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NCCN Guidelines Panel: Colon and Rectal Cancer

On behalf of the Society of Interventional Oncology, we respectfully request the NCCN Colon and Rectal Cancer Guideline panel review the enclosed data for inclusion in the management of metastatic colon and rectal cancers.

Requested Change 1: Acknowledge recent data demonstrating non-inferiority of thermal ablation to surgical resection in selected patients with small colorectal cancer liver metastasis in respect to overall survival, while providing improvement results in respect to complications, hospital stay, and local disease control. Specifically:

- Modify the statement "Resection (preferred)^{aa} and/or Local therapy" to "Resection or thermal ablation (preferred)^{aa} and/or Local therapy". COL-10 (page 16), COL-15 (page 21)
- Modify the statement "liver or lung resection (preferred) and/or local therapy^{bb}" to "liver resection or thermal ablation (preferred) or lung resection (preferred) and/or local therapy^{bb}" COL-6 (page 12), COL-14 (page 20)
- Modify the statement "and resection (preferred) and/or local therapy^{bb}" to "and resection or thermal ablation (preferred) and/or local therapy^{bb}" COL-6 (page 12), COL-14 (page 20)
- In the section "Local Therapies for metastases", consider the addition of the following statement following the statement "The standard... is surgical resection". "Image-guided thermal ablation can be considered as a first local-therapy for selected patients with small colorectal liver metastasis where sufficient ablative margins can be achieved". MS-29 (page 90)

Rationale: Recently presented results of a multi-center phase 3 non-inferiority trial (COLLISION Trial) at ASCO 2024 demonstrated that the use of thermal ablation was non-inferior to surgical resection in respect to overall survival. Moreover, transitioning from surgical resection to thermal ablation as standard of care for patients with small-size (≤ 3 cm) colorectal cancer liver metastasis reduced complications, shortened hospital stay and improved local control. Likewise, there is increasing evidence in the literature that image-guided thermal ablation can achieve similar outcomes in terms of local tumor control and survival when compared to surgery in selected patients presenting with small (< 3 cm) colorectal liver metastasis where ablation can be done with sufficient minimal ablative margins (> 5 mm).

This is consistent and further clarifies the statements made in “Principles of Surgery, Criteria for Resectability of Metastases and Locoregional Therapies within Surgery” (COL C, page 35). Furthermore, the statement “Ablative techniques can be considered alone or in conjunction with resection. All original sites of disease need be amenable to ablation or resection” is made for both liver and lung metastases.

References:

Colorectal Liver Metastases

1. Martijn Ruben Meijerink et al. Surgery versus thermal ablation for small-size colorectal liver metastases (COLLISION): An international, multicenter, phase III randomized controlled trial. *JCO* 42, LBA3501-LBA3501(2024).
2. Vasiniotis Kamarinos N, Vakiani E, Gonen M, et al. Biopsy and Margins Optimize Outcomes after Thermal Ablation of Colorectal Liver Metastases. *Cancers (Basel)*. 2022;14(3):693. Published 2022 Jan 29.
3. Lin YM, Paolucci I, O'Connor CS, et al. Ablative Margins of Colorectal Liver Metastases Using Deformable CT Image Registration and Autosegmentation. *Radiology*. 2023;307(2):e221373.
4. Tinguely P, Ruiter SJS, Engstrand J, et al. A prospective multicentre trial on survival after Microwave Ablation VErSUS Resection for Resectable Colorectal liver metastases (MAVERRIC). *Eur J Cancer*. 2023;187:65-76.
5. Tinguely P, Dal G, Bottai M, Nilsson H, Freedman J, Engstrand J. Microwave ablation versus resection for colorectal cancer liver metastases - A propensity score analysis from a population-based nationwide registry. *Eur J Surg Oncol*. 2020;46(3):476-485.
6. Shady W, Petre EN, Do KG, et al. Percutaneous Microwave versus Radiofrequency Ablation of Colorectal Liver Metastases: Ablation with Clear Margins (A0) Provides the Best Local Tumor Control. *J Vasc Interv Radiol*. 2018;29(2):268-275.e1.

Colorectal Lung Metastases

1. Kurilova I, Gonzalez-Aguirre A, Beets-Tan RG, et al. Microwave Ablation in the Management of Colorectal Cancer Pulmonary Metastases. *Cardiovasc Intervent Radiol*. 2018;41(10):1530-1544.
2. de Baère T, Aupérin A, Deschamps F, et al. Radiofrequency ablation is a valid treatment option for lung metastases: experience in 566 patients with 1037 metastases. *Ann Oncol*. 2015;26(5):987-991.

Specific Change 2: Modify Footnote “bb” from “Resection is preferred over locally ablative procedures (e.g., image-guided ablation or SBRT)” to “Resection or thermal ablation is preferred over stereotactic body radiation therapy [SBRT].” COL-6 (page 12), COL-7 (page 13), COL-10 (page 16), COL-11 (page 17), COL-14 (page 20), COL-15 (page 21)

Rationale: The interchangeable use of the term “ablative” for image-guided thermal ablation, other forms of ablation, and SBRT is not in keeping with current clinical practice and level of evidence on literature. It is also not consistent with the statements provided in COL C “Principles of Surgery, Criteria for Resectability of Metastases and Locoregional Therapies within Surgery”. As depicted on the “Tumor Ablation” discussion session, there are several level 1 and 2 studies that support thermal ablation (microwave, RFA, and cryoablation) as the main alternative to surgical resection for liver and lung colorectal cancer metastasis. Other local therapies/energy modalities such as irreversible

electroporation, brachytherapy, and SBRT currently lack the same level of evidence as thermal ablation and therefore should not be discussed in conjunction with thermal ablation (please see “specific change 1” request). In COL C, the statement “Ablative techniques can be considered alone or in conjunction with resection. All original sites of disease need be amenable to ablation or resection” refers to thermal ablation (RFA and or MWA) based on a higher level of evidence than any other image guided local therapy (IRE, SBRT, Cryoablation, Radioembolization etc.). We feel this needs to be properly reflected throughout the guidelines and discussion sessions for both lung and liver colorectal cancer metastasis.

References:

Colorectal Liver metastases

1. Puijk RS, Dijkstra M, van den Bemd BAT, et al. Improved Outcomes of Thermal Ablation for Colorectal Liver Metastases: A 10-Year Analysis from the Prospective Amsterdam CORE Registry (AmCORE). *Cardiovasc Intervent Radiol*. 2022;45(8):1074-1089.
2. Nieuwenhuizen S, Dijkstra M, Puijk RS, et al. Thermal Ablation versus Stereotactic Ablative Body Radiotherapy to Treat Unresectable Colorectal Liver Metastases: A Comparative Analysis from the Prospective Amsterdam CORE Registry. *Cancers (Basel)*. 2021;13(17):4303.
3. Ruers T, Van Coevorden F, Punt CJ, et al. Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial. *J Natl Cancer Inst*. 2017;109(9):dix015.
4. Tanis E, Nordlinger B, Mauer M, et al. Local recurrence rates after radiofrequency ablation or resection of colorectal liver metastases. Analysis of the European Organisation for Research and Treatment of Cancer #40004 and #40983. *Eur J Cancer*. 2014;50(5):912-919.
5. Di Martino M, Rompianesi G, Mora-Guzmán I, Martín-Pérez E, Montalti R, Troisi RI. Systematic review and meta-analysis of local ablative therapies for resectable colorectal liver metastases. *Eur J Surg Oncol*. 2020;46(5):772-781.

Colorectal Lung metastases

1. Hasegawa T, Takaki H, Kodama H, et al. Three-year Survival Rate after Radiofrequency Ablation for Surgically Resectable Colorectal Lung Metastases: A Prospective Multicenter Study. *Radiology*. 2020;294(3):686-695.
2. Li G, Xue M, Chen W, Yi S. Efficacy and safety of radiofrequency ablation for lung cancers: A systematic review and meta-analysis. *Eur J Radiol*. 2018;100:92-98.

Specific Change 3: Create “Principles of Locoregional Therapy”.

Rationale: Interventional oncologists play a critical role in the management of patients with metastatic colorectal cancer, similarly to medical oncologists, surgeons, and radiation oncologists. This rapidly evolving field encompasses various image-guided locoregional therapies with distinct clinical applications, evidence levels, and incorporation of novel technologies. The creation of a specific "Principles of Locoregional Therapy" section would ensure consistency between the "principles" and "discussions" sessions, enabling a more nuanced discussion on the well-established role of interventional oncology in colorectal cancer management. It is worth noting that the NCCN guidelines for hepatocellular carcinoma (HCC) and Neuroendocrine Tumors already incorporate "principles of locoregional therapy”.



Specific Change 4: Increase number of Interventional Radiologists on the panel.

Rationale: In 2012, ABMS approved IR as a primary specialty, with an ACGME-approved residency. IR is a clinical patient-oriented specialty, combining clinical care, medical imaging, and image-guided procedures. Interventional Oncology is now a well-recognized subspecialty of interventional radiology. Interventional Oncologists/Radiologists collaborate on a multidisciplinary fashion, providing complementary expertise. They are involved in patient care, outpatient clinic and inpatient consultations, hospital admissions, conferences, and follow cancer management guidelines. Their expertise in image-guided therapies is crucial throughout cancer care. As essential members of the multidisciplinary team, interventional oncologists should be equally represented at the NCCN with same numbers as surgeons, and radiation oncologists. Interventional Oncologist should be seen as separate and unique experts from diagnostic radiologist in the panel. We would respectfully request the addition of one more interventional radiologist to the panel.