**Patient information leaflet on the "TRAPISTtrial": A study comparing early versus late intervention for twin reversed arterial perfusion sequence**

Dear parent(s),

Following the conversation that you had with one of the investigators, please find here the written information about the research study for which we have requested your participation.

**Introduction**

Your twins have been diagnosed with twin reversed atrial perfusion (TRAP) sequence and you have been offered treatment for this condition. As you heard from your doctor, TRAP may have serious consequences for your pregnancy. TRAP is a very rare condition occurring in 1 in a 100 monochorionic twin pregnancies or 1 in 35 000 pregnancies. Monochorionic twins are identical and share a single placenta with vascular anastomoses that connect the two fetal circulations. TRAP is a complication of this shared circulation and occurs if one of the twins dies in early pregnancy.

In TRAP, blood flows from the healthy twin in a reverse direction towards its demised co-twin. The demised twin has no longer any heart activity from its own and that is why it is also called the acardiac twin. The healthy twin pumps blood towards the acardiac twin, hence the name pump twin. Thanks to the reverse blood flow, the acardiac twin continues to grow. However, the reverse flow strains the heart of the pump twin, which may lead to heart failure and increased urine output. Subsequently, heart failure may cause the demise of the pump twin and the increased urine production may lead to too much fluid and trigger preterm birth.

Without treatment, about 80% of pump twins will die either because of heart failure or very preterm birth. As such, untreated TRAP twins are born on average at 30 weeks (2.5 months too early). The consequences of TRAP for the long-term development of the children are unknown. An intrauterine intervention to arrest the reverse flow improves the prognosis for the pump twin. Although TRAP sequence is nowadays diagnosed at the time of the first trimester scan, as it was in your situation, such interventions are performed only after 16 weeks because the membranes surrounding the twins are not fused yet prior to 16 weeks.

There are 2 types of interventions. Your physician may choose to use a fine needle that produces heat to arrest the reverse follow. The needle is positioned near to the acardiac's blood vessels using ultrasound guidance (see Figure). Alternatively, your physician may opt to burn the cord or communicating vessels of the acardiac twin using a miniature 1 mm endoscope. After such intervention, the chances of survival for the pump twin are 80% and the pregnancy can be prolonged on average to 36 weeks. The survival rate is not a 100% because the pump twin may die or the intervention may cause rupture of the membranes and thereby lead to miscarriage or very preterm birth. There is limited information on the long-term development of these children, but the outcome seems very good if the child is not born too early.

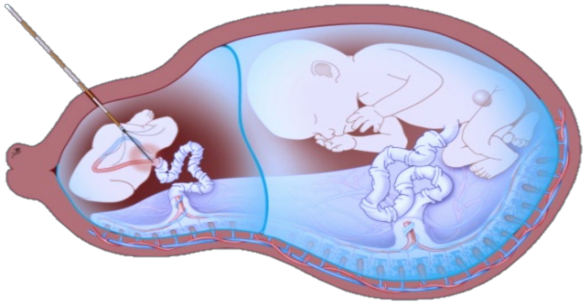

Figure illustrating the needle intervention to arrest the reverse flow

Since TRAP is now diagnosed in the first trimester, it appears that about 1 in 3 to 1 in 4 pump twins dies between the diagnosis in the first trimester and the planned intervention after 16 weeks. On the other hand, in another 1 in 4 cases, the flow towards the acardiac stops spontaneously, such that the planned intervention is no longer necessary at 16 weeks. At the time of the first trimester ultrasound scan; it is not possible to identify those pregnancies that will result in subsequent demise of the pump twin, spontaneous resolution or persistent flow. An intervention in the first trimester may prevent these early demises, but it may also increase the risk of miscarriage due to rupture of the membranes because these are not fused yet at the time of diagnosis. Also, for the 1 in 4 pregnancies in which the flow will have stopped spontaneously by 16 weeks, an intervention in the first trimester is unnecessary. Small reports have shown that interventions can be done safely in the first trimester, but a large study is necessary to demonstrate that an intervention in the first trimester results in better outcomes than waiting until after 16 weeks. We therefore request your participation in an international research project that is coordinated by the University Hospitals Leuven in Belgium (the sponsor) and that involves several other fetal medicine centers around the world in order to include 126 patients.

**Aim of the study**

The purpose of the study, for which your participation is requested, is to examine the outcome of the pump twin comparing an intervention prior to 14 weeks (early intervention) to the standard intervention after 16 weeks (late intervention). We will compare the survival rate, the risk of an early birth, the problems after birth and the development of the child when he/she is 2 years old.

**Study design**

If you agree to participate in this study, then fate will determine if you receive either an early or rather a late intervention. Therefore, there will be 1 chance out of 2 you either receive the early or the late intervention.

**Course of the study**

The treatment before and after the surgery will be the same in both groups. Also, there is no difference in the duration of hospitalization or in the frequency of follow-up visits. When your child reaches the age of 2 years, you will be asked to fill out a questionnaire about the development of your child.

**Extra burden for the participants**

There are no additional costs related to participation in this study (no extra blood samples or hospital visits). As mentioned above, we will ask you to fill out a questionnaire when your child is 2 years old to examine his/her development.

**Possible risks of participating in this study**

Recent small studies have shown that an intervention can be done safely in the first trimester. However, an early intervention may increase the risk of miscarriage due to early membrane rupture or may involve other risks, which are currently unforeseeable. Whether these risks outweigh a possible better outcome is unknown.

**Voluntary participation**

Your collaboration to this study is voluntary. In case you decide to participate in the study, you have the right to withdraw your permission at any time. There is no need to give any reason for this. Whether you participate or not will not have any consequences for the relationship with your physician. If you decide not to participate or if you withdraw your participation, you will be treated with the standard intervention after 16 weeks.

**Confidentiality of the data**

Your participation in the study means that you agree to the investigator collecting data about you and to these data being used for research purposes and in connection with scientific and medical publications. You are entitled to ask the investigator what data are being collected about you and what is their use is in connection with the study. You have the right to inspect these data and correct them if they are incorrect.

The investigator has a duty of confidentiality vis-à-vis the data collected, and you are assured that all data will be handled confidentially and that unauthorized persons will have no insight in your data. The investigator will never to reveal your name in the context of a publication or conference but also he/she will encode (your identity will be replaced by an ID code in the study) your data before sending them to the manager of the database of collected data (UZ Leuven). The investigator and his/her team will therefore be the only ones to be able to establish a link between the data transmitted throughout the study and your medical records. The personal data transmitted will not contain any combination of elements that might allow you to be identified. The results of this study may be used in a scientific publication, but the data cannot be related to you personally. If you want, we can communicate the results of this study to you. We will inform your referring obstetrician and general practitioner of your participation in the study and if your child is transferred to another unit, we will inform the pediatrician.

If you withdraw your consent to take part in the study, to guarantee the validity of the research, the data encoded up to the point of your withdrawal, will be retained. To verify the quality of the study, it is possible that your medical records will be examined by persons subject to professional secrecy and designated by the ethics committee, the coordinating center of the University Hospital Leuven or by an independent audit body. In any event, this examination of your medical records may only take place under the responsibility of the investigator and under the supervision of one of the collaborators designated by him/her.

Your consent to take part in this study therefore also implies your consent to the use of your encoded medical data for the purposes described in this information form and to their transmission to the aforementioned people and authorities.

**Insurance**

To be filled out according to local legislation

**Responsible researchers at the principle investigator's site**

The Ethical Committee of the PI site has approved this study. If you still have questions concerning this study, you can always contact your physician or one of the investigators that are mentioned below. In case you decide to take part in this research we kindly ask you to sign the informed consent on the next page. With the signature you indicate that you have received and understood this information.

Name and contact details of PI(s)

**Informed Consent for participation in the research study: Early versus late intervention for twin reversed arterial perfusion sequence-TRAPIST: an open-label randomized controlled trial**

I have been informed satisfactorily concerning the study. I have read the written information carefully. I have had the opportunity to ask questions concerning the study. My questions have been answered satisfactorily. I have been able to think about the participation properly. I have the right to withdraw my consent at any time without giving any reason.

**Surname and initials: ……**

**Date of birth: ……**

**Signature: .....** **Date:…….....**

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**For the physician:**

Signatory states that abovementioned individual has been informed both orally and in writing about the above-mentioned study. He/she declares that a premature stopping of the participation by above-mentioned person will absolutely not influence the care to which she is entitled.

**Surname and initials: …….**

**Signature: .....** **Date:…….....**

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