NIPT INFO BROCHURE

The Non - Invasive Prenatal Test (NIPT) is a DNA test on maternal blood to safely and reliably screen pregnancies for the most common fetal chromosome anomalies : Trisomy 21 (Down syndrome), Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome).

Also the sex of the fetus and anomalies of the sex chromosomes X and Y (Turner, Klinefelter, Triple X-XXX and XYY syndrome) can be tested upon request.

Chromosome anomalies diagnosed with NIPT :

Trisomy 21 (Down syndrome)	This is caused by an extra copy of chromosome 21 and is also called Down syndrome. This is the most common genetic cause of intellectual disability. Individuals with Down syndrome have some degree of intellectual disability (average IQ of 50). Some children with Down syndrome have congenital defects of the heart or other organs that may require surgery or medical treatment. Some have other medical conditions including hearing or vision loss, and at a later age dementia.
Trisomy 18 (Edwards syndrome)	This is caused by an extra copy of chromosome 18 and is also called Edwards syndrome. Most babies with trisomy 18 have multiple severe birth defects of the brain, heart and other organs. Poor growth during pregnancy is common and many babies are miscarried or stillborn. Of those babies born alive, most die before one year of age. Babies who survive have profound intellectual disabilities and growth and developmental problems.
Trisomy 13 (Patau syndrome)	This is caused by an extra copy of chromosome 13 and is also called Patau syndrome. Most babies with trisomy 13 have multiple severe birth defects of the brain and other organs. Many babies are miscarried or stillborn. Of those babies born alive, most die before one year of age.

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SAMPLES : At least 10 ml blood in a specific blood tube (STRECK) available from GENDIA is required from the mother. The maternal blood can be taken from week 11 of the pregnancy. The sample has to be sent by Express mail to GENDIA's lab in Antwerp, Belgium, and arrive there within 3 days of withdrawal.

METHODS : DNA isolated from maternal blood, which contains fetal DNA, is sequenced using an high-throughput next generation sequencer (NGS). Sequencing data are analyzed to determine the fetal copy number for chromosomes 21, 18, 13, thereby identifying any aneuploidy of any of these 3 chromosomes.
The determination of fetal sex and exclusion of anomalies of the sex chromosomes (X and Y), including Turner, Klinefelter, XXX and XYY syndrome, are optional.
This NIPT test (VERISEQ V2 test) was developed by ILLUMINA in the United States and is carried out by the AML laboratory in Antwerp, Belgium.

Also the exclusion of 3 monogenic molecular anomalies (cystic fibrosis, B-thalassemia, and sickle cell disease) is possible. Cystic fibrosis (CF) is the most common severe genetic disorder in Western populations. Sickle cell anemia and B-thalassemia are the most common genetic disorders in Mediterranean countries (Spain, Italy, Greece, Turkey, North Africa), India and the Middle East.
The NIPT for these 3 monogenic molecular anomalies costs 650 Euro extra, takes 3 weeks, and a blood or DNA sample from the father is also needed.

TURNAROUND TIME : NIPT takes approximately 1 week from arrival of the sample in the GENDIA lab.

INDICATIONS : Although NIPT can be performed without specific indication, it might be most appropriate in pregnancies with an increased risk for fetal aneuploidy based upon a high maternal age (> 35 yrs.) or abnormal result of the or first trimester Down syndrome screening (NT measurement in combination with determination of free beta-hCG and PAPP-A in maternal blood) or triple test (determination of AFP, oestriol, beta-hCG in maternal blood).
In these cases NIPT is an alternative to chromosome studies after amniocentesis (AC) or chorion biopsy (CVS).

CONTRAINDICATIONS : Samples from triplet pregnancies cannot be accepted for testing, but (vanishing) twin testing is possible. Also pregnancies after egg donation are no contraindication. NIPT is not a good option in case of ultrasound anomalies of the fetus or genetic anomalies that can not be diagnosed with NIPT.

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TWIN PREGNANCY : The procedure and costs in a twin pregnancy are the same.
The sensitivity for Down syndrome in single-egg monozygotic twins is just as high as in singles (99%).
The sensitivity to Down syndrome in 2-egg dizygotic twins is 90 - 95%.
With a vanishing twin (fetus that disappears) NIPT is possible, but without gender determination.

LIMITATIONS OF NIPT : In line with international recommendations the samples are analyzed for the most common fetal chromosome anomalies : Trisomy 21 (Down syndrome), Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome). The determination of fetal sex and sex chromosome (X and Y) anomalies (Turner, Klinefelter, XXX and XYY syndrome) is optional.
Aneuploidy of other chromosomes, other chromosome anomalies (including mosaicism for chromosomes 21, 18, 13, and microdeletions or microduplications), and triploidy cannot be excluded.

RELIABILITY OF NIPT RESULT : The reliability of NIPT results is very high. The test has very high sensitivity and specificity for trisomy 21, 18 and 13, and very high reliability for the determination of fetal sex.

The sensitivity for the detection of trisomy 21, 18, 13 is so high that a normal NIPT result means that the chance of a trisomy 21, 18, 13 is less than 1 in 1,000 (false negatives).
The specificity of NIPT is also > 99.9 % for the 3 chromosomes: this means that fewer than 1 in 1000 tests are false positive with a different NIPT result while the fetus has no trisomy 21, 18 or 13.
If the NIPT test is abnormal, then it is not certain that the fetus also has the chromosome anomaly because some NIPT anomalies are limited to the placenta, and therefore do not occur in the fetus. For this reason, we always recommend amniocentesis in the event of an abnormal NIPT result.

The reliability for the determination of fetal sex is very high (> 99.9 %), but the sensitivity and specificity of NIPT for anomalies of the sex chromosomes (Turner, Klinefelter, Triple X-XXX and XYY syndrome) is not entirely clear.

NIPT FAILURE : In a limited number of pregnancies (< 1 %) NIPT cannot be performed for technical reasons (damaged sample or other technical reasons) or biological reasons (not enough fetal DNA, fetal demise, chromosome anomaly). In these pregnancies NIPT can be repeated at no extra cost on a repeat maternal blood sample.

NIPT RESULT : The NIPT result will be sent to the patient and physician or midwife who ordered the test within a week after the blood arrives.
If you have indicated on the submission form that you want to know the sex of the fetus, this will be stated in the result. Anomalies of the sex chromosomes (Turner, Klinefelter, XXX and XYY syndrome) are then also reported.
If you have indicated on the submission form that you do not want to know the fetal sex, the fetal sex and eventual anomalies of the sex chromosomes are not reported. However, you can request these results later by email (NIPT@GENDIA.net).

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FOLLOW UP STEPS :

1. In case of a normal NIPT result : no specific follow up is necessary apart from the routine ultrasound examinations of the fetus.

2. In case of test failure : in a limited number of pregnancies (< 1 %) NIPT cannot be performed for technical or biological reasons. In these pregnancies NIPT can be repeated at no extra cost on a repeat maternal blood sample.

3. In case of an abnormal NIPT result : in case of an abnormal result with the finding of an abnormal number (aneuploidy) of any of the chromosomes tested, the physician/genetic counselor/midwife will discuss the implications of such chromosomal anomaly with the patient, who can then decide to confirm the NIPT results with chromosome studies after amniocentesis (AC) or chorion biopsy (CVS).

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