

Impact of the Recurrence Score (RS) result and mismatch repair status (MMR) on agreement between oncologists (MDs) for stage II colon cancer (CC) recurrence risk (RR) assessment: A novel clinical utility endpoint for prognostic markers.

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Background: Appropriate use of prognostic and predictive markers depends on quality of evidence for clinical utility in addition to clinical validity. In stage II CC, RR assessment is based traditionally on clinicopathologic factors (CP) with limited clinical validation and varies substantially across providers. We hypothesized that the validated Oncotype DX Colon Cancer RS and MMR tests may impact clinical decision-making by decreasing variation in RR assessment across MDs. We conducted a survey to compare the level of MD agreement on stage II CC RR assessment using CP alone vs CP+RS+MMR (CP+).

Methods: A clinical trial database was randomly sampled for 100 cases of stage II CC stratified on T-stage, MMR and RS groups. Anonymous internet surveys asked each MD to assess 3-year RR for 10 cases with CP and 10 different cases with CP+. MDs were divided into panels of 5; all members of each panel reviewed the same cases. Agreement in RR among MDs was assessed using within-panel mean squared difference in RR assessments and analyzed using generalized linear models. **Results:** 30 community (C) and 20 university-based (U) MDs (Assoc of Northern California Oncologists or NCCN, respectively) completed evaluable surveys April-June 2012. For C vs U, median years in practice were 5 and 2; prior use of RS 13% vs 25%; and routine MMR use 21% vs 55%. The standard deviation of the differences (SDD) in RR assessments for CP alone was high overall (7%), and greater for U vs C MDs (8.2% vs 6.4%). CP+ produced higher agreement in RR assessments vs CP for both C ($p<.001$) and U ($p=0.04$) MDs, with 23% and 20% proportional reduction in SDD. For T3 MMR-proficient (P) patients ($n=70$), CP+ produced higher agreement in RR for both C ($p<0.001$) and U ($p=0.01$) MDs with 37% and 29% reduction in SDD. **Conclusions:** Addition of RS+MMR to CP significantly increased MD agreement on RR assessment in stage II CC, including T3 MMR-P patients. Agreement was higher among C than U MDs. MD agreement on stage II CC RR assessment and Tx decision-making warrants consideration as a novel endpoint for clinical utility of RS, MMR, and other prognostic markers.