

Digital Consultation: “Meet the expert” about personalized gene therapy

Q&A

Disclaimer

The PCH2 treatment options listed here are based on data from the 2023 Natural History Study on PCH2 and personal experience from parents. The answers make no claim to be exhaustive and represent neither a specific recommendation nor an endorsement of the drugs or PCH2 treatment options mentioned. It is a compilation of measures that have been tried in the past and is intended for informative purposes only. PCH2cure assumes no liability in this respect.

Q&A session

My 5-month-old child has been diagnosed with PCH, is there any possibility of using gene therapy on him?

- Unfortunately **not yet**, for details please watch the video of the presentation on the topic.
- More steps are needed to develop a gene therapy for PCH → We are working hard to achieve this goal as soon as possible.

Q&A session

What prerequisites would a child need to be eligible for gene therapy?

- Viral vectors, such as AAV9, cause various **side effects**.
- One problem is that viral vectors often cause **liver inflammation** (hepatitis) → Screening of liver enzyme values will be necessary and elevated liver values could be a contraindication for therapy (liver problems are rare in PCH).
- As viral vectors often trigger **immune reactions**, patients should be tested in advance for the presence of antibodies.
- The exact requirements that a child must fulfill to receive gene therapy cannot be determined at this time.

Q&A session

Does age play a role in the use of gene therapy?

- In general, **the earlier** gene therapy is used, **the better!** → However, there is currently **no fixed age limit**.
- Although gene therapy can stop ongoing pathological processes, it cannot reverse existing damage.
- The earlier gene therapy can be administered, the more likely it is that certain damage in neurodegenerative diseases can still be prevented due to **brain plasticity**.
- The use of viral vectors, such as AAV9, is easier in infants <1 year of age, as the blood-brain barrier is not yet fully developed at this age.

Q&A session

The paper on gene therapy for baby “KJ” was published quickly. To what extent can statements already be made about the effect of the therapy?

- According to the publication, the success was monitored up to 7 weeks after the first therapy by measuring the **ammonia levels in the blood** and by means of the **clinical course**.
- Further examinations, such as a liver biopsy, were not carried out at this time. This would show the proportion of liver cells reached by the therapy.
- At the time of publication, it was still necessary to intercept the ammonia produced, so the therapy significantly improved KJ's situation, but it is not possible to speak of a complete cure after the described doses of the therapy.

Q&A session

Are there already gene therapies for neurodegenerative diseases?

- No.
- However, there are already approved gene therapies for some other pediatric diseases:
 - **Neuromuscular diseases:** Spinal muscular atrophy and Duchenne muscular atrophy
 - **Metabolic diseases:** Leukodystrophy
 - **Haemato- and oncologic diseases:** Sickle cell anemia or leukemia
- There are also research approaches for gene therapies for Parkinson's and Alzheimer's disease
- Overview of the approved gene therapies in the EU (links to a german website):
<https://www.vfa.de/de/forschung-entwicklung/datenbanken/datenbanken-zu-arzneimitteln/atmp?sort=MedikamentIndikation#listmedikamenteatmp-118727>

Q&A session

Would gene therapy also have an impact on movement disorders in children with PCH2?

- Yes, gene therapy would have an impact on all symptoms of PCH.
- Currently there is already some **evidence on movement disorders in children with PCH2**, see for example the following resources:
 - <https://www.pch2cure.org/en/event/online-consultation-meet-the-expert-on-the-topic-of-restlessness-in-pch2/>
 - <https://www.pch2cure.org/en/healthcare-professionals/treatment-options/>
 - <https://www.pch2cure.org/wp-content/uploads/2025/02/2025-01-30-pch-broschure-englisch-mit-titel.pdf>