GynTect

oncgnostics
MOLECULAR CANCER DIAGNOSTICS

GynTect®

Epigenetic biomarkers for reliable cervical cancer diagnostics

CE-IVD-marked diagnostic test
developed by oncgnostics GmbH

GynTect® in clinical routine

Step 1: Visit at gynecologist

The patient has an abnormal Pap smear (Pap III, Pap IIID) and/or is tested HPV-positive: With a GynTect® result the gynecologist has a better option to assess the situation of the patient. GynTect® allows to distinguish between cervical lesions that require biopsy and eventually conization and those lesions that will regress with high probability.

Step 2: Smear collection and shipping

The gynecologist takes a cervical smear using the corresponding collection device and medium. The smear material may be shipped at room temperature by normal mail. You may obtain the corresponding collection devices through the diagnostic lab or through oncgnostics. The patient bears the costs for GynTect®, clarifies a possible coverage through her health insurance.

Step 3: Performance of GynTect®

The laboratory may run GynTect® within a work day. The result is then passed to the gynecologist.

Step 4: Clear decision

The gynecologist discusses the result with the patient. A negative GynTect® result indicates that at the time of test the patient has no severe lesion that may proceed to a carcinoma. Further observation of the abnormal Pap smear result/the HPV infection should be performed. In case of a positive GynTect® result a colposcopy with biopsy is recommended, which may lead to further invasive measures.

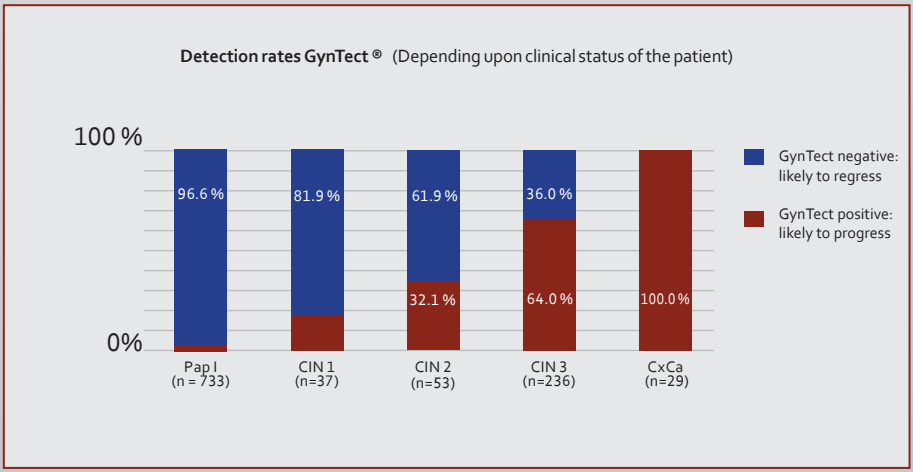
GynTect® clarifies abnormal screening results

Persistent infection with HPV may lead to genetic instability of the infected cells, and these cells may undergo a malignant transformation. During this process of carcinogenesis changes in the genetic material occur, especially enhanced methylation of certain DNA regions.

With GynTect® the methylation of six DNA regions in the human genetic material is detected. Methylation in these regions only occurs during cervical carcinogenesis. Thus, GynTect® allows to differentiate between patients with lesions that may heal, and those who have malignant lesions.

Trial results available for GynTect® suggest that the test allows a definitive judgement of the malignancy status of patients with abnormal Pap smear: in all studies performed to date, GynTect® allowed the detection of all cervical cancer cases (sensitivity = 100%). In cytologically inconspicuous patients GynTect® is only rarely false-positive (specificity = 96.6%). The GynTect® detection rate increases with the severity of the cervical lesions CIN1, CIN2 and CIN3 – this indicates that the GynTect® markers have prognostic potential.

Figure 1:



Clinical performance of GynTect®

The clinical performance of GynTect® was evaluated in several clinical trials using in total 1088 cervical scrapes collected for routine testing. Histopathology results were available for 32.6% of the samples: in 37 cases CIN1, in 53 cases CIN2, in 236 cases CIN3 and in 29 cases cervical carcinoma (CxCa) was diagnosed. 67.4% of all samples had a normal cytology finding (PAP I, NILM), thus no biopsy was taken.

GynTect® detected all cervical carcinomas. Only 3,4% of the samples with normal cytology (PAP I) were GynTect®-positive in the older age group and none in the younger group, which could significantly reduce unnecessary colposcopies. The clinical performance is depicted in Table 1. GynTect® showed high sensitivity and specificity for the detection of CIN3+ in HPV-positive women.
GynTect® performed less sensitive regarding the detection of CIN1 and CIN2. This finding has to be seen in the light that especially in younger women many CIN lesions regress spontaneously[1,2]. Therefore, future work may provide more information that a certain proportion of CIN3 cases may not need to be detected yet.

Based on the current data, GynTect® is suitable for triaging PAP-abnormal and/or HPV-positively tested women. Besides, it is intended as an aid in the diagnosis of cervical (pre)cancer.

Table 1: Clinical performance (CIN3+ and CIN2+)

	Sensitivity	Specifity	PPV	NPV
Performance CIN3+	78.6 %	90.1 %	67.9%	94.0%
Performance CIN2+	86.0 %	85.9 %	61.9%	95.8 %

[1] Trimble et al. 2005 Spontaneous regression of high-grade cervical dysplasia: effects of human papillomavirus type and HLA phenotype. Clin Cancer Res. 2005 Jul 1;11(13):4717-23.
[2] Ostör 1993 Natural history of cervical intraepithelial neoplasia: a critical review. Int J Gynecol Pathol. 1993 Apr;12(2):186-92.

GynTect® in cervical cancer screening

In cervical cancer screening GynTect® may take over where established methods have their limitations: Pap smear and HPV tests have led to a tremendous decrease of incidence and mortality due to cervical cancer. Both tests, however, only indicate that a cervical disease leading to cancer may be present. As a result repeated diagnostics and invasive measures are performed in the course of watchful waiting or therapy, which upon accurate diagnostics using GynTect® could be limited to the relevant cancer risk cases. Furthermore it would decrease the psychological burden for women in the clarification process. GynTect® clarifies early if a patient with abnormal Pap smear findings develops or already has cervical cancer.

Positive GynTect® result

» Development or presence of clinically relevant cervical lesion is highly probable.

» Further clarification, biopsy and eventually conization required.

Negative GynTect® result

» The presence of a clinically relevant cervical lesion at the time of test is highly unlikely; no invasive intervention required.

» Watchful waiting is recommended due to the initially abnormal Pap smear/positive HPV test result.

GynTect®: advantages for the gynecologist

» The patient receives an objective result.

» Referral to specialized consultancy in relevant cases only.

» Defined measures may be scheduled immediately, repeat diagnostics may be minimized.

» No change in the frequencies of visits.

GynTect®: advantages for the patient

» Short waiting time between screening result and clarification.

» Definitive result: unnecessary invasive interventions may be avoided.

» Clear diagnostic situation decreases psychological burden.

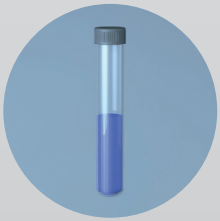
» No change in the regular gynecologist appointment.

GynTect® – assay principle and workflow

The GynTect® assay principle is based on the detection of DNA methylation of human marker gene regions. DNA methylation is a process during which methyl groups are added to the DNA, more specifically, to cytosines followed by guanines, so-called CpG dinucleotides.

The analysis of a patient sample comprises two steps. First, the methylation status of the human DNA in a cervical sample is "fixed" by a so-called bisulfite treatment. In the second step the bisulfite-converted DNA is analyzed in the regions of interest by applying several sensitive real-time PCR reactions. Using specific PCR primers, only the marker regions originally methylated in tumour DNA are selectively amplified, and a PCR product can be detected. Therefore, this procedure is called methylation-specific PCR (MSP).

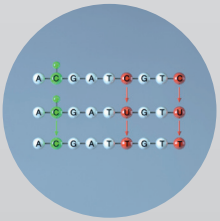
For a highly reliable workflow, the assay includes several internal sample quality control markers. Additionally, separate positive and negative control materials are provided with the kit.



Patient sample:
Direct
cell lysis

1

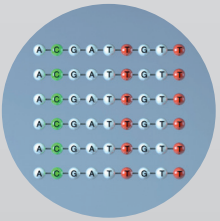
Duration: 30 min
Thereof hands-on time
5 – 15 min
Sample collection via STM™ (Qiagen) or ThinPrep PreservCyt® (Hologic)



Bisulfite treatment:
"Fixation" of
DNA methylation

2

Duration: 90 min
Thereof hands-on time
60 min
Bisulfite conversion with the EpiTect® Fast Bisulfite Kit (Qiagen).
Order via oncgnostics recommended.



Analytical PCR:
Detection of the
DNA marker regions

3

Duration: 130 min
Thereof hands-on time
10 – 30 min
GynTect® PCR: ABI 7500 real-time PCR System, Life Technologies; cobas Z480 Analyzer, Roche Diagnostics.

Data analysis:
Evaluation of the
PCR result

4

Hands-on time:
15 min
The algorithm if GynTect® is scored positive is applied using a calculation software such as Microsoft Excel.

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