Society of Interventional Oncology

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NCCN Guidelines Panel: Neuroendocrine and Adrenal Tumors

On behalf of the Society of Interventional Oncology, we respectfully request the NCCN Neuroendocrine and Adrenal Tumors guideline panel review the enclosed data for updating the role of liver-directed therapies (LDT) in the clinical practice guidelines in oncology (NCCN guidelines).

LDT is inclusive of ablative therapies, such as radiofrequency (RF) and microwave (MW) ablation, as well as embolotherapies, including transarterial embolization (TAE), conventional transarterial chemoembolization with ethiodized oil (cTACE), drug-eluting bead chemoembolization (DEB-TACE), and transarterial radioembolization with Yttrium-90 microspheres (TARE).

Specific change 1: Include a section "Principles of Liver-DIrected Therapy" to follow the existing "Principles of Surgery" section.

Rationale: Since liver-directed therapies are an integral part of the treatment algorithm of neuroendocrine tumor patients, a more detailed summary of LDT and its appropriate application(s) would be useful to include as general guidelines.

Specific change 2: In NET-7 "Neuroendocrine Tumor of the GI tract, lung, and thymus (carcinoid tumors) – management of locoregional unresectable disease – bronchopulmonary/thymus" => Add ablation as potential alternative treatment for unresectable primary typical carcinoid (2B)

Rationale: Growing volume of literature shows the safety and efficacy of thermal ablation for control of primary and secondary malignancies of the lung measuring < 3.5 cm in diameter. While the evidence for stereotactic radiation is more robust, thermal ablation offers a noninferior therapeutic alternative to radiation therapy, particularly in patients with underlying pulmonary fibrosis.

- Lencioni R Lancet Oncol 2008;9,621-628
- Uhlig et al Radiology 2018;289:862-870
- Chen et al Int J Radiat Oncol Biol Phys 2017;98:622-631
- Bahig et al. Pract Radiat Oncol;6:367-374

Specific change 3: NET-9 "Neuroendocrine Tumor of the GI tract, lung, and thymus (carcinoid tumors) – management of distant metastases – bronchopulmonary/thymus" => Add LDT for liver dominant liver metastases (2B)

Rationale: Liver-directed therapies for neuroendocrine liver metastases have demonstrated efficacy for tumor growth control and symptomatic relief.

- Gupta et al Cancer 2005l104:1590-1602
- Ruutiainen et al J Vasc Intervent Radiol 2007;18:847-855
- Ho et al AJR Am J Roentgenol 2007;188:1201-1207
- Maire et al Neuroendocrinoloy 2012;964:294-300
- Sommer et al Eur Radiol 2013;23:3094-3013
- Fiore et al Endocrine 2014;47:177-182
- Pericleous et al. Asian Pac J Clin Oncol 2016;12:61-69

Specific change 4: NET-10 "Neuroendocrine Tumor of the GI tract, lung, and thymus (carcinoid tumors) – management of locoregional advanced disease and/or distant metastases gastrointestinal tract" => Change from hepatic-directed therapy for hepatic predominant disease to liver-directed therapy (LDT) and refer to principles of LDT (new). No difference in evidence level between TARE and TAE/TACE (all 2B).

Rationale: Growing literature on image-guided interventions has provided some insight into prioritization of liver-directed therapies in different clinical scenarios. For example, the use of transarterial bland embolization (TAE) or conventional transarterial chemoembolization with ethiodized oil (cTACE) is now preferred over drug-eluting beads chemoembolization (DEB-TACE), due to increased risk of bile duct injuries. Use of transarterial radioembolization with Yttrium-90 microspheres (TARE) carries a lesser risk of hepatobiliary infection over thermal ablation, TAE and TACE, in the setting of prior biliary tract instrumentation. These updates and others are included in the new principles of LDT page.

- Chen et al Cardiovasc Intervent Radiol 2017;40:69-80
- Pitt et al J Gastrointest Surg 2008;12:1951-1960
- Bhagat et al Cardiovasc Intervent Radiol 2013;36:445-458
- Guiu et al J Hepatol;5:609-617
- Soulen MC et al J Vasc Interv Radiol 2019; 30, Supplement, Pages S49–S50
- Devulapalli et al Radiology 2018:774-781
- Cholapranee et al Cardiovasc Intervent Radiol 38:397-400
- Tohmasawa et al J Vasc Intervent Radiol 2018;29:858-865
- Currie et al J vasc Intervent Radiol 2019;S1051-0443

Specific change 5: PanNET-7 "Neuroendocrine Tumors of the pancreas – management of locoregional advanced disease and/or distant metastases gastrointestinal tract" => Change from hepatic-directed therapy for hepatic predominant disease to liver-directed therapy (LDT) and refer to principles of LDT (new). No difference in evidence level between TARE and TAE/TACE (2B).

Rationale: As above for specific change 4

Specific change 6: AGT-5=> "Adrenal gland tumors – Workup" – Consider changing RFA to ablative therapies (2B). Add consider LDT for liver metastases and refer to new principles of LDT.

Rationale: Local treatment of adrenal neoplasms has been shown to improve patient survival. When surgery is not feasible or operative risk is considered unacceptable, ablative therapies represent a safe and effective approach for treatment of adrenal tumors. Modern ablative therapies available to treat adrenal tumors include cryoablation, microwave ablation, and radiofrequency ablation.

- Howell et al Ann Sug Oncol 2013;20:3491-3496
- Gunjur et al Cancer Treat Rev 2014;40:838-846
- Hasegawa et al Radiology 2015;584-593
- Frenk et al J Vasc Intervent Radiol 2018;2:276-284

Thank you for your consideration,

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