Case Study: Achieving and Exceeding Clinical Trial Participant Diversity Targets

Using Customized Tools, Applications and a Dynamic Enrollment Tracker [1]

Summary

Hepatitis C Virus (HCV) infection is a potentially curable chronic liver infection that can cause cirrhosis, liver cancer, and even death. HCV affects approximately 170 million individuals worldwide and disproportionately impacts Blacks and Latinos.[2,3] Blacks demonstrate lower responses to some treatments (i.e., interferon-alpha) compared to other racial subgroups.
Also, the major HCV genotypes vary in prevalence (based on regional and ethnic/racial demographics), severity, and treatment response (see Section 16.2.2 "Hepatitis C, genomics, geographic region, ethnicity" in *MRCT Center Diversity Guidance Document*), thus amplifying the importance of participant diversity in clinical trials of the treatment for Hepatitis C.[4]

In its pivotal phase 3 "C-EDGE" program evaluating the combination of two products, elbasvir/grazoprevir (Zepatier®), Merck[5] demonstrated that enrolling a diverse population can be improved and targets exceeded through the use of customized tools and applications, and by utilizing a dynamic participant enrollment tracker. Although there were significant program challenges (short enrollment period, competitive landscape, aggressive timelines, managing enrollment on a global basis, and requirement for reliable, real-time reporting and site communication), the goal for minority enrollment of 20% was exceeded.

The activities of Merck to increase clinical trial diversity include a 'Diversity in U.S. Clinical Trials Core Team' that supports company efforts to develop a sustainable process to ensure inclusion of underrepresented diverse patient populations with regard to sex, age, race, and ethnicity in its research and clinical trials. An overall objective of the team is to support the development and implementation of sustainable solutions aimed to make diversity a standard part of the company's commitment to conducting research to develop innovative medicines and vaccines that address important, unmet medical needs to help improve the quality and quantity of life for all people and communities. In 2015 Merck collaborated with the Association of Black Cardiologists, academia and others, to complete an intensive research effort, involving patients, investigators, referring physicians, and study coordinators,

[1] This Case was developed by utilizing the information provided in the webinar hosted by DrugDev. https://www.drugdev.com/uncategorized/merck-improved-clinical-trial-patient-diversity-using-dynamic-enrollment-tracker/

[2] Melia MT, Muir AJ, McCone J, Shiffman ML, King JW, Herrine SK, Galler GW, Bloomer JR, Nunes FA, Brown KA, Mullen KD. Racial differences in hepatitis C treatment eligibility. Hepatology. 2011 Jul;54(1):70-8.

[3] Vutien P, Hoang J, Brooks Jr L, Nguyen NH, Nguyen MH. Racial disparities in treatment rates for chronic hepatitis C: analysis of a population-based cohort of 73,665 patients in the United States. Medicine. 2016 May;95(22).

[4] Reddy, K. Rajender, et al. "Racial differences in responses to therapy with interferon in chronic hepatitis C." *Hepatology* 30.3 (1999): 787-793.

[5] For simplicity, we use "Merck" to reference the company's full legal name, Merck & Co., Inc., Kenilworth, NJ, USA.

to investigate the barriers to minority participation in U.S. clinical trials and to identify potential solutions with respect to implementation, recruitment, retention, and communication.[6] Key barriers were identified including mistrust and lack of comfort with the clinical trial process. Referring physicians were recognized as key drivers of minority patients' participation in clinical trials. They represent the most trusted source of medical information for their patients, and need to feel engaged, informed, and appreciated by study teams.

Challenges and approach

The C-EDGE Program presented the Clinical Trials Core team with a short enrollment period in a competitive landscape. The Core Team had only eight weeks to activate sites and an additional eight weeks to enroll participants. Further, it was necessary to have flawless and reliable medication adherence by the participants. An additional challenge was managing enrollment at a global level in all the sites, across different time-zones, holidays, etc. A reliable, real-time reporting and site communications tool was needed to provide multiple status updates per day, accessible across all sites in different countries, and specifically available for headquarter teams involved in the program management of the trial.

The C-EDGE phase 3 program committed to a certain percentage of minority enrollments as a goal and that goal was set to be higher than those of earlier trials. The program used targeted site selection and made the difficult decision to work only with those centers and sites that were confident in their ability to meet the recruitment goals in the aggressive timelines set. The program partnered with The Center for Information and Study on Clinical Research Participation (CISCRP) to develop customized tools and minority patient education materials. These resources included tools for sites to use such as cultural pointers for healthcare professionals, implementation guides for sites, and bi-lingual consumer materials and brochures that emphasized how patients had been part of the healthcare team designing the trial and not just as recipients of healthcare treatment. The tools highlighted the values of clinical research, the rights of patients and participants in research, and expectations of the participants.

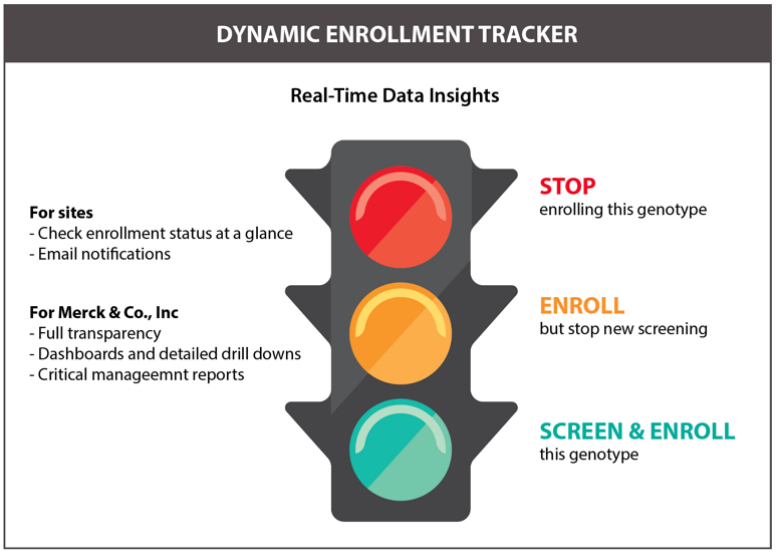
The program developed a communication strategy focused on community building and site engagement using the DrugDev Spark[7] platform. This portal was used as a central cloud-based platform that allowed all staff conducting a study to access materials securely and efficiently. It had multiple features including study dashboards, enrollment update emails, educational videos, team photos, electronic newsletters, and operational spotlights with key materials and best practices. The tools in the platform helped sites trust and rely on the content and the extended network.

[6] Clark LT, Watkins L, Piña IL, Elmer M, Akinboboye O, Gorham M, Jamerson B, McCullough C, Pierre C, Polis AB, Puckrein G. Increasing diversity in clinical trials: overcoming critical barriers. Current Problems in Cardiology. 2019 May 1;44(5):148-72.

[7] For more information, see http://drugdevspark.com/

Figure 1: High-level dynamic enrollment tracker

The dynamic enrollment tracker (see Figure 1) provided real-time data feedback by leveraging the integrated platform system. The tracker was used in tandem with targeted email blasts in addition to an automatic document notification system that deployed a “stop-light" method. This transparent and identifiable visual imagery allowed study leads to check enrollment status and critical management reports quickly.



The enrollment tracker was designed and configured to meet specific study needs. Functionalities were adjusted for specific protocols depending on the study as were subgroups that were important to include and track. The platform was designed to be visually appealing so that sites and other staff members would be comfortable and engage with the tracker. The dashboard within the platform had clear and direct messaging to internal and external study stakeholders, as well as a virtual protocol guide so all information required by a coordinator would be available. Further, the platform contained a ‘Document Exchange’ – a secure repository of all the study documents with a uniform folder structure that was applied to all studies in the program. The standard configuration made it easier for all staff to locate and access necessary information in a timely fashion and decreased barriers to uptake and implementation.

Key components of the program

- **Targeted site selection** including only those sites confident in their ability to meet the diversity recruitment goals;
- **Partnering with CISCRP** to develop customized education materials and resources for healthcare professionals, implementation guides for sites, and bi-lingual communication materials for patients;
- **A communication strategy** focused on community building and site engagement using a central cloud-based platform that allowed all staff access to materials securely and efficiently;
- **A dynamic enrollment tracker** that provided real-time data feedback by leveraging the integrated platform system and transparently allowed study leads to check enrollment status and critical management reports quickly.

Results and key takeaways

- The C-EDGE program exceeded the minority enrollment goals of 20%. The actual number screened was 26.6% and the actual randomized minority population was 26.5%.
- Creating a plan with diversity goals that are clear is key.
- Monitoring execution against plan is a critical element for success.
- Building a clinical trial community is essential.
- Celebrating and sharing those successes continuously promote utilization.
- Engaging sites requires easy, direct, and focused communication to align partners.
- Execution entails partner awareness and tracking through customized tools and applications.