

# Non-invasive diagnosis of urinary bladder cancer

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<b>Registration date</b> 04/09/2020	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 04/05/2023	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Urothelial cancer (cancer in the bladder, ureter or renal pelvis) is amongst the most common malignancies in the world. The disease mainly affects the elderly, while it is uncommon among those younger than 50 years of age, with a median age of 73 years at diagnosis. About three quarters of patients diagnosed with urothelial cancer (UC) are men.

The most common symptom of UC is macroscopic haematuria (visible blood in the urine). According to clinical guidelines, macroscopic haematuria should be investigated with cystoscopy and computed tomography with urographic imaging (CT urography) of the upper urinary tract (ureter and renal pelvis). In Sweden, a standardised care pathway has been in effect since 2015 which mandates this investigation for all patients older than 50 years of age with macroscopic haematuria, and which should be completed within one week. More than 90 % of UC is located in the bladder (bladder cancer), with about 2500 new cases in Sweden annually, most of which are diagnosed with cystoscopy.

Among patients investigated in such a standardised care pathway, 8-10 % are diagnosed with UC. Both cystoscopy and radiologic imaging of all patients with macroscopic haematuria are very resource-intensive, leading to delays completing the investigations beyond the mandated week. In addition, cystoscopy is an invasive procedure with significant discomfort, and which leads to infections in up to 5 % of patients. It is therefore desirable to develop a non-invasive assay to better select patients for whom cystoscopy can be avoided, and thus be able to concentrate resources on the patients who are more likely to need timely investigations.

Non-invasive tests have been studied previously. The first was urine cytology, which shown however to have a high variability between those assessing the results and low sensitivity, especially for low-grade tumours. UroVysion was developed as an adjunct to cytology and is a fluorescence in-situ hybridisation (FISH) analysis of urine cytology, which detects specific genetic amplifications in urothelial cells. However the sensitivity of this test is still too low to be used to exclude further investigations, and it still suffers from a high variability.

Recently, newer mRNA and epigenetic-based assays have been reported and made commercially available. Xpert Bladder Cancer Detection is an assay based on levels of specific mRNA in urine,

which are elevated in UC. It has reported a very high sensitivity, but only where data has been assessed retrospectively after a diagnosis of UC. The result is given as a risk of cancer so that the threshold for further action can be modified depending on the clinical setting.

CT urography, which is the clinical standard used to detect urothelial cancer in the upper urinary tract, can also visualise urinary bladder cancer. It has previously been shown that by timing the contrast phases appropriately, bladder cancer can be detected with high sensitivity without performing more series or using a higher radiation dose. This protocol is therefore currently in clinical use at most centres. However, the results have not been validated outside the initial investigation centre.

The aims of this project are therefore to evaluate the Xpert Bladder Cancer Detection test and CT urography, separately and combined, in a prospective study of patients investigated in a standardised care pathway.

Who can participate?

All patients referred for evaluation of macroscopic haematuria according to the standardised care pathway at participating centres will be offered participation.

What does the study involve?

Prior to cystoscopy participants will give a urine sample and fill out a questionnaire regarding their symptoms. Participants will undergo cystoscopy (A thin camera inserted into the urethra) and CT urography (a scan of the pelvis). Participants with signs of, or suspected signs of, urothelial cancer from these tests will have the urine sample analysed with GeneXpert Bladder Cancer Detection. Subjects with negative findings of urothelial cancer will be randomised for analysis or not. The outcome of investigations for urothelial malignancy up to one year after enrolment will be collected retrospectively from medical records.

What are the possible benefits and risks of participating?

The participants and clinical physicians will be blinded to the results of the urine analysis, so participants will not themselves have any benefits, but there are no physical risks associated with participation.

Where is the study run from?

The Department of Urology, Sahlgrenska University Hospital (Sweden), in collaboration with the Department of Surgery, NU-sjukvården (Sweden)

When is the study starting and how long is it expected to run for?

From September 2019 to January 2024

Who is funding the study?

Grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (ALFGBG-873181), and from the Swedish Society of Medicine (SLS-890771)

Who is the main contact?

Dr Henrik Kjölhede

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## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Henrik Kjölhede

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**Contact details**

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**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number****ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

Nil known

**Study information****Scientific Title**

Non-invasive diagnosis of urothelial carcinoma with urinary biomarkers and imaging after macroscopic haematuria

**Study objectives**

Urine analysis using GeneXpert Bladder Cancer Detection and/or CT urography can be used to select patients with macroscopic haematuria, for whom the risk of underlying urothelial malignancy is so low that cystoscopy is not needed.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 11/12/2019, Swedish Ethical Review Authority (Box 2110, 750 02 Uppsala; +46 10-4750800; [registrator@etikprovning.se](mailto:registrator@etikprovning.se)), ref: 2019-05582

## **Study design**

Prospective observational case-control single-centre study

## **Primary study design**

Observational

## **Secondary study design**

Case-control study

## **Study setting(s)**

Hospital

## **Study type(s)**

Diagnostic

## **Participant information sheet**

Only available for patients at participating centres

## **Health condition(s) or problem(s) studied**

Diagnostic workup in patients with macroscopic haematuria

## **Interventions**

Patients undergoing diagnostic workup according to a standardised care pathway for macroscopic haematuria will leave urine sample prior to cystoscopy. For the participants where cystoscopy detects a suspected urinary bladder cancer (expected 8% of all included participants) and a random sample of 1 in 15 with normal cystoscopy, GeneXpert Bladder Cancer Detection analysis will be performed. All participants will also undergo a computed tomography urography, including an image sequence with contrast in late arterial phase, according to the standardised care pathway.

## **Intervention Type**

Other

## **Primary outcome measure**

Diagnosis of urinary bladder cancer within one year of enrolment collected retrospectively from medical records at 1 year after enrolment

## **Secondary outcome measures**

There are no secondary outcome measures

## **Overall study start date**

01/08/2019

## **Completion date**

01/01/2024

# **Eligibility**

## **Key inclusion criteria**

1. Aged  $\geq 50$  years
2. Referred to participating centres for evaluation of macroscopic haematuria according to standardised care pathway
3. Able to give signed informed consent

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

2000

**Total final enrolment**

1516

**Key exclusion criteria**

1. History of urothelial carcinoma
2. Unable to give voided urine sample/has urine catheter

**Date of first enrolment**

09/09/2020

**Date of final enrolment**

31/12/2022

**Locations****Countries of recruitment**

Sweden

**Study participating centre**

Kirurgmottagning Uddevalla Sjukhus

Fjällvägen 9

Uddevalla

Sweden

45180

**Sponsor information**

**Organisation**

Västra Götaland Regional Council

**Sponsor details**

Regionens hus  
Vänersborg  
Sweden  
462 80  
+46 10 441 00 00  
gothia.forum@vgregion.se

**Sponsor type**

Government

**Website**

<https://www.vgregion.se>

**ROR**

<https://ror.org/00a4x6777>

**Funder(s)****Funder type**

Government

**Funder Name**

Svenska Läkaresällskapet

**Alternative Name(s)**

Swedish Society of Medicine, Swedish Medical Society, SLS

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

Sweden

**Funder Name**

ALF-agreement: Swedish state under the agreement between the Swedish government and the county councils

# Results and Publications

## Publication and dissemination plan

Planned publication in peer-reviewed journal

## Intention to publish date

01/09/2025

## Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Henrik Kjölhede, henrik.kjolhede@vgregion.se, on publication of results and for 10 years, for research purposes by researchers in public institutions within the European Union, in anonymised form.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>		04/09/2020	08/09/2020	No	No