

Evidence Discussion (ONC 5)

Evidence Discussion for Non-Melanoma Skin Cancers:

General Considerations (ONC 5.5): Advanced imaging to include PET/CT is generally not indicated for basal cell (BCC) or squamous cell (SCC) skin cancers. The incidence of metastatic BCC was found to be < 1% at 14 years of follow-up while metastatic SCC is noted to be rare. 8, 9 Merkel cell carcinoma, due to its high propensity (25-33%) for regional lymph node spread as well as distant metastases (12-20%), conventional imaging is indicated initially prior to considering PET scan. 10

Initial Work-up/Staging (ONC 5.6): A body area with unexplained signs or symptoms can undergo imaging with CT with contrast. For SCC, MRI or CT of the primary site with MRI favored if there is perineural or deep soft tissue involvement while CT is preferred for bone disease. 6, 7 If the skin lesion is felt to be a dermal metastasis from a distant primary, CT CAP with contrast is the initial recommended imaging with PET/CT indicated if conventional imaging is unable to identify a primary site and especially if the primary tumor may involve an extremity. 10

Restaging/Recurrence (ONC 5.7): For recurrences where planned therapy is more extensive than simple wide local excision, CT with contrast of primary site and recurrent site(s) is indicated. Merkel cell carcinoma recurrence can be evaluated with CT CAP plus any other symptomatic areas. PET/CT can be done for inconclusive findings on conventional imaging. MRI brain indicated for signs or symptoms of CNS involvement.

Surveillance/Follow-up (ONC 5.8): For SCC and BCC, long term follow-up is mandatory due to high risk of developing new primary lesions with imaging indicated as clinically indicated following the pathway for initial work-up and staging. In node positive Merkel cell carcinoma, recurrence rates have been found to be up to 33% at 5 years of follow-up (11) hence the recommendation for CT CAP every 6 months for 5 years as well as CT neck if known prior neck/facial/scalp disease. Routine imaging is not indicated for SCC or BCC in the absence of signs and symptoms of recurrence.

Ocular Melanoma (ONC 5.9): Approximately 95% of ocular melanoma occur in the uvea and 5% from the conjunctiva or orbit. Biopsy may not be mandatory for diagnosis but should be performed if diagnosis is uncertain or for prognostic analysis and risk stratification. Less than 3% of cases present with metastatic disease with 5 year risk of metastasis ranging from 3-5% in Stage I to 44% or higher in Stage III. 1 The most common site of metastatic disease is the liver (80%) but may also spread to the lungs, bone, skin/soft tissue and lymph nodes. 2, 4 Surveillance of the affected eye is with clinical examination only with advanced imaging supported based on individual risk factors. Initial staging includes MRI orbits/face/neck to determine extraocular extension that impacts treatment planning (radiation therapy versus enucleation). While the risk of baseline metastases may be low, the NCCN favors baseline staging before treatment to include CT CAP in addition to aforementioned MRI. 3 MRI brain indicated with any neurologic signs or symptoms. Restaging/recurrence with same imaging as

initial staging as well as including MRI brain. Surveillance: Local recurrence is rare (< 10%) and the development of metastatic disease is much more common (up to 70% up to 20 years after initial diagnosis) hence the following recommendations for surveillance that does not include local imaging unless clinically indicated. 4 For low risk disease, CT chest with CT or MRI of the abdomen annually for 10 years. For medium risk disease, same as low risk but every 6 months for 2 years then annually for a total of 10 years. For high risk disease, same as low risk but every 3 months for 2 years, every 6 months for 3 years then annually for a total of 10 years. The NCCN recognizes the optimal surveillance strategy is an issue of debate due to overall low yield of testing and the risk of cumulative radiation exposure. 5

1. NCCN Guidelines Version 1.2024, Melanoma: Uveal (MS-2)
2. National Organization for Rare Disorders (2022): [Ocular Melanoma - Symptoms, Causes, Treatment | NORD \(rarediseases.org\)](#)
3. NCCN Guidelines Version 1.2024, Melanoma: Uveal (MS-9; MS-12)
4. NCCN Guidelines Version 1.2024, Melanoma: Uveal (MS-18; MS-19)
5. NCCN Guidelines Version 1.2024, Melanoma: Uveal (MS-21; MS-22)
6. NCCN Guidelines Version 1.2024, Squamous Cell Cancer (MS-3)
7. NCCN Guidelines Version 3.2024, Basal Cell Skin Cancer (MS-3)
8. Shreve C, Shropshire C, and Cotter, D. Metastatic Squamous Cell Carcinoma: A Cautionary Tale. *Cureus*, October 2020; 12(10): e10879
9. Nguyen-Nielsen M, Wang L, Pedersen L, et al. The incidence of metastatic basal cell carcinoma (mBCC) in Denmark, 1997-2010. *Eur J Dermatol* 2015; 25:463-468
10. NCCN Guidelines Version 1.2024, Merkel Cell Carcinoma (MS-3)
11. NCCN Guidelines Version 1.2024, Merkel Cell Carcinoma (MS-16)