

Prospective evaluation of a 12-gene assay on treatment recommendations in patients with stage II colon cancer.

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Author(s): Geetika Srivastava, Lindsay Anne Renfro, Robert J. Behrens, Margarita Lopatin, Calvin Chao, Gamini S. Soori, Shaker R. Dakhil, Rex Bradford Mowat, J. Phillip Kuebler, George P. Kim, Miroslaw Mazurczak, Mark Lee, Steven R. Alberts; Mayo Clinic, Rochester, MN; National Surgical Breast and Bowel Project; Iowa Oncology Research Association, Des Moines, IA; Genomic Health, Redwood City, CA; Missouri Valley Cancer Consortium CCOP, Omaha, NE; Cancer Center of Kansas, Wichita, KS; Toledo Clinic, Toledo, OH; National Surgical Adjuvant Breast and Bowel Project and CCOP Columbus, Columbus, OH; Mayo Clinic, Jacksonville, FL; Sanford Cancer Center, Sioux Falls, SD

Background: A 12-gene assay (Oncotype DX Colon Cancer) has been clinically validated as a predictor of recurrence risk in stage 2 colon cancer patients following surgery. We conducted the first prospective study to characterize the impact of Recurrence Score results on medical oncologists' recommendations regarding adjuvant chemotherapy in T3, Mismatch Repair-proficient (MMR-P) stage 2 colon cancer patients. Methods: Consecutive patients with resected stage 2A colon cancer who were candidates for adjuvant chemotherapy were consented and enrolled by 105 medical oncologists from 17 sites in the Mayo Clinic Cancer Research Consortium. Each patient's tumor specimen was assessed by the Recurrence Score test (quantitative RT-PCR) and MMR (IHC). Prior to and after receiving these results, physicians completed surveys indicating their planned treatments given hypothetical or known MMR results, recorded as Observation (Obs), 5FU-based chemotherapy (5FU), or 5FU + Oxaliplatin (Oxal). Change in treatment recommendation intensity from baseline to follow-up was defined as: increased if change from Obs to 5FU +/- Oxal or from 5FU to 5FU+Oxal, decreased if change from 5FU + Oxal to 5FU or Obs, or from 5FU to Obs, or no change. Results: 187 of 221 patients enrolled were evaluable including 141 who were MMR-P (avg age 63, 65% ECOG PS 0, med tumor size 5 cm, 11% high grade, 91% with 12+ nodes examined). In the primary analysis treatment recommendations changed for 63 (45%) of 141 MMR-P patients, with intensity decreasing for 47 (33%) and increasing for 16 (11%). Recommendations for chemotherapy (5-FU +/- Oxal) decreased from 73 (52%) patients pre-assay to 42 (30%) post-assay. Increased treatment intensity was more likely at higher Recurrence Score values and decreased intensity at lower Recurrence Score values ( $p=0.011$ ), and any change was more likely when MMR status was unknown at baseline ( $p = 0.041$ ). Conclusions: In this prospective study, quantitative recurrence risk information provided by the Recurrence Score test was associated with treatment recommendation changes for 45% of T3 MMR-P stage II colon cancer patients. Use of the 12-gene assay may lead to overall reductions in chemotherapy.