Cerba Research

Case Study

Lab Support for the Largest Global Phase III NASH Study to Date

The Ask

In a meta-analysis of several studies using various methodologies, worldwide prevalence of NAFLD (Non-alcoholic fatty liver disease) is 25.2% and 6.45% for NASH (Non-Alcoholic SteatoHepatitis).[1] NASH prevalence is expected to increase by 63% between 2015 and 2030,[2] yet the condition is still poorly understoodand there is no known treatment. The need for therapeutic agents is urgent. At Cerba Research, we are committed to improving the diagnosis and treatment for NASH.

In 2016, after we successfully supported their Phase II NASH study, a midsize biotech engaged our services for Phase III. Gratified to have gained their trust and eager to continue our productive collaboration with this meticulous client, we rolled up our sleeves and took on the challenge of supporting the largest NASH Phase III study to date.

> "For NASH, the quality of the biopsy slides is pivotal."
>
> Global Head of Project Management

2016 – 2019

5000+
liver biopsies

2000+
patients randomized

600+
sites

31+
countries

NA, EU, AUS, AF

Challenges

Global Scale

NASH is a special therapeutic area with significant operational complexity. Successfully managing these trials on a global scale — encompassing many sites, countries, and patients — requires experienced teams and a wide-reaching host of local affiliates accustomed to NASH protocols and adept at handling liver biopsies.

Liver Biopsy Quality

In NASH studies, the liver biopsy is the gold standard for screening and is often the primary endpoint in monitoring disease progression. A proven process for managing complexity at every step, from biopsy processing through staining and reporting, is paramount. In this case, the critical biopsy hurdle would have to be cleared 5,000 times.

Consistent Readings

Because the histological changes are subtle, reading NASH biopsies is practically an art form, one that has been mastered by only a handful of key opinion leaders worldwide. A good relationship with these top pathologists and impeccable slide preparation facilitate the kind of consistent biopsy readings needed for a successful study.

Right Biomarker Testing

From non-invasive tests for fibrosis scoring to biochemical urine markers to liver tissue tests for inflammatory, glycemic, lipid, and genetic biomarkers, NASH trials can require a vast range of validated testing. With a global trial, provision must be made for comparability of results and easy data access by study teams.

Solutions

Quality Processes

NASH is a key indication for Cerba Research. Through experience, flexibility, and attention to detail, we were able to apply robust quality processes at every step of the complex biopsy workflow for more than 5,000 patients, screened at more than 600 sites in 31 countries.

Our teams leveraged expertise in:

- Liver biopsy performance
- Logistics around biopsy blocks and slides
- Custom staining
- Relationship with key opinion leader (KOL)
- In-house NASH testing
- Flexibility to adjust processes toward agency updates/requirements

Expert staining enables consistent results. During this study, we developed an excellent relationship with a prominent pathologist. While we have outstanding capabilities for embedding, cutting, and staining slides across the globe, in this case, they were prepared at our central lab in Belgium under a modified staining protocol specified by the KOL. With liver biopsy results as primary endpoints, this degree of cooperation paves the way for success.

Central & Specialty Lab Solutions

- Global liver biopsy, slide handling, and processing for KOL investigator
- Safety analysis, patient monitoring for response to drug and placebo
- Biomarker testing
- Project management
- Site support
- Unified global study database

In-House NASH Biomarker Testing

Because Cerba Research offers a vast portfolio of biomarkers required for NASH, our client had no difficulty obtaining what was needed. When necessary, we provide guidance for narrowing the selections. Our biomarkers are set up and validated at Cerba Research labs, with management of all variability factors. Testing may include anything from basic NASH necessities to exploratory options. Any assay we don't normally carry can be added and validated in-house. Generally, our testing covers:

- Genetic predisposition
- Inflammatory biomarkers
- Glycemic and lipid biomarkers
- Safety and serology

End-to-End Global Project Management

Lab support for NASH studies has a definite learning curve, so our experience was a key factor in successful conduct in a global trial this large. We established detailed operational workflows and internal monitoring with a focus on the primary endpoint liver biopsy.

Our worldwide affiliates' regional PMs supported local requirements and helped maintain global consistency and standardization. Cerba Research proactive site training and monitoring reinforced sites' compliance with protocol expectations, including quality slide production and correct blinding practices. Furthermore, a unified global study database enabled study teams around the globe to access all trial data via our online portal.

Close Partnerships

We believe customer-focused project management is essential to conducting a smooth trial. It took a lot of collaboration to manage every component of this project. Our SMEs and PMs communicated openly and proactively with our client throughout to optimize processes and services. The Cerba Research team can help with optimal biomarker selection given the study requirements, molecule, and budget. We can also help ensure the proposed protocol will be compliant with evolving FDA, EMA, or other regulatory body suggestions or regulations.

Additionally, we partner effectively with CROs offering NASH expertise. A joint CRO-lab offering, integrated seamlessly, can be a win-win solution and deliver great results and efficiencies for sponsors.

Minding the Budget

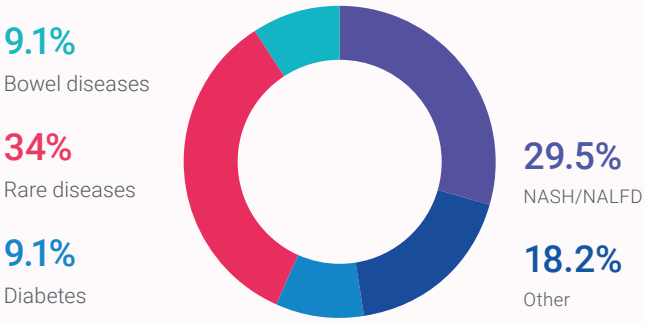
NASH studies are notorious for high screen-failure rates and ballooning costs. We monitor the budget closely throughout the trial, tracking expenditures and flagging any outliers or excesses right away to address potential overages proactively.

Results

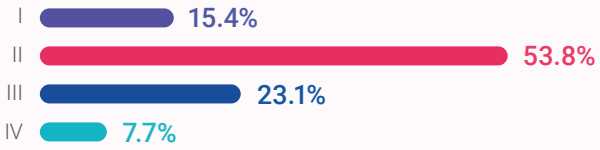
>5,000 liver biopsies processed and certified by leading KOL further innovation

Reaching a global patient base can be challenging, but Cerba means certainty. Close partnership with Cerba Research gave this midsize biotech company global access to the industry-leading laboratories, scientific experts, and skilled project management required to support this challenging NASH trial successfully.

Metabolic Areas Clinical Trials



Clinical Trial Phases Metabolic Diseases



Innovation to Anticipate the Evolving Landscape

Change is a given in clinical research, especially in indications as new as NASH. We have used learnings from this Phase III NASH trial to develop an improved suite of offerings that increase efficiency for our clients and address forthcoming regulatory updates. In particular, we were inspired by the new requirement for multiple biopsy readers and the expected progression to digitalization and evaluation by AI. Our liver biopsy services include now:

- Digitalized slides
- Integrated platforms
- Next-generation image analysis
- An app to improve processes

Other novel offerings are:

- Metabolomics, whereby a mass spec profile of serum metabolites is analyzed against a NASH/steatosis database. This method can be used to evaluate short interval responses to therapy, investigate a drug's mechanism of action, or tailor a companion diagnostic.
- Patient recruitment service — BioKortex — a patient-centric solution that uses the vast Cerba HealthCare patient database to save sponsors time and expense through customized digital tools, patient enriched data, and partnership with strong medical laboratory networks.
- Research technician training program and site performance management and a data management solution to ensure the success of your studies.

References

1. Wong RJ, Aguilar M, Cheung R, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterology. 2015;148:547-555.
2. Estes C, Razavi H, Loomba R, et al. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. Hepatology. 2018;67(1):123-133.

About Cerba Research

Cerba Research provides the highest quality specialized laboratory and diagnostic solutions while leveraging patient data and scientific insight to shape and advance clinical trials. With our global footprint and access to leading regional labs, data, patients, technology, and partnered resources, we support global biotech, pharma, and IVD organizations to improve the lives of patients around the world.

From the translation of preclinical to clinical, through commercialization, our expert scientists collaborate with you to optimize your therapeutic development and obtain critical insights earlier. We help accelerate your therapies through the development of highly specialized custom assays, deep biomarker expertise, and a passion for scientific innovation across complex therapeutic areas. Our global network of leading, specialty laboratories ensures you have access to quality data and can reach your patients. Together, we'll improve patients' lives around the globe.

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