcinoma&rank=13

**Anti-PD-L1 and Adoptive T cells:**
https://clinicaltrials.gov/ct2/show/NCT02584829?term=Merkel+cell+carcinoma&rank=11

**Anti-PD-1 and anti-CTLA-4:**
https://clinicaltrials.gov/ct2/show/NCT02488759?term=nivolumab+and+virus+associated+cancers&rank=1

**mTOR inhibitor:**
https://clinicaltrials.gov/ct2/show/NCT02514824

**VEGF & other tyrosine kinase inhibitor (Cabozantanib):**
https://clinicaltrials.gov/ct2/show/NCT02036476

5. **MCC incidence is increasing in Sweden: An epidemiologic analysis**
John Paoli, MD (Sahlgrenska University Hospital, Sweden)

Dr. Paoli reviewed results of population-based data collected by the Swedish Cancer Registry to determine the incidence of MCC in Sweden and the clinical characteristics of these tumors including demographics (from 1993 to 2012). He found that the incidence (per 100,000) of MCC in Sweden in 1993-2012 increased from 0.09 to 0.20 for men and 0.12 to 0.17 for women, adjusted for age to the world standard population. For both sexes, the increase was from 0.11 to 0.19 per 100 000, **an increase of 73%.** The most common site of the primary tumor was the head and neck, representing 52% of cases.

These data were recently published in the Journal of the European Academy of Dermatology and Venereolgy (link below).

Publication: http://www.ncbi.nlm.nih.gov/pubmed/27136306

Political Lore article: http://www.politicallore.com/rare-and-aggressive-merkel-cell-skin-cancer-on-the-rise/3587

## In attendance at the 2016 Washington DC MMIG meeting:

Arron, Sarah (San Francisco)
Bichakjian, Chris (Ann Arbor)
Brownell, Isaac (Bethesda)
Doan, Hung (Galveston)
Fu, Teresa (Stanford)
Gelb, Tara (Bethesda)
Harms, Kelly (Ann Arbor)
Huang, Victor (Boston)
Luo, Su (Boston)
Nghiem, Paul (Seattle)
Paoli, John (Gothenburg, Sweden)
Perlis, Cliff (Philadelphia)
Shinohora, Michi (Seattle)
Seely, Jill (Philadelphia)
Swetter, Susan (Stanford)
Stasko, Tom (Oklahoma City)
Sober, Arthur (Boston)
Schoenfeld, Jason (Buffalo)
Tarabadkar, Erica Shantha (Seattle)
Thakuria, Manisha (Boston)
Wu, Julie (Las Vegas)
Yu, Siegrid (San Francisco)
Zeitouni, Nathalie (Tucson)
Zhang, Lin (Boston)

**Goals of the Merkel cell carcinoma Multi-center Interest Group (MMIG)**

- Promote communication and collaborative studies on MCC
- Enhance access to patient data and specimens
- Expand evidence-based care for MCC

*The homepage for MMIG contains photos, meeting summaries and more at:*
*http://merkelcell.org/MMIG.html*

*MMIG is funded in part by donations from Merkel cell carcinoma patients.*

*Please note that in many cases, these summaries reflect unpublished data and are provided to help MMIG members manage their patients and give an overview of what is being done at different centers for care and research.*