CASE STUDY

# Unique insights gained from multiple NASH studies.

## Overcoming key challenges to design and execute more efficient clinical trials

Sponsors face several challenges in nonalcoholic steatohepatitis (NASH) clinical trials. Issues such as nonperforming sites, the limited availability of experienced investigators and the hesitancy of patients to undergo invasive liver biopsies as an enrollment requirement all contribute to the inherent complexity in NASH clinical trials.

Modern challenges in the NASH clinical landscape have not diminished, but we have gained valuable, experienced-based insight and extensive data on screening, recruitment and dropout to deliver more efficient and expedited trials. **Here, we summarize the key lessons we've learned after 14 trials over the last four years.**

### Taking on NASH challenges

**Patient recruitment improvements:**
***Reducing screen failure rates (SFRs) from as high as 80% to as low as 30%***

When Fortrea first began conducting NASH clinical trials four years ago, we observed SFRs as high as ~80% due to lack of detailed screening paradigms and limited availability of the tools required to pre-identify patients. By carefully reviewing and applying real-world data, Fortrea has been able to design better screening paradigms with specific cutoff values and has put into place processes to provide sites with the necessary tools.

The main challenge in our approach is to find the right balance between identifying potential eligible patients while keeping the SFRs low and not losing potentially eligible patients. Our proprietary algorithm is based on data from more than 2,000 randomized patients. Through our efforts, we are routinely observing average SFRs of 55% with some sites achieving as low as 30%. This reduction in SFRs has not only limited the number of unnecessary liver biopsies but has also helped reduce study costs and resulted in enhanced site motivation.

**Designing more efficient trials:**
***Identifying high-performing NASH sites and selecting the right patients***

In the first generation of NASH trials (i.e., those starting 2015 and 2016), nonperforming sites reached as high as 30% due to poor understanding of sites' capabilities across the globe.

### KEY REASONS FOR CHOOSING FORTREA

**Liver disease experts to optimize protocol design, streamline costs and minimize patient and site burden**

**Operational experts in nonalcoholic fatty liver disease (NAFLD)/NASH Phase I to IV studies to design efficient clinical plans and deliver results on time and on budget**

**Flexibility to effectively adapt to our sponsors' highest priorities**

**Institutional knowledge on NAFLD/NASH across all departments**

**An extensive data set on NAFLD/NASH site performance**

**Strong knowledge of site capabilities**

**Experienced project management and leadership teams who will proactively mitigate risks and resolve challenges**

Fortrea

Building on the experience gained from 14 clinical trials (ranging from Phases I-IV) and enrolling more than 4,000 biopsy-confirmed patients in 700 study sites in 28 countries, the Fortrea NASH team has gained strong insight into which sites can deliver NASH patients—and which cannot. For example, some previous studies enlisted as many as 400 sites to recruit their biopsy-confirmed NASH patients. Currently, however, by capitalizing on our understanding of site performance, a similar study design would require approximately half the number of sites. Overall, our data and experience enable us to design more efficient trials with fewer nonperforming sites, shorter recruitment periods and lower budgets.

With data driven site selection and patient centric recruitment strategies, Fortrea is uniquely placed to support our sponsors identifying the right population to meet both recruitment goals and study objectives.

**KEY ACHIEVEMENTS**

**Acquired access to more than 30 billion patient-level data points**

**Randomized more NASH patients than any other CRO**

**Enrolled more than 4,000 biopsy-confirmed patients in 700 study sites across 28 countries**

**Site engagement and motivation:**
***Proactively managing sites to keep timelines on track***

Even with the use of known, high-performing sites, the Fortrea NASH team has recognized the importance of ongoing site management. By staying connected with sites throughout screening and recruitment, our team of medical and operational experts can help solve screening and recruitment issues as they arise and help maintain compliance with study protocol requirements. We have successfully applied this approach across several studies and, as a result, have now randomized more NASH patients than any other CRO.

## Building a path to success

With the high prevalence of NASH, there is an urgent need to develop effective and safe treatments.

While the current competitive landscape offers unique challenges, our sponsors are capitalizing on the experience, data and relationships with NASH sites that we can offer at Fortrea to help deliver studies on-time and on-budget.

In our most recent biopsy-confirmed NASH study, we were able to draw on our data, experience and key relationships to activate sites as early as two months after being selected and deliver both on-time and on-budget patient recruitment.

Fortrea offers comprehensive and multifunctional experience available in NAFLD/NASH clinical trials across many functions including:

- Scientific and medical input
- Operational strategy and planning
- Regulatory strategy and interactions with health authorities
- Protocol development
- Feasibility
- Site selection
- Operational delivery
- Liver biopsy processing and handling
- Biomarker analysis and imaging

Based on our lessons learned from 14 NASH trials over the last four years, our team understands the best way to design and conduct a highly efficient program. Together, we can design the trial that best meets your needs while also minimizing SFRs, maximizing recruitment rates, lowering your overall risks and keeping costs low.

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