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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.

**Specific Change 1: In “Principles of Surgery, Criteria for Resectability of Metastases and Locoregional Therapies within Surgery” add yttrium-90 radioembolization radiation lobectomy to portal vein embolization and staged liver resection as options to induce future liver remnant hypertrophy when hepatic metastatic disease is not optimally resectable based on insufficient remnant liver volume.**

**Rationale:** Unilobar Y-90 radioembolization to the tumor-bearing hepatic lobe results in hypertrophy of the contralateral lobe (future liver remnant) in the range of 26 to 47% between 44 days and 9 months. This compares favorably to portal vein embolization, but provides the additional advantages of treating the hepatic disease and obtaining tumor control in the interval to hypertrophy, as well as possibly facilitating R0 surgical resection by causing retraction of the hepatic tumor(s) away from critical structures.

#### References:

Teo JY et al. HPB 2016; 18:7-12

Vouche M et al. J Hepatol 2013; 59:1029-1036

Melstrom L et al. HPB 2019; S1365-182X(19)30491-5 [Epub ahead of print]

**Specific Change 2: In “Principles of Surgery, Criteria for Resectability of Metastases and Locoregional Therapies within Surgery,” consider updating the section header “Evaluation for Conversion to Resectable Disease” to “Evaluation for Conversion to Resectable or Ablatable Disease,” and add to the first bullet point that initially unresectable patients should be re-evaluated for resection and ablation after 2 months of preoperative chemotherapy and every 2 months thereafter. Similar wording can be considered to the treatment algorithm on COL-11 and REC-14.**

**Rationale:** In a randomized phase II trial, patients who received radiofrequency ablation in addition to systemic therapy showed statistically significant improvement in overall survival compared to patients treated with chemotherapy alone. It would be important to highlight the importance of assessing whether patients are or might become eligible for RFA throughout the course of their treatment, even if they are not be candidates for surgical resection, considering the substantial improvement in long term survival when radiofrequency ablation is added to systemic therapy.

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**Reference:**

Ruers T et al. J Natl Cancer Inst 2017;109

**Specific Change 3: mFOLFOX + bevacizumab + DEBIRI may be considered as first line therapy for patients with liver-limited metastases.**

**Rationale:** In a randomized trial of irinotecan drug-eluting beads with simultaneous FOLFOX and bevacizumab for patients with unresectable colorectal liver-limited metastases, there was significantly more downsizing to resection in the FOLFOX-DEBIRI arm versus the FOLFOX/bevacizumab arm and there was significantly improved progression-free survival in the treatment arm.

Reference: Martin et al. Cancer 2015; 121:3649-58

**Specific Change 4: Consider the addition of a footnote or other statement within the algorithms of COL-D and REC-F addressing the consideration of locoregional therapies for highly selected patients who have developed chemotherapy-resistant/-refractory disease with predominant hepatic metastases.**

**Rationale:** The algorithms of COL-D and REC-F make it appear that regorafenib or trifluridine + tipiracil are the only therapeutic options for patients who have developed chemotherapy-resistant/-refractory metastases, with the consideration of locoregional therapies figuring only as a secondary discussion, even though according to the current guidelines, “consensus amongst panel members is that arterially directed catheter therapy and, in particular, yttrium-90 microsphere selective internal radiation is an option in highly selected patients with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases.”

We would like to thank the NCCN panel members for their time and effort in reviewing this submission.

Sincerely,

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