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Immunotherapy and Biomarker Testing in Recurrent and Metastatic Head and Neck Cancers

ASCO Guideline

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1 Background & Methodology

Introduction

- HNSCC accounts for ~4% of all cancers in the US, with an estimated 66,470 new diagnoses and 15,050 deaths in 2022.[1] HNSCC frequently arises from the oral cavity, oropharynx, larynx, hypopharynx, or nasopharynx, and more rarely from salivary glands or paranasal sinuses.
- Patients with HNSCC commonly present with locoregionally advanced disease and often receive multimodality treatments.
- Recurrent or metastatic HNSCC is typically treated with systemic therapy involving chemotherapy and/or immunotherapy.
- Immune-checkpoint inhibitors were first approved in the treatment of patients with platinum-refractory HNSCC and later in first-line treatment with or without chemotherapy.[2-4]
- With the advent of ICIs in cancer treatment, biomarkers such as PD-L1 and TMB are gaining importance in selecting treatment options.[5,6]
- The purpose of this guideline is to provide recommendations regarding immunotherapy and biomarker testing for this diverse and complex group of diseases.

ASCO Guideline Development Methodology

- The ASCO Evidence Based Medicine Committee (EBMC) 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 EBMC

- 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 biomarkers are recommended for selecting HNSCC patients for anti-PD-1 immune-checkpoint inhibitor therapy?
2. What is the optimal first-line treatment regimen for recurrent or metastatic HNSCC patients based on PD-L1 status?
3. What is the effect of immunotherapy compared to other systemic treatments in platinum-refractory recurrent or metastatic HNSCC?
4. What is the role of immunotherapy for patients with recurrent or metastatic NPC?
5. What is the effect of radiation therapy in combination with anti-PD-(L)1 immunotherapy compared to immunotherapy alone for the treatment of locoregionally recurrent or oligometastatic HNSCC?
6. What is the role of immunotherapy for rare head and neck cancers?

Target Population and Audience

Target Population

- Patients with head and neck cancers

Target Audience

- Medical oncologists, radiation oncologists, surgical oncologists, clinical oncologists, radiologists, nurses, pathologists, oncology pharmacists, caregivers, and patients.

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2 Summary of Recommendations

Summary of Recommendations

Clinical Question 1

- What biomarkers are recommended for selecting HNSCC patients for anti-PD-1 immune-checkpoint inhibitor therapy?

Recommendation 1.1

- PD-L1 immunohistochemistry testing should be performed in patients with recurrent or metastatic HNSCC.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Summary of Recommendations

Recommendation 1.2

- PD-L1 CPS ≥ 1 should be interpreted as positive and correlates with a clinical benefit to PD-1 inhibitors.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Recommendation 1.3

- TMB testing may be performed in patients with recurrent or metastatic HNSCC when CPS is not available or in patients with rare tumors.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Summary of Recommendations

Recommendation 1.4

- TMB ≥ 10 should be interpreted as high and correlates with a clinical benefit to PD-1 inhibitors.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Summary of Recommendations

Clinical Question 2

- What is the optimal first-line treatment regimen for recurrent or metastatic HNSCC patients based on PD-L1 status?

Recommendation 2.1

- Pembrolizumab monotherapy or pembrolizumab, platinum, and 5-FU should be offered as first-line treatment for patients with recurrent or metastatic HNSCC with a CPS ≥ 1.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Summary of Recommendations

Recommendation 2.2

- Pembrolizumab, platinum, and 5-FU may be offered as first-line treatment for patients with recurrent or metastatic HNSCC with a CPS < 1.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
Moderate	Strong

Summary of Recommendations

Clinical Question 3

- What is the effect of immunotherapy compared to other systemic treatments in platinum-refractory recurrent or metastatic HNSCC?

Recommendation 3.1

- Pembrolizumab or nivolumab should be offered to patients with platinum-refractory recurrent or metastatic HNSCC, regardless of CPS status.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

Summary of Recommendations

Clinical Question 4

- What is the role of immunotherapy for patients with recurrent or metastatic NPC?

Recommendation 4.1

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
High	Strong

- Toripalimab, camrelizumab or tislelizumab, with gemcitabine and cisplatin, should be offered as first-line treatment for patients with recurrent or metastatic nasopharyngeal cancer.

Qualifying statement: Pembrolizumab or nivolumab may be offered with gemcitabine and cisplatin if the immune checkpoint inhibitors in Recommendation 4.1 are unavailable.

Summary of Recommendations

Recommendation 4.2

- PD-1 inhibitors may be offered to patients with recurrent or metastatic nasopharyngeal cancer who have progressed following platinum-based therapy.

Informal consensus benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
Low	Weak

Summary of Recommendations

Clinical Question 5

- What is the effect of radiation therapy in combination with anti-PD-(L)1 immunotherapy compared to immunotherapy alone for the treatment of locoregionally recurrent or oligometastatic HNSCC?

Recommendation 5.1

- For patients with oligometastatic HNSCC, radiation therapy is safe to give concurrently with immunotherapy for the purpose of palliation or local control, but should not be given to enhance response to immunotherapy outside of a clinical trial.

Evidence-based no net benefit	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

Summary of Recommendations

Clinical Question 6

- What is the role of immunotherapy for rare head and neck cancers?

Recommendation 6.1

- Pembrolizumab may be offered to patients with TMB-high recurrent or metastatic rare head and neck cancers.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

Summary of Recommendations

Recommendation 6.2

- Pembrolizumab may be offered to patients with PD-L1 positive recurrent or metastatic salivary gland cancer.

Evidence-based benefits outweigh harms	
Evidence Quality	**Strength of Recommendation**
Moderate	Weak

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3 Discussion

Patient and Clinician Communication

- With the improvement of screening and surgical techniques, patients have more options available to them.
- Strategies to manage cancer in the head and neck vary according to a surgeon's experience and the availability of different technologies.
- Head and neck cancer clinicians face challenges given the potential adverse impacts many of these treatments have on a patient's quality of life – including treatment impacts on speech, taste, saliva, chewing, swallowing, lymphatic processes, nerve damage, teeth, facial bone structure, and physical appearance.
- The clinician needs to discuss these potential impacts with the patient to balance the most effective treatment with the patient's quality of life objectives.

Patient and Clinician Communication

- By recommending which patients would most benefit from immunotherapy and biomarker testing, the Expert Panel hopes to give clearer guidelines to treating clinicians, without placing additional burdens on patients.
- The goal of these recommendations is so patients will receive more specific, targeted treatments to manage their cancer, resulting in higher success rates. This guideline does not seek to encompass all approaches but serves as a helpful framework for critical discussions among the multidisciplinary treatment team, the patient, and their families.

Cost Implications

- As part of the guideline development process, ASCO may opt to search the literature for published cost-effectiveness analyses that might inform the relative value of available treatment options.
- Three cost-effectiveness analyses were identified to inform the topic.[7-9]
- Each analysis similarly dealt with the particular case of nivolumab monotherapy for recurrent or metastatic HNSCC.
- Both Haddad et al.[7] and Ward et al.[9] found that nivolumab was cost-effective up to a willingness-to-pay threshold of $150,000 per quality-adjusted life-year (QALY);[7] however, Tringale et al.[8] concluded nivolumab was not cost-effective if a threshold of $100,000 per QALY was used.

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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Abbreviations

- ASCO, American Society of Clinical Oncology
- CPS, combined positive score
- EBMC, Evidence Based Medicine Committee
- HNSCC, head and neck squamous cell carcinoma
- ICI, immune checkpoint inhibitors
- NPC, nasopharyngeal carcinoma
- PD-1, programmed cell death protein 1
- PD-L1, programmed death-ligand 1
- QALY, quality-adjusted life-year
- TMB, tumor mutational burden
- US, United States

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