Colon and Rectal Cancers Clinical Trials Planning Meeting Executive Summary

Meeting dates: January 7-8, 2011

Prepared by meeting co-Chairs and NCI Staff

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The NCI Gastrointestinal Cancer Steering Committee Colon and Rectal Task Forces held a Clinical Trials Planning Meeting (CTPM) in Bethesda, MD on January 7-8, 2011. The overall goal of the meeting was to develop a blueprint for the next generation of clinical trials for patients with colorectal cancer. The meeting included 103 invited guests, representing NCI and extramural participation, with expertise in colorectal cancer patient management, clinical trials, biostatistics, translational science, and patient advocacy. The meeting included separate agendas for colon cancer and rectal cancer participants, with conjoint sessions as appropriate. Interaction between meeting participants was fostered through small group breakout sessions, and discussion following more formal scheduled presentations.

This Executive Summary presents the consensus arising from the CTPM. It is organized by disease site. These recommendations are not meant to address all clinical contexts, but rather represent priorities for publicly-funded clinical research.

General

- Advances in understanding molecular characterization of tumors and germline variation requires a national infrastructure to provide real-time clinical testing of patient specimens for treatment assignment.
- Integral marker studies are a high priority.
- Existing tissue banks should be exploited for predictive classifier discovery; treatment-classifier-response relationships defined in banked tissue are necessary to design prospective validation studies.
- Banking of patient tumors and germline DNA for future research is an imperative.
- High-priority therapeutic targets include signaling kinases, stem cells, DNA damage response, host response.

Colon Cancer

Early Stage Adjuvant Therapy

- There is not currently a new agent of sufficient promise to warrant testing in a phase III adjuvant study.
- A triple drug combination regimen, FOLFOXIRI should be tested against standard FOLFOX as adjuvant therapy in high-risk stage III colon cancers.
- Neoadjuvant approaches in early stage colon cancer should be considered to establish a model for evaluation of agents potentially active in the adjuvant setting.
- Discovery efforts should continue to focus on identification of populations at particularly high risk of recurrence, as a setting for testing new agents in early stage disease.

Resectable liver-confined metastatic disease

- Preoperative treatment with a new agent will permit in vivo pharmacodynamic assessment of treatment effect.
- "Adjuvant" treatment after potentially curative resection will allow testing of new approaches in this high-risk setting using resected stage IV disease as a model for micrometastatic disease.

Oligometatatic disease with extrahepatic component

- A common clinical setting is liver metastasis with intraabdominal extrahepatic disease. A study is suggested to test the combination of surgical (resection/ablation) plus systemic approach in the setting where minimal residual disease can be accomplished with surgical treatment.

Unresectable metastatic disease

- Tumors with BRAF mutations have a poor prognosis. A first-line randomized phase II study involving new agents, with or without conventional cytotoxics is suggested in this population.
- Patients often have a period of stable disease after initial treatment response. This "window" after response is an opportunity to test targeted approaches in molecularly-defined patient groups. A randomized phase II study of combinations of signaling inhibitors is suggested.
- Irinotecan is commonly administered as a component of second-line treatment. A phase II trial of irinotecan plus novel agent(s) with treatment assignment based on tumor molecular characterization is suggested.
- "Last-line", salvage settings present a patient population of high clinical need with opportunities for drug development.

Rectal Cancer

- Current treatment algorithms typically involve trimodality therapy in a "one-size fits all" approach. Future trials should tailor treatment to patient risk of local and distant recurrence.
- For upper rectal cancer, studies should explore the selective use of radiotherapy.
- For lower rectal cancer or upper rectal cancer at high risk for local recurrence, studies should explore novel agents in addition to a backbone of neoadjuvant fluoropyrimidine plus radiation.
- Explore the role of 5 x 5 radiation therapy in high risk rectal cancer.
- Examine/identify appropriate early end-points/prognostic markers for neoadjuvant clinical trials that can subsequently be integrated into future trials. These endpoints and classifiers will correlate with local recurrence and overall, and include pathological assessment, imaging biomarkers, and molecular classifiers.

NCI Colon/Rectal Cancer Clinical Trials Planning Meeting Attendees
January 7-8, 2011
Bethesda, Maryland

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