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NRG GI008: Colon adjuvant chemotherapy based on evaluation of residual disease (CIRCULATE-US)

Christopher H. Lieu

Yan Lin

Scott Kopetz

Samuel A. Jacobs

Peter C. Lucas

See next page for additional authors

Authors

Christopher H. Lieu, Yan Lin, Scott Kopetz, Samuel A. Jacobs, Peter C. Lucas, Ibrahim H. Sahin, Dustin A. Deming, Philip A. Philip, Theodore S. Hong, Yesenia Rojas-Khalil, Jonathan M. Loree, Norman Wolmark, Greg Yothers, Thomas J. George, and Arvind Dasari

TPS260 **Trials in Progress Poster Session**

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Background: Currently, there are no biomarkers validated prospectively in randomized studies for resected colon cancer (CC) to determine need for adjuvant chemotherapy (AC). However, circulating tumor DNA (ctDNA) represents a highly specific and sensitive approach (especially with serial monitoring) for identifying minimal/molecular residual disease (MRD) post-surgery in CC patients (pts), and may outperform traditional clinical and pathological features in prognosticating risk for recurrence. CC pts who do not have detectable ctDNA (ctDNA-) are at a much lower risk of recurrence and may be spared the toxicities associated with AC. Furthermore, for CC pts with detectable ctDNA (ctDNA+) who are at a very high risk of recurrence, the optimal AC regimen has not been established. We hypothesize that for pts whose CC has been resected, ctDNA status may be used to risk-stratify for making decisions about AC. **Methods:** In this prospective phase II/III trial, up to 1,912 pts with resected stage III A, B (all pts) and stage II, IIIC (ctDNA+ only) CC will be enrolled. Based on the post-operative ctDNA status using personalized and tumor-informed assay (Signatera™, bespoke assay), those who are ctDNA- (Cohort A) will be randomized to immediate AC with fluoropyrimidine (FP) + oxaliplatin (Ox) for 3-6 mos per established guidelines *vs.* serial ctDNA monitoring. Patients who are ctDNA+ post-operatively or with serial monitoring (Cohort B) will be randomized to FP+Ox *vs.* more intensive AC with addition of irinotecan (I) for 6 mos. The primary endpoints for Cohort A are time to ctDNA+ status (phase II) and disease-free survival (DFS) (phase III) in the immediate *vs.* delayed AC arms. The primary endpoint for Cohort B is DFS in the FP+Ox *vs* FP+Ox+I arms for both phase II and phase III portions of the trial. Secondary endpoints include prevalence of detectable ctDNA post-operatively, time-to-event outcomes (overall survival and time to recurrence) by ctDNA status, and the assessment of compliance to adjuvant therapy. Biospecimens including archival tumor tissue, as well as post-operative plus serial matched/normal blood samples, will be collected for exploratory correlative research. Active enrollment across the NCTN started in June, 2022. Support: U10-CA-180868, -180822; UG1CA-189867; Natera, Inc. Clinical trial information: NCT05174169. Research Sponsor: U.S. National Institutes of Health, Natera, Inc.