Management of Salivary Gland Malignancy: ASCO Guideline

Geiger et al.
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Background & Methodology
Introduction

- Salivary gland malignancies (SGMs) are rare neoplasms accounting for less than 1-5% of all head and neck cancers.\(^1,2\)

- Given the rarity of the disease, there are limited clinical trial data to help guide therapy, and no formal evidence-based or consensus guidelines have previously been published as far as the expert panel was aware.

- This guideline aims to provide up-to-date diagnosis, workup, and management recommendations for patients with SGM based on literature and expert panel consensus.

- The intricacies of patient management decisions for SGM are best decided in the context of a multidisciplinary tumor board and with careful consideration of histology, disease burden and distribution, the patient’s overall health and co-morbidities, potential treatment-related toxicities, and function.

- It is the Expert Panel’s goal that this guideline will provide a framework and the best current evidence for managing the care of patients with SGM from diagnosis to treatment.
ASCO Guideline Development Methodology

• The ASCO Clinical Practice Guidelines Committee guideline process includes:
  ▪ a systematic literature review by ASCO guidelines staff
  ▪ an expert panel provides critical review and evidence interpretation to inform guideline recommendations
  ▪ final guideline approval by ASCO CPGC

• The full ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology
Clinical Questions

This clinical practice guideline addresses six clinical questions:

1. What is the appropriate pre-operative evaluation for patients with salivary gland malignancy (SGM)?
2. What are the proper surgical procedures for SGM?
3. What are the treatment considerations and appropriate radiotherapy technique for patients with SGM?
4. What is the role of systemic therapy in the management of SGM?
5. What is the appropriate post-treatment follow-up and evaluation of patients with SGM?
6. What are treatment options in recurrent/metastatic disease for patients with SGM?
Target Population and Audience

Target Population

• Patients with SGM

Target Audience

• Medical oncologists, radiologists, radiation oncologists, clinical oncologists, surgeons, nurses, pathologists, oncology pharmacists, caregivers and patients
Summary of Recommendations
Summary of Recommendations

Clinical Question 1

• What is the appropriate pre-operative evaluation for patients with SGM?

Recommendation 1.1

• Providers should perform imaging (neck ultrasound, CT with IV contrast and/or MRI of the neck and primary site) in patients with a suspicion of a salivary gland cancer.
Summary of Recommendations

**Recommendation 1.2**

- Providers should perform computed tomography of the neck with IV contrast for patients with suspicion for salivary gland cancer and involvement of adjacent bone.

**Recommendation 1.3**

- Providers should perform contrast-enhanced MRI with a diffusion sequence of the neck and skull base for patients with suspicion for salivary gland cancer with concern for perineural invasion and/or skull base involvement.
Summary of Recommendations

Recommendation 1.4

- Providers may perform a CT/positron emission tomography from the skull base to mid-thighs for patients with advanced stage high-grade salivary gland cancers.

Recommendation 1.5

- Providers should perform a tissue biopsy (either fine needle aspiration biopsy or core needle biopsy) in order to support distinction of salivary gland cancers from non-malignant salivary lesions.
Summary of Recommendations

Recommendation 1.6

• Providers may perform core needle biopsy if fine needle aspiration biopsy is inadequate or subsite precludes fine needle aspiration biopsy such as deep minor salivary glands

Recommendation 1.7

• Pathologists should report risk of malignancy using a risk stratification scheme for salivary fine needle aspiration biopsies with particular attention to high-grade features.
Summary of Recommendations

Recommendation 1.8

• Pathologists may perform ancillary testing (immunohistochemical or molecular studies) on fine needle aspiration biopsies and core needle biopsies to support diagnosis and risk of malignancy.
Clinical Question 2

• What are the proper surgical procedures for SGM?

Recommendation 2.1

• Surgeons should offer open surgical excision for histologically confirmed salivary gland malignancies.
Summary of Recommendations

Recommendation 2.2

- Surgeons may request intraoperative pathologic examination to support immediate alterations in intraoperative management (extent of resection, neck dissection). Decisions that would result in major harm such as facial nerve resection should not be based on indeterminate preoperative or intraoperative diagnoses alone.

Recommendation 2.3

- Surgeons may perform partial superficial parotidectomy for appropriately located superficial T1 or T2 low grade salivary gland cancers.
Summary of Recommendations

Recommendation 2.4

• Because of the risk of intraparotid nodal metastases in high-grade or advanced stage parotid cancer, surgeons should perform at least a superficial parotidectomy with consideration of a total or subtotal parotidectomy for any high-grade or advanced (T3 - T4) parotid cancer.

Recommendation 2.5

• Surgeons should perform facial nerve preservation in patients with intact preoperative facial nerve function when a dissection plane can be created between the tumor and the nerve.
Summary of Recommendations

Recommendation 2.6

• Surgeons should perform resection of involved facial nerve branches in patients with impaired facial nerve movement preoperatively or when branches are found to be encased or grossly involved by a confirmed malignancy.

Evidence-based

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<th>Evidence Quality</th>
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Recommendation 2.7

• Surgeons should offer an elective neck treatment over observation in a clinically negative neck in T3 and T4 tumors and high-grade malignancies.

Evidence-based

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Summary of Recommendations

**Recommendation 2.8**

- For operative elective neck management of salivary cancers, ipsilateral selective neck dissection should be performed with levels dependent on the primary site. For parotid malignancies, levels may include 2-4.

**Recommendation 2.9**

- For a cN+ neck, surgeons may perform an ipsilateral neck dissection of involved and at-risk levels and may extend to adjacent levels, up to levels 1-5.
Summary of Recommendations

Recommendation 2.10

• In the setting of resectable, recurrent locoregional disease and no distant metastatic disease, regardless of prior treatment type, patients should be offered revision resection and appropriate surgical reconstruction and rehabilitation.
Summary of Recommendations

Recommendation 2.11

• In the setting of resectable, recurrent locoregional disease and distant metastatic disease, regardless of prior treatment type, treatment may include palliative revision resection and appropriate surgical reconstruction and rehabilitation, if the metastatic disease is not rapidly progressive or imminently lethal.

Recommendation 2.12

• Patients undergoing revision surgery for recurrent salivary gland cancer should be evaluated for potential adjuvant therapy.
Summary of Recommendations

Clinical Question 3

• What are the treatment considerations and appropriate radiotherapy technique for patients with SGM?

Recommendation 3.1

• Post-operative RT should be offered to all patients with resected adenoid cystic carcinoma.

Evidence-based

Evidence Quality

Intermediate

Strength of Recommendation

Strong
Summary of Recommendations

Recommendation 3.2

• Post-operative RT should be offered to patients with tumors with the following features: high grade tumors, positive margins; perineural invasion; lymph node metastases; lymphatic/vascular invasion; and T3-T4 tumors.

Recommendation 3.3

• Post-operative RT may be offered to patients with tumors with close margins, or intermediate grade tumors.
Summary of Recommendations

Recommendation 3.4

- In post-operative cases, the high dose target should cover the salivary gland surgical bed and appropriate nodal levels.

Recommendation 3.5

- In the case of perineural invasion, the associated nerve(s) may be covered with an elective/intermediate dose to the skull base.
Summary of Recommendations

Recommendation 3.6

• Elective nodal coverage may be offered for T3-T4 primary and high-grade malignancies.

Recommendation 3.7

• Radiation should be initiated within 8 weeks of surgery.
Summary of Recommendations

Recommendation 3.8

- Particle therapy, including proton, neutron, and carbon ion therapy, may be used for patients with SGM; there are no indications for use of heavy particle therapy over photon/electron therapy.

Recommendation 3.9

- Elective neck irradiation may be offered in patients with cN0 disease for the following indications: T3 - T4 cancers or high-grade malignancies.
Summary of Recommendations

Recommendation 3.10

- Radiotherapy should be offered to patients with SGM who are not candidates for surgical resection (due to extent of disease or medical comorbidity).

- *Note: The high dose target should cover the gross disease in the salivary gland and any appropriate nodal levels.*
Summary of Recommendations

Clinical Question 4

• What is the role for systemic therapy in the management of SGM?

Recommendation 4.1

• In the setting of patients undergoing adjuvant radiotherapy, the addition of concurrent chemotherapy may not be routinely offered outside of a clinical trial.

Evidence-based

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Summary of Recommendations

Recommendation 4.2

- In the setting of patients undergoing radiotherapy for non-operable salivary gland cancer, the addition of concurrent chemotherapy may not be routinely offered outside of a clinical trial.

Evidence based

Evidence Quality

Insufficient

Strength of Recommendation

Moderate

Recommendation 4.3

- In patients with salivary gland tumors expressing androgen receptor and/or Her2-Neu, adjuvant endocrine or targeted therapy may not be routinely offered outside of a clinical trial.

Informal consensus

Evidence Quality

Insufficient

Strength of Recommendation

Moderate
Summary of Recommendations

Clinical Question 5

• What is the appropriate post-treatment follow-up and evaluation of patients with SGM?

Recommendation 5.1

• Clinical follow-up with history and physical exam should be completed on a regular basis with decreasing frequency as time elapses from completion of treatment of salivary gland cancer.
Summary of Recommendations

Recommendation 5.2

- Post-treatment baseline imaging with contrast CT or MRI (for patients without contraindications) of the primary site, and/or PET/CT should be obtained 3 months after completion of all treatment.

Recommendation 5.3

- Follow-up surveillance imaging of the primary site (contrast CT or MRI) and the chest CT may be obtained every 6-12 months for the first 2 years after treatment.
Summary of Recommendations

Recommendation 5.4

- Follow-up imaging of the primary site and the chest from years 3-5 should be directed by symptoms and physical exam findings. Yearly follow-up imaging may be offered in cases of high-grade histology or poor prognostic clinicopathologic features.

Recommendation 5.5

- Long-term follow-up (beyond 5 years) with yearly exam should be offered in all salivary gland cancer patients. Yearly chest CT may be offered especially in patients with high-grade histology or poor prognostic clinicopathologic features.
Summary of Recommendations

Clinical Question 6

- What are treatment options in recurrent/metastatic disease for patients

Recommendation 6.1

- Patients presenting with metastatic disease may be evaluated for further treatments such as local ablative treatments or systemic therapy. These options should be discussed with the patient and will depend on the patient and tumor factors.

Informal consensus

Evidence Quality

- Low

Strength of Recommendation

- Weak
Summary of Recommendations

Recommendation 6.2

- In the setting of adenoid cystic carcinoma and/or low grade tumors with indolent biology with limited metastases (i.e. ≤ 5 metastases), local ablative treatments such as surgery (metastatectomy) or stereotactic body radiation (SBRT) may be offered to delay local disease progression.
Summary of Recommendations

Recommendation 6.3

• Patients may be considered for initiation systemic therapy in the following circumstances: 1) metastatic deposits are symptomatic and not amenable to palliative local therapy, 2) growth has the potential to compromise organ function, or 3) lesions have grown more than 20% in the preceding 6 months.
Summary of Recommendations

Recommendation 6.4

• For patients with adenoid cystic carcinoma who are candidates for initiation systemic therapy, a multitargeted tyrosine kinase inhibitor, such as lenvatinib, or sorafenib may be offered if a clinical trial is not available.

Recommendation 6.5

• For patients with non-adenoid cystic salivary gland cancer who are candidates for initiation of systemic therapy, targeted therapy based on tumor molecular alterations (i.e. AR, HER2, NTRK) may be offered if a clinical trial is not available.
Summary of Recommendations

Recommendation 6.6

• Cytotoxic chemotherapy combinations may be offered to patients with symptomatic disease.

Evidence Quality
- Low

Strength of Recommendation
- Weak

Recommendation 6.7

• For patients who are candidates for systemic therapy, checkpoint inhibitors should not be routinely offered at this time except for patients with select molecular alteration (high tumor mutational burden, MSI-H).

Evidence Quality
- Low

Strength of Recommendation
- Weak
Summary of Recommendations

Recommendation 6.8

- For patients with histologic tumor types with a high prevalence of targetable molecular alterations (i.e. AR in salivary duct carcinoma, NTRK3 in secretory carcinoma) confirmatory target specific testing should be performed.
Summary of Recommendations

Recommendation 6.9

• Patients who may be potential candidates for systemic therapy with histologic tumor types with low prevalence of targetable molecular alterations and unknown driver mutation status should be screened using a comprehensive panel for driver mutations; patients with driver mutation negative tumors may then be offered target specific testing (i.e. AR, NTRK3).
Discussion
Patient and Clinician Communication

• Head and neck cancer clinicians need to consider how treatment might have acute and late toxicities for the patient affecting speech, taste, saliva, chewing, swallowing, lymphatic processes, nerves, teeth, facial bone structure, and physical appearance.

• Clinicians need to discuss these potential impacts with patients to balance the most effective treatment with the patient’s quality of life objectives.

• A personal discussion among the multidisciplinary team, the patient, and their families is critical to optimal modern care.

• Many centers have developed navigators to facilitate processes and minimize the challenge patients face when they first encounter large systems of physicians and providers. Navigators can also help identify resources such as support groups to share information and strategies that can improve the patient treatment experience.

• Strong and clear communication between physicians, patients, caregivers, and families is paramount for delivering the best quality care.
Cost Implications

- Increasingly, individuals with cancer are required to pay a larger proportion of their treatment costs through deductibles and co-insurance.\(^3,4\)

- Higher patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended cancer treatments.\(^5,6\)

- Discussion of cost can be an important part of shared decision-making.\(^7\)

- Clinicians should discuss with patients the use of less expensive alternatives when it is practical and feasible for treatment of the patient’s disease and there are two or more treatment options that are comparable in terms of benefits and harms.\(^7\)

- Patient out of pocket costs may vary depending on insurance coverage.

- When discussing financial issues and concerns, patients should be made aware of any financial counseling services available to address this complex and heterogeneous landscape.\(^7,8\)
Additional Resources

• More information, including a supplement and clinical tools and resources, is available at www.asco.org/head-neck-cancer-guidelines

• Patient information is available at www.cancer.net
# Guideline Panel Members

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References

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