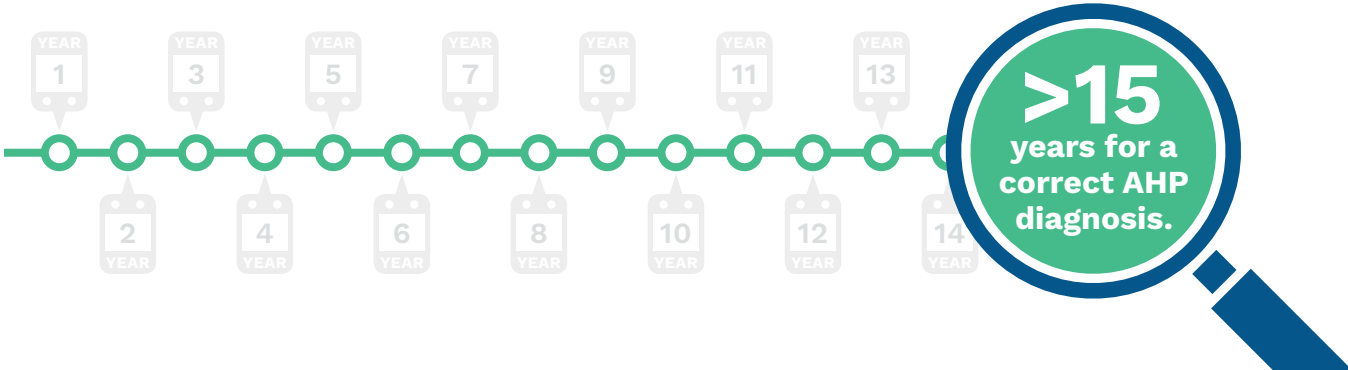
InformedDNA®
Genetics, Decoded.

Accelerating Clinical Trials for Patients with Rare Diseases

— A CASE STUDY —

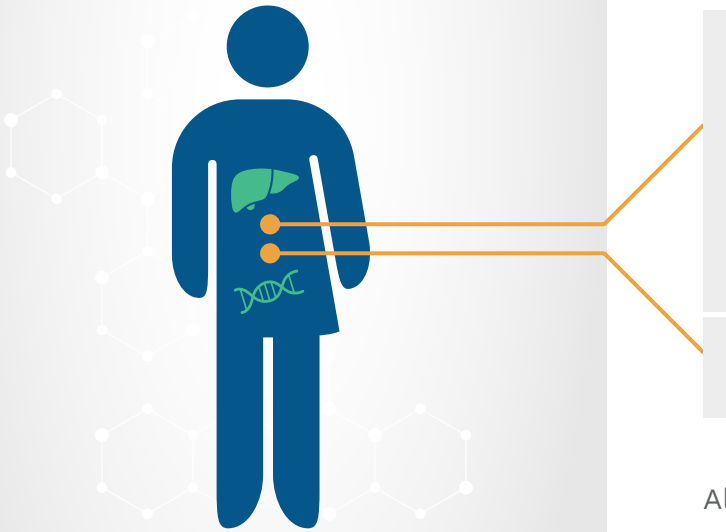
Background

Having a genetics services partner throughout the clinical trial and pre- and post-market stages of rare disease drug development is an asset to pharmaceutical companies as well as patients. As our client worked its way through the complex process of gaining FDA approval for the first-ever treatment for adults with the rare disease Acute Hepatic Porphyria (AHP), they chose to partner with InformedDNA to support their efforts. From guiding patients through a remote screening process to providing pre- and post-test genetic counseling about the disease and treatment options, we worked hand-in-hand.



Who Should Receive Genetic Testing for AHP?

The unique nature of AHP and other rare genetic testing is essential. Candidates for AHP genetic testing might have a variety of symptoms such as:



The Challenges

On average, it takes up to 15 years from symptom onset for a patient to receive a correct diagnosis of AHP[1]. Misdiagnoses include conditions such as chronic pain syndrome, fibromyalgia, and inflammatory bowel disease (IBD). This is partly due to AHP being a rare disease. The most common form of AHP has a prevalence of only five per 100,000 in the United States. Further complicating an accurate diagnosis is that porphyria is a complex disease including at least eight subtypes, each with distinct symptoms that can differ by gender and age. Additionally, due to the low penetrance of clinical manifestations for AHP, a significant proportion of individuals with the associated gene mutation are asymptomatic. This results in most patients reporting a negative family history, masking the hereditary nature of their symptoms.

- Severe, acute episodes of unexplained, recurrent, diffuse (non-localized) abdominal pain, especially if accompanied by symptoms such as:
  - Mental status changes, including confusion, anxiety, memory loss
  - Nausea, vomiting, diarrhea
  - Fatigue
  - generalized weakness
  - Seizures
- A known or suspected family history of porphyria.

All of these factors can prevent the patient from obtaining an accurate diagnosis and being offered the clinical trial opportunity or treatment they are eligible to receive. Physicians are eager to incorporate genetics into the personalized care of their patients, however many feel ill-equipped to interpret and communicate genetic test results[2]. As a result, our client faced significant challenges in identifying appropriate candidates for clinical trials and, later, approved therapy. These challenges are not unique to this client. The largest driver of clinical trial costs and delays are often due to patient recruitment issues.

1. Bonkovsky HL et al., 2014

2. Haga et al., 2019

The Solutions

A collaborative program utilizing our InformedRECRUIT™ service was developed to reduce barriers to genetic testing and counseling to help individuals make more informed decisions about their health. Genetic counseling and testing was made available at no-cost to patients in order to facilitate patient identification and reduce recruitment time and minimize delays.

1. Patient identification strategies
2. Patients referred to InformedDNA
3. Remote screening based on personal and family history
4. Subset undergo targeted genetic testing
5. High-touch test result disclosure, discussion of trial, referral to clinical trial site

Telemedicine services delivery

Working with our team of genetics experts, our client was able to implement criteria for no-cost genetic counseling and meet the needs of patients who do — and do not — test positive for AHP. This created a funnel so that only the most appropriate patients were referred for evaluation at a clinical research center. Porphyria is a diagnosis that some patients reach by self-diagnosis. However, porphyria symptoms overlap with other diagnoses and receiving a negative genetic test result can be particularly difficult for patients who believed they had finally found the answer to their symptoms and a potential therapy. The availability of genetic counseling removes the burden from the patient's healthcare provider to explain the negative test result and screens out these patients early in the process.

Our client was able to screen a much larger population of patients in ways that engage the patient community more quickly, in part due to our telemedicine model. The program resulted in confidence in their diagnosis and care options as well as time savings for patients, and both time and cost savings for our client.

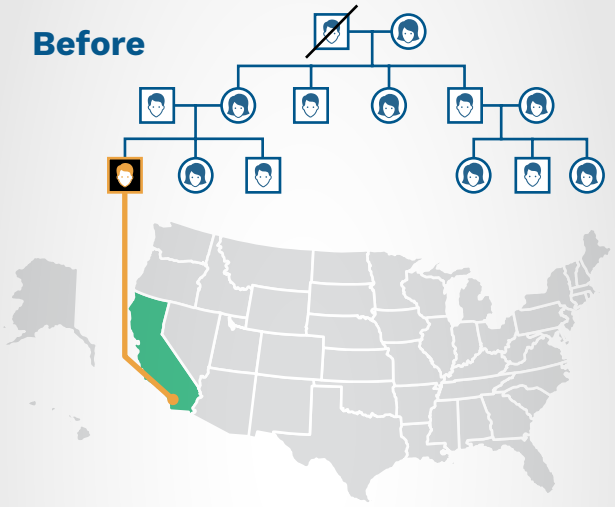
InformedRECRUIT™
Screening Process

- ✓ Significant cost savings for the sponsor.
- ✓ Greater engagement in the patient community.

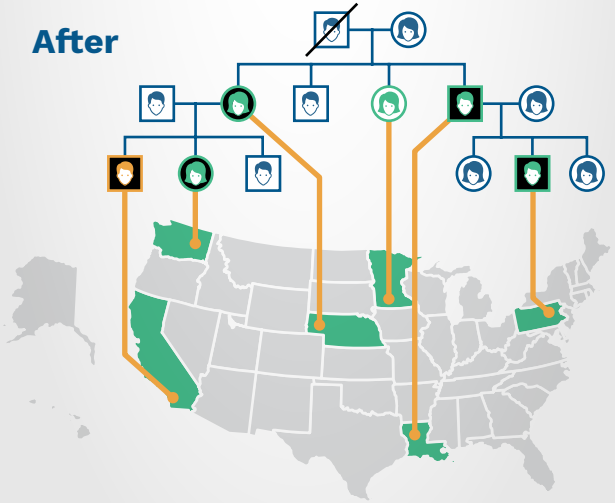
Family Member Outreach

- Patient
- Symptomatic or At Risk
- Unaffected
- Genetic Test Positive

Before



After



Genetics specialists with rare disease expertise

With access to board-certified genetic counselors who have deep clinical expertise, patients may be more comfortable participating in a pharma-sponsored program because they know they are receiving a high level of impartial and personalized information. The genetic counselor is also a resource for the patient's physician to provide genetics-related education and support through the testing process.

Patient identification

Through pre-test counseling, InformedDNA is able to identify patients who are good candidates for genetic testing. Genetic counselors obtain a detailed medical and family history to assess whether a patient meets clinical criteria for further testing. (InformedDNA offers test ordering capabilities, a planned future element for this client's program.) If they do, counselors help patients understand next steps and what to expect. If they don't, counselors help patients understand why and can suggest other avenues to pursue for further diagnostic help.

Genetic test result interpretation and disclosure

Post-test genetic counseling involves explaining test results and what they mean for the patient and their family. How is the disease inherited? Who's at risk? Which family members should be tested? Who might qualify for therapy or a clinical trial? What are the next steps if testing was negative? When appropriate, patients are referred back to their physicians for decision-making about treatments.

At-risk family member engagement and identification

After our client gained FDA approval, they leveraged our InformedACCESS™ service to expand patient identification to at-risk family members. Cascade testing in an autosomal dominant condition is a highly efficient method of identifying additional patients because siblings, parents and children of the proband have a 50% chance of sharing the genetic mutation.

The Results

Previously, treatment options for patients with AHP included only partial relief from the intense and unremitting pain of porphyria attacks. While there was still high value in getting to a diagnosis, there weren't good treatment options. With the exciting development of an approved therapy, interest from patients and their families will likely grow, leading to earlier diagnosis and treatment.

This collaborative genetic counseling and testing program supports the patients, the providers and our client in the journey from clinical trial to pre- and post-market stages of drug development. The program has:

- Shortened the time to diagnosis and prevented misdiagnoses
- Identified patients who are eligible to participate in clinical trials and now approved therapy
- Helped patients to get screened remotely, avoiding an unnecessary trip to a research center should they not be eligible for the clinical trial
- Educated at-risk family members on their testing and care options
- Connected patients and their healthcare providers to support resources and patient advocacy organizations

Patients participating in the genetic counseling program report a very high appreciation for the appointments, the information provided, and the support received.

The InformedDNA Advantage

Nation's largest staff of board-certified genetics specialists, covering all genetics specialties, enables rapid deployment of resources to accelerate patient recruitment

Support for sponsors at every stage of the drug development pipeline:

- ✔ **For preclinical development programs:** InformedRESEARCH™ enables sponsors to engage patients through trusted IRB-approved screening programs prior to active clinical trial enrollment
- ✔ **For actively enrolling clinical trials:** InformedRECRUIT™ optimizes patient identification by uncovering and screening targeted populations at the community level
- ✔ **For post-market programs:** InformedACCESS™ leverages our extensive payor network to ensure successful coverage policies while identifying rare disease therapy candidates

InformedDNA®

Genetics, Decoded.

Founded in 2007, InformedDNA is the authority on the appropriate use of genetic testing. With the largest, lab-independent, full-time staff of board-certified genetics specialists in the U.S., InformedDNA helps to ensure that pharmaceutical and biotech companies, health plans, hospitals, employers, clinicians and patients all have access to the highest quality genetic services. Key offerings for pharmaceutical and biotech companies include support for clinical trial design, patient identification, recruitment and support; clinical genetic counseling; and, test ordering and interpretation services.

For more information, contact us:

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