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Systematic Survey of Therapeutic Trials for Metastatic Colorectal Cancer: Room for Improvement in the Critical Pathway

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Purpose: The current strategy of drug development has been criticized as being highly inefficient. In 2004, the US Food and Drug Administration (FDA) released recommendations to improve this process, including a push for increased use of enrichment trials. It is unclear to what extent aspects of this “Critical Path Initiative” have been adopted in trial designs in metastatic colorectal cancer.

Patients and Methods: A systematic review was conducted of actively enrolling treatment trials in metastatic colorectal cancer. Trials were identified from the National Cancer Institute’s *clinicaltrials.gov* and Investigative Drug Branch databases. Trials were categorized based on the number of previous treatments allowed, phase of the trial, agent mechanism of action, and FDA-approval status of agents under investigation.

Results: One hundred and two trials are enrolling with a combined enrollment goal of more than 20,000 patients. Twenty five percent of trials are investigating an agent not yet FDA-approved for any oncology indication, although for many of these trials, the stated therapeutic target duplicates an agent already FDA-approved for colorectal cancer. The most common study design is a phase II study limited to previously untreated patients; compared to the remaining trials, these phase II trials are over 10 times more likely to only use agents FDA-approved for colorectal cancer. Even in trials limited to

previously treated patients, few refractory patients (27%) are enrolled on trials with a novel agent. Three percent of patients are enrolled in trials enriched for tumor characteristics that were hypothesized to improve clinical benefit.

Conclusions: Current clinical trials for metastatic colorectal cancer are deficient in the investigation of agents directed at a novel therapeutic target, over-utilize phase II studies of FDA-approved agents, and fail to incorporate enrichment trial designs as encouraged by the FDA initiative.