Summary of the International CAA Conference Munich 2024

Every two years, researchers from around the world gather at the international CAA (Cerebral Amyloid Angiopathy) conference. The Dutch DCAA patient association usually sends two representatives to learn about the latest research, network with researchers and physicians, and voice the perspectives of families affected by Dutch-type CAA. This October, we met in Munich. Since the conference was "close to home," as the patient association, we had extra room in our budget (aka our government subsidy), allowing a larger part of our board to attend. This year, Maike, Koos, Janny, Martina, Nicole, and Sanne were all present.

Sporadic CAA and Dutch-type CAA

As you may know, sporadic CAA is the non-hereditary form of Dutch-type CAA, also called sCAA. Since sCAA remains difficult to diagnose with certainty and cannot be predicted, Dutch-type CAA research is valuable for understanding sporadic CAA as well. There is no association for people with sCAA, so our association, representing families with hereditary CAA, are the only patient advocates at the conference.

sCAA is still far less known than diseases like Alzheimer's, though brain studies show about one in four people over 65 has sCAA, with higher risk over age 80. Awareness and research are growing quickly, and this 9th edition of the conference saw record attendance, with almost 200 participants. While still small compared to Alzheimer's conferencees, with thousands of researchers, the intimacy has an advantage: researchers are more collaborative.

Many of these researchers work at LUMC in Leiden, recognized as a center of expertise for both hereditary and non-hereditary CAA, conducting extensive research. Our consortium was well represented, including the Dutch CAA Foundation board (which funds and helps organize these conferences), a research team from Perth, Australia, part of the Alnylam team, and of course, Steven Greenberg, a pioneer in sCAA research. Many members of his Boston team were also present.

What Does a Three-Day CAA Conference Look Like?

The conference spanned three days of presentations, including "poster presentations" during breaks. These are posters with summaries of specific research and findings. The long breaks facilitated valuable networking. On the first evening, there was a networking dinner, fostering knowledge exchange, inspiring new ideas, learning from each other, and preventing redundant research efforts worldwide.

Topics covered at the conference included:

- Factors influencing sporadic CAA development (since it's not caused by a DNA mutation, like Dutch-type CAA, making it harder to predict).
- Knowledge on brain inflammation in CAA (ARIA and CAA-ri).
- The brain's clearing system (glymphatic system).
- Current treatments (e.g., blood pressure control and lifestyle adjustments).
- Methods for visualizing CAA in the brain (e.g., MRI and cerebrospinal fluid protein analysis).
- What occurs in the brain during CAA.
- Guidelines for diagnosing sporadic CAA.
- Potential future treatments (e.g., Alnylam's RNA therapy).
- Considerations on researching immunotherapies for CAA, as being studied in Alzheimer's.

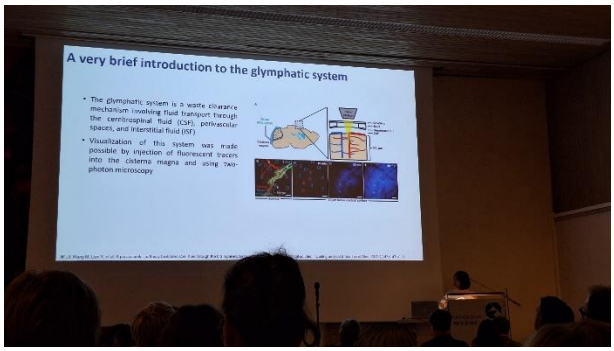
While we couldn't always understand every detail, we attended nearly every presentation. This helps us inform you better about the disease and research progress and clarify to researchers what matters to patients based on stories from those dealing with the disease daily.

Researchers' curiosity often leads to more research, yielding important findings but not always aligning with the daily priorities of people living with the disease. Thus, we're focusing on studies most relevant to you.

Research Relevant to Dutch-type CAA Families

Brain Clearance (Glymphatic System)

Much research on the brain's "clearing system" is conducted in mice, as some methods are currently unsafe for humans. Presently, researchers are studying the glymphatic system and its interaction with brain blood vessels, crucial in removing toxic proteins that accumulate in blood vessel walls in both Dutch-type and sporadic CAA.



Additionally, researchers are exploring imaging methods for observing this clearance in humans, using contrast agents administered via infusion or lumbar puncture, along with MRI scans. Leon Munting from the LUMC, presented his ongoing research on enhancing glymphatic clearance in mice.

Furthermore, lessons learned are being applied in the new Clear-Brain study. This LUMC study aims to improve sleep, the optimal time for glymphatic activity, in people DCAA. The LUMC team has developed an MRI-based method for visualizing the glymphatic system, investigating whether improving sleep improves clearing toxic proteins from the brain.

Blood Pressure, Blood Thinners, and Lifestyle

It's well known that reducing blood pressure during a brain hemorrhage is crucial. Researchers are also investigating whether blood pressure medications can prevent brain damage. Studies are examining blood thinners, usually discouraged due to hemorrhage risk, but they may offer benefits in early disease stages. Additionally, lifestyle factors like BMI, smoking, and alcohol use are under scrutiny for their potential impact on CAA risk and symptom progression.

Immunotherapies

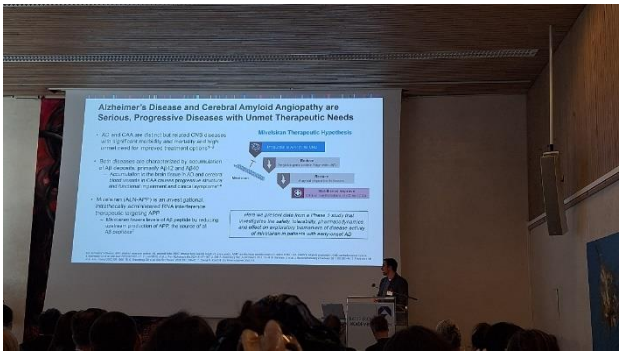
Alzheimer's research has long explored ways to clear toxic proteins from the brain, including immunotherapy. These therapies use a vaccine-like substance that binds to the toxic protein, enabling its removal from the brain. Despite extensive research, no therapy has shown clear benefits in Alzheimer's, partly due to complications like brain inflammation or CAA. At the conference, Alzheimer's studies raised questions on whether these therapies should be trialed in CAA patients. Opinions were mixed, as the risks must be carefully weighed.

Genes and CAA

Since sporadic CAA is not genetically driven, like Dutch-type CAA, understanding its origins and associated "risk factors" is crucial. Researchers are examining whether certain genes may increase CAA risk, possibly influencing how the disease progresses in Katwijk families.

Mivelsiran

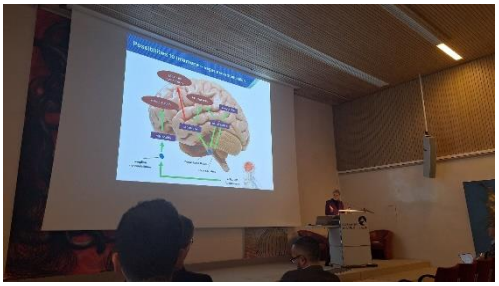
Alnylam's team, including our collaborator Robert Deering, presented their RNA therapy, Mivelsiran (formerly ALN-APP), sharing early results with 34 early-stage Alzheimer's patients who received different doses. Promising effects were observed, particularly with the 75 mg dose, which reduced toxic proteins in cerebrospinal fluid (measured via lumbar puncture) with no adverse events reported.



Neal Parikh, a neurologist from Alnylam, further explained Mivelsiran's mechanism in potentially reducing toxic amyloid beta proteins. The phase 2 trial, involving CAA patients, is underway globally as "cAPPricorn-1." In time, DCAA family members may also participate. You can request links to previous presentations by Alnylam to DCAA family members through Maike Hoek via mhoek@hchwa-d.nl.

Minocycline

Professor Marieke Wermer concluded the conference with an update on her BATMAN study on minocycline, an antibiotic potentially useful in addressing brain inflammation. She urged researchers to continue exploring treatment options, given the pressing needs of hereditary CAA patients, listing several promising medications.



Our Role at the Conference

Patient Perspective

During conferences, our representative Sanne always raises awareness for the “patient perspective”. This time, during the “networking event”, she was given the time to address the attendees. She used the “compendium”, a document that was compiled in the 1990s by professor Luyendijk and doctor Timmers, who, together with others, pioneered DCAA research.

Sanne emphasized the contributions that people from families with DCAA have been making for decades to what we know about (D)CAA. Like her grandfather, who was one of the first to participate, and helped to track DCAA in families in Katwijk and Scheveningen. But certainly also her mother, Janny, who founded the Association in 2007, which gave research a real boost. Janny received a long lasting applause from the audience.

Sanne then put the entire board in the spotlight and told each of them how important their (voluntary) contribution is for the families with DCAA, and how important it is to commit ourselves, also within research, because research can only improve from that.

Sanne also emphasized how important it is to listen to Nicole's podcast “Zieke Erfenis” and experience her lived experience. Finally, Sanne emphasized that she thinks it is important that more is known about CAA, but that people with Dutchtype CAA should not be forgotten. Steven Greenberg emphasized after the talk that she did not have to worry about thatSome researchers indicated that this story was the most important of the conference for them, because it reminded them why and for whom they do it. It brings the human aspect closer to their work. Watch Sanne’s speech here: https://youtu.be/Otu49qkAqc4?si=U8K9UTLRg58xfn__

Network

We also networked. A lot. It is always good to have all Leiden researchers in one place and to be able to talk to everyone informally. This often leads to new ideas. It was also good to see the Australian team and to talk to them about how the research in Perth is going and what we as an Association can do for it.

Maike and Sanne also had lunch with the Alnylam team and Thijs, Ellis and Ellen from the LUMC to talk about the status of the Mivelsiran trial in Leiden. More information about that will follow later.

Furthermore, we spoke with the organization about how the patient perspective can become a permanent part of each biennial conference, for example in the form of a workshop, how the international CAA association (the association of international CAA researchers) can focus more on patient participation (in addition to the collaboration with us) and how we can connect representatives from different parts of the world.

Conclusion

It was another intensive, educational and important meeting. We see that the knowledge about what happens in the brain, and how we can visualize and hopefully influence that, is still growing. A lot of attention is paid to sporadic CAA worldwide, but for the Leiden and Australian research groups, DCAA is still very much in the spotlight.

The development of Mivelsiran and thus a possible treatment for (hereditary) CAA is very important, because it is the first treatment that has a direct effect on the toxic protein. Everyone is eagerly awaiting the phase II study to get momentum and for the results.

In addition, it is important to keep in mind that (hereditary) CAA is a complicated disease that may need to be treated with multiple treatments at the same time. That is why a lot of research is still being done into other processes in the brain, such as inflammation and the glymphatic system, in order to hopefully be able to treat symptoms better.

A conference always fries our brains a bit, because of all the impressions and information. What we mainly take away is that there are hopeful developments and that at the same time, from our perspective, it really always takes too much time.