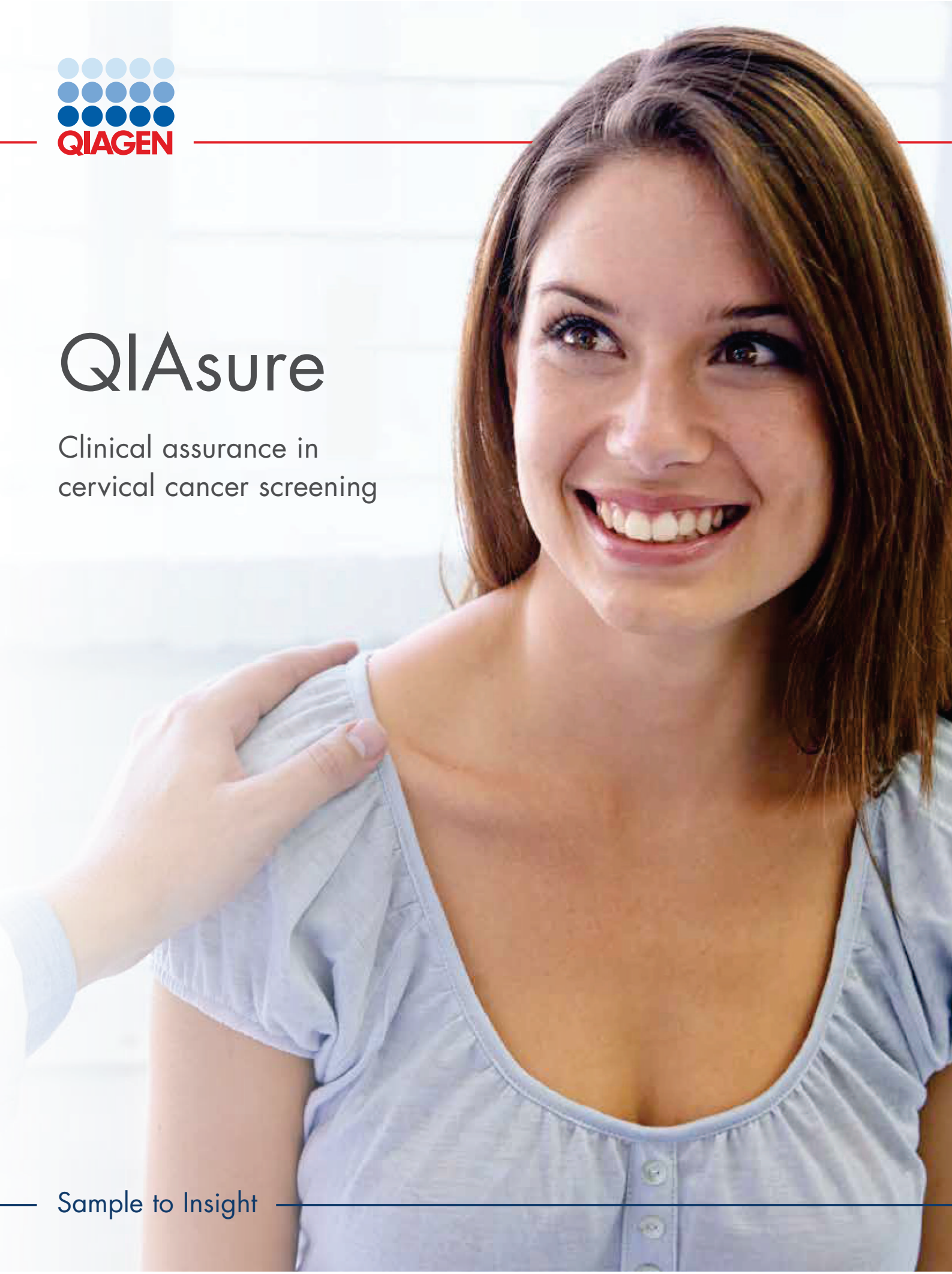
QIAGEN

QIAsure

Clinical assurance in
cervical cancer screening



Sample to Insight

QIAsure: A new cervical cancer screening test

QIAGEN, the developer of the gold-standard HPV screening test *digene*® HC2 High-Risk HPV DNA Test®, brings to market the QIAsure Methylation Test—a new cervical cancer screening test that gives clinicians molecular insight into whether an HPV infection is actively transforming cervical cells into cancer.

The need for clinical assurance in cervical cancer screening

Adoption of HPV testing into cervical screening has created the need for more effective ways to manage patients with a positive HPV test or abnormal cytology. High-risk HPV (hrHPV) is the cause of cervical cancer. However, only 10% of women with hrHPV will go on to develop precancer and cancer (1). The current clinical focus on hrHPV testing and genotyping lets clinicians know whether a patient *could* develop cervical cancer; however hrHPV infection is a risk factor, not an indicator of cervical cancer. Further testing is needed to identify patients who need immediate follow-up and treatment versus close surveillance.

QIAsure provides an effective triage test in cervical screening to fulfill the need for more actionable molecular insight into whether a patient has cervical precancer or cancer.

What is QIAsure?

QIAsure is a quantitative methylation specific PCR (qMSP) test that lets clinicians see what's happening at a molecular level so they can determine whether a hrHPV positive patient is at short-term risk of developing cervical cancer. QIAsure detects the presence of biomarkers associated with cervical carcinoma and advanced transforming cervical intraepithelial neoplasia (CIN), to objectively discern passive HPV infections from ones that need immediate attention.

QIAsure can be used to triage a positive hrHPV test on the same specimen used for the HPV test or liquid-based cytology. It can also be used as a confirmatory test to an atypical squamous cells of undetermined significance (ASC-US) cytology result. QIAsure looks for methylation of the host cell genes *FAM19A4* and *miR124-2* in the cervical cells. Methylation of these genes indicates carcinogenic cell transformation and high short-term risk of developing cervical cancer; absence of methylation indicates low short-term risk of developing cervical cancer.

With these molecular insights, QIAsure can eliminate overtreatment by identifying women who need immediate treatment and those who need monitoring.

How does it work?

QIAsure uses DNA methylation analysis to look for biomarkers in patient specimens. The test can be performed on the same sample that you send to the lab for HPV testing and/or liquid based cytology (LBC). Abnormal patterns of DNA methylation have been implicated in various cancers, including cervical cancer where promoter hypermethylation of the tumor suppressor genes *FAM19A4* and/or *miR124-2* has been reported (2–9). QIAsure measures the methylation status of these genes in a multiplex qMSP test. Hypermethylation of these genes indicates a presence of advanced transforming CIN and a high short-term risk of developing cervical cancer; absence of hypermethylation indicates a low short-term risk of developing cervical cancer (3–9).

With the results, clinicians can protect their patient's reproductive health and be confident in recommendations for surveillance or treatment.

"QIAsure is an important advance for women's health. When a woman screens positive for HPV, or cytology shows abnormal cells, she is at risk of developing cervical cancer. The QIAsure test is the next logical step to pin it down. This highly sensitive, specific molecular test identifies epigenetic changes in cervical cells and enables the physician to assess whether the HPV infection is progressing toward cancer – a valuable insight that provides timely reassurance and guidance to treatment for each individual patient."

– Tadd S. Lazarus, M.D., Chief Medical Officer of QIAGEN

Key benefits:

Accurate

QIAsure is a quantitative methylation-specific PCR test with high sensitivity and 100% accuracy in detecting biomarkers associated with cervical carcinoma in patients.

Objective

QIAsure provides object results on whether your patient has a hrHPV infection that is actively transforming cervical cells into cancer.

Simple

Sample collection is streamlined, so that QIAsure can be performed on the same sample as the primary screening HPV test.

Economical

By helping to reduce unnecessary colposcopies and cervical treatments, QIAsure helps save time and money for both you and your patients.

Convenient

QIAsure can be performed on self-samples collected by the patient without a speculum exam, making it easy and convenient to be tested early and often.

Reassuring

QIAsure provides you and your patients who test negative with peace of mind that they may be at low short-term risk of cervical cancer.

Transforming information into insight

QIAsure transforms information into insight through DNA methylation analysis that objectively determines the presence of biomarkers associated with cervical precancer and cancer. QIAsure can be performed in the PCR lab through industry-standard methods of sample prep/extraction and automation platforms for analysis (clinically validated for Rotor-Gene® Q MDx instrument). Using a qMSP test, QIAsure can detect the presence of carcinogenic cervical cells and advanced transforming CIN lesions. QIAsure has been clinically proven to detect the transformation of cervical cells and advanced transforming CIN 2/3 lesions, even in patients with normal cytology.

Clinical examples

Sophie (age 32) undergoes primary screening for HPV and discovers she is at risk for cervical cancer due to detection of hrHPV. QIAsure is performed on the same sample to detect the presence of precancer or cancer. QIAsure produces a negative result and the clinician schedules a six-month follow-up appointment. QIAsure separates transforming hrHPV infections from non-transforming infections so that Sophie can be confident she is safe from cancer.

Veronica (age 30) has a high-risk HPV infection and returns for her six-month follow-up appointment. A pap smear discovers abnormal cytology and she undergoes colposcopy to look for CIN lesions. CIN 1 and 2 are present; however the level of short-term risk is unclear since there is no molecular insight into whether the lesions are actively transforming into cancer or could subside on their own. The patient and clinician discuss options for treatment since treatment could inhibit Veronica's ability to carry a pregnancy to term. QIAsure is performed providing the clinician more insight into what's happening at a molecular level and providing critical information to make the best clinical decision.

Emma (age 34) has hrHPV, but normal cytology. A confirmatory QIAsure test is performed and produces a positive result, indicating the presence of transforming precancer. Emma is sent straight to colposcopy and treated for CIN 3. If she hadn't had the QIAsure test, she would have had to wait 6 months before being re-tested, putting her life and reproductive health at risk. QIAsure identifies transforming hrHPV infections that can be missed by cytology and genotyping so that Emma is safe from dangerous precancer that could have rapidly progressed to cancer.

Objective clinical assurance

QIAsure delivers objective assurance that women are safe from cervical cancer following a positive hrHPV result or an abnormal cytology result. The high sensitivity and specificity of QIAsure offers reassurance for absence of cervical cancer in test negative women; a positive test identifies women who need immediate treatment. It can separate out patients with hrHPV infections that are transforming into cancer from patients who may have low short-term risk of developing cancer. By including this test as part of the clinical assessment, QIAsure can help guide treatment decisions and prevent women with non-transforming infections from receiving unnecessary treatments.

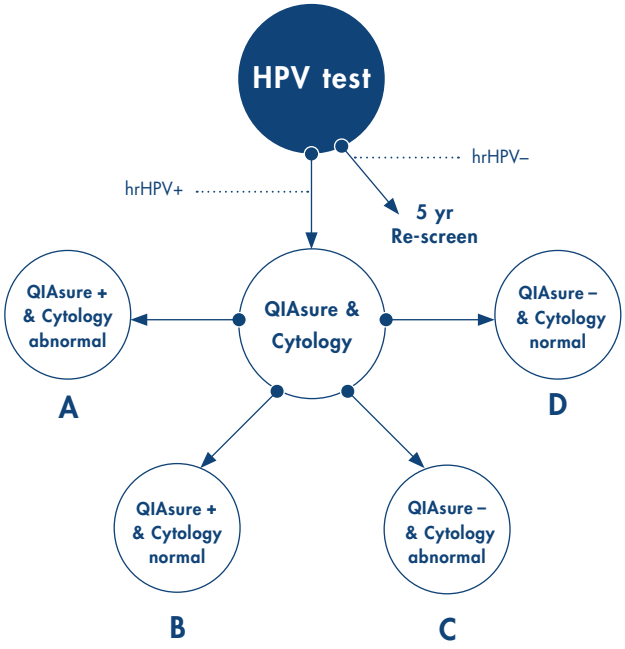
QIAsure has been developed as a cervical cancer screening triage test to fit into current cervical screening algorithms. The flowchart diagram on the top right follows HPV primary screening. The flowchart diagram on the bottom right follows cytology primary screening.

Frequently Asked Questions about QIAsure

What sample type is best for QIAsure?

QIAsure has equal performance on self-collected and phsyician collected samples. The same sample used for high-risk HPV testing or liquid-based cytology may be used for QIAsure.

HPV Primary Screening



Cytology Primary Screening

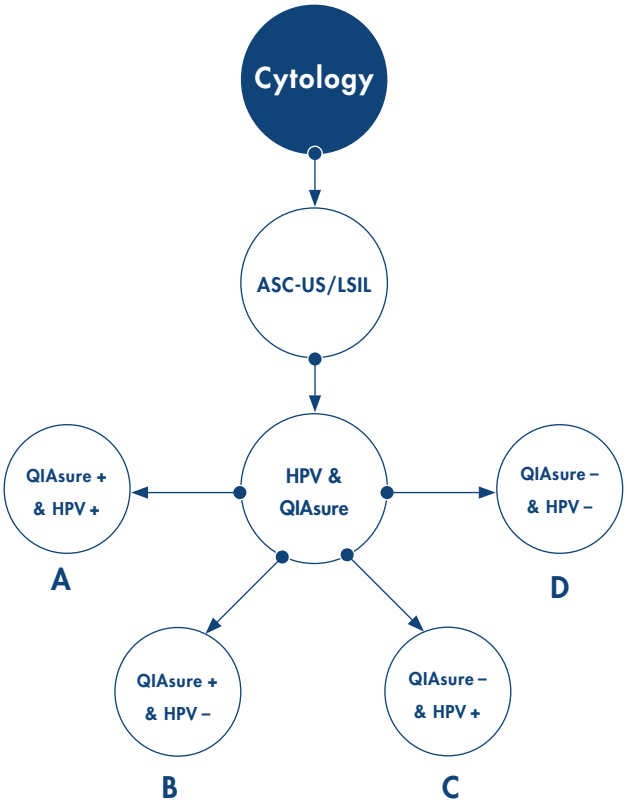


Figure 1. Screening flowcharts.
Proposed guidelines for primary screening scenarios

A. High risk of advanced transforming CIN, refer to colposcopy.

B. High risk of advanced transforming CIN, refer to colposcopy.

C. Low risk of advanced transforming CIN, refer to colposcopy—be conservative in treatment vs. surveillance decision.

D. Low risk of advanced transforming CIN, recommend increased surveillance.

How accurate is QIAsure?

In clinical trials, QIAsure testing was performed on physician-collected cervical specimens from 258 hrHPV-positive women including 117 without evidence of CIN 2 or worse after 18 months follow-up (CIN≤1), 42 with CIN 2, 30 with CIN 3, 50 with squamous cell carcinoma, and 10 with adenocarcinoma. QIAsure detected 100% of carcinomas (squamous cell carcinoma and adenocarcinoma) in these samples, but varied in detection of other grades of CIN, from 88.9% in CIN 3+ to lower sensitivity for CIN 1/2. Transforming CIN (CIN 2/3) can be divided into early and advanced transforming CIN based on the level of genetic and epigenetic alterations, which is measured in this test by analysis of *FAM19A4* and *miR124-2* hypermethylation. This explains why QIAsure had a sensitivity of 88.9% for CIN 3 and 52.4% for CIN 2. QIAsure identifies patients with advanced transforming CIN for immediate treatment and allows those who have early transforming CIN to undergo intensified surveillance.

Does QIAsure replace the need for cytology?

QIAsure is not intended to replace cytology. When used to triage a positive hrHPV primary screening test result, QIAsure gives complementary information when combined with cytology. When used to triage a cytology primary screening finding of ASCUS, QIAsure can be combined with hrHPV testing to give complimentary information. Unlike cytology, *FAM19A4/miR124-2* methylation analysis on hrHPV-positive cervical specimens detects 100% of biomarkers associated with cervical cancer, and identifies advanced transforming CIN2/3.

Peace of mind for your patients

QIAsure bridges a gap in cervical screening as an accurate and objective triage test that can be performed on the same sample used for hrHPV testing or liquid-based cytology. It is a unique and effective method to see beyond HPV and gain molecular insights into whether a hrHPV infection is actively transforming into cervical cancer. It provides clinicians with a new way to detect the presence of cervical precancer and make informed decisions about follow-up treatment. Moreover, QIAsure provides peace of mind for patients so they can live their lives safe, confident, and sure of their reproductive health.

QIAGEN and cervical cancer prevention

QIAGEN is a worldwide leader in innovative Sample to Insight® solutions for molecular diagnostics, applied testing, advanced genomics, and clinical and academic research.

Since the launch of the *digene* HPV Test in 1999, QIAGEN has been at the forefront of advanced HPV screening and cervical cancer prevention. Considered the gold standard for HPV testing, the *digene* HPV Test uses advanced molecular technology to provide a highly accurate means of identifying women at risk for cervical cancer. For almost 20 years, clinicians around the world have used the *digene* HPV Test to routinely screen more than 100 million women for the presence of HPV. QIAGEN is deeply committed to helping women in developing nations around the world gain access to essential cervical cancer screening through its QIAGEN*cares* and *care*HPV® initiatives.

QIAGEN is excited to bring its newest Women's Health solution to market—QIAsure, a qMSP triage test for objective detection of cervical precancer and cancer.

Ordering Information

Product	Content	Cat no.
QIAsure Methylation Test	For 72 reactions: 2 Master Mixes, 2 Calibrators.	616014
Related Products		
Rotor-Gene® Q MDx 5plex HRM System	Real-time PCR cycler and High Resolution Melt analyzer with 5 channels (green, yellow, orange, red, crimson) plus HRM channel, laptop computer, software, accessories: includes 1-year warranty on parts and labor, installation and training	9002033
Rotor-Gene Q MDx 5plex HRM Platform	Real-time PCR cycler and High Resolution Melt analyzer with 5 channels (green, yellow, orange, red, crimson) plus HRM channel, laptop computer, software, accessories: includes 1-year warranty on parts and labor, installation and training not included	9002032
Rotor-Gene AssayManager®	Software for routine testing in combination with the Rotor-Gene Q and QIAsymphony® RGQ instruments; single license software for installation on one computer	9022739

For more information about QIAsure testing, visit **www.qiagen.com/qiasure**.

References

1. Molano, M., et al. (2003). Am. J. Epidemiol. **158**, 486–94.
2. Wilting, S.M., et al. (2010). Mol. Cancer **9**, 167.
3. De Strooper, L.M., et al., (2014). Cancer Prev. Res. **7**, 1251–7.
4. De Strooper, L.M., et al. (2014). J. Clin. Pathol. **67**, 1067–71.
5. De Strooper, L.M., et al. (2016). Int. J. Cancer **138**, 992–1002.
6. De Strooper, L.M., et al. (2016). Gynecol. Oncol. **14**, 341–7.
7. Bierkens, M. et al. (2013). Int. J. Cancer **133**, 1293–9.
8. Luttmer, R., et al. (2015). Int. J. Cancer **138**,992–1002.
9. Steenbergen, R. D. et al. (2014). Nature Rev. **14**, 395–405.