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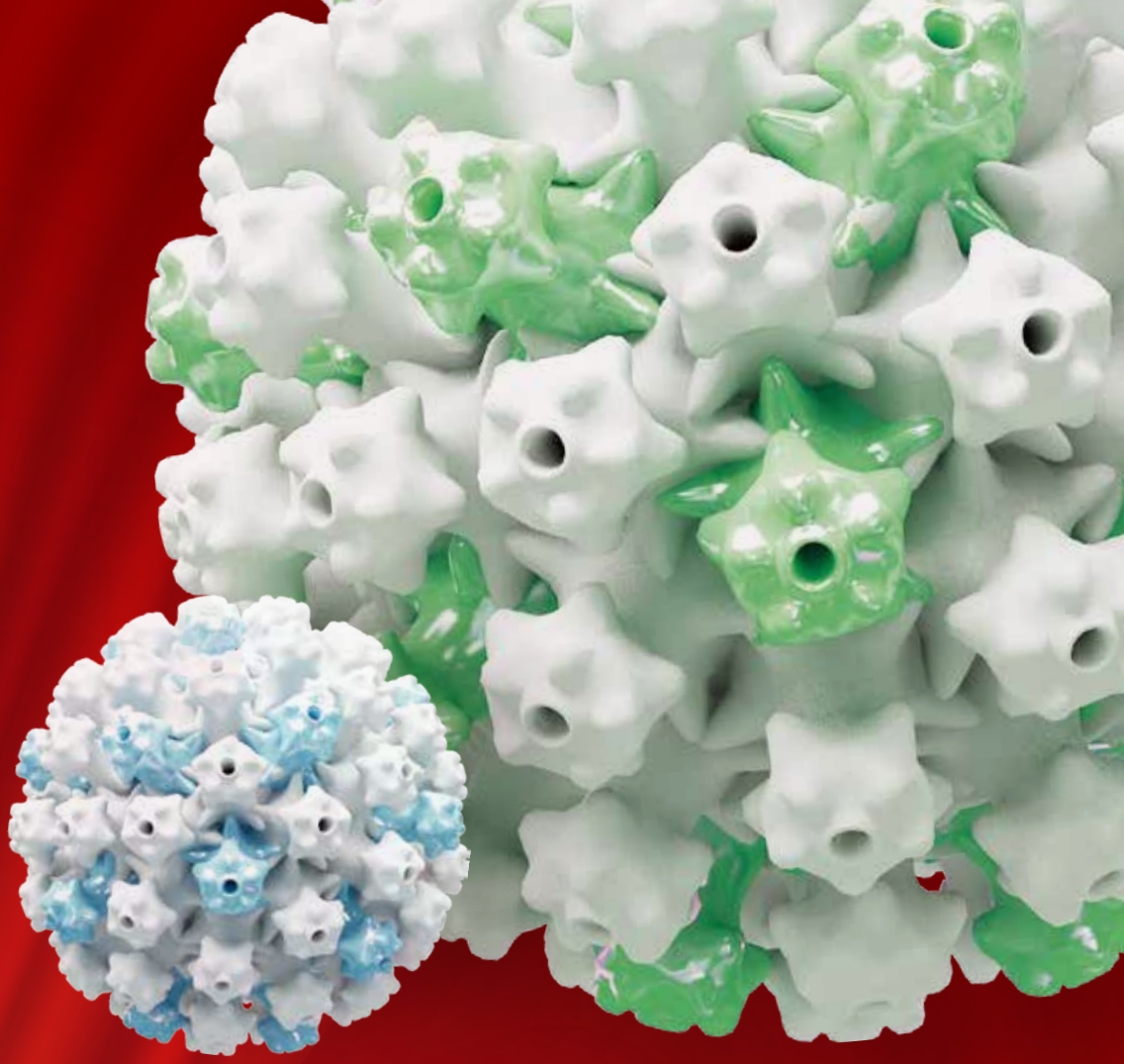


Anyplex™ II

HPV HR Detection

Screening of 14 high-risk HPVs with genotypes by real-time PCR

- **14 High-risk HPV genotypes :** 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

CE-IVD Marked

Superior

HIGH SENSITIVITY & SPECIFICITY

Multiplex real-time PCR with high sensitivity and specificity by utilization of DPO™ and TOCE™ technologies

Seegene

Anyplex™ II

REAL TIME PCR

CE-IVD Marked

HPV HR Detection

Human papillomavirus (HPV) has been identified as the leading cause of cervical cancer in women as well as a growing risk factor in oropharyngeal cancer. Although over 150 related HPV strains have been identified, only a subset of whole HPV was identified as major risk factors for cervical cancer. While HPV16 and HPV18 have clearly been implicated as causative agents, the influence of other high-risk HPV genotypes on the severity and progression of cervical cancer (e.g., viral load; persistence and clearance rates of virus over time) have been reported. In particular, the co-infection of high-risk HPV strains has now been identified as risk factors for increased co-morbidity and disease progression. Outcome-based clinical studies in regard to HPV vaccines have demonstrated the advantages of long-term monitoring of infected HPVs in association with persistent efficacy and cross-genotype protection. Unfortunately, current HPV diagnostic tools are restricted to use for the detection, identification and quantitation of multiple HPV genotypes.

Anyplex™ II HPV HR Detection is specifically designed for simultaneous detection of 14 high-risk HPV genotypes including HPV16 and HPV18 which contributes to cervical cancer. Anyplex™ II HPV HR Detection is a fast and reliable solution for the detection of HPV infection, providing a much-needed multiplex diagnostic solution to assist in prognosis and long-term patient outcome.

Analytes

- **14 High-risk HPV genotypes :**
  16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68
- Internal Control

Specimens

- Cervical swab
- Liquid based cytology specimen
  (e.g., ThinPrep® and Surepath™)

Seegene's automated platform (CE-IVD Marked)

- **Automated Extraction & PCR setup**
  Seegene NIMBUS / Seegene STARlet
- **Automated Pre-analytic System**
  VCMS (Vial Cap Management System)
- **Real-time PCR**
  CFX96™ Dx

Seegene's VCMS*

*STARlet IVD with VCMS (vial cap management system) automates pre-analytic steps for primary vial, ThinPrep® and Surepath™, such as de-capping, aliquot and re-capping.

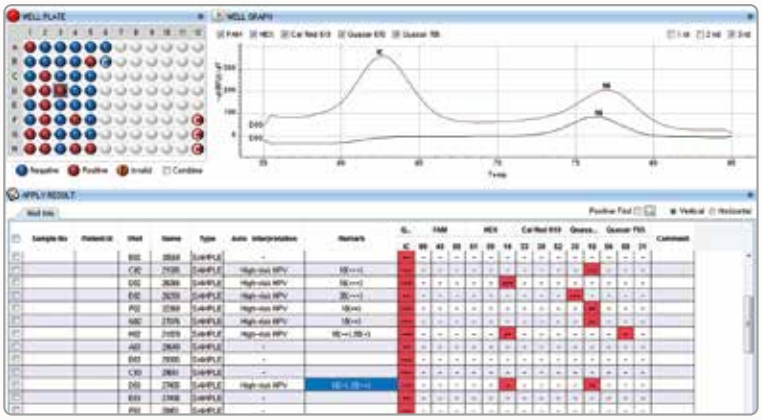
Features

a. Screening of 14 high-risk HPV genotypes in a single reaction
b. Multiplex real-time PCR for reliable results by utilization of DPO™ and TOCE™ technologies
c. Amenable to automated sample handling and assay systems
d. Utilization of the UDG system to prevent carry-over contamination
e. Endogenous Internal Control for assay validity
f. Convenient data interpretation by the Seegene Viewer

Seegene Viewer

Quick and easy data analysis & interpretation

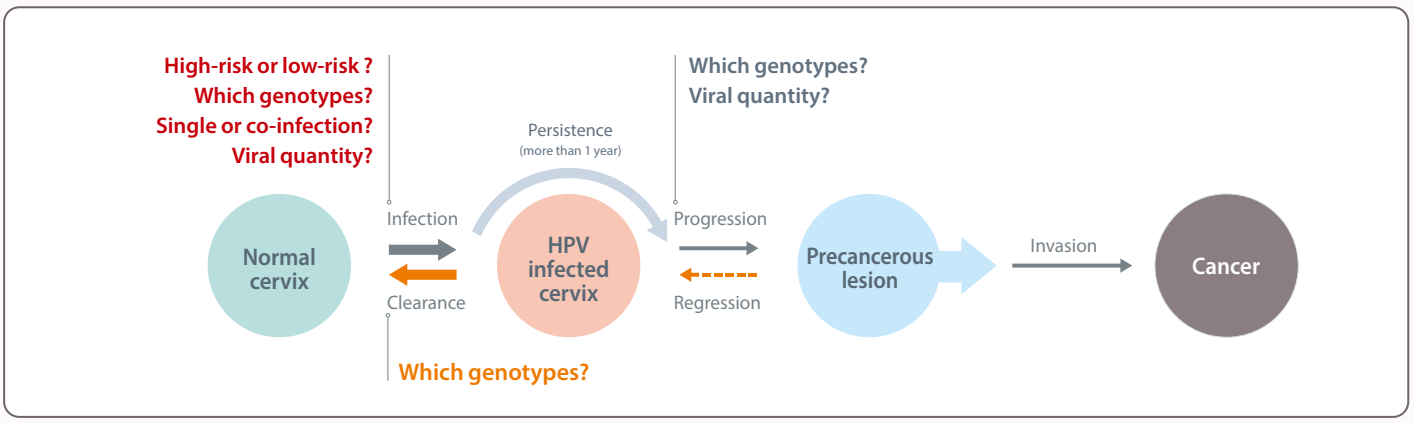
a. Interface specialized for multiplex testing
b. Interlocked with LIS
c. Patient information input via barcode scanning system or LIS system
d. Printable in various formats
e. Downloadable results in a CSV file
f. Convenient read out for quantitative analysis result



Purpose of HPV DNA Test

HPV DNA tests should provide maximum information (genotype, co-infection, quantitative result) about the infection to facilitate the clinical follow up of the patient.

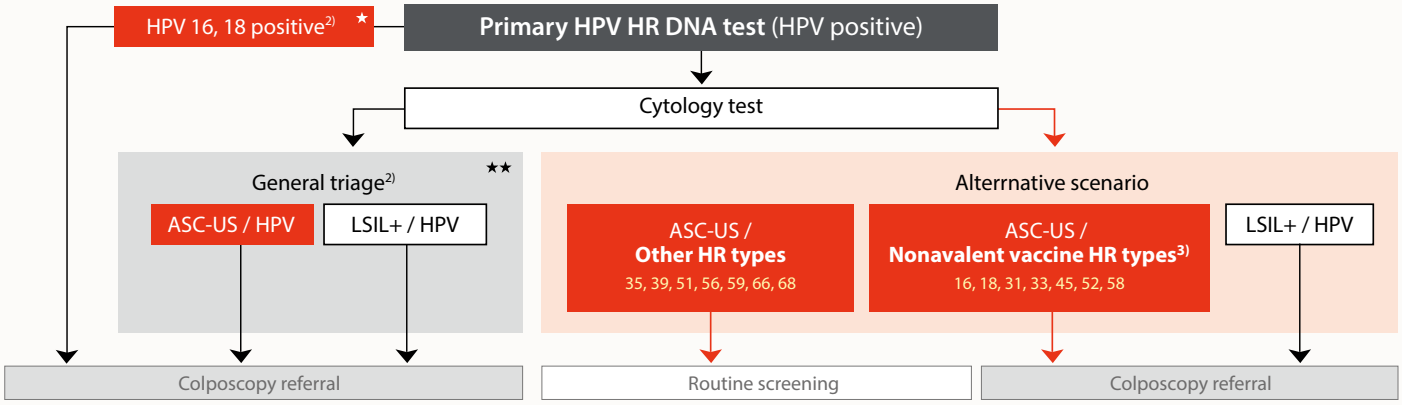
Natural history of cervical cancer [1)]



1) Shiffman M *et al.* The promise of global cervical cancer prevention. *N Engl J Med* (2005) **353**(20) : 2101-4

Optimizing HPV-based primary screening program

General primary HPV screening with cytology triage vs. Alternative triage based on the HPV genotype



General example of triage algorithm for primary HPV screening[2)]

1. HPV genotyping for HPV16, HPV18 and cytology in US
2. HPV positive and cytology in Europe
: Women with ASC-US or higher are referred to colposcopy

A new screening approach is required[2)]

1. **Vaccination effect** : An increase of HPV vaccination coverage is likely to leading lower prevalence
2. **Low specificity** : Referring HPV+ women with ASC-US to colposcopy is not efficient, because the large number of women do not have precancer or anything related to cervical cancer
3. **Management trend** : Risk thresholds* rather than individual results

★ The primary HPV screening program in USA.

★★ The primary HPV screening program in the Netherlands.

2) *Wentzensen N. et al. Triage of HPV positive women in cervical cancer screening (2016)*

3) *A nonavalent vaccine targets seven carcinogenic types (HPV16/18/31/33/45/52/58) that contribute to 90% of cervical cancer cases*

For primary HPV screening,
Anyplex™ II HPV HR detection can help

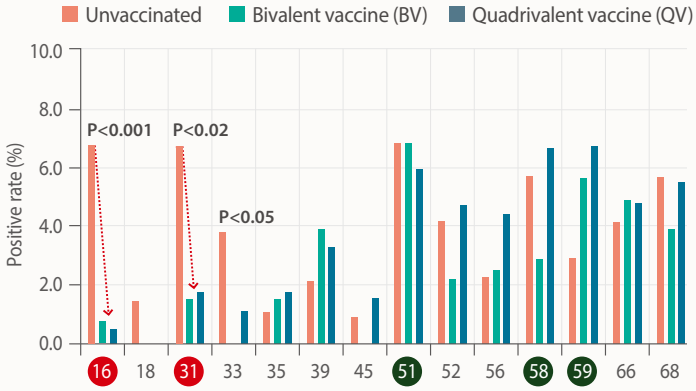
1. Setting risk threshold
2. Considering new alternative scenario
3. Proposing better algorithm

through identifying major high-risk HPV including vaccine-covered type

Effective tool for national cervical cancer screening in post-vaccination era

The HPV vaccination had a substantial impact on genotype distribution.

1. Monitoring infection dynamics such as type replacement or unmasking in a vaccinated population[5)]



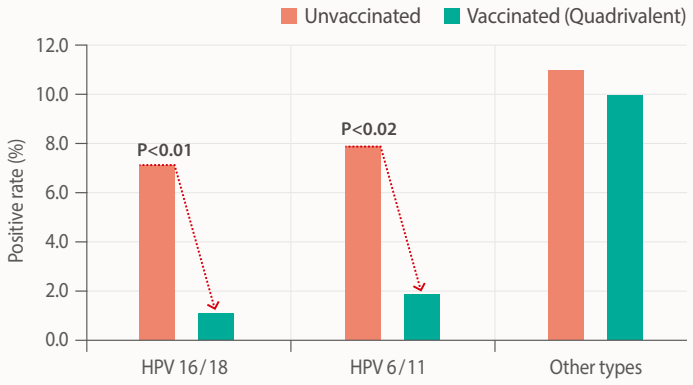
18~29 Yrs women (participant no.: 401)	Unvaccinated	Vaccinated
HPV positive rate	53.5%	46.4%
		42% (BV), 49% (QV)
Most prevalent type	16, 31, 51	51, 58, 59

5) *Latsuzbaia et al. Caner Epider. (2019) 63:101593*

Study 1. HPV prevalence and vaccine efficacy 8 years following the implementation of the vaccination program in Luxembourg

The overall prevalence of HPV showed a very similar rate between the two groups, however, the type distribution was dramatically changed in certain types covered by HPV vaccine and other types assuming cross-protection. For instance, HPV 16, 31, and 33 were significantly decreased in vaccinated women, but not in the unvaccinated group. Instead, other types such as HPV 51, 58, and 59 were found as the most frequent types in vaccinated women.

2. Measuring the efficacy affecting the vaccine policies and strategies[6)]



18~31 Yrs women (participant no.: 409)	Unvaccinated	Vaccinated
HPV 16/18 positive rate	7.2%	1.1%
HPV 6/11 positive rate	8.3%	2.1%
Other HR-HPV prevalent type	11.2%	10.3%

6) *Jeannot et al. Int. J. Environ. Res. Public Health (2018) 15:1447*

Study 2. Prevalence of vaccine type HPV in vaccinated and non-vaccinated women in Switzerland

The prevalence of four types, HPV6/11 and HPV 16/18, covered by the quadrivalent vaccine was significantly lower in vaccinated women, whereas cross-protection was not observed in this study.

The impact of Seegene's HPV assay in the post-vaccination era:

- Monitoring changes of HPV types in a vaccinated population
- Evaluating the prevalence of HPV vaccine types
- Measuring the efficacy and cross-protection of vaccine

Anyplex™ Ⅱ HPV HR Detection is

clinically validated assay for primary cervical cancer screening[1)]

Anyplex™ Ⅱ HPV HR Detection meets the international consensus validation metrics for HPV DNA tests for cervical cancer screening[1) 2)]

Clinical sensitivity & specificity of Anyplex™ Ⅱ HPV HR Detection

Category		Clinical sensitivity	Clinical specificity
Test population & number		60 samples with ≥ CIN2	816 samples with < CIN2
Result	Reference Test (GP5+/6+-PCR)	98.3% (59/60)	94.1% (768/816)
	Anyplex™ Ⅱ HPV HR	98.3% (59/60)	93.6% (764/816)
Relative analysis to reference test		100%	99.5%
Requirements		≥ 90%	≥ 98%

▶ **The clinical sensitivity and specificity for CIN2+ of Anyplex™Ⅱ HPV HR Detection were non-inferior to those of GP5+/6+-PCR.**

Inter-lab agreement & intra-lab reproducibility of Anyplex™ Ⅱ HPV HR Detection

Category		Intra-laboratory reproducibility	Inter-laboratory agreement
Test population & number		505 samples	505 samples
Result	Agreement (95% CI)	96.0% (94.3~97.4)	96.8% (95.3~98.1)
	kappa value	0.91	0.93
Requirements	Lower 95% CI	≥ 87%	≥ 87%
	kappa value	≥ 0.5	≥ 0.5

▶ **Anyplex™Ⅱ HPV HR Detection displayed sufficient intra-laboratory reproducibility and inter-laboratory agreement.**

1) Hesselink AT *et al*. (2016) *Journal of Clinical Virology* 76:36-39
2) Meijer CJLM *et al*. (2009) *Int J Cancer* 124(3):516~20

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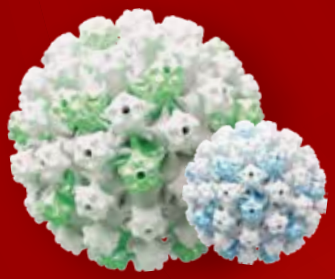

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Ordering Information

Not Available for Sale in the United States

Product	Package Volume	Cat. No.
Anyplex™ II HPV HR Detection	100 rxns	HP7E00X
Anyplex™ II HPV28 Detection	100 rxns	HP7S00X
Instrument	**Type**	**Cat. No.**
CFX96™ Dx	Real-time PCR _ Optical Reaction Module	1845097-IVD
	Real-time PCR _ Thermal Cycler	1841000-IVD
Seegene NIMBUS	Automated extraction & PCR Setup	65415-03
Seegene STARlet	Automated extraction & PCR Setup	67930-03
VCMS (Vial Cap Management System)	Automated Pre-analytic System	6600532-01
STARMag 96 X 4 Universal Cartridge kit	Nucleic acids extraction reagent	744800.4.UC384

Seegene

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