Email: Guidelines@astro.org

Date of Request: May 28, 2020

The American Society for Radiation Oncology has reviewed the 2020 NCCN Head and Neck Cancers guideline for gaps relative to radiation therapy and offers 5 key recommendations supported by evidence-based rationales and 6 additional suggestions for your consideration.

We hope you find these recommendations useful to your panel as you review and update the guidelines.

Sincerely,

Laura I. Thevenot
Chief Executive Officer, American Society for Radiation Oncology

Recommendation 1: Throughout the guideline, IMRT should be emphasized over 3D-CRT as the standard-of-care in mucosal H&N cancers treated with curative intent.

Rationale: Multiple randomized trials have confirmed that IMRT is superior to 3D-CRT in multiple outcomes including xerostomia, quality of life, rates of skin or mucosal toxicity, feeding tube use, and stimulated parotid salivary flow.

References:

**Recommendation 3:** HYPO-A and MS-27 – The recommended fractionation scheme with concurrent chemotherapy in hypopharyngeal cancer is 70 Gy in 35 fractions, as no prospective data has validated other regimens with concurrent chemotherapy in the setting of hypopharyngeal cancer.

**Rationale:** Though the guideline cites RTOG 0615 and RTOG 0022 for alternative fractionation regimens, neither were a trial of hypopharynx cancer patients.

**Recommendation 4:** GLOT-2/SUPRA-2 – Select T3N0 patients should be removed from the decision tree, as there is no obvious reason why a subset of T3N0 disease should be treated with radiation alone over chemoradiation, given these patients were eligible for the VA Larynx and RTOG 91-11 trials, the latter of which showed improved locoregional control and laryngeal preservation outcomes with concurrent chemotherapy.

**References:**

**Recommendation 5:** GLOT-3, GLOT-4, GLOT-6, SUPRA-3, SUPRA-8 – For T3 tumors requiring (amenable to) total laryngectomy (N0-N3) and selected T4a patients who decline surgery, the algorithm should reflect that chemoradiation is preferred over induction chemotherapy.

**Rationale:** Although long-term follow up of RTOG 91-11 showed similar laryngectomy-free survival between chemoradiation and induction chemotherapy followed by radiation, there was higher local control and laryngeal preservation with chemoradiation; further, both PARADIGM and DeCIDE trials showed no difference oncologic outcomes but worse Grade 3/4 toxicity with induction chemotherapy followed by chemoradiation versus chemoradiation alone.

**References:**

**Additional Suggestions:**

**Recommendation 6:** Hypofractionation should be marked as preferred for T2N0 (as it is for T1N0).
Rationale: Multiple non-randomized studies have shown not only improved local control, but also improved survival when hypofractionated RT is compared to conventional RT.

References:

Recommendation 7: ETHM-2 – For sinonasal cancers (ethmoid and maxillary sinus tumor sections), induction/neoadjuvant chemotherapy should be added as an option for T3-T4 tumors where upfront surgery or radiation would compromise organ function (i.e., the orbit or skull base is involved such that there would sacrifice of structures surgically or to exceed dose tolerances with radiation).

Rationale: Given the lack of a prospectively validated standard-of-care in sinonasal cancers, it is reasonable to offer upfront chemotherapy for these situations, as multiple retrospective series show favorable response rates for sinonasal squamous cell carcinomas and this is being investigated in the ongoing clinical trial EA3163.

References:

Recommendation 8: ETHM-2 – Anatomic location (including tumors located at the orbit/cribiform plate/pterygomaxillary fossa), perineural invasion and lymphovascular space invasion should be incorporated as additional considerations for post-op RT for T1-T2 tumors.

Rationale: Tumors at the orbit/cribiform plate/pterygomaxillary fossa may be at higher risk for recurrence after surgery alone.

References:

Recommendation 9: ADV-2 – We recommend re-structuring the algorithm for M1 disease by breaking off the first branch into:
Clinical trial preferred

Diffuse metastases: systemic therapy with consideration of palliative radiotherapy

Oligometastatic disease
PS 0-1 [systemic treatment] with surgery/RT/CRT for selected patients
PS 2-3: systemic treatment with consideration of palliative radiotherapy

Rationale: Patients with newly diagnosed metastatic head and neck cancer with limited systemic burden may benefit from aggressive locoregional therapy based on analogy from lung cancer data (such as SABR-COMET), but the data specific to head and neck cancers are limited.


**Recommendation 10**: ADV-3 – The indications for consideration of postoperative chemoradiation should be specified for previously irradiated patients and should include patients with positive margins and extranodal extension.

Rationale: No direct specification on which patients should be reirradiated after surgery is mentioned and given the lack of prospective data in the reirradiation setting, reasonable analogy can be made using the features predictive for the benefit of adjuvant chemoradiation in the EORTC 22931 and RTOG 9501 trials (ECE and positive margins).

References:

**Recommendation 11**: ADV-4 – Curative-intent reirradiation as part of initial therapy should not be initially recommended for patients with recurrent or persistent disease with distant metastases.

Rationale: High-dose reirradiation carries significant toxicities and should not be considered as part of the initial treatment paradigm if distant metastases are also present, though palliative reirradiation in this setting is reasonable.

References: