Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
SYST-A (2 of 4) External request: Submission from Merck & Co., Inc., on 03/20/20 to consider the inclusion of pembrolizumab in the treatment of advanced MSI-H head and neck squamous cell carcinoma be added as a category 2A based on the efficacy data from the publication by Marabelle et al.	Based on the review of the data in the noted reference, the panel consensus was to include pembrolizumab as an option for advanced MSI-H head and neck squamous cell carcinoma (non-nasopharygneal). This is a category 2A, useful in certain circumstances recommendation. Reference: Marabelle et al. Efficacy of pembrolizumab in patients with non-colorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase 2 KEYNOTE-158 study. J Clin Oncol 38:1-10.	24	0	0	6
STST-A (2 of 4) External request: Submission from Merck & Co., Inc., on 04/29/20 to consider the inclusion of the updated dosing recommendations for pembrolizumab, either 200 mg every 3 weeks or 400 mg every 6 weeks administered as a 30-minute intravenous (IV) infusion until disease progression, unacceptable toxicity, or up to 24 months for the treatment of adult patients with head and neck squamous cell carcinoma (HNSCC).	Based on a review of the data and discussion, the panel consensus did not support the addition of these specific recommendations in the Guideline. See Submission for references.	0	24	0	6
SALI-B & NASO-B External request: Submission from Merck & Co., Inc., on 06/17/20 to consider the inclusion of pembrolizumab as a treatment option for patients with advanced tumor mutational burden-high (TMB-H) salivary gland tumors who have progressed following prior treatment and have no satisfactory alternative treatment. Submissions from Foundation Medicine on 06/22/20 and 09/15/20 to consider: • Amend the algorithm for distant metastases on page SALI-4 to recommend tumor mutational	Based on a review of the data and discussion, the panel consensus supported the inclusion of pembrolizumab as a treatment option for: • Patients with advanced tumor mutational burden-high (TMB-H) salivary gland tumors. This is a category 2A, useful in certain circumstances recommendation. • Patients with TMB-H recurrent, unresectable, or metastatic nasopharyngeal cancers. This is a category 2A, useful in certain circumstances, subsequent-line therapy recommendation.	24 24	0 0	0 0	6 6

burden (TMB) as determined by a validated and/or FDA-approved assay to inform the use of pembrolizumab and add a footnote referencing Merino DM, et al. J Immunother Cancer 2020;8:e000147. • Add pembrolizumab as a treatment option for patients with unresectable or metastatic salivary or nasopharyngeal tumors with tissue tumor mutational burden-high (TMB-H) ⩾10 mutations/megabase, as determined by an FDA-approved test, who have progressed following prior treatment and who have no satisfactory alternative treatment options.	The panel consensus did not support the addition of a footnote recommending TMB as determined by a validated and/or FDA-approved assay to inform the use of pembrolizumab. Reference: Marabelle A, Fakih M, Lopez J, et al. Association of tumour mutational burden with outcomes in patients with advanced solid tumours treated with pembrolizumab: prospective biomarker analysis of the multicohort, open-label, phase 2 KEYNOTE-158 study. Lancet Oncol. 2020;21(10):1353-1365.	0	24	0	6
NASO-B Internal request: Comment to consider the inclusion of recommendations for cisplatin-ineligible patients.	Based on the discussion, the panel consensus was to include carboplatin + RT followed by carboplatin/5-FU as an option for patients with nasopharyngeal cancer if cisplatin ineligible or intolerant.	24	0	0	6
Multiple Pages External request: Submissions from ASTRO on 08/13/2019 and 05/28/20 to consider multiple recommendations for consideration. • Throughout the guideline, IMRT should be emphasized over 3D-CRT as the standard-of-care in mucosal H&N cancers treated with curative intent. • OR-2: There is a recommendation for resection of primary (without neck dissection). Add detail in the decision tree on which patients this is appropriate for. A depth of invasion cut off should be considered. Page SURG-A, 6 of 9, indicates dissection should be strongly considered for >4 mm, only used in selective situations for < 2 mm, and be subject to clinical judgement for 2-4 mm, which should be reflected on page OR-2 as well. • ORPH-A: In the Principles of Radiation Therapy (page ORPH-A 1 of 2), the guideline suggests 44-50 Gy (2.0 Gy/fraction) for low to intermediate risk disease. This should be broken down further to indicate that for IMRT a biologically equivalent dose of approximately 50 Gy in 2 Gy fractions or	Based on a review of the data and discussion, the panel consensus was to include the following edits in the NCCN Head and Neck Guidelines V.1.2021: • ORPH-A (1 of 2): ○ Added, “IMRT planning can consist of sequential IMRT (S-IMRT) or simultaneous integrated boost (SIB) techniques. Equivalent doses in 2Gy (EQD2) can be used to determine appropriate fractionation schemes when using SIB techniques.” ○ Low to intermediate risk, modified: 44–50 Gy (2.0 Gy/fraction) *used for S-IMRT or the use of an anterior neck field and* to 54–63 Gy (1.6–1.8 Gy/fraction) *when using SIB techniques.* ○ Add “See discussion” in footnote 6. Information about cetuximab will be included in the Discussion section.	24	0	0	6

slightly higher should be prescribed (e.g., 50 Gy [2 Gy/fraction] or 54-56 Gy [1.54 Gy-1.63 Gy/fraction] in a dose-painting fashion where all target volumes receive 33-35 fractions), or 44 Gy in 22 fractions if using a low neck matched AP field. • ORPH-A: In footnote 6 on page ORPH-A 1 of 2, the guideline discusses altered fractionation with chemotherapy. It should be expanded to specifically include cetuximab, now level 2B for use concurrently with RT. Alternate fractionation should be suggested with concurrent cetuximab. • HYPO-A: 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. • 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. • GLOT-2: Since the guideline groups T1 and T2 tumors with T3 ones, systemic therapy and RT should be recommended as another option for post-operative patients with T1-T2, N0 or select T3, N0 tumors and positive surgical margins. • 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. • Hypofractionation should be marked as preferred for T2N0 (as it is for T1N0). • ETHM-2: For ethmoid sinus cancers, the use of postop RT for T1-2 cancers is based on features including negative margins, favorable histology,	• ETHM-2: Revised adverse features in footnote “o” for consideration of adjuvant systemic therapy/RT: Adverse features include positive margins, close margins *(tumors adjacent to the cribriform plate and/or medial wall of the orbit), unfavorable histology (*high grade, *adenoid cystic),* ~~high-grade lesions~~, ~~and~~ intracranial *and/or intraorbital extension, cribriform plate location, medial wall of orbit location, perineural invasion, and lymphovascular space invasion.* • ETHM-2: The panel consensus was to consider the inclusion of induction/neoadjuvant chemotherapy as an option for T3-T4 ethmoid sinus tumors where upfront surgery or RT would compromise organ function. (See Transparency dated 09/03/2020 for vote). • The panel consensus was not to include induction/neoadjuvant chemotherapy as an option for T3-T4 maxillary sinus tumors. • ADV-2/ADV-4: Add “+/- palliative RT or palliative surgery” as an option for PS-2/3, metastatic head and neck cancer. The panel consensus did not support the addition of any other specific recommendations.				

central tumors, and low-grade tumors. Anatomic location should be incorporated as another consideration. • ETHM/MAXI: 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). • ADV-2/ADV-4: Consider re-structuring the algorithm for M1 disease. 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. • 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. • 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.					
SYST-A (EB-3) External request: Submission from Merck & Co., Inc., on 06/18/20 to consider an increase in the number of Evidence Blocks for efficacy of the regimen for pembrolizumab combination therapy (pembrolizumab/platinum/5-FU).	The NCCN Evidence Blocks™ have been updated to reflect the panel consensus.				