

TITLE OF FORM:

“Evaluation of the antioxidant activity of lutein/zeaxanthin early administered to premature newborns”

Date: 09/06/2017

INFORMED CONSENT

Dear parents,

it has been proposed you to participate in a clinical trial and this document is intended to inform you about it. In this brochure you will find details on the research procedures and the duration of the project.

Please read carefully the informations here written before taking a decision on a possible participation in the study. You will have all the time to decide whether to participate or not.

You can also freely ask any clarifying question and repeat every question that has not received a clear and comprehensive answer.

In the eventuality that, having read and understood all the information provided therein, you decide you want to participate in the study, we will ask you want to sign and personally date the informed consent form attached to this document.

What it implicates to participate in the study?

Dear parents,

Premature birth is the most common cause of mortality, morbidity and disability. Premature infants have a higher risk of developing damage in eye (retinopathy of prematurity ROP), in the central nervous system (intraventricular haemorrhage IVH), in the lungs (bronchial pulmonary dysplasia BPD), in the intestine (NEC) and infections.

Oxidative stress has been implicated in various capacities, in the etiology of these conditions. Lutein and zeaxanthin are powerful anti-oxidants and are commonly assimilated with different foods. They are present at level of umbilical cord, in the breast milk particularly in colostrum and they pass the placental barrier. Concerning supplementation, the lutein presents, for its specific characteristics, a high bioavailability after oral administration.

In the last few years there have been more and more studies which have shown that lutein can constitute a valid and important preventive and protective factor against certain diseases related to oxidative stress.

The preparations of lutein and zeaxanthin have never pointed out in man (included in the term newborn) adverse or toxic effects after supplementation, nor gastrointestinal level or systemically, or any interaction with other fat-soluble nutrients were reported.

This spontaneous / non-commercial pilot study involves the administration of a dietary supplement containing lutein / zeaxanthin, as the health care structures need to identify a natural antioxidant product that can reduce the incidence of serious diseases related to oxidative stress in the perinatal period.

This study aims to evaluate whether the administration of lutein in aqueous solution is capable of reducing the free radicals rates in preterm infants and therefore reduce the incidence of pathologies related to free radicals diseases.

How the study is conducted?

After the consent your son / daughter becomes part of the study protocol. He/she will be assigned randomly to one of the two candidate groups (group A or group B).

To group A will be administered **LUTEINofta 0,5 drops**, to 5% by weight solution of lutein and 2.5% by weight of zeaxanthin with the excipients (corn starch, glucose, potassium sorbate, xanthan gum, citric acid).

To the group B will be administered placebo solution, (demineralised water, potassium sorbate, xanthan gum, citric acid).

The manner and timing of administration will be the same between the two groups.

Group A will be treated with 0.5 LUTEINofta drops, (1 ml for Kg of 0.5 mg of lutein and 0.05 mg of zeaxanthin), in 2 doses throughout the day, in addition to the standard hospital therapy expected. The first dose will be given within 36 hours of life, the last to 30th day of life.

The B group will be treated with the placebo solution in addition to the standard hospital treatment planned. The first dose will be given within the first 36 hours of life, the last to 30th day of life.

The product administered will be added to the milk (human or artificial) or in a small amount of glucose orally or by gavage.

Duration of patient observation period enlisted:

From birth until discharge.

Total duration of the study:

The study will run for a year: the first 6 months will be spent to enroll infants in the centers concerned.

Method:-

All newborns in the period of observation, will be subjected to collection (1 ml) of umbilical cord and peripheral blood (to coincide with routine withdrawals) on which will be performed blood gas analysis and assay of markers of oxidative stress (TH and BAP).

Times Survey:

- T0, baseline at birth, before starting treatment: drawing blood from the umbilical vein.
- T1, the first control, 15 days after initiation of therapy: removal of peripheral blood to be performed prior to administration of lutein / zeaxanthin.
- T2, the second control, to 30th day of therapy: sampling of peripheral blood to be carried out before administration of lutein / zeaxanthin.

What are the benefits that your son / daughter will receive by participating in the study?

The results of these investigations will be used in the future for infants with problems of immaturity or other diseases.

What are the risks arising from participation in the study?

The risks to your son/daughter resulting from participation in the study, although not elevated are not entirely known.

What happen if you decide not to participate in the study or retire later?

You are free not to participate in the study; if you decide to participate, you will have the right to retire from the study at any time and without the obligation to provide explanations.

Study interruption

The doctor may decide to stop the study at any time it seems appropriate, also in the interest of the patient, without that being detrimental to the health of the newborn.

Confidentiality of personal data

Pursuant to Legislative Decree n. 196 of 30.6.03 (new privacy code), we inform you that the personal information of your son / daughter, collected for scientific research purposes will be treated in full compliance with the above provisions, in order to ensure respect for human rights, fundamental freedoms and dignity of individuals, with particular reference to privacy and personal identity. All documents related to the study and especially the personal data of your son / daughter will remain strictly

confidential. These data will be used exclusively for scientific research purposes and in anonymous form. The security and confidentiality of the data will be guaranteed by appropriate protective measures regarding minimum security measures, in order to reduce the risk of destruction or loss, even accidental, of data, unauthorized access or treatment not allowed or not in accordance with the purposes of collection. The study data will be recorded in anonymous form in a computer database by the Universities participating in the study. The study results will be presented at scientific congresses or used for the preparation of a clinical study report to the regulatory authorities, or to the publication. The identity of patients will never be revealed in any of these occasions. Samples collected for this study will be stored and sent for analysis to other centers that collaborate with the study. All data will be protected in accordance with legal rules on personal data protection (Legislative Decree 30/06/2003 n. 196 and subsequent amendments) and any identification will not be possible by a third party.

Place of the study: Hospital.....

Doctors conducting the Study: Dr.

I, the undersigned

born in _____, resident in _____

, address _____

I declare that:

- I have voluntarily chosen to involve my baby in the study titled above;
- I received from Dr. _____ exhaustive explanations about the request of participation in the study, its purposes and procedures;
- I have read and understood the information sheet that was handed to me with early enough time, and that confirms what I have been told verbally;
- to have had the opportunity to ask questions and have received satisfactory answers;
- I have been informed about possible risks or reasonably foreseeable discomforts;
- to be aware that participation is voluntary and that any refusal will not affect neither assistance nor on subsequent medical care to my child;
- It was satisfied that:
 - I could retire from the study already started in any moment and this will have no negative consequences on subsequent medical care to my child;

- medical records remain confidential and the data will be used for study purposes only;
- I will be informed of any new information which might influence the risks and benefits of participation in the study of my child;
- a copy of the information sheet I have read and a copy of the informed consent document will remain in my possession;

Place and Date

Signature of patient

Signature of doctor