Protocol Title: Sentinel Lymph Node Localization and Biopsy for Sebaceous Gland Carcinoma of the Eyelid

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1.0 Objectives

Primary Objectives:

a) Identify the rate of SLN (sentinel lymph node) positivity for eyelid sebaceous gland carcinomas.

b) Identify the false negative events associated with SLN biopsy for sebaceous gland carcinomas.

Secondary Objective:

Record any side effects associated with SLN biopsy for sebaceous gland carcinoma of the eyelid.

2.0 Background

Sebaceous gland carcinoma of the eyelid is a rare cancer with a tendency for regional nodal metastasis. Clinically obvious regional nodal metastasis is detected in 10-20% of patients with sebaceous gland carcinoma of the eyelid according to most series.

Sentinel lymph node mapping and selective lymphadenectomy is a technique that has been successful in identifying patients with cutaneous melanoma who have microscopic regional lymph node metastasis. An early therapeutic lymph node dissection is subsequently performed in patients proven to harbor occult metastatic disease. This technique is well characterized for cutaneous melanomas in most locations. Our group has adapted SLN biopsy technique for conjunctival melanoma and eyelid sebaceous gland carcinoma.[5,8-11,13] The potential survival benefit for patients with nodal metastasis treated with neck dissection followed by radiotherapy or systemic adjuvant therapy provides an important impetus for accurate assessment of nodal status in patients with eyelid sebaceous gland carcinoma.

The primary objective of this study is to identify the rate of SLN positivity in patients with eyelid sebaceous gland carcinoma and to determine the false negative events for the same. The SLN positivity rate refers to the number of patients who had a positive SLN on biopsy divided by the total number of patients. The false negative events refer to recurrence in a lymphatic basin that was previously deemed to harbor a "negative" SLN within the first 3 years of follow-up.

3.0 Patient Eligibility

Inclusion Criteria:

a) Participant must be 18 years of age or over.

b) Possible or Suspicious sebaceous gland carcinoma of the eyelid.

c) A CXR (chest x-ray), liver enzymes, and a head and neck CT,a (SPECT/CT) or magnetic resonance imaging (MRI) , and an ultrasound negative for clinical evidence of metastasis.

d) Patient provided written informed consent. In the event that non-English speaking participants are eligible for this study, a short form (if applicable) or an ICD in their language, will be utilized and completed in accordance with the MDACC Policy for Consenting Non-English Speaking Participants.

Exclusion Criteria:

a) Pregnant or nursing females.

4.0 Pretreatment Evaluation

Patients who meet the inclusion criteria are evaluated in the Ophthalmology Clinic with a complete ophthalmologic examination. The tumor size, location and extent are characterized. The pathology slides are reviewed by the pathology department at M.D. Anderson and the diagnosis of eyelid sebaceous gland carcinoma is confirmed. A CXR, a CT or MRI of head and neck or a SPECT /CT scan and an ultrasound of regional nodes are obtained to establish lack of clinically identifiable metastatic disease. The patient's ability to undergo surgery under general anesthesia will also be evaluated/assessed at this time. The eligible patients then undergo preoperative lymphoscintigraphy.

NOTE: A serum/blood pregnancy test (i.e., 10cc's) will be obtained, within 7 days prior to SLN mapping and biopsy, for all female patients of child-bearing potential, unless previously ordered as part of standard of care prior to surgery. A negative pregnancy test will be verified on all female patients of child-bearing potential prior to any SLN mapping and biopsy. If beta hcg is outside normal range, a 2nd test will be obtained. If beta hcg is out of range a second time, a gynecologic consult will be obtained.

Women of child-bearing potential (WOCBP) include any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation or bilateral oophorectomy) or is not postmenopausal [defined as amenorrhea 12 consecutive months; or women on hormone replacement therapy (HRT) with documented serum follicle stimulating hormone (FSH) level 35mIU/mL]. Even women who are using oral, implanted or injectable contraceptive hormones or mechanical products such as an intrauterine device or barrier methods (diaphragm, condoms, spermicides) to prevent pregnancy or practicing abstinence or where partner is sterile (e.g., vasectomy), should be considered to be of child bearing potential.

5.0 Methodology and Treatment Plan

Within 24 hours prior to planned surgery, patients will be injected with 0.3-0.4 mci of Tc99m-sulfur colloid in 0.15-0.2 cc volume intradermally in 2-4 spots around the eyelid sebaceous gland carcinoma. Multiple standard of care images of the head and neck including SPECT/CT will be obtained in the Nuclear Medicine Department following standard of care

protocols at MD Anderson Cancer Center.. At this point transmission images of the head and neck region will be performed.

Intra-operative Mapping and Sentinel Node Biopsy

On the day of surgery, 0.15-0.2 cc (0.3-0.4 mCi) of Tc99m-Sulfur colloid will be injected intradermally around the primary lesion approximately one hour prior to the procedure, only if it has been more than 24 hours since the prior injection of Tc99m-sulfur colloid. Intraoperative lymphatic mapping and SLN identification are performed based on the localization of the radioactive colloid in regional lymph nodes. The hand-held gamma probe is used to localize the SLN transcutaneously before a small skin incision is made over the corresponding nodal basin(s), and identification of a SLN is attempted. An SLN is defined as one that collects radiolabeled colloid (at least twice background) within a regional nodal basin. The maximal ex-vivo counts per second are recorded for each SLN. The SLN harvest is considered to be complete when radiotracer uptake in the draining nodal basin(s) is less than twice background. All patients will undergo wide local excision of the eyelid sebaceous gland carcinoma if needed during the same anesthesia session.

The intradermal injection of Tc99m-Sulfur colloid as well as resection of the eyelid tumor will be done by the PI. The intraoperative localization of SLN will be performed by a surgeon from Surgical Oncology or from Head & Neck Surgery.

Excised SLNs are analyzed following the same methodology as in other anatomic locations. Briefly, the SLNs are breadloafed at 2 mm interval. Formalin-fixed, paraffin-embedded and serially sections at 4-µm intervals are obtained. Initially, one hematoxilin and eosin (H&E) stained slide is examined by routine microscopy. If a metastasis is identified, the diagnosis is rendered. In the report, the size (two dimensions) of the largest metastatic focus, the localization of metastasis (subscapular, intraparenchymal or both) and the presence or absence of the extracapsular extension will be included. If metastasis is not identified in the initial H&E section, a serial level will be obtained and another H&E-stained slide will be examined, along with an immunohistochemical study performed on paraffin-embedded sections. The immunohistochemical study will include a pan-keratin cocktail (containing antibodies against high and low molecular-weight keratins), as well as antisera against epithelial membrane antigen (EMA). The combination of immunohistochemical studies is performed in order to expand the sensitivity of sebaceous carcinoma metastases detection method in SLNs.

6.0 Evaluation During Study

An ophthalmologic exam to check for recurrence of the eyelid tumor is undertaken every three months (+/- 6 weeks) during the first year and every 6 months (+/- 6 weeks) during years 2-5. A CXR will be performed 1 year (+/- 6 weeks) after removal of the primary tumor. A head and neck CT or MRI or a SPECT /CT scan is done once every 6 months (+/- 6 weeks) during the first year and then once a year (+/- 6 weeks), thereafter and as needed. An ultrasound of regional nodes will be repeated 1 year (+/- 6 weeks) after removal of primary tumor.

A study participant's inability to comply with study policies and procedures, including the inability to comply with recommended follow up visits and testing, will be withdrawn from the study by the study PI.

7.0 Evaluation of Side Effects

There are no significant ocular toxicity expected from SLN biopsy in the periocular region.8-11 One potential side effect of the SLN biopsy for periocular tumors is the likelihood of involvement of the preauricular (parotid) lymph nodes and the risk of damage to the facial nerve during the dissection and biopsy. In our experience so far, in over 40 patients, there have been no cases of permanent facial nerve paralysis, although 3 patients with ocular tumors have had mild, temporary marginal mandibular nerve paresis, which resolved spontaneously after three weeks. This risk will be discussed with each patient prior to sentinel node biopsy. If facial nerve weakness occurs, the patient will be promptly evaluated by the ophthalmologist for protection of the corneal surface and consideration will be given to periocular reconstructive surgery, if the paresis or palsy is not improved after several months of observation.

8.0 Number of Patients

This study will be conducted at M.D. Anderson Cancer Center only. Given the rare nature of eyelid sebaceous gland carcinoma, we estimate that accrual will be about 8-10 participants a year. Our goal is to enroll 20 patients in this study. All will be enrolled at M.D. Anderson only.

9.0 Statistical Considerations

The rate of SLN positivity and the false negative events will be reported using descriptive statistics. Given the rare nature of this cancer, a total patient number of 20 is likely the maximum number that we can feasibly accrue in a few years. The estimated rate of positivity for SLN is about 15% and the estimated rate of false negative events is 8%. Based on these assumptions, the widths of 95% binomial confidence intervals based on 20 patients would be: 5%: 0.25; 10%: 0.30; 15%: 0.35; 20%: 0.38.

10. Data Analysis

Data analysis will be done at the end of patient accrual and follow up.

11.0 References

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