## S1 Patient consent form

**TITLE OF THE TRIAL:** Assessment of an intervention to OPTIMize antenatal management of women admitted with PreTerm Labor and intact membranes using amniocentesis-based predictive risk models: study protocol for a randomized controlled trial (OPTIM-PTL study).

**Version and date:** v4 May 10th, 2021

**Principal investigator at Promotor center*:*** Teresa Cobo Cobo. Maternal and Fetal Medicine Department. Hospital Clinic Barcelona (email: tcobo@clinic.cat)

**CENTER:** Hospital Clínic Barcelona

**INTRODUCTION**

We are writing to inform you about a research study in which you are invited to participate. According to the prevailing Royal Decree 1095/2015. the study has been approved by an ethics committee.

The aim of this document is to provide you with correct and sufficient information so that you can evaluate and judge whether you wish to participate in the study or not. Please read this information sheet carefully, and we will clarify any doubts or questions you may have. In addition, you can consult with other people who you deem appropriate.

**VOLUNTARY PARTICIPATION**

You should know that your participation in this study is voluntary, and that you can decide not to participate or change your decision and withdraw your consent at any time, without interfering with the relationship with your doctor or leading to any change in your usual treatment.

**OVERALL VIEW OF THE STUDY**

Preterm birth is the main cause of adverse neonatal outcomes. Despite the clinical importance of this problem, current prediction of preterm birth (based on the presence of uterine contractions or vaginal examination) is poor. Only 10% of pregnant women who are admitted with a diagnosis of threatened preterm labor deliver within the following 7 days, and 70% deliver above 37 weeks.

It is clinically relevant to target the low- and the high-risk group of preterm birth because it allows individualizing antenatal management according to the risk. In the high-risk group, treatment with all the antenatal strategies available has shown to improve the prognosis of preterm babies (e.g steroids) and to plan preterm delivery. However, in the low-risk group, the current management with steroids, tocolysis, magnesium sulphate might be unnecessary. Unnecessary over-treatment can be associated with negative side effects. In this regard, neurodevelopmental impairment and cardiovascular risk has been

reported in babies antenatally exposed to steroids who were finally born at term (above 37 weeks). This is why it is important to treat if there is high-risk of preterm birth and not to over-treat if the risk is low.

One of the known causes of preterm birth is intra-amniotic infection, but diagnosis of this problem requires performing amniocentesis. Our group has developed a model with good diagnostic performance to predict the risk of delivery within 7 days or the presence of intra-amniotic infection. The result can be obtained within a few hours. However, before being implemented in clinical practice we need to test whether the use of amniocentesis-based predictive risk models improves the antenatal management of a woman like you without affecting perinatal outcome.

We request your participation in this study with the objective to optimize the antenatal management of women with threatened preterm labor without affecting maternal or perinatal outcomes and to demonstrate that it is a cost-effective strategy.

The initial management of women with preterm labor will follow the standard institutional management of each center and include a first dose of corticosteroids and tocolysis. After providing informed written consent, you will be randomly assigned to one of the two study arms.

In the intervention arm, the management will be optimized according to the amniocentesis-based predictive risk models. If the risk is low, hospital discharge within 24h of results with no further medication will be recommended. If there is high-risk of spontaneous delivery within 7 days or the presence of intra-amniotic infection, antibiotics will be added to the standard management, at least until the amniotic fluid culture result.

In the control arm, you will be managed according to the standard institutional management protocols of each center, including hospital admission, corticosteroids and tocolysis without amniocentesis.

The planned duration of the study is 2 years.

We have estimated that a total of 340 women will be sufficient to show we can optimize the antenatal management of women such as you admitted with threatened preterm labor using amniocentesis-based predictive risk models, without affecting neonatal or maternal outcomes.

**BENEFITS AND RISKS RELATED TO YOUR PARTICIPATION IN THIS STUDY**

There is no inconvenience or risk related to the study due to the fact that the initial management with treatments that have shown to improve neonatal prognosis (steroids and/or magnesium sulfate) will be similar in the 2 study arms until randomization. In the intervention arm, we will reduce the duration of treatment if there is low risk, and we will start with antibiotics if there is high risk (due to the high-risk of intra-amniotic infection).

**ALTERNATIVE TREATMENTS**

Your participation in the study will not modify your current treatment. It will only modify

the management as explained above.

**CONFIDENTIALITY**

The Hospital Clínic of Barcelona, with CIF 0802070C, is responsible for the treatment of your data, and states that the treatment, communication and transfer of personal data of all participants will comply with European Union regulations EU 2016/679 of the European Parliament of April 27th, 2016 regarding the processing of personal data and the free circulation of data and with Organic Law 3/2018 of December 5th on the Protection of Personal Data and guarantee of digital rights.

The data collected for these studies will be identified only by a code, and therefore, there will be no information to identify the participants. Only the Principal Investigator and collaborators with specific permission can relate your data collected in the study with your medical history.

Your identity will not be revealed to any other person except for a medical emergency or legal requirements. The health authorities, the Research Ethics Committee and personnel authorized by the study promoter may have access to your personal information when necessary in order to verify data and study procedures, while always maintaining confidentiality in accordance with the prevailing legislation.

Only coded data will be transferred to third parties and other countries, which in no case will contain information that can directly identify the participants (such as name and surname, initials, address, social security number, etc.). In the event of data transfer, it would be for the same purpose as the study described, and confidentiality would be guaranteed.

If encrypted data is transferred outside the EU to entities related to your hospital center to service providers or to researchers who collaborate with your doctor your data will be protected by safeguards such as contracts or other established mechanisms.

In addition to the rights contemplated in the above mentioned legislation (access, modification, opposition and cancellation of data, deletion in the new regulation) you can now also limit the processing of incorrect data and request a copy of data transferred to a third party (portability). To exercise these rights, or if you wish to know more about confidentiality, you should contact the Principal Investigator of the study or the Data Protection Delegate of the *Hospital Clínic de Barcelona* at protecciodades@clinic.cat. They also have the right to contact the Data Protection Agency if they are not satisfied.

In order to ensure the validity of the research and to comply with legal duties and drug authorization requirements, data already collected cannot be deleted even if you withdraw from the study. However, no new data will be collected if you withdraw from the study.

The Researcher and the Sponsor are obliged to keep the data collected for the study for at least 25 years after its completion. Subsequently, the personal information will only be kept by your health care center and by the promoter for other scientific research purposes if you provide consent to this, and if this is allowed by the law and applicable ethical requirements.

**ECONOMIC COMPENSATION**

Your participation in the study will not incur any expense.

**OTHER RELEVANT INFORMATION**

Your doctor will immediately communicate any new information, which is discovered regarding the treatment used in the study that may affect your willingness to participate.

If you decide to withdraw your consent to participate in this study, no new data will be added to the database and you can demand the destruction of all identifiable samples previously retained to avoid further analysis.

It is also important to know that you may be excluded from the study if the promoter and / or the study investigators consider it appropriate, either for safety reasons, due to any adverse event that occurs and in relation to your participation in the study or because they consider that you are not complying with established procedures. In any case, you will receive an adequate explanation of the reason that led to your withdrawal from the study.

By signing the attached consent sheet, you agree to comply with the study procedures that have been set forth to you.

**PATIENT CONSENT FORM**

**Title:** "Assessment of an intervention to OPTIMize antenatal management of women admitted with PreTerm Labor and intact membranes using amniocentesis-based predictive risk models: study protocol for a randomized controlled trial (OPTIM-PTL study).

**Version and date: v4 4 May 2021**

I, *(Patient'sName and surnames)* .....

- I have read the information sheet given to me about the study.

- I have been able to ask questions about the study.

- I have received enough information about the study.

- I have spoken with: (Investigator's name)

- I understand that my participation is voluntary.

- I understand that I can withdraw from the study:

  - Whenever I wish.
  - Without having to explain.
  - Without this affecting my medical care.

- In accordance with the provisions of Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 regarding the protection of natural persons with regard to the processing of personal data and the free movement of these data and Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, I declare to have been informed of the existence of a file or processing of personal data for the purpose of the collection of these and the recipients of the information.

Given the information that the Data Controller has provided and having understood it, I consent to the treatment of:

□ My personal data to carry out the research project.

□ My personal data to carry out research projects related to the present project or in the same research area.

I freely give my consent to participate in the study.

Participant signature Principal investigator signature

*Model de FIP/CI Projectes, EPA, PS amb marca CE v6 de 12.06.2019*

Date: ____/____/____ Date: ____/____/____

I would like to receive information derived from research that may be relevant to my health:

☐ YES ☐ NO

Participant signature Principal investigator signature

Date: ____/____/____ Date: ____/____/____