CONCERT study 2.0 information folder
Participation in treatment research

You received a letter along with this folder. The letter contains general information about the study. This folder contains more information about cytomegalovirus (CMV) and the study.

CMV as the cause of hearing loss

There are several causes of hearing loss in children, one of which is a congenital virus infection (infection occurred in the womb) with cytomegalovirus (CMV) . CMV is a commonly occurring virus that generally does not produce any symptoms in adults. However, if a pregnant woman becomes infected, the fetus can also become infected by transmission through the placenta. In the Netherlands about 5 in every 1000 newborn infants are infected with CMV in the womb. The most common sequela is hearing loss. In about half of children with hearing loss due to CMV, the hearing loss worsens in the first few years of life. If a child becomes infected with CMV in the womb, the risk of hearing loss developing by the age of 7 years is about 1 in 10. Children with hearing loss and congenital CMV infection are currently supervised in an Audiology Centre, but no standard medical treatment is given.

Why is research being done into congenital CMV infection?

Small studies have shown that medical treatment of children with a congenital CMV infection can prevent worsening of their hearing. To obtain more information about the effect of treating children with congenital CMV infection and hearing loss, it is necessary to conduct a large and soundly based study. For the CONCERT study 2.0, all parents of newborn children with suspected hearing loss in the Netherlands are being approached.
The aim of the study is to investigate whether worsening of the hearing loss can be limited to improve the chance of good speech and language development.

Why are we asking you to participate?

Your child has been diagnosed with congenital CMV infection. In addition, hearing loss has been measured at an Audiology Centre. If your child is younger than 13 weeks old (after birth), your child can be considered for inclusion in the second part of the CONCERT study 2.0 .

What does the trial involve?

If you grant written permission for your child to participate in the study, your child will be given antiviral medication (valganciclovir) for 6 weeks.. It is also possible for your child to participate in the study even if you don’t want your child to be treated. You will sign a different informed consent form. At 1.5-2 years of age, all children will undergo a development test at home conducted by the investigator. In addition, all children will have their hearing tested at home.

Which tests are we going to conduct on your child?

A summary of the study is given as a timeline on the last page.

House visit

First of all, the entire study will be discussed with you and any questions you might have answered. Next, the medical history will be discussed, especially concerning the pregnancy. A questionnaire will be administered. Your child will undergo a physical examination by the investigator. Blood will be sampled from the mother and child. Several determinations will be done on your child's blood sample to confirm that your child may be treated. The results will be available later the same day or the next day, and you will be informed of them by telephone.

The 6 weeks of treatment

You will be given the medicinal product by the investigator during the house visit. The treatment must be started before the age of 13 weeks. You will be instructed in how to adminster the medicinal product (with a syringe in the mouth before breastfeeding or bottle feeding in the morning and evening). The treatment will take 6 weeks.
You will be given a diary to note down anything unusual briefly every day. You will also receive a special 'filter paper' that you place in your child's diaper once a week to obtain a urine sample. Your child will not notice this. The envelope marked 'Diaper paper' contains these papers together with a brief explanation.
Even if you do not want your child to be treated, you still receive a diary and the 'filter paper'.

Follow-up study at 1.5-2 years of age

House visit for development test:

During a house visit the investigator will discuss with you how things are going with your child. The investigator will conduct an extensive development test with your child. You will be given a questionnaire. This questionnaire concerns your child's general development, with specific questions about language and speech development. You can complete the questionnaire at any convenient time.

The hearing test:

Your child's hearing will be tested in both ears with audiological equipment. This hearing test will be done at home. For this hearing test, which involves sticking leads to your child's head, your child does not have to be asleep. The development and hearing tests will probably be scheduled for two separate house visits.

The treatment: valganciclovir

The medicine vlaganciclovir is adminstered to your child twice daily before breastfeeding or bottle feeding with a syringe in the mouth. The fluid has an orange flavour. There is already extensive experiencewith valganciclovir in other patients. Adverse effects found in animals include: reduced fertility, cancer and birth defects. These adverse effects have not been noted in people.
The most common adverse effect is a lowering of the white blood cell count. Lowering of the white blood cell count is a reversible effect of valganciclovir, which means it recovers after the treatment is stopped.

If your child is treated, blood will be sampled weekly to check this. If the number of white blood cells falls too low, the quantity of medicine administered to your child will be halved. If necessary, the treatment will be stopped.

What happens if you prefer your child not to be treated?

Participation in the treatment is voluntary. You can decide not to let your child be treated. In that case, you can still choose to participate in the untreated “refusal” group. Your child will not be treated, but will receive additional attention as deescribed above under “House visit” and “Follow-up study at 1.5-2 years of age”. We would like to draw blood twice from your child and once from the mother. This can be done at home by an experienced doctor or nurse. We also ask you to collect a bit of urine even week (total of 7 times) on a filter paper in the diaper. For participation in the “refusal” group, we ask you to complete an informed consent form.

What are the possible advantages of participation in this study?

The advantages for all children participating in this study is the supervision and additional care, development test and hearing test. The children who are treated may also benefit from the treatment if it is shown after conclusion of the study that this treatment prevented worsening of the hearing.

What are the possible disadvantages of participation in this study?

The disadvantages are that blood will be sampled from the treated children 8 times , specifically to examine any possible lowering of the white blood cell count. This will be done at your home by experienced medical staff, twice from a bloodvessel on the hand and 6 times with a heel prick. The untreated children will also have blood sampled twice at home (from a blood vessel on the hand) to determine virus activity. In both groups, urine will be sampled 7 times with a paper in the diaper.
The follow-up study at 1.5-2 years of age takes a lot of time (about 3 hours in total).

What happens to your child’s standard care?

The monitoring of you and your child at the Audiology Centre continues as usual during the study. It is possible that your child will be given a hearing aid. We recommend that you visit a paediatrician for standard care. We can establish this contact for you. This care is separate from the study and will continue on indefinitely.

What happens if you do not wish to take part in this study or want to stop?

You decide yourself whether you wanttoparticipatein the study or not. Participation is voluntary. If you decide not to take part, you do not need to do anything further. You do not need to sign anything. You do not have to say why you do not want to take part.
You can always withdraw your participation in this study without having to give a reason for doing so.

Can the treatment be stopped?

There are several reasons to stop the treatment. If you wish, you can stop the treatment without giving any reason for doing so. If there aretoo many adverse effects, the investigatorcan stop the treatment.

Will my GP/paediatrician/ENT spcialist/youth health care physician be informed about my participation?

Your GP will be informed that your child is participating in this studyand whether your child is being treated. If your child is registered with a paediatrician and/or ENT-specialist, they will alsobe informed that your child is participating in this study. You will be given an envelope containing a letter for the youth health care physician at the well-baby clinic. You can deliver it to the well-baby clinic yourself. The Audiology Centre will also be informed about your participation in this study.

Is your child insured if he/she participates in the study?

An insurance has been arrangedby the LUMC to cover any possible harm that your child might suffer as a consequence of participating in this study.

What costs are involved?

Participation in this study does not involve any costs for you. All costs involved in participation (blood tests, house visits by the investigator, development test and hearingtest) will be paid by the study.

What will happen to your data and your child's data?

The data will be handled with full medical confidentiality and coded before analysis. Your child's data will not be provided to third parties. The results of the study will be published as group results.

Which medical ethics review committee approved this study?

The Mediical Ethics Committee of the Leiden University Medical Center evaluated and approved this study. You can find more information about the approval in the general brochure "Medical-scientific research with human subjects".

Questions

If you have any questions or would like more information, please contact:
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Would you like any independent advice about participating in this study? You can contact an independent paediatrician:
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For more information or answers to frequently asked questions, please look at the study website, *www.lumc.nl/concert*.

Timeline

This timeline shows you the process of what will be done in the study from the moment that your child participates up to the age of 18-22 months. Age is given in the boxes at the top. This is an example, so the age of your child may differ from what is given here. Underneath the timeline is a description of what is done for the study at each age of your child.