BACKGROUND

Colorectal polyposis is the primary reason for declining colorectal cancer incidence and mortality. However, many of the ~50,000 annual colorectal cancer (CRC) deaths can be attributed to 1/3 of eligible Americans not following screening guidelines or approximately 1/2 of the population not adherent to the follow-up post-polypsectomy guidelines. CRC is among the most preventable cancers when adenomatous polyps are detected and removed at an early stage because of its slow progression. The new understanding of the natural history and shared etiology of adenomas and CRC inform integration of the most preventable cancers when guidelines or approximately 1/2 of the population not adherent to the follow-up post-polypectomy guidelines. CRC is among the ~50,000 annual colorectal cancer (CRC) deaths can be attributed to 1/3 of eligible Americans not following screening guidelines or approximately 1/2 of the population not adherent to the follow-up post-polypsectomy guidelines. CRC is among the most preventable cancers when adenomatous polyps are detected and removed at an early stage because of its slow progression. The new understanding of the natural history and shared etiology of adenomas and CRC inform integration of the most preventable cancers when

METHODS

A single-center, IRB-approved, prospective, blinded study was conducted at the Veterans Affairs Palo Alto Health Care System (VA PAHCS) to assess a blood test (FirstSight) detecting adenoma-carcinoma pathway markers in a sample of blood. The test analyzes two biomarkers: circulating gastrointestinal epithelial cells (CECs) and somatic mutations of cell-free tumor DNA. CECs are captured and quantified using the CellMax CMx platform, a highly sensitive proprietary platform that has been used in several clinical studies outside of the U.S., with results presented at the 2018 and 2019 ASCO GI conferences.

RESULTS

Interim results for 458 patients with no prior diagnosis of colorectal cancer (CRC) are presented. The cohort included both screening (239) and surveillance (219) subjects. Indicators for colonoscopy were 86% asymptomatic and 14% with symptoms or positive-FIT. Balanced distribution of roughly 3/4th subjects in each disease category were randomly selected for training and algorithm development and the remaining 1/4th subjects were used for validation. A cutpoint was selected to obtain a test specificity (non-neoplastic finding or negative colonoscopy) of 90% resulting in a sensitivity of 100% and 80.0% for detection of CRC and advanced neoplasia (AN = CRC+AA), respectively, on the training subjects.

The area under the ROC curve is 0.91. Validation using the fixed cutoff and 112 test subjects achieved 91.4% specificity and 100% and 75.0% sensitivity for CRC and AN, respectively.

CONCLUSIONS

A noninvasive multimodal FirstSight blood test that analyzes cell-free tumor DNA and circulating epithelial cells, and integrates SEER incidence risk is developed for the early detection of colorectal neoplasia.

This blood test has high sensitivity for colorectal advanced neoplasia while retaining high specificity. The quantitative nature of the score has the potential to enable prognostic stratification of patients for screening or post-polypectomy surveillance colonoscopy.

The authors sincerely appreciate the help and contributions from staff at the Veterans Affairs Palo Alto Health Care System and all patients who contributed samples to this study.

Research Highlights

- Analysis of the blood-based FirstSight test revealed 90% specificity, with sensitivity of 100% and 80% for detection of CRC and advanced neoplasia, respectively, on training set subjects

- The quantitative nature of the FirstSight score has the potential to enable prognostic stratification of patients for screening or post-polypectomy surveillance colonoscopy.