ISRCTN25823942 https://doi.org/10.1186/ISRCTN25823942

Haematuria Biomarker Study (HaBio)

Submission date 16/11/2012	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/01/2013	**Overall study status** Completed	
Last Edited 31/10/2022	**Condition category** Signs and Symptoms	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-study-help-develop-test-find-causes-blood-in-urine-habio

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
A study investigating the use of protein measurements as diagnostic tests for the causes of blood in the urine

Acronym
HaBio

Study objectives
Collectives of biomarkers aligned with demographics and/or clinical variables can predict bladder cancer in haematuria patients with 90% accuracy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Office of Research Ethics Committee Northern Ireland, 23/12/2012, ref: 11/NI/0164

Study design
Case control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Haematuria

Interventions
At the clinic the Research Nurse will record height, weight and blood pressure, medical history and ask questions about lifestyle and occupations before collecting one urine and one blood sample. The first 20 patients in this part of the study will be asked to provide approximately 25ml urine sample (approximately 5 teaspoons), and a 45ml blood sample (9 teaspoons). All patients after this will be asked to provide approximately 25ml sample of urine (5 teaspoons) and approximately 35ml sample of blood (7 teaspoons). If diagnosis is confirmed using bladder tissue removed during the surgical procedure the researchers will review the tissue and use small samples to identify protein and other constituents including DNA and RNA within the

tissue structures. The patients notes will be reviewed by members of the HaBio clinical team. The HaBio clinical team will inform the patients consultant of their review findings should this be appropriate. This will be beneficial for patients. Members of the HaBio clinical team will review the patients notes for a second time 3 years after recruitment to obtain updated information about the patients health.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Single biomarkers and/or multivariate algorithms will significantly improve on the predictive power of an algorithm based on demographics for prediction of causes of haematuria in patients presenting with haematuria.

Secondary outcome measures
1. Patient age, gender, current medications, date of cystoscopy and date of initial diagnosis of bladder cancer (if relevant) are recorded from the patient notes by a Clinical Research Nurse (CRN) or the HaBio clinician at the time of recruitment
2. Blood pressure and body mass index (BMI) measurements, together with dip-stick analyses are undertaken by the CRN or the HaBio clinician at the time of recruitment
3. A detailed history of smoking, cancers, hypertension, renal stones, pelvic irradiation, and urinary tract infections; weekly alcohol consumption; present and past occupations; lower urinary symptoms; and whether the patient presented with visible or non-visible haematuria are recorded by the CRN or the HaBio clinician following discussion with each patient at their time of recruitment
4. Urine and blood samples are obtained from each patient by the CRN or the HaBio clinician at the time of recruitment
5. Scientists complete analyses of ~ 60 biomarker levels for each patient at Randox Laboratories Ltd (Country Antrim, Northern Ireland) as soon as possible after recruitment
6. Investigation results, details of positive micro-organism findings, causes of infection, causes of benign disease and levels of clinical biomarkers are recorded following review of the patient notes by a consultant urologist at least six weeks after recruitment
7. One or more causes of haematuria are recorded for each patient following review of the patient notes by a consultant urologist at least six weeks after recruitment
8. Where applicable, cause of death, details of chronic kidney disease, non-urological cancers, biomarkers measured in NHS, bladder cancer treatments, prostate and kidney pathology are recorded following review of the patient notes by the HaBio Clinician at the time of follow up
9. Where applicable, pathological review to obtain dates of recurrences and progression and pathology reports for tissue removed at the time of recruitment are recorded for all patients following review of the patient notes by the HaBio Clinician at the time of follow up
10. A detailed pathological review including details of pathological variants is completed by a consultant pathologist following completion of follow up
11. Patterns of expression and cell type location of key biomarkers using appropriate immunohistochemistry (IHC) on sections from diagnostic bladder tissue samples from patients is completed for each patient after completion of the diagnostic review by a Consultant Pathologist

Overall study start date

17/10/2012

Completion date
21/02/2020

Eligibility

Key inclusion criteria
Bladder cancer patients
Patients with pathologically proven bladder cancer, newly diagnosed or recurrent, will be recruited prior to transurethral resection of the bladder tumour at pre-assessment clinics, as in-patients on urology wards or at planned cystoscopy sessions.
1. Written informed consent to participate in the study
2. Aged between 40 and 80 years
3. Current haematuria or a history of haematuria
4. Cystoscopy within the last 6 months or planned cystoscopy
5. No chemo- or radio- therapy in the three weeks prior to recruitment
6. No previous history of cancers other than bladder cancer
7. Suspicion of bladder cancer or proven bladder cancer

Control patients
These patients will be recruited from haematuria clinics following negative cystoscopy and negative findings for other bladder cancer investigations.
1. Written informed consent to participate in the study
2. No previous history of cancer
3. Of the same gender, approximate age and smoking status (where possible) to a bladder cancer patient already recruited to HaBio
4. Current haematuria or a history of haematuria
5. Negative cystoscopy within the last 3 months, but at least 48h after the procedure
6. No chemo- or radio- therapy in the three weeks prior to recruitment

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
999

Total final enrolment
677

Key exclusion criteria
Bladder cancer patients:
1. No written informed consent to participate in the study
2. Aged <40 or >85 years

3. No history of haematuria
4. No recent or planned cystoscopy
5. Chemo- or radio- therapy in the three weeks prior to recruitment
6. Previous history of cancer(s), other than bladder cancer
7. No suspicion of bladder cancer or proven bladder cancer

Control patients:
1. No written informed consent to participate in the study
2. Previous history of any cancer
3. Not of the same gender, approximate age and smoking status of a patients already recruited as a bladder cancer patient
4. No history of haematuria
5. No recent or planned cystoscopy
6. Chemo- or radio- therapy in the three weeks prior to recruitment

Date of first enrolment
27/11/2012

Date of final enrolment
28/06/2017

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Study participating centre
Belfast City Hospital
Department of Urology
Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
Ulster Hospital Dundonald
Upper Newtownards Road
Dundonald
United Kingdom
B16 1RH

Study participating centre
Craigavon Hospital
68 Lurgan Road
Portadown
United Kingdom
B63 5QQ

Sponsor information

Organisation
Queens University Belfast (UK)

Sponsor details
c/o Ms Louise Dunlop
Head of Research Governance
Research and Enterprise
Room 114 Lanyon North
Belfast
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BT7 1NN

Sponsor type
University/education

Website
http://www.qub.ac.uk

ROR
https://ror.org/00hswnk62

Funder(s)

Funder type
Industry

Funder Name
Randox Laboratories Ltd (UK)

Results and Publications

Publication and dissemination plan

Publication and dissemination plan, as of 12/04/2021:
We are currently preparing the following manuscripts which will
i) describe adherence to STARD guidelines and the characteristics of the patients
ii) present our findings about the impact of smoking on bladder carcinogenesis in the HaBio cohort
iii) will discuss our interpretation of the biomarker data in the context of risk stratification of patients presenting with haematuria in a Northern Ireland population
iv) will report on the characteristics of the diabetic sub-populations within the HaBio cohort
Further manuscripts will be written to describe findings from our Tissue Microarray studies.

Publication and dissemination plan as of 19/12/2018:
We plan to submit five manuscripts based on the HaBio data, during the Spring/Summer of 2019. One manuscript will report on smoking and occupational carcinogen exposure in the development of bladder cancer in a Northern Ireland population. A second paper will focus on the causes of haematuria. A third manuscript will report on the characteristics of the diabetic sub-populations within the HaBio cohort. Further manuscripts will be written to describe findings from our Tissue Microarray studies.

Previous publication and dissemination plan:
HaBio is the follow-on study from a trial published, following peer-review, in Cancer in 2012 (https://www.ncbi.nlm.nih.gov/pubmed/21918968) which described the feasibility of producing diagnostic algorithms for bladder cancer in patients presenting with haematuria. One publication will present the HaBio findings in a similar fashion. There are plans to submit this manuscript to a high impact journal in the Autumn 2017. Another manuscript on the cost effectiveness of a diagnostic classifier for risk stratification of haematuria patients (DCRSHP) compared to flexible cystoscopy in the diagnosis of bladder cancer is also being prepared, as well as plans to submit data on risk stratification to the NCRI Conference that will take place in Liverpool in November 2017.

Intention to publish date
01/01/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study may be available for research collaborations (k.williamson@qub.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2022	31/10/2022	Yes	No