Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
COL-2 External request from Gabriel Brooks, MD, MPH and Ken Surprenant, patient advocate to include a footnote "Germline polymorphisms of the DYPD gene are known to increase risk for grade 3-5 toxicity among patients receiving fluoropyrimidine chemotherapy. Consider pharmacogenomic or phenotypic testing to assess for risk of severe toxicity prior to initiation of fluoropyrimidine chemotherapy."	Based on review of the data, the Panel consensus did not support the addition of the suggested footnote to the algorithm. Information will be added to the discussion section. • See Submission for references.	0	23	0	3
COL-2/3 External request from the American Society for Radiation Oncology (ASTRO) requesting the addition of concurrent capecitabine or 5-FU + RT as a treatment option for clinical T4b (COL-2) and T4, N1-2; T Any, N2 (COL-3).	Based on review of the data, the Panel consensus did not support the addition of concurrent capecitabine or 5-FU + RT as a treatment option. For COL-2, the Panel felt that this layout clearly displays neoadjuvant chemoradiation as the preferred option for patients with initially unresectable disease which would potentially include clinical T4b patients. For COL-3, adjuvant radiation therapy is listed as an option for high-risk stage III disease under footnote p. • See Submission for references.	7 5	14 17	1 1	4 3
COL-3/COL-B External request from HalioDx to review the data for inclusion of Immunoscore colon testing as part of the standard of care management of patients with localized colon cancer as an adjunct to the TNM staging in the postsurgical pathologic review.	Based on review of the data, the Panel consensus did not support the addition of Immunoscore testing to the Guidelines. The Panel does not believe that the results of this test would impact treatment decisions. • See Submission for references.	0	23	0	3
COL-6/REC-9 Internal request to review the data for inclusion of the combination regimen FOLFOXIRI ± cetuximab/panitumumab as a treatment option for patients with unresectable synchronous liver and/or lung metastases only.	Based on review of the data, the Panel consensus supported the addition of FOLFOXIRI ± cetuximab/panitumumab as a treatment option for patients with unresectable synchronous liver and/or lung metastases only. This is a category 2B recommendation. Geissler M, Martens UM, Knorrenschield R, et al. mFOLFOXIRI + panitumumab versus FOLFOXIRI as first-line treatment in patients with RAS wild-type metastatic colorectal cancer: a randomized phase II VOLFI trials of the AIO (AIO-KRK0109). Annals of Oncology 2017;28:Issue suppl_5(abstract 4750).	14	6	3	3

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
COL-6/COL-D External request from Sirtex to review the data to support the addition of yttrium 90 resin microspheres to standard first-line mFOLFOX6 chemotherapy in patients with right-sided primary colon cancer with liver-dominant or liver-only metastases.	Based on review of the data, the Panel consensus did not support the addition of yttrium 90 resin microspheres to standard first-line mFOLFOX6 chemotherapy in patients with right-sided primary colon cancer with liver-dominant or liver-only metastases. • See Submission for references.	0	21	1	4
COL-6/COL-11/COL-D External request from Sirtex for formatting revisions to the guideline with the purpose of clarifying and supporting patient access and coverage of the existing NCCN recommendation of yttrium 90 treatment for chemo-refractory/chemo-intolerant colon cancer. **COL-6**: "Unresectable synchronous liver and/or lung metastases only", after "Remains unresectable": revise to "Systemic therapy **or radioembolization for highly select patients (see COL-E)**" **COL-11**: "Unresectable metachronous metastases", after "Remain unresectable": revise to "Systemic therapy **or radioembolization for highly select patients (see COL-E)**" ADD Footnote: "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." **COL-D1:** "Continuum of care", "Patient not appropriate for intensive therapy", after "No improvement in functional status": revise to "Best supportive care **or radioembolization for elderly patients (see COL-E)**"	Based on review of the data, the Panel consensus did not support the modifications as requested for COL-6 or COL-11. This information is addressed in the Principles of Radiation Therapy (COL-E). The Panel consensus also did not support the addition of radioembolization for elderly patients to COL-D 1. • See Submission for references.	1 0	19 20	2 0	4 6
COL-11/COL-D REC-14/REC-F External request from Bristol-Myers Squibb for the inclusion of the following footnote based on the recent FDA dosing update: FDA approved dose is 240mg IV every 2 weeks administered over 30 minutes until disease progression or unacceptable toxicity.	Based on review of the data, the Panel consensus did not support the addition of the suggested footnote to pages COL-11/REC-14/COL-D/REC-F. Dosing information is included on COL-D/REC-F 9 of 12. • See Submission for references.	0	23	0	3

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
COL-B 4 of 5 External request from Foundation Medicine to review the data to support the following updates to the Principles of Pathologic Review: 1. Indicate that testing for KRAS, NRAS, BRAF, and Microsatellite instability (MSI)/MMR status might be most efficiently performed by a single validated comprehensive genomic profiling (CGP) assay (as opposed to sequential testing of single biomarkers or use of limited molecular diagnostic panels) in order to conserve tissue and to obtain as much information as possible to inform the use of currently available biomarker driven therapies and define/refine clinical trial options. 2. Add evaluation of tumor mutational burden (TMB) as a recommendation in addition to MSI or mismatch repair (MMR) testing, to identify additional patients who are likely to benefit from immunotherapies. 3. If tissue is unavailable, suggest genomic testing via a validated, blood-based liquid biopsy, such as FoundationACT, to identify genomic alterations that may inform the patient's treatment, including the option to enroll in genomically matched clinical trials.	Based on review of the data, the Panel consensus did not support the modifications as requested for COL-D 4 of 5. Voting is noted for specific requests: 1. Indicate that testing for KRAS, NRAS, BRAF, and Microsatellite instability (MSI)/MMR status might be most efficiently performed by a single validated comprehensive genomic profiling (CGP) assay (as opposed to sequential testing of single biomarkers or use of limited molecular diagnostic panels) in order to conserve tissue and to obtain as much information as possible to inform the use of currently available biomarker driven therapies and define/refine clinical trial options. *clarified that testing could be made individually or as part of a next-generation sequencing pane. 2. Add evaluation of tumor mutational burden (TMB) as a recommendation in addition to MSI or mismatch repair (MMR) testing, to identify additional patients who are likely to benefit from immunotherapies. 3. If tissue is unavailable, suggest genomic testing via a validated, blood-based liquid biopsy, such as FoundationACT, to identify genomic alterations that may inform the patient's treatment, including the option to enroll in genomically matched clinical trials. • See Submission for references.	0 0 2	20 22 18	1 0 2	5 4 4
COL-D/REC-F External request from Genentech to review the data for inclusion of trastuzumab in combination with pertuzumab for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-amplified/overexpressing metastatic colorectal cancer.	Based on review of the data, the Panel consensus did not support the addition of trastuzumab in combination with pertuzumab for the treatment of patients with HER2-amplified/overexpressing metastatic colorectal cancer. Initial trial results and references will be updated in the discussion section. • See Submission for references.	5	15	3	3
COL-D/REC-F External request from Genentech to review the data for atezolizumab in chemotherapy-refractory metastatic colorectal cancer.	Based on review of the data, the Panel consensus did not support the addition of atezolizumab in in chemotherapy-refractory metastatic colorectal cancer. • See Submission for references.	0	23	0	3

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
COL-E External request from ASTRO requesting the following changes: 1. *Fourth line*: Small bowel dose should be limited to ~~45~~ **50** Gy**, with a max point dose of 55 Gy for conventional fractionation.** 2. *Third bullet*: "If radiation therapy is to be used, conformal external beam radiation should be routinely used and intensity-modulated radiation therapy (IMRT) should be reserved only for unique clinical situations such as re-irradiation of previously treated patients with recurrent disease or anatomical situations **where IMRT facilitates the delivery of recommended target volume doses while respecting accepted normal tissue dose-volume constraints."** 3. To simplify different radiation dose options, consider this format: **Neoadjuvant and adjuvant radiation therapy:** 45-50 Gy in 25-28 fractions **For close or positive margins, 10-20 Gy external beam radiation or brachytherapy to a limited volume could be considered soon after surgery, pending cumulative dose constraints, prior to adjuvant chemotherapy** **IORT: 10-20 Gy** **Unresectable disease: 54 Gy if technically feasible** **SBRT metastasis: Doses depend on the fractionation and location of tumor. Single fraction treatments: 14-26 Gy, 3 fraction: range 28-60 Gy, 5 fraction: range 50-60 Gy.** 4. In patients with a limited number of ~~**liver and lung**~~ **oligo**metastases, radiotherapy to the metastatic site can be considered in highly selective cases or in the setting of a clinical trial. The techniques can include 3-D conformal radiation therapy, **image-guided radiotherapy (IGRT), fiducial placement, and respiratory-gated radiotherapy,** IMRT or SBRT.	Based on review of the data, the Panel consensus related to the recommended revisions is noted below. 1. The panel felt that the dose limits in the current version of the guidelines were appropriate. 2. The Panel felt that the qualifying statement for the use of IMRT in either the re-irradiation setting or particular anatomical situations where dose constraints cannot be met utilizing conformal external beam radiation therapy was appropriate to include in the guidelines. 3. The Panel appreciates the comment regarding the format of the radiation dose options to make them easier to read. We added additional commentary to clarify that the decision to offer a post-operative or brachytherapy boost in the setting of close or positive margins should be made taking into account the cumulative dose to adjacent organs at risk. 4. The Panel agrees that SBRT can be and is used to treat oligometastatic disease outside of the liver and lung and that practices vary across the country. However, at this time, the panel felt that high quality data regarding the efficacy and safety of SBRT outside of these sites is lacking, and until such data exist, should not be included in the NCCN guidelines. • See Submission for references.				

NCCN Guidelines for Colon Cancer and Rectal Cancer 1.2019 – Meeting on 08/30/18

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
REC-2 External request from ASTRO requesting the addition of: "fertility risk discussion/counseling in appropriate patients" To the workup section.	The Panel consensus supported the addition of fertility risk discussion/counseling as part of the workup for appropriate patients.	23	0	0	3
REC-3/REC-4/REC-6 External request from ASTRO requesting consistency with the headings by providing descriptors under the different treatment algorithms such as "Sandwich therapy" and "Concurrent therapy" and Chemo>ChemoRT and Chemo.	The Panel consensus did not support the requested modifications. The sections are sufficiently clear in the current format.	0	23	0	3
REC-7/REC-10 External request from ASTRO requesting the addition of local ablative therapy as a treatment option for synchronous unresectable metastases of other sites (REC-7) and nonobstructing, synchronous abdominal/peritoneal metastases (REC-10)	Based on review of the data, the Panel consensus was that SBRT can be and is used to treat oligometastatic disease outside of the liver and lung and that practices vary across the country. However, at this time, the panel felt that high quality data regarding the efficacy and safety of SBRT outside of these sites is lacking, and until such data exist, should not be included in the NCCN guidelines. • See Submission for references	0	23	0	3
REC-C 1 of 3 External request from ASTRO requesting the bolded edit to be consistent with REC-5 and REC-E recommendations, "Surgery should be 5-12 weeks following conventional dose 5.5-week neoadjuvant chemoradiation. **For short course neoadjuvant radiation therapy, surgery can be considered at 3-7 days or 4-8 weeks.**	Based on review of the data, the Panel consensus was that the guidelines should be consistent and that surgery can be considered at 3-7 days or 4-8 weeks after completion of short course neoadjuvant radiation therapy per the Stockholm III trial. • See Submission for references	23	0	0	3

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
REC-E External request from ASTRO requesting the following changes: 1. Removing the following statement: Intensity modulated radiation therapy (IMRT) should only be used in the setting of a clinical trial or in a unique clinical situation such as re-irradiation of previously treated patients with recurrent disease or unique anatomical situations. And replace with the following: If radiation therapy is to be used, conformal external beam radiation should be routinely used and intensity-modulated radiation therapy (IMRT) should be reserved only for unique clinical situations such as re-irradiation of previously treated patients with recurrent disease or anatomical situations where IMRT facilitates the delivery of recommended target volume doses while respecting accepted normal tissue dose-volume constraints. 2. Make the bolded changes. **Long-course radiation therapy**: ~~45~~-50 Gy in 25-28 fractions to the pelvis Small bowel dose should be limited to ~~45~~ **50** Gy**, with max point dose of 55 Gy for conventional fractionation**. Short-course radiation therapy: 25 Gy in 5 fractions **to the pelvis** **IORT: 10-20 Gy** **For close or positive margins, 10-20 Gy external beam radiation or brachytherapy to a limited volume could be considered soon after surgery, pending cumulative dose constraints, prior to adjuvant chemotherapy.** **Unresectable: 54 Gy if technically feasible** **SBRT metastasis: Doses depend on the fractionation and location of tumor. Single fraction treatments 14-26 Gy. 3 fraction range 28-60, 5 fraction range 50-60 Gy.**	Based on review of the data, the Panel consensus related to the recommended revisions is noted below. 1. The Panel agreed that the use of IMRT and radiation doses for rectal cancer needs to be clarified. 2. The Panel felt that the dose constraints in the current version of the guidelines were appropriate. • See Submission for references				