EUROIMMUN Medizinische Labordiagnostika AG

GynTect®

Epigenetic markers for cervical cancer diagnostics

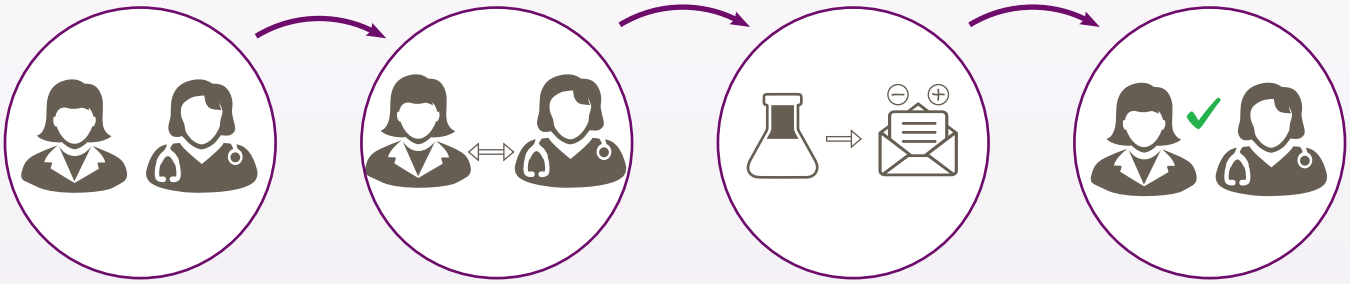
- **CE-IVD approved diagnostic test* identifying patients with malignant changes of the cervix**
- **Performance possible in one working day**
- **Performed on cobas® z 480 Analyzer**
- **Evaluation using common calculation software**

** The product is currently only available in the following countries: Canada, Italy, Poland, Portugal and Turkey.*

GynTect® – reliable and fast diagnostics

If the cervical cancer screening result is **abnormal** with the **Pap test** and/or **positive** with the **HPV test**, patients suddenly find themselves in an exceptional situation. Even though both tests indicate a possible cancer, **in many cases** there is **no malignant disease** and the positive test result was a false alarm. Further examinations are necessary for reliable clarification, such as a colposcopy with biopsy, if required. If abnormalities are detected, the presumably affected tissue is often removed.

GynTect® is a fast and non-invasive test for clarification of abnormalities in cervical cancer screening. Just one further smear allows for a reliable result to be obtained within a few days.



Step 1:
Visit at gynaecologist

Step 2:
Cervical smear is sent to the lab

Step 3:
GynTect® is performed

Step 4:
Result is discussed with patient

An existing infection with **HPV** may lead to **genetic instability of the infected cells** and eventually cervical cancer. In the course of **carcinogenesis**, **changes (methylations)** occur **in the DNA**.

GynTect® recognises six areas of the human genome, which only exist methylated during the development of cancer cells. **GynTect®** thus identifies patients with malignant cervical cell changes.

Decision-making based on reliable results

With a **negative GynTect®** result, a **cancer diagnosis** could be **excluded** at the time of testing. If there was an abnormal Pap test result or HPV infection present prior to the test, it is recommended to observe them further.

If there is a **positive GynTect®** result, a **malignant precursor or** even **cancer** is **very likely**. Further steps such as diagnostics assisted by colposcopy and surgical therapies are recommended.

Based on available study data, **GynTect®** provides a clear indication of malignancy status in patients with abnormal Pap smear: In all previous studies, **GynTect®** was able to detect all cases of cervical cancer (sensitivity = 100 %).

GynTect® is rarely positive in patients with inconspicuous cytological findings (specificity = 96.6 %). Cancer develops via the histopathologically defined dysplasias CIN1, CIN2 and CIN3. **GynTect®** detection rates for these dysplasias increase continuously. This indicates a prognostic value of the **GynTect®** cancer markers.

Negative GynTect® result

Cervical cancer is very unlikely at the time of testing.

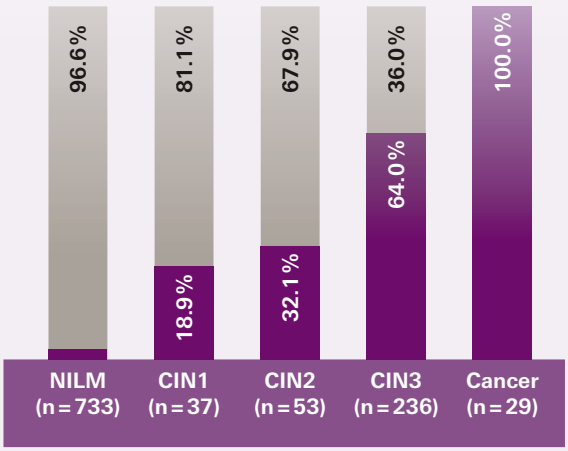
If there is a dysplasia, it is very unlikely to be malignant.

Positive GynTect® result

Cervical cancer or a malignant precursor is very likely.

Therapeutic action is recommended!

Study data GynTect®



Detection rate GynTect® (dark purple bar) depending on the clinical status of the patient

Confidence interval for confidence level = 95%:

NILM: 2.22–4.99 %
CIN1: 7.96–34.16 %
CIN2: 19.92%–46.32 %
CIN3: 57.5–70.11 %
Cancer: 88.06–100 %

Assay principle and workflow

The **GynTect®** assay principle is based on the detection of **DNA methylation** in human gene regions that occurs **specifically during carcinogenesis**. In the process of DNA methylation, methyl groups are added to the DNA. These are always cytosines located next to guanines (**CpG dinucleotides**).

The analysis of a patient sample comprises two steps:

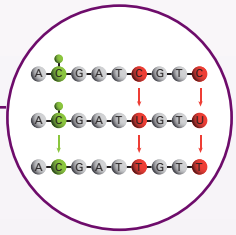
1. First, methylation is fixed by **bisulphite treatment**.
2. Subsequently, specific regions of the genome are analysed by **PCR** and an **evaluation** is carried out using common spreadsheet software.

Step 1

Patient sample:
Preparation

Hands-on time: 15 min

Sample collection:
STM™ (Qiagen) or
ThinPrep PreservCyt® (Hologic)

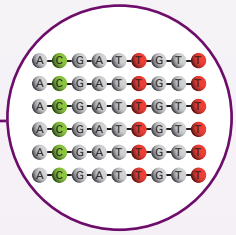


Bisulphite treatment:
Fixation of DNA methylation

Duration: 70 min
Hands-on time: 25 min

Bisulphite conversion using EpiTect® Fast Bisulfite Kit (Qiagen)

Step 2



Analytical PCR:
Detection of the DNA marker regions

Duration: 100 min
Hands-on time: 35 min

GynTect® PCR:
cobas® z 480 (Roche Diagnostics)

Data analysis:
Evaluation of the PCR result

Hands-on time: 30 min

Data analysis for GynTect® evaluation using a calculation software, e.g. Microsoft Excel

Only originally methylated DNA regions are amplified in the PCR. Therefore, this procedure is also called **methylation-specific PCR (MSP)**.

The **GynTect®** assay includes **several internal controls** to ensure a highly reliable and robust workflow. Moreover, positive and negative controls are included.