UZ LEUVEN | GYNAECOLOGIE EN VERLOSKUNDE
Leuvens universitair fertiliteitscentrum

www.uzleuven.be/lufc › tel. +32 16 34 36 24

INFORMATION CONCERNING PREIMPLANTATION GENETIC TESTING USING NEXT GENERATION SEQUENCING (NGS) AS A METHOD FOR DETECTING SERIOUS CHROMOSOMAL ABNORMALITIES

Preimplantation genetic testing (PGT) is an analysis that makes it possible to detect serious chromosomal abnormalities in embryos obtained via in-vitro fertilisation (IVF) with intracytoplasmic sperm injection (ICSI), before they are transferred to the uterus.

Background and purpose of IVF/ICSI with PGT

PGT is used to detect genetic abnormalities in embryos obtained via IVF/ICSI before they are transferred to the uterus. Couples at an increased risk of passing on a serious genetic abnormality to their children qualify for IVF/ICSI combined with PGT. PGT makes it possible to avoid a pregnancy in which a baby inherits a serious genetic abnormality prevalent in the family.

Procedure of IVF/ICSI with PGT

During IVF/ICSI treatment the woman's ovaries are hormonally stimulated to promote the ripening of several eggs. As soon as there are sufficient mature eggs, they are removed from the ovaries (oocyte aspiration). The eggs are then fertilised with sperm via ICSI (injection of one sperm in one egg). The fertilised eggs are placed in a culture medium in the fertility laboratory to develop into embryos.

In order to carry out PGT a biopsy is taken from each embryo, which involves removing one or several cells from the embryo. Two biopsy options are available, depending on the embryo's development stage:

1. On day 3 after fertilisation one cell is removed for genetic analysis from each embryo of sufficient quality.
2. On day 5/6 after fertilisation the embryo is more developed and a section of trophectoderm (cells from the embryo's outer layer that will eventually form the placenta and other membranes) is removed for genetic analysis.

All embryos are kept in culture medium until day 5/6 after fertilisation and embryos of sufficient morphological quality are frozen. No embryo will consequently be transferred in the fresh IVF/ICSI cycle.

The genetic laboratory will analyse the biopsied cell(s) using next generation sequencing (NGS), thus making a specific diagnosis for each frozen embryo. It provides an answer to the question as to whether the embryo is affected. The results of an NGS analysis are known within a month of freezing the embryos.

Only non-affected embryos are eligible for transfer to the uterus in a subsequent thawing cycle. One or two non-affected embryos are transferred in line with the available options and legal stipulations.

Embryos for which the genetic analysis indicates that they are affected, or embryos with trisomy 21 or other serious chromosomal abnormalities, or embryos for which the results of the genetic analysis are inconclusive, are not eligible for transfer. However, these embryos qualify for scientific research, providing the prospective parents agree to this. Further information on scientific research is provided in the LUFC form entitled "Agreement on scientific research with gametes and embryos that you cannot use yourself".

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Who can PGT using next generation sequencing be useful for?

Only couples who know that they are at an increased risk of having a child with a serious chromosomal abnormality are eligible for PGT. Gender selection for non-medical reasons is not an option. The genetic defect in the chromosomes or gene must be identified. No specific preparation is required for PGT using NGS.

Success rate of IVF/ICSI with PGT

In general, the chance of a woman having a baby following an IVF/ICSI cycle with PGT treatment is 20 to 25%. The woman's age, the quality of the embryo(s) suitable for transfer and the inheritance pattern of the genetic abnormality for which PGT is carried out, will affect the number of available embryos and consequently the success rate. The prospective parents are aware that treatment by the Leuven University fertility centre (LUFC) and the Centre for Human Genetics (CME), University Hospital Leuven, constitutes a best-effort commitment only, and that a positive outcome of the treatment cannot be guaranteed.

How reliable and safe is IVF/ICSI with PGT using next generation sequencing?

Despite the fact that studies have demonstrated that IVF/ICSI with PGT using NGS is highly reliable, an error may occur during IVF/ICSI with a PGT procedure in less than 3% of cases. That is why additional checks are desirable and in the event of a pregnancy the possibility of NIPT, and/or prenatal diagnosis via chorionic villus sampling/amniocentesis, will be discussed with the prospective parents.

Monitoring of babies born following IVF/ICSI with PGT has shown that there is no increased risk of children with congenital abnormalities.

Important information of IVF/ICSI with PGT

In order to assess the IVF/ICSI with PGT application, provide appropriate explanation and organise the necessary preparations, prospective parents will be invited to attend consultations with a clinical geneticist and gynaecologist/fertility specialist. Where necessary prospective parents will also be invited to attend a consultation with a fertility psychologist.

We ask to use protection during intercouse both one week before and one week after oocyte aspiration and one week before and one week after embryo transfer, because there is a risk of a spontaneous pregnancy involving a fertilised egg that has not be subjected to genetic analysis.

Financial aspects of IVF/ICSI with PGT

The IVF/ICSI with PGT procedure is mostly covered by the mandatory Belgian health insurance. A fixed fee will be charged for the embryo biopsy. Patients who do not have Belgian health insurance will have to meet the cost of the IVF/ICSI with PGT procedure in full.

A cost estimate can be found at www.uzleuven.be/kostenraming under Gynaecology and Obstetrics.

For further information, please contact the PGT midwives of the LUFC, on +32 (0)16 34 36 24 or by e-mail PGT-LUFC@uzleuven.be.

This document 'Information concerning preimplantation genetic testing using next generation sequencing (NGS) as a method for detecting serious chromosomal abnormalities' is intended for you. If you agree to this treatment, you should complete and sign the attached 'Agreement concerning preimplantation genetic testing using next generation sequencing (NGS) as a method for detecting serious chromosomal abnormalities' and return it to LUFC, 'contractenadministratie', UZ Leuven, Herestraat 49, 3000 Leuven or to contractenLUFC@uzleuven.be.

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AGREEMENT CONCERNING PREIMPLEMANTATION GENETIC DIAGNOSIS USING NEXT GENERATION SEQUENCING (NGS) AS A METHOD FOR DETECTING SERIOUS CHROMOSOMAL ABNORMALITIES

Between Leuven university fertility centre,
UZ Leuven,
represented by
prof. dr. Karen Peeraer,

hereinafter 'the LUFC', on the one hand,

and Ms .....
born on ...../...../.....
Partner .....
born on ...../...../.....
resident at .....
.....

hereinafter 'the prospective parents', on the other hand,

the following has been agreed:

- The prospective parents declare that they have been properly informed by the LUFC about the IVF/ICSI with PGT procedure and that they have received, read and understood the document entitled 'Information concerning preimplantation genetic testing using next generation sequencing (NGS) as a method for detecting serious chromosomal abnormalities'. They consent to the LUFC proceeding with IVF/ICSI with PGT treatment. The procedure involves removing (biopsy) one or several cells from each embryo of sufficient quality, followed by genetic analysis of these cell(s).
- The prospective parents declare that the advantages and disadvantages of this procedure have been thoroughly discussed with them and that they are well aware that:
  - IVF/ICSI with PGT is used for couples at an increased risk of passing on a serious genetic abnormality to their children. This procedure may lead to parenthood, but there is no guarantee.
  - they have been asked to use protection during intercourse both one week before and one week after oocyte aspiration and one week before and one week after embryo transfer.
  - only non-affected embryos are eligible for transfer to the uterus. Embryos for which the genetic analysis indicates that they are affected, or embryos with trisomy 21 or other serious chromosomal abnormalities, or embryos for which the results of the genetic analysis are inconclusive, are not eligible for transfer to the uterus. This technique does not allow all potential genetic defects to be detected.
  - despite the fact that studies have demonstrated that IVF/ICSI with PGT using next generation sequencing is highly reliable, an error may occur during IVF/ICSI with a PGT procedure in less than 3% of cases. That is why additional checks are desirable and in the event of a pregnancy the possibility of NIPT, and/or prenatal diagnosis via chorionic villus sampling/amniocentesis, will be discussed with you.
  - The IVF/ICSI with PGT procedure is mostly covered by the mandatory Belgian health insurance. A fixed fee will be charged for the embryo biopsy. This amount is 415,80 euros on 1 January 2018. This amount will be adjusted on the 1st of January each year in line with the health index (http://statbel.fgov.be/nl/statistieken/cijfers/economie/consumptieprijzen/gezondheidsindex) in December of the preceding year. Patients who do not have Belgian health insurance will have to meet the cost of the IVF/ICSI with PGT procedure in full.
  - The prospective parents were assumed to be informed that the Belgian health insurance will only provide a reimbursement of the PGT preparation once. If they choose to have a second preparation carried out in another PGT center, then they will pay the costs themselves.
  - After the birth of a child conceived with IVF/ICSI with PGT their ongoing development may be monitored by asking the parents to complete questionnaires.

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Drawn up in duplicate in Leuven on ……../……../……., one copy being intended for the LUFC and the other for the prospective parents.

	Name Madam	Name Partner
	.....	.....
	.....	.....
	born on ……/……. / …….	born on ……/……./…….

prof. dr. Karen Peeraer
Administrator Tissue Bank LUFC

read and approved
signature Ms

read and approved
signature Partner

Please complete and sign this agreement and return it to Leuvens universitair fertiliteitscentrum, 'contractenadministratie', UZ Leuven, Herestraat 49, 3000 Leuven or contractenLUFC@uzleuven.be.