

Arctic Therapeutics research suggests preventative strategy against HCCAA

- N-acetylcysteine (NAC) shows promise to treat hereditary cystatin C amyloid angiopathy (HCCAA)
- HCCAA – a subtype of cerebral amyloid angiopathy (CAA) – is an ultra-rare Icelandic amyloid disease due to a mutation in the *CST3* gene encoding for the protease inhibitor, cystatin C.
- HCCAA causes cerebral hemorrhages in asymptomatic carriers of the L68Q variant due to amyloid aggregation with precipitation in brain vessels and tissue.
- Findings could guide the development of preventative therapies for related CAAs.

Reykjavik, Iceland– April 2, 2025 – Icelandic drug discovery and development company Arctic Therapeutics (ATx) today announced the publication of research in *JAMA Neurology*, which informs a possible therapeutic strategy to treat a rare form of familial dementia.

The publication, titled *N-Acetylcysteine for hereditary cystatin C amyloid angiopathy (HCCAA), a nonrandomised clinical trial*, details a new treatment approach for HCCAA, a rare and fatal genetic brain disorder that primarily affects young Icelandic adults, with the disease process beginning in childhood.

The research provides insights into the potential of N-acetylcysteine (NAC) as a treatment for HCCAA, a disease with no currently approved therapeutic options. The study highlights how NAC may reduce disease-associated biomarkers and slow disease progression.

The study is the first phase 2a clinical trial to assess the safety and therapeutic potential of high-dose NAC in patients carrying the L68Q-CST3 sequence variation of HCCAA. Results indicate that NAC is well tolerated, reduces disease specific biomarkers and stabilises disease progression, suggesting NAC may offer a preventative strategy against HCCAA.

These findings could accelerate the development of preventative therapies for individuals at risk of HCCAA and other forms of CAAs.

“These promising results provide hope to HCCAA patients and their families,” Dr Ásbjörg Ósk Snorradóttir, lead author of the study explained.

Senior author, Dr. Hákon Hákonarson, director of the Center for Applied Genomics at the Children's Hospital of Philadelphia and founder of Arctic Therapeutics added: “This study provides the first clinical evidence that NAC, by breaking disulfide bonds and other aberrant molecular interactions, can disrupt cystatin C oligomers and prevent amyloid aggregation that ultimately accumulates in brain vessels. By targeting the root biochemical process behind HCCAA pathology, NAC may ultimately offer a novel disease-modifying approach, not only for this devastating condition, but potentially for other forms of CAAs and protein aggregation disorders where toxic oligomers are central to disease progression”.

The open-label phase 2a clinical trial was conducted at Iceland’s Landspítali University Hospital from March 2019 to December 2021. A total of 17 participants were enrolled, all confirmed carriers of the L68Q-CST3 mutation. The study assessed:

- **Safety & tolerability:** NAC was well tolerated, with no drug-related severe adverse events. Five participants experienced cerebral hemorrhages, but none resulted in permanent neurological damage.

- **Biomarker reduction:** Significant reductions were observed in collagen IV, fibronectin, vimentin, and SMAD levels—key indicators of disease progression.
- **Plasma & skin biomarker changes:** NAC was shown to increase reduced glutathione levels, a protective antioxidant, and reduce high-molecular-weight cystatin C aggregates, which are linked to amyloid buildup in the brain.
- **Cognitive stability:** No measurable decline in cognitive function was observed during the study period.

Building on these findings, as well as internal in-vitro data that demonstrates that NAC-amide (NACA) has more than 10-fold higher potency in preventing or dispersing amyloid complex aggregates than NAC and increased ability to penetrate the blood brain barrier and get into cells involved in the disease pathogenesis, ATx has launched a European Medicines Agency-approved registration study to monitor safety, tolerability, and efficacy using NACA in patients with HCCAA.

For more details, read the full study in *JAMA Neurology*: [Original Investigation](#).

About Arctic Therapeutics

Arctic Therapeutics is an Icelandic drug discovery and development company established in 2015, which has licensed intellectual property from Children's Hospital of Philadelphia. ATx leverages the transformative power of applied genomics, steering the course of drug development towards safer, more effective treatments for some of the world's most challenging diseases. The company has operations in Iceland, the US and multiple collaborations across Europe. For more information, please visit: www.arctictherapeutics.com and follow us on [LinkedIn](#)

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