Near-infrared Fluorescence-Enhanced Identification of the Ureters using ZW800-1

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Primary objectives: To assess the feasibility of ZW800-1 in intraoperative detection of the urinary tract using the NIR fluorescence imaging system. Secondary objectives: To define the optimal dose of ZW800-1 for intraoperative imaging of the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Urinary tract signs and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON44580

Source
ToetsingOnline

Brief title
NIRF imaging of ureters with ZW800-1

Condition

- Urinary tract signs and symptoms

Synonym
Preventing iatrogenic ureteral damage; preventing unneccessary damage to urinary tract

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NIH en KWF grants

Intervention

Keyword: Detection, Fluorescence imaging, Phase 2., Ureters

Outcome measures

Primary outcome

Efficacy endpoint: Signal-to-background ratio, defined as fluorescence signal in the ureters compared to fluorescence signal of the surrounding tissue, at different doses.

Secondary outcome

Safety and tolerability endpoint: The occurrence or absence of adverse events following administration of ZW800-1 in patients.

Pharmacokinetic endpoint: Analysis of blood and urine samples for serum biochemistry, hematology and pharmacokinetics.

Study description

Background summary

Iatrogenic ureteral injury during abdominal surgery is a rare but serious complication with incidences varying from 0.7% to 10%.(1) When this complication is detected during surgery, the damage can often be repaired. However, most injuries remain unnoticed, resulting in severe long-term complications such as urogenital fistula or kidney failure. About 44% of all cases with iatrogenic ureteral injuries occur in patients with malignancies. Important risk factors include, previous surgery in the pelvic area, obesity and previous radiotherapy in the pelvic area. A preventive measure is inserting a double J catheter, which can be palpated during surgery to identify the ureters. However this method has its disadvantages, as it may injure or infect the ureter and most importantly it cannot be used during laparoscopic surgery.

Over the last years, near-infrared fluorescence imaging has emerged to empower surgeons to identify anatomical structures in real-time during surgery.

Fluorescence imaging using near-infrared (NIR) light (700-900 nm) can assist surgeons in recognizing structures that need to be spared, such as blood vessels and ureters, and structures that need to be resected, such as tumors(2). These imaging systems work with an external light source with a defined wavelength (700-900 nm) to illuminate the injected fluorescent agent. As the light travels through the tissue, it excites the fluorescent agent and releases light which is subsequently detected by the NIR imaging system, permitting high sensitivity detection of a desired target within the surgical field. Currently, the only clinically available NIR fluorophores are methylene blue, 5-ALA, and indocyanine green (ICG), but these fluorophores cannot easily be conjugated covalently to other molecules. Moreover, the fluorescence emission intensity and clearance routes are far from optimal. New fluorophores are needed with improved optical qualities and in vivo properties.

ZW800-1 is a novel fluorophore engineered with geometrically balanced, net neutral polyionicity. In pre-clinical studies it has proven to be a valid agent for molecular imaging, due to low non-specific binding and uptake, and an exclusive renal clearance, permitting imaging of the gastrointestinal tract. In rat studies, the ureters became fluorescent for several hours after a low dose of ZW800-1. More importantly, ZW800-1 has been proven safe. The safety, tolerability and pharmacokinetics have been studied in a phase 1 study in 16 healthy volunteers, without signs of safety concern. Based on the characteristics, safety and distinctive pharmacokinetics we believe that ZW800-1 is an ideal candidate to visualize the urinary tract during surgery to prevent iatrogenic ureteral damage. The NIR fluorescence signal of ZW800-1 can penetrate through 5-10 mm of tissue and is invisible to the naked eye.

Study objective

Primary objectives: To assess the feasibility of ZW800-1 in intraoperative detection of the urinary tract using the NIR fluorescence imaging system.

Secondary objectives: To define the optimal dose of ZW800-1 for intraoperative imaging of the urinary tract.

Study design

The study is an open-label, single ascending dose, exploratory study, consisting of 12 patients undergoing laparoscopic abdominal surgery. The study will consist of 3 cohorts where 3 different doses of ZW800-1 will be explored to select the optimal dose for surgery. The selected doses are based on the pre-clinical and phase I results. ZW800-1 will be administered in a bolus injection during surgery after exposure of the ureters. Patients will be under anesthesia during administration.

* Cohort 1 (up to 4 patients): 2.5 mg ZW800-1

* Cohort 2 (up to 4 patients): 5 mg ZW800-1
* Cohort 3 (up to 4 patients): 10 mg ZW800-1 / 1 mg ZW800-1 / repeated dose of 2.5 mg ZW800-1

Study burden and risks

The risks of participation for the patients in the trial include hypersensitivity reactions. These risks are deemed minimal. Nevertheless precautionary measures (supervised administration by qualifîed staff and availability of medical treatment to treat hypersensitivity reactions) are in place and these effects are generally well manageable. The burden of the trial is minimal, the research will for the largest part coincide with routine care and the proposed procedures are minimally invasive. This research could possibly provide a useful tool to enhance visualization of ureters and, hence, reducing the risk of ureteral damage. We believe therefore that this study is justified.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Patients 18 years or older;;2) Patients scheduled and eligible for laparoscopic surgery in the lower abdominal or pelvic area; ;3) Patients should be capable and willing to give informed consent before study specific procedures;;4) No unacceptable known cardiovascular or pulmonary disease, renal or liver dysfunction;;5) The screening ECG and laboratory test results are within normal limits, or if any are outside of normal limits they are considered to be clinically insignificant;;6) Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial.

Exclusion criteria

1) History of a clinically significant allergy;;2) Patients pregnant or breastfeeding, lack of effective contraception in male or female patients with reproductive potential;;3) Any condition that the investigator considers to be potentially jeopardizing the patients well-being or the study objectives.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-03-2018

Enrollment:	12
Type:	Actual

Medical products/devices used

Generic name:	1) InfraVision Imaging System & 2) Lab-FLARE Model RP2
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	ZW800-1
Generic name:	not applicable

Ethics review

Approved WMO Date:	03-08-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-11-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-001954-32-NL
CCMO	NL61892.058.17