



Diagnostics Health

Large PMA Study of CRC Diagnostic

Test Diagnostic: Multi-target screening test utilizing quantitative molecular assays for KRAS mutations, aberrant NDRG4 and BMP3 methylation, and β -actin, plus a hemoglobin immunoassay.

Study Design: Enroll approximately 12,000 subjects between the ages of 50 and 84 with average risk of developing colorectal cancer, stopping enrollment upon obtaining 43-49 cases of confirmed colorectal cancer.

Publication: Imperiale TF, Ransohoff DF, Itzkowitz SH, et al N Engl J Med 370:1287-1297, 2014.

Challenges Faced:

- Ensuring that complex sample-management requirements were met
- Improving patient compliance with study obligations
- Monitoring data quality, including critical data on cancer staging
- Ensuring adequate sample count and efficient sample collection with attention to distribution by age cohort

Risk Management and Mitigation:

The following strategies for risk management and mitigation were among those that Health Decisions utilized in this study.

Complex Sample Management Requirements – Health Decisions has supported a variety of trials worldwide with multipart sample logistical requirements. This case study was unique because it required subjects to self-collect samples at home. The samples were important because of the low prevalence rate of the screening disease; therefore, the Sponsor wanted to ensure the CRO would be able to track each sample throughout its life cycle, reinforcing the surety and integrity of the data. Health Decisions utilized a sample tracking system that allowed for coordination/management of the kit producers, the clinical research sites, a call center, FedEx and a

Study at a Glance

Type of Study:

PMA

Objective:

Determine sensitivity and specificity 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.

Active Sites:

90

Subjects Enrolled:

12,779

Evaluable Samples:

9,989

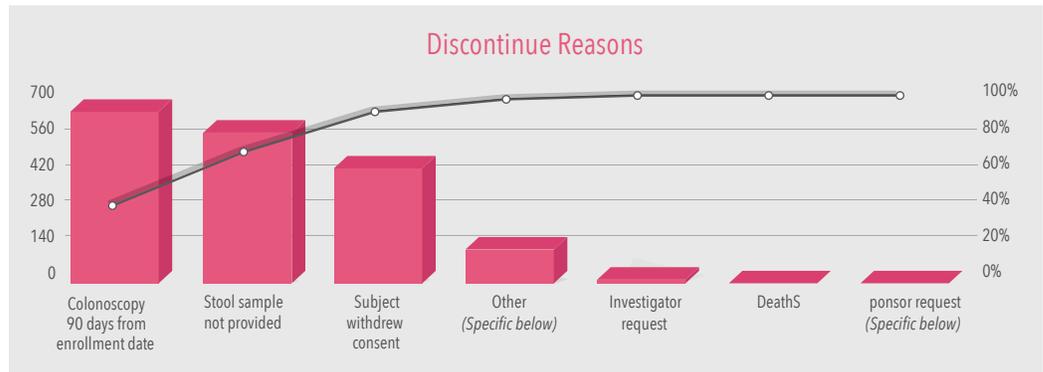
Patient Population:

Patients ages 50 – 84 with average risk of developing colorectal cancer

biostorage bank in order to minimize lost study samples. 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 subject enrollment. After contacting subjects to ensure sample collection within protocol-defined windows, the call center alerted FedEx of upcoming shipments to minimize lost study samples. Samples were then routed to a biostorage bank ahead of randomization for processing. Of over 36,000 samples collected, only nine were unaccounted for, all due to FedEx internal issues.

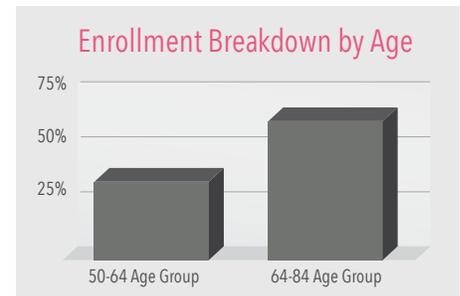
Improving Subject Compliance – As in clinical practice, many subjects failed to keep commitments to collect a stool sample. Other subjects failed to keep the commitment to undergo colonoscopy within 90 days of sample collection. Health

Decisions utilized a call center to remind subjects to use the provided sample-collection kits within protocol-defined windows. Health Decisions closely tracked discontinuation reasons (see chart at right) and adjusted recruitment plans accordingly.



Meeting Age Stratification Requirements for Subjects Providing Samples

– Health Decisions continuously tracked age of subjects providing samples by site and for the study as a whole and advised sites to adjust enrollment to ensure an adequate number of samples for each age group. A continuously updated chart showed enrollment breakdown by age. Health Decisions analyzed optimal age stratification to support timely completion of sample collection consistent with other study requirements.



Analysis showed CRC prevalence almost triple for the older age group, suggesting collecting more samples from the older cohort would increase efficiency. This was consistent with the sponsor’s initial plan to collect 75% of samples from the older cohort. However, older subjects proved more difficult to enroll than the younger cohort. The Health Decisions project team performed an analysis and determined that we could obtain the required number of confirmed CRC cases more rapidly by enrolling a greater number of younger subjects than planned. Because this would reduce site and staffing costs by allowing earlier completion of the study, this approach was more economically efficient despite lower prevalence in the younger group. With the sponsor’s agreement, Health Decisions implemented a late initiative to enroll a greater percentage of subjects in the age 50-64 group. Closely tracking enrollment and productivity by cohort for each site enabled rapid, efficient adjustments to enrollment strategy and accelerated completion of the study.

The Leading Full-Service Women’s Health CRO from Pre-IND or -IDE to Regulatory Approval and Beyond

Health Decisions is a full-service CRO offering therapeutic, operational and regulatory excellence for clinical development of drugs, diagnostics, medical devices and combination drug/devices in all areas of women’s health. Our experience, expertise, site network and KOL and investigator relationships enable us to address the challenges of developing products in areas including general gynecology indications, contraception, sexual health, infertility, obstetrics, menopause and osteoporosis and other indications that affect women disproportionately and profoundly, including autoimmune disorders and male-factor infertility. If it matters to women’s health, it matters to Health Decisions. Health Decisions is headquartered in Durham, NC and operates on five continents.



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