Test results and actions

- **Normal:**
  - ✓ No indication of fetal trisomy 21, 18 or 13
  - ✓ Standard pregnancy follow-up
- **Abnormal:**
  - ✓ Strong indication of fetal trisomy 21, 18 or 13
  - ✓ Confirmation by amniocentesis
- **Inconclusive result for chromosome 21, 18 or 13:**
  - ✓ Trisomy 21, 18 or 13 cannot be excluded
  - ✓ Repeat NIPT on new blood sample (no extra cost) OR amniocentesis
- **Failed test:**
  - ✓ No reliable analysis possible
  - ✓ Repeat NIPT on new blood sample (no extra cost)

Quality control

We appreciate your feedback!

Please update us with the outcome of the pregnancy after NIPT via *cme.nipt@uzleuven.be*

- Ultrasound abnormalities
- Spontaneous miscarriages
- Discrepant results (false positives/negatives)
- Invasive testing:
  - ✓ Tissue type: CVS / amniotic fluid
  - ✓ Type of analysis: array / FISH / qPCR
  - ✓ Result (as compared to NIPT)

Scientific publications

(1) Bayindir, B. *et al.* Noninvasive prenatal testing using a novel analysis pipeline to screen for all autosomal fetal aneuploidies improves pregnancy management. Eur J Hum Genet 23(10): 1286-93 (2015)

(2) Vandenberghe, P. *et al.* Non-invasive detection of genomic imbalances in Hodgkin/Reed-Sternberg cells in early and advanced stage Hodgkin's lymphoma by sequencing of circulating cell-free DNA: a technical proof-of-principle study. Lancet Haematol 2(2):e55-65 (2015)

(3) Amant, F. *et al.* Presymptomatic identification of cancers in pregnant women during noninvasive prenatal testing. JAMA Oncology 1(6): 814-9 (2015)

(4) Brady, P. *et al.* Clinical implementation of NIPT – technical and biological challenges. Clin Genet 89(5): 523-30 (2016)

(5) Brison, N. *et al.* Accuracy and clinical value of maternal incidental findings during noninvasive prenatal testing for fetal aneuploidies. Genet Med 113 (2016)

(6) Brison, N. *et al.* GIP-sequencing combined with fetal fraction determination predicts fetoplacental mosaicism. *Manuscript in preparation.*

Disclaimer:

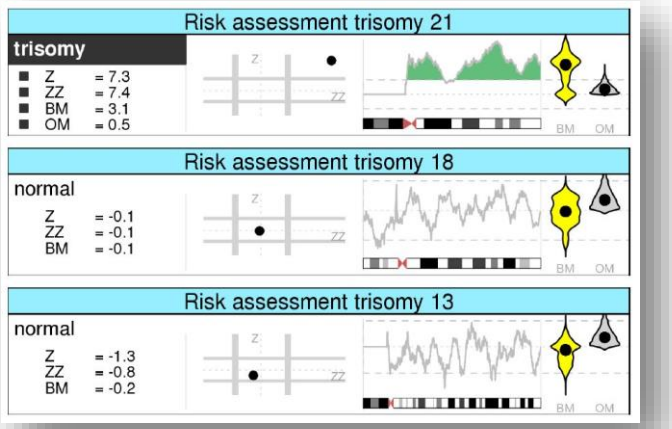
NIPT is a non-invasive prenatal screening test for detection of trisomy 21, 18 and 13 from 10 weeks of gestation onwards. An abnormal result should always be confirmed by invasive prenatal testing (preferably by amniocentesis). NIPT also detects the sex of the fetus. However, sex chromosomal aneuploidies cannot be detected. In rare cases, NIPT may detect other chromosomal abnormalities such as other fetal autosomal trisomies or a clinically relevant chromosomal abnormality in the pregnant mother. When ultrasound abnormalities are present in the fetus, an invasive test is indicated. NIPT is not able to detect mosaicism, microdeletions, microduplications or monogenic disorders. NIPT should be performed with caution in cases of (vanishing) twin or multiple pregnancies, when the mother has (had) cancer, when the mother recently had heparin therapy or a blood transfusion, and when the mother has had immunotherapy, a stem cell transplant or an organ/tissue transplant within 3 months prior to the pregnancy.

Contact us at:
cme.nipt@uzleuven.be
+32 (0)16 34 59 03

More information:
www.uzleuven.be/nipt

NON-INVASIVE PRENATAL TESTING

NIPT



First centre in Belgium and in Europe to perform NIPT

In-house developed and optimized genome-wide analysis

Validated and accredited for the detection of trisomy 21, 18 and 13 as well as fetal sex

ISO 15189

Diagnostic Experience at UZ Leuven

November 2013 – Mid April 2017

Over 21,000 samples have been analyzed

>99% of cases received a result on first sampling

Test Performance

Unprecedented sensitivity of almost 100% for detection of fetal trisomy 21, 18 and 13 in singleton pregnancies

Much more reliable than the combined test

No false negatives for trisomy 21 and 13

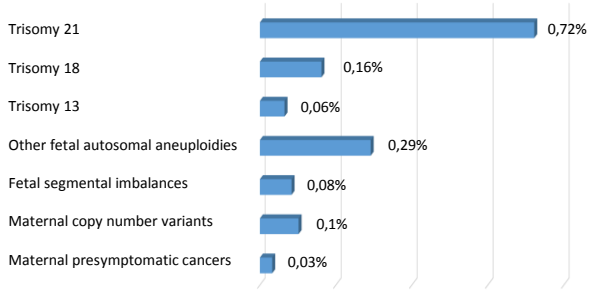
False positive in <0,05% of cases

	Observed sensitivity	Observed specificity	PPV	NPV
Trisomy 21	100%	99,99%	98,12%	100%
Trisomy 18	97,14%*	100%	97,14%	99,99%
Trisomy 13	100%	99,98%	64,29%	100%

* 1 false negative trisomy 18

Incidental Findings

Genome-wide analysis allows detection of other clinically relevant maternal / fetal chromosomal abnormalities



IMPORTANT NOTICE:

NIPT at CME-UZ Leuven is offered in full compliance with the BeSHG National Guidelines for NIPT testing and management of incidental findings (www.BeSHG.be). CME-UZ Leuven is part of the national consortium which drafted and issued good practice guidelines. The consortium is comprised of 8 genetic centres, all of which are nationally accredited by the Ministry of Health.

FAQs

When? ≥10 weeks of gestation

Blood collection?

- cfDNA tubes [Roche] (white cap) = **preferred**
- Streck tubes (camouflage pattern)

Contra-indications?

- Ultrasound abnormalities (incl. NT>3,5mm)
- Mothers on heparin therapy or who had a blood transfusion
- Mothers who had immunotherapy, a stem cell transplant or an organ/tissue transplant within 3 months prior to the pregnancy
- Mothers with a chromosome abnormality
- Mothers with cancer

Test accuracy in twin pregnancies?

- Monozygotic twins ≈ singleton pregnancies
- Dizygotic twins / vanishing twins:

  accuracy = less than singleton pregnancies

  accuracy = higher than combined test

High pre-pregnancy Body Mass Index (BMI)?

Increases the probability of low fetal fraction, which could reduce the reliability of the results

Cost for the pregnant women?

- Pregnant women with a Belgian medical insurance: 8,68€ (as from July 1, 2017)
- Others: 260€