Premier Insight 280

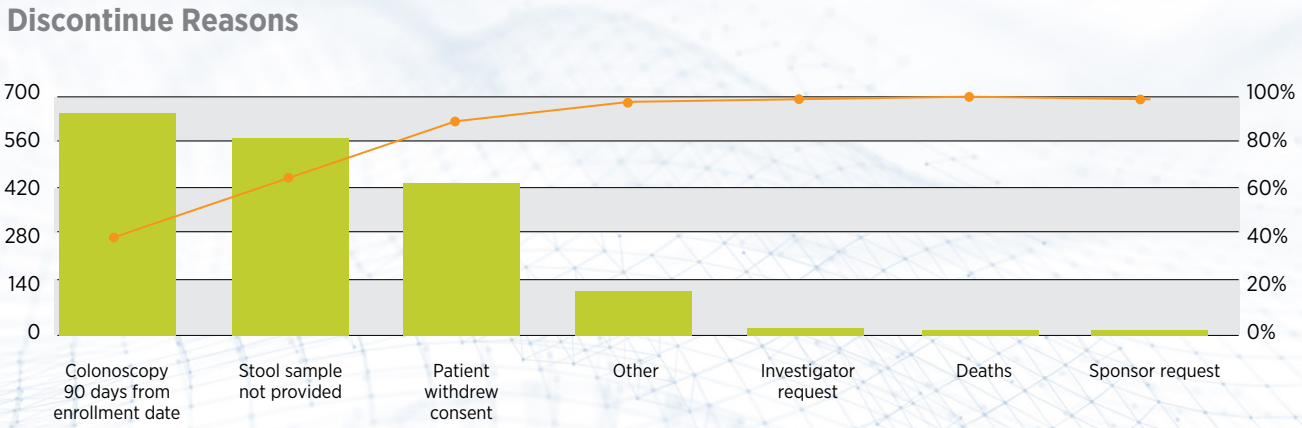
Engineering a PMA Study for a First-of-its-kind Oncology Dx

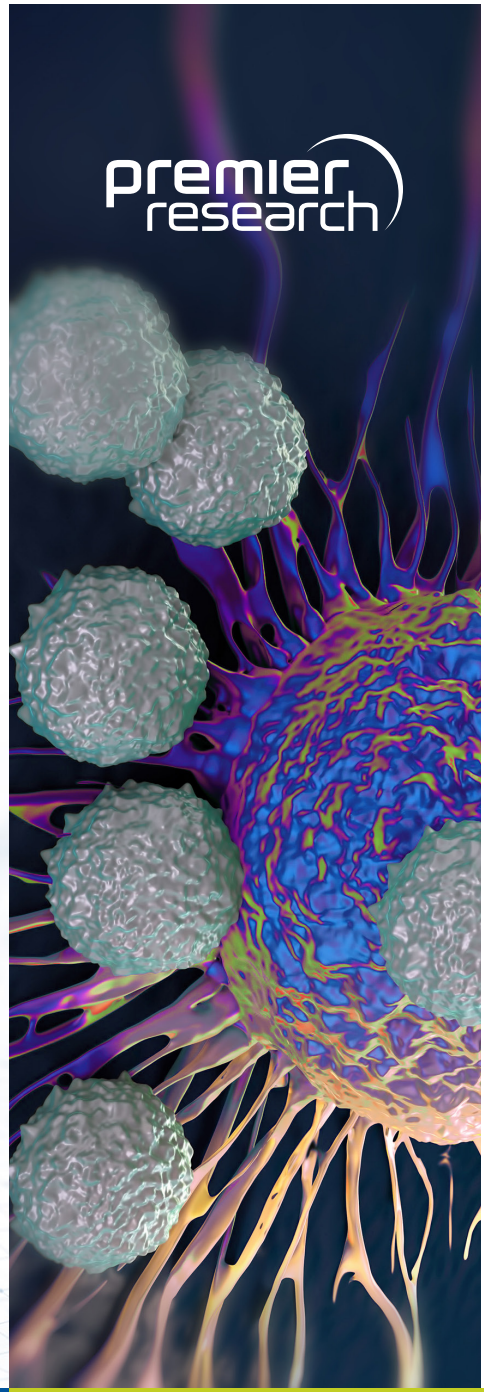
Background

Colorectal cancer (CRC) is the second most deadly form of cancer – although it is among the most curable and the easiest to detect in its early stages. The reason: patients notoriously avoid colonoscopy, placing themselves at unnecessary risk. Our client developed a unique solution – a multi-target, noninvasive screening test that could be facilitated by patients in their homes. They came to Premier Research to conduct the pre-market approval (PMA) study.

Objective

Premier was asked to determine the sensitivity and specificity of this product using colonoscopy as the reference method, with lesions confirmed as malignant by histopathologic examination, quantitative molecular assays for KRAS mutations, aberrant NDRG4 and BMP3 methylation, and β-actin, plus a hemoglobin immunoassay.





D I A G N O S T I C S

Meeting the Challenges

Challenge #1

Due to the low prevalence of the screening disease, the sponsor wanted to ensure we could track each sample throughout its lifecycle, reinforcing the surety and integrity of the data.

Our Strategy

To minimize lost study samples, Premier employed a sample tracking system that coordinated the kit producers, the clinical research sites, a call center, FedEx, and a biostorage bank. The kit production team provided pre-labeled sample collection kits along with pre-filled shipping documents for air transportation. The clinical research sites inventoried shipments and stored the kits ahead of patient enrollment. After contacting patients to ensure sample collection within protocol-defined windows, the call center alerted FedEx of upcoming shipments. Samples were then routed to a biostorage bank for processing ahead of randomization. Of over 36,000 samples collected, only nine were unaccounted for, all due to FedEx's internal issues.

Challenge #2

We anticipated that patient compliance would be an ongoing challenge, requiring careful monitoring and additional enrollment to ensure adequate sample count.

Our Strategy

Premier enlisted a call center to remind patients to use their sample-collection kits within protocol-defined windows. Still, even with the convenience of home testing, many patients failed to collect a stool sample; others missed their colonoscopy. We closely tracked discontinuation reasons and adjusted recruitment plans accordingly.

Challenge #3

The sponsor originally asked that 75 percent of patients be between 64 and 84, with the balance being 50 to 64. We needed to ensure adequate sample count and efficient sample collection with attention to age distribution. We found something surprising.

Our Strategy

Premier continuously tracked the age of the study's patients both by site and for the entire study, charting patients in order to adjust enrollment in real time. Analysis showed CRC prevalence was almost triple for the older age group. Since the study endpoint was obtaining 43-49 cases of confirmed CRC, that statistic suggested that collecting more samples from the older cohort would increase efficiency. However, older patients proved more difficult to enroll than the younger cohort; we determined that we could obtain the required number of confirmed CRC cases more rapidly by enrolling a greater number of younger patients than planned. With the sponsor's agreement, we implemented a late push to accept a greater percentage of patients in the age 50-64 group. We were able to successfully complete the study ahead of schedule, thus reducing site and staffing costs.

Takeaway

Conducting a PMA study for a novel diagnostic presents novel challenges – some foreseeable, others unforeseen. Partnering with a team that closely tracks critical variables and makes rapid, efficient adjustments can not only deliver success, but do so with time- and cost-savings.

Study Description

To compare safety and efficacy of a novel diagnostic with standard colonoscopy, patients submitted self-collected stool samples, then underwent a traditional colonoscopy within 90 days.

Therapeutic Area

Oncology

Geographic Scope

United States

Number of Study Sites

90

Number of Patients Enrolled

12,779

Evaluable Samples

9,989

Outcome

The assay received FDA approval; it is the only approved stool-DNA noninvasive colorectal cancer screening test available today.

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