INFORMED CONSENT FORM
AUTHORIZATION FOR ONCOLOGY RESEARCH

TITLE:	A Phase 3 Multicenter Trial Evaluating the Efficacy and Safety of MitoGel™ (UGN-101) on Ablation of Upper Urinary Tract Urothelial Carcinoma
PROTOCOL NO.:	TC-UT-03
SPONSOR:	UroGen Pharma Ltd
INVESTIGATOR:	Name Address City, State Zip Country
SITE(S):	Name Address City, State Zip Country
STUDY-RELATED PHONE NUMBER(S):	Name Number(s) (24 hour required)

INTRODUCTION

You are invited to consider participating in a research study. You were selected as a possible participant in this study because you have upper tract urothelial carcinoma (UTUC), and because you appear to meet the requirements for admission to this clinical trial.

Please take your time to make your decision. It is important that you read and understand several general principles that apply to all who take part in our studies:

a) Taking part in the study is entirely voluntary.
b) Personal benefit to you may or may not result from taking part in the study, but knowledge gained from your participation may benefit others;
c) You may decide not to participate in the study or you may decide to stop participating in the study at any time without [21]penalty or loss of any benefits to which you are entitled.

The purpose and nature of the study, possible benefits, risks, and discomforts, other options, your rights as a participant, and other information about the study are discussed below. Any new information discovered which might affect your decision to participate or remain in the study will be provided to you while you are a participant in this study. You are urged to ask any questions you have about this study with members of the research team. You should take

whatever time you need to discuss the study with your physician and family. The decision to participate or not to participate is yours. If you decide to participate, please sign and date where indicated at the end of this form.

The research study is being sponsored by UroGen. UroGen is called the Sponsor and [Site/Institution Name] is being paid by UroGen to conduct this study. [PI Name] is the primary investigator.

The study will take place at [Site/Institution Name].

WHY IS THE STUDY BEING DONE?

The purpose of this study is to evaluate the effectiveness and safety of MitoGel on patients with UTUC. This research study is being done because this is a potentially beneficial new treatment for Low Grade UTUC.

Mitomycin C (MMC) is FDA approved for other clinical indications and commercially available for the treatment of bladder cancer. UroGen's MitoGel™ (a combination of MMC and TC-3 gel) has not been approved by the FDA and is not commercially available. The gel is designed to safely maintain the MMC within the body to treat the urinary tract urothelial carcinoma.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Participants in the study are referred to as subjects. About 74 subjects will take part in this study worldwide; about [Number of Subjects] subjects will be recruited at this site.

WHAT IS INVOLVED IN THE STUDY?

If you take part in this study, you will have the following tests and procedures:

You will receive 6 MitoGel instillations (treatments with the MitoGel) into upper urinary tract (specific area in the kidney) once per week for 6 weeks. MitoGel for the treatment of upper tract urothelial carcinoma (UTUC) contains the drug Mitomycin C. The administration of MitoGel will be performed under fluoroscopy (medical imaging that shows a continuous x-ray image on a monitor) and cystoscopy (procedure to examine the lining of your bladder and the tube that carries urine out of your body) through a standard ureteral catheter. Your physician will review the details of the instillation procedure, which are similar to a cystoscopy.

Entering this study will delay any other method of care for your situation by at least 3 months.

Such delay is considered low risk in patient with low grade upper tract urothelial carcinoma.

If the treatment succeeds, meaning, the tumor(s) disappeared after 6 instillations (Complete Response=CR), you will receive up to an additional 11 (eleven) maintenance instillations.

This is a multi-center open label, single arm, safety and efficacy study.

- "Multi-center" means that this study will be done in approximately 40-50 medical centers across the US, Europe, Israel and Canada in approximately 74 individuals.
- "Open label" means that everyone participating in this study will be treated with UroGen's MitoGel™ procedure.

Your treating urologist within this trial will inform you of any new findings, during the course of your treatment that might affect your willingness to continue receiving this treatment.

[21]A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identity you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

STUDY PARTICIPATION

This study involving UroGen's MitoGel™ procedure has 5 phases:

Screening for eligibility	1 to 4 weeks
Treatments with UroGen's MitoGel™	Once weekly for 6 weeks (Visits 1 through 6)
Primary Disease Evaluation (PDE)	Approximately 4 to 6 weeks after last treatment visit (Visit 9)
MitoGel Maintenance Treatment	Only for complete response (CR) patients- monthly, up to a total of 11 (Eleven) treatments
Follow-up visits	Approximately 3, 6, 9 and 12 months after the primary disease evaluation visit (Visits 12, 15, 18, 21)

Total length of study: 16 months

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the treating urologist and your primary physician first.

If you decide to discontinue your participation, your urologist will discuss your options for continued care.

Note: You will be requested by signing this informed consent to allow your urologist to provide your relevant medical records to UroGen and to the coordinating investigator of this trial which is not your doctor for review of your eligibility to the trial.

You will also be requested by signing this Informed Consent Form to allow sending of the biopsy and urine cytology slides/tissues taken prior to the trial which are relevant for eligibility and those taken during the trial, to central laboratory for a second reading.

Your medical records and cytology/biopsy slides provided to UroGen and central lab, respectively will not contain your personal identification information (de-identified).

SCREENING FOR ELIGIBILITY

If you agree to participate in this study, the following may happen for participation up to 28 days before starting experimental treatment:

- You must first consent to participate in this study
- You will undergo a detailed evaluation. This will include a collection of your medical history information, a physical examination, including a measurement of your vital signs, fulfillment of eligibility criteria, and a review of your current and past medications.
- We will be collecting a urine sample for urinalysis and urine culture, which are all standard urine tests.
- We will collect 20 ccs of blood (4 teaspoons) for routine testing, including kidney, liver, blood count, and coagulation tests.
- If you are a woman of child bearing potential, 5ccs (1 teaspoon) blood will be drawn for a pregnancy test.

Prior to Instillation (during the screening period):
We will conduct a pyelography, which is an examination to assess the upper urinary tract, to determine the volume of MitoGel to be instilled in each visit. (Details below)

During this examination, we will also conduct the following procedures, if they
a) Have not already been completed for your care within the past two (2) months, and
b) Records and slides are available for the study sponsor for review
c) Or if it is not informative enough for the study requirement:

- A biopsy of lesions within the upper tract
- Upper tract urine cytology (a washing cytology)
- A video recording or photography of the diagnostic ureteroscopy & upper urinary tract lesion assessment. (Under anesthesia)

The volume of your kidney will be measured with a contrast agent (This is a commonly used substance that enhances the ability to see the specific parts inside the body during medical imaging), during the Ureteroscopy or during the first treatment through the ureter catheter. This measured volume will be the volume of the MitoGel you will receive each treatment.

If you have not had a recent CTU (CT urography) scan within the past –Three (3) months or if your doctor believes it is necessary to a better evaluation of your current disease, you will be required to repeat CTU scan. In the event that CTU cannot be performed due to any reason, an MRI should be performed instead.

Medication:
In order to facilitate the instillations, you will be prescribed with 1.3 g Sodium bicarbonate tablets (a type of salt), to help lower the acidity levels in your urine, as acidic urine can cause the fast breakdown of the Mitomycin C. These tablets are to be taken the night before each instillation, the morning of instillation, and again 30 minutes prior to each instillation procedure.

In order to avoid allergic symptoms, you may be prescribed with prophylactic anti-allergic treatment –Anti-histaminic agents. These tablets are to be taken the day before instillation, on the day of instillation and the day after the instillation.

It is preferred that diuretics not be taken the night before and prior to the instillation. If you are on diuretic medications, your doctor will determine whether the medication can be skipped prior to the instillations.

To the extent that it is possible, drinking should be avoided in the 4-6 hours prior to the instillation.

- Post instillation drinking should be limited. A recommended drinking schedule follows:
- 0-2 hours post instillation: refrain from drinking any liquid
- 2-4 hours post instillation: 1 cup of water every 2 hours
- 4 hours post instillation: resume normal liquids consumption

Following instillation, you will be carefully monitored for urine output and clinical symptoms, which might indicate urinary obstruction.

Aiming to minimize the risk for Urinary Tract Infections (UTI), an antibiotic will be prescribed, as is normal for this kind of procedure.

Your doctor might prescribe you with Diazepam, an anti-anxiety medication to be taken 1 hour prior to each instillation.

You will be given separate written instructions for each of these steps, and will also receive a phone call from a member of the study team to remind you.

Treatments with UroGen's MitoGel™

You will have 6 treatments performed once weekly for 6 weeks. Each treatment will include MitoGel™ will contain 4 mg of Mitomycin C per 1 mL of TC-3 gel (4:1 ratio) which will be administered through an ureteral catheter into the upper urinary tract. The procedure will take approximately 30 minutes. After MitoGel™ administration (MitoGel injection will be performed under fluoroscopy and cystoscopy through a standard ureteral catheter as explained above)., the gel will form a reservoir in the renal pelvis, which will dissolve over several hours, delivering the drug to cover the surface during that time.

Upon consultation with your urologist, in very rare cases, the catheter may be kept in place for the 6 weeks duration, instead of having new ones put in every week (and removed). Your care team will provide home care instructions.

Instillation through a nephrostomy tube may be an option, if necessary.

It may be required that an educational trainer from the sponsor will be present during some of the treatments to support the clinical team with the proper instructions of use.

During the first instillation visit

You will undergo a standard urology-oriented physical exam, including vital signs measurement, and we will collect information about your medications. We will collect 20 cc of blood (4 teaspoons) for routine testing, including kidney, liver, blood count, and coagulation tests.

- Urine will be collected for standard urologic assessment tests, including urinalysis, and urine culture. If you are a woman of child bearing potential, some of the urine will be used for a pregnancy test (If the urine test is positive, a blood (1 teaspoon) pregnancy test will be performed).

If not done during screening, the volume of your kidney will be measured with a contrast agent through the ureter catheter. This measured volume will be the volume of the MitoGel you will receive each treatment

After the treatment you will be provided with a Visual Analogue Scale (VAS) form and requested to mark the degree of pain during the instillation procedure on a scale of 0-10. You will also be given a Post-Treatment questionnaire to evaluate your post-treatment experience with the following questions:

1. How long after the treatment did you have your first urination?
2. How long after the treatment was the urine clear (no purple color) for the first time?

Thereafter, 24 to 32 hours post treatment, you will be contacted via telephone to review the completed questionnaire. Please keep the completed questionnaire as it will be collected at the next visit.

Following this first visit, we will monitor you for 6-23 hours after the instillation for observation, at the investigator's discretion, to monitor for side effects. This initial treatment will be done in the clinic/office or in the operating room with anesthesia

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☐ If you allow, on the visit for the first instillation, for this, we will collect blood samples, to monitor the drug distribution (Pharmacokenetic assessment). PK will be performed with just 6 first patients who provide informed consent. This will be done prior to instillation, thirty minutes after the instillations, and then again 1, 2, 3, 4, 5, and 6 hours post instillation. Each sample will require 5 mL of blood. **Yes, I agree to the collection of serial blood samples during the first instillation visit.**

☐ **No, I do not agree to the collection of serial blood samples during the first instillation visit.**

Instillation Visits 2 through 6

Prior to visits 2 through 6 -up to 3 days prior to treatment day, your blood (approximately 20 mL) will be tested for safety evaluation (check your blood count, liver enzymes, kidney function, electrolytes and coagulation).

On treatment day the following procedures will be conducted:

1. A standard urology-oriented physical examination, including a measurement of your vital signs, and a review of your current medications as well as any side effects.
2. Urine will be collected for standard urologic assessment tests, including urinalysis and urine culture.
3. If you are a woman of child bearing potential, a urine pregnancy test will be conducted. If the urine test is positive, a blood pregnancy test will be performed.
4. In case not all blood test were preformed prior to treatment – your blood (up to 20 mL) will be tested according to missing test (blood count/ liver enzymes/ kidney function/ electrolytes / coagulation)..

After each treatment, you will be requested to mark the degree of pain during the instillation procedure on a scale of 0-10. You will also be given a questionnaire to evaluate your post-treatment experience with the following questions:

1. How long after the treatment did you have your first urination?
2. How long after the treatment was the urine clear (no purple color) for the first time?

Thereafter, 24 to 32 hours post treatment, you will be contacted via telephone to review the completed questionnaire. Please keep the completed questionnaire as it will be collected at the next visit.

If necessary, you may be called for an unscheduled visit to follow up on any post-treatment issues or problems that require clinical evaluation or follow-up.

You will undergo safety evaluation after each instillation including adverse event rate and laboratory evaluation.

In the event of a urinary tract infection or another safety reason which causes the investigator to postpone a treatment, the MitoGel treatment will be postponed until the event is resolved and not over 4 weeks; In case treatment has been delayed beyond 4 weeks due to adverse drug reaction MitoGel treatment will be stopped permanently, however, you will continue to follow up visits.

Following Installation Visits

One week, and again three weeks following the 6th installation, your blood (up to 20 mL/ 4 teaspoons) will be tested (a CBC, liver function, renal function and coagulation will be taken). If necessary, this can be done at your local clinic or doctor's office.

Primary Disease Evaluation Visit (PDE)

About five weeks following the completion of treatment visits, you will be scheduled for an evaluation visit. This will involve the following procedures:

1. A full physical examination, including a urology oriented physical exam, vital signs measurements and a review of your current medications as well as any side effects.

2. Your blood will be tested to check your blood count, liver enzymes, kidney function, electrolytes and coagulation (4 teaspoon).
3. Urine will be collected for urinalysis and urine culture.
4. You will undergo Ureteroscopy evaluation under anesthesia to evaluate the area of treatment, which include an upper urinary tract cytology, and biopsy of lesions, if applicable.

At the evaluation, if no detectable disease is found, you will be considered a Complete Response (CR) patient and continue with the study as described below. You will receive up to an additional 11 (eleven) maintenance treatments.

If you responded partially or did not respond to the treatment, you will be considered as a Non-Complete Response and your participation in the study will be terminated.
In the event that your cytology test results are equivocal, you will undergo re-cytology test after several weeks. This sentence apply also to each of the follow-up visits.

Your urologist will discuss the results with you and will determine which standard of care treatment is best, and information about the disease will be collected.
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Study continuation for Complete Response patients only:

Maintenance Instillation Visits
In the case that you are a complete response patient (no detectable disease on the PDE visit), you will be scheduled for monthly visits, during which MitoGel will be instilled as described in the visits above. This will occur once per month (+- 2 week) for eleven months, (one month prior to last FU visit within the study - see below) or until tumor first recurrence.

The following procedures will be conducted:

- Standard urology-oriented physical examination
- Your blood (approximately 20 mL) will be tested to check your blood count, liver enzymes, kidney function, electrolytes and coagulation and medication review.
- Urine will be collected for standard urologic assessment tests, including urinalysis and urine culture.
- Review of your current medications and adverse events, if any.

The tests will be conducted while you are at the clinic for your monthly treatments. If the disease reoccurs, you will stop treatment in the study and your urologist will review your treatment options. If you decide to stop study participation, you will be asked to perform a safety visit.

Follow-up Visits
During the time of the maintenance instillation visits, you will have an up to a 4 standard-of-care follow-up visits done every 3 months.

Three months after your evaluation visit, the first follow-up (FU) visit will be conducted. During this visit, follow-up data on your disease outcome will be collected. As per standard of care, you will undergo these follow-up visits every three months.

These visits may include:

1. A review of your current medications, vital signs and reporting of any adverse events.
2. Endoscopy of the kidney (ureteroscopy under anesthesia) where the upper urinary tract will be examined and photographed to record number, size, appearance and location of tumors if any are present. This will also include a biopsy sample of the tumor, if lesions are detected. If present, the tumor(s) may be surgically ablated (destroyed)
3. Upper urinary tract urine cytology will be performed to confirm the absence of cancer.

The final follow up visit will happen 12 months after the post-instillation evaluation visit, or until tumor first recurrence, at which time, additional follow-up data on disease outcome will be collected.

CTU Scan

At the 4th follow up visit, we will obtain a final CTU scan.

Note: In case of recurrence or progression at the original treated area, assessed during the follow-up period, you will be considered as having completed the trial and will not be summoned for further follow-up visits, but for a single termination visit for safety evaluation.

FOLLOW-UP VISITS AND END OF STUDY PARTICIPATION

Unscheduled Visit

An unscheduled visit may be performed at any time during the trial if the investigator decides that the clinical state of the patient does not permit instillation of the IP, for assessment of safety, at the Patient's request, or as deemed necessary by the investigator.

You should provide the trial urologist information about any medications you are taking. In addition, if you are taking any over-the-counter drugs or herbal supplements which you have obtained from the drug store, grocery store, etc., this information should also be provided to the urologist.

Withdrawal by investigator, physician, or sponsor

The investigators may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The investigators or the study sponsor might also decide to stop the study at any time.

The investigators, physicians or sponsors may stop the study or take you out of the study at any time should they judge that it is in your best interest to do so, if you experience a study-related injury, if you need additional or different medication, or if you do not comply with the study

plan. They may remove you from the study for various other administrative and medical reasons. They can do this without your consent.

If you decide to stop being in the study or are removed from the study or the study is stopped the investigator will ask you to do a follow-up visit to complete an exit interview. The data collected about you up to the point of withdrawal will remain a part of the study and may not be removed from the study database.

If you decide to stop receiving the study treatment prior the 6th instillation, the investigator will ask you to continue being in the study up to the PDE visit. In the event that you didn't complete the study treatment, but have a Complete Response to the treatment, you will be advised to continue with the follow-up visits as long as possible even without having the study treatment, but in consultation with your study doctor it may be re-considered continuing with monthly instillations until 1-year follow-up or disease recurrence. The data collected about you up to the point of withdrawal will remain a part of the study and may not be removed from the study database.

Note: Your follow up data may be collected up to 3 years from PDE visit (visit 9) to evaluate long term safety and efficacy of the investigational product.

WHAT ARE THE RISKS OF THE STUDY?

For drug and device trials, there may be risks. These risks will be discussed with you by the research urologist.

Each treatment may have possible adverse events. In the current treatment there might be Mitomycin C-related adverse events and Catheter insertion related adverse events.

Many side effects go away shortly after treatment is stopped, but in some cases, side effects may be serious, long-lasting or permanent, and may even result in hospitalization.

Inflammation causing narrowing in the ureters is a common phenomenon, most of the cases resolve with or without intervention, for example placing a stent in the ureter. In some cases, the narrowing persists, or resolves with some residual damage.

MMC+TC-3 Side Effects

Based upon limited information regarding upper urinary tract irrigation with MMC+TC-3 (based on data from 22 compassionate treatments of upper tract urothelial carcinoma and the patients treated in the study so far):

The following were reported more than once in the compassionate treatment series as probably or possibly related to study drug:

- Allergic Reaction (n=2)
- Dysuria (burning or painful urination) (n=2)

- Weakness/ Fatigue (n=4)
- Fever/chills (n=2)
- Aggravation of renal failure (n=2)
- Blood line suppression (n=2) - decreased white blood cells (increases infection risk), red blood cells (increases fatigue risk), and platelets (increases bleeding and bruising risk)
- Nausea (n=3)

Catheter Insertion Related Side Effects
Trauma to the bladder/ upper urinary tract creating:

Common:
Adverse events affecting the ureter including, but not limited to inflammation of the ureter and narrowing of the ureter.

Less Common or Rare:

- Urinary tract infections resulting from the presence of a foreign body (the catheter) in the urinary tract
- Urethral stenosis- narrowing of the urethra (passage from which urine leaves the bladder)
- Urethral tear- due to traumatic insertion of the catheter
- Ureteral perforation (tearing, breakage, or holes on the ureter)

Mechanical Manipulations related Side effects (Including catheter Insertion and nephrostomy tube related side effects)

Catheter insertion to the upper tract is well-practiced worldwide and widely used for many indications for example during kidney stones removal, the following are the known side effects of this procedure, including those evident in the upper urinary tract instillations (as seen in the CUP described above:

- Flank (between the ribs and the hip) pain (n=6)
- Mild pressure/fullness at instillation site (n=4)
- Acute Pyelonephritis (acute infection of the kidney)(n=3)
- Asymptomatic Bacteriuria (n=2)
- Macroscopic Hematuria (visible blood in urine)(n=2)

Apart from the above- any adverse event mentioned in the information leaflet of mitomycin C may appear during the study.

Regarding **Mitomycin C-**related adverse events, please note:

- Mytomicin C may cause burning sensation in the ureter, hand skin exfoliation (removal of dead skin cells), blood count changes, inflammation of the organ, soreness/pain in the area, soreness of the skin in the area around the openings of the urethra.

- Mitomycin C can have also some side effects, including cystitis (bladder infection), frequent and / or painful urination, night-time urination or blood in the urine, allergic reactions in form of rashes or erythema (redness of the skin or painful itching) of a portion of the skin (i.e. palms and feet) or of the entire skin surface, contact dermatitis, generalized exanthemas (skin breakouts), skin peeling on the palms with/without generalized rash.

Rare:

- Blood line suppression - decreased white blood cells (increases infection risk), red blood cells (increases fatigue risk), and platelets (increases bleeding and bruising risk)

- Death of cells of the urinary tract
- Narrowed urethra (stenosis) Necrotizing severe cystitis (inflammation and dying of cells) are also very rare.
- Cases of bladder shrinking with reduced bladder capacity have been described
- Teratogenic effects (developmental disturbances) on embryo/foetus have been previously described.

Previous studies using the MMC in association with TC-3 gel showed few side effects from the treatments which are related and expected to the treatments with MMC. Among the side effects have been found also urinary burning, urinary tract infections (UTI) and dysuria, which were resolved with or without any treatment.

Anticipated TC-3 Gel Related Adverse Events:

Common:

- A sensation of bladder contractions due to the cold temperature of the instilled gel.
- A sensation of upper urinary tract contractions due to the cold temperature of the instilled gel.

- Rare:Upper urinary tract obstruction which occurred once due to violation of treatment instructions.

Anticipated MitoGel-Related Phenomena (not an adverse event)

- Purple colored urine
- Urination of gel particles

MMC+TC-3 may cause low blood cell counts (red blood cells, white blood cells, and/or platelets) that may require a transfusion, but this is very rare in local administration.
Following are rare some side effects that were noticed during compassionate treatments:

- "Cool" flank sensation due to low temperature of instilled drug.
- narrowing of the ureter at location of the previously available tumor (Narrowing originated either from drug effect on the tissue or mechanical injury by rapidly inserted ureteral catheter). The event resolved following local treatment.
- Bladder inflammation and upper tract inflammation (due to treatment drug)
- Enhanced frequency of urination (probably due to bladder irritation by the drug)
- Hydronephrosis (distention of the kidney with urine as a result of obstruction of the outflow of urine) due to local edema caused by inflammation of the upper tract.

Risks and side effects associated with Bicarbonate

Sodium bicarbonate (baking soda) is generally well tolerated. However, high doses may cause headache, nausea or irritability. If any of these effects continue or become bothersome, inform your doctor.

Risks and side effects associated with a biopsy

Having biopsies performed in the upper urinary tract may cause pain, local bruising, bleeding, redness, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Cytoscopy

Cystoscopy is generally a safe procedure. Serious complications are rare. However, as with any surgery, there is the risk of infection, bleeding, and complications from the anesthesia. In all but the simplest procedures, antibiotics are used before the surgery to reduce the incidence of urinary tract infection.

Side effects due to Blood Draws

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions, but in this study the amount of blood drawn is limited and the risk for blood transfusion is extremely rare.

This study involves exposure to radiation, and that exposure is increased the more often such tests are done. Radiation exposure at certain doses can potentially cause cancer. Any possible increase in cancer risk associated with participation in this study is within acceptable limits for human research subjects.

Fluoroscopy

Fluoroscopy involve the risks of radiation. Radiation-related risks associated with fluoroscopy include:

- Radiation-induced injuries to the skin and underlying tissues ("burns"), which occur shortly after the exposure, and
- Radiation-induced cancers, which may occur [22]sometime later in life.

The probability that you will experience these effects from a fluoroscopic procedure is statistically very small.

CT Scan Risks

CT scans involve the risks of radiation (above) .In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock, or rarely, death. The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan.

Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time. If contrast material is used, you may feel discomfort when it is injected. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting or a headache.

MRI Risks

An MRI scan is a painless radiology technique that has the advantage of avoiding x-ray radiation exposure. There are no known side effects of an MRI scan. During the MRI scan, patient lies in a closed area inside the magnetic tube. Some patients can experience a claustrophobic sensation during the procedure. If you have history of claustrophobia please relate this to the treating urologist, as well as the radiology staff.
If you have any metallic materials within the body please notify your treating urologist prior to the examination or inform the MRI staff. Metallic chips, materials, surgical clips, or foreign material (artificial joints, metallic bone plates, or prosthetic devices, etc.) can significantly distort the images obtained by the MRI scanner. If you have a heart pacemakers, metal implants, or metal chips or clips in or around the eyeballs you should not be scanned with an MRI because of the risk that the magnet may move the metal in these areas. If you have artificial heart valves, metallic ear implants, bullet fragments, and chemotherapy or insulin pumps you should not have MRI scanning.

Reproductive Risks:

You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. Therefore, you need to use effective birth control while on this study. You must use at least 2 acceptable and effective methods of birth-control (like implants, injectable, combined estrogen/progesterone oral contraceptives and/or condoms with spermicide).

Unknown Risks to Women of Child Bearing Potential and Pregnant Women: The effects of the study medication on fertility or a fetus are not known. For this reason, if you believe that you are pregnant or have a chance of becoming pregnant you should not participate in this study. A urine pregnancy test will be performed before the start of study procedures. If you are pregnant, you will not be allowed to participate in the study. If you do participate in this study, you must use a medically effective form of birth control before entering the study, while participating in the study, and for at least 6 months after stopping the study. If you become pregnant during the study, tell the researchers right away.

Unknown risks to infants: The side effects of the study medication on infants are also not known, therefore if you are currently breastfeeding you cannot participate in this study.

Unknown risks and discomforts

The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

As with any other new treatment this treatment may involve unpredictable risks to you

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

You may or may not benefit from participation in this study. Treatment with the drug may help to control the disease, but there may be no benefits to you for receiving this treatment.

The following are possible benefits from study treatment:

- The tumors might disappear and subsequently no need for surgical removal would exist.
- Additionally, in case of reduction of the number or size of the lesion(s) in comparison with baseline, the following surgical removal would be more limited;
- A more efficient preventive effect of tumor recurrence might be proven.

From what has been shown so far in the sponsor trials in urothelial carcinoma in the bladder, Mitomycin C appears to have a high potential for tumor removal, with more than 70% of the patients showing complete response to the treatment, and more than 80% of the patients showing either complete response or partial response. Moreover, the results suggest that the treatment appears to be generally safe and there has been no indication of a significant rise in risk related to the Mitomycin C dose used.

The information generated by your participation may help future patients with Low Grade Upper Urinary Urothelial Carcinoma (UTUC).

ALTERNATIVE TREATMENT

If you decide not to take part in this study, or if you withdraw from this study before it is completed, the following alternative procedures or courses of treatment are available:

- There may be an opportunity to take part in other studies of investigational treatments, which your doctor will be happy to discuss with you.
- You may be a candidate to undergo another approach of endoscopic management-like series of laser ablation or a kidney removal, partial or complete.
- Alternatively, you may choose not to have any treatment directed at the cancer, but receive full supportive care, including treatment for pain and other symptoms of cancer.

The risks, benefits and any questions you have regarding these other treatments will be explained to you by your doctor.

FINANCIAL INFORMATION

Any tests, procedures, and/or drugs that you may receive as part of this treatment will be without cost to you. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the procedures and/or drugs, including hospitalization, nausea, vomiting, low blood cell counts, and dehydration. Standard medical care that you receive under this treatment will be billed to your insurance provider and/or you in the ordinary manner. Before receiving this treatment, you may ask about which parts of the treatment-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this treatment.

UroGen will reimburse traveling expenses upon receipts and limited up to $50 per visit (higher reimbursed will be consider for exception cases)

If you also participate in the PK trial, UroGen will reimbursed you $120 for your spent time.

INJURE OR HURT

If you are injured or harmed as a result of participating in the study and receive medical care through [Site Name/Institution] or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your health insurance. If a Study patient suffers an illness or injury as a result of participating in this Study, the Sponsor shall reimburse the patient for the costs of diagnosis and treatment. The Sponsor, however, is not offering to reimburse for Study injuries that are caused by (i) Institution's negligence or willful misconduct or (ii) the natural progression of an underlying or pre-existing condition, unless participating in the study made such condition worse. The study sponsor is also not offering to pay for medical expenses that are covered by your insurance provider or if your injury was not caused by the study drug or a study procedure.

CONFIDENTIALITY

Your research records will be handled as confidentially as possible. No individual identities will be used in any reports or publications resulting from this study. In order to verify the study data,

the primary coordinating Investigator, clinical monitors authorized by the sponsor of this study and monitors from the Food and Drug Administration or the Institutional Review Board (IRB) may be allowed to see some specific records, including yours. This information may include personal identifying information about you (such as your name, race, date of birth, gender, city, and zip code), your medical history, treatment schedule, and the results of any of your tests, therapies, and/or procedures. The purpose of collecting and sharing this information is to learn how the treatment procedures may affect the disease and any treatment-related side effects.

[Site Name/Institution] will take appropriate steps to keep your protected health information private and protected according to state and federal law. However, there is no guarantee that your information will remain confidential, and it may be re-disclosed at some point. Federal agencies (such as the FDA, OHRP, or National Cancer Institute [NCI]), UroGen Pharma Ltd, and the IRB of Name of Institute where study will be performed might view or receive your record in order to collect data and/or meet legal, ethical, research, and safety-related obligations. In some situations, the FDA could be required to reveal the names of patients.

You have the right to see and reproduce your records related to the treatment, and ask for corrections, for as long as this information is held by your doctor and/or [Site Name/Institution] where study will be performed.

CONTACT INFORMATION

If you have any other questions[21], concerns or complaints about the study, your rights as a research subject or about an injury from the study, you may call the [Site Name] at [Contact Number(s)] between 8:00 am to 4:00 pm on weekdays and ask to speak to [PI/Contact Name]. During non-office hours or on weekends, you may call the office and ask to be connected to the physician on call. If you have any questions about your rights as a research subject [21]or if you have questions, concerns, or complaints about the research,, you may contact IRC, an independent review research board. They are available from time they are open, at phone number.

RECORD OF INFORMATION PROVIDED

I will be given a copy of this consent form to keep.

SIGNATURES

PARTICIPATION IN RESEARCH IS VOLUNTARY. I have the right to decline to participate or to withdraw at any point in this study without jeopardy to my medical care at the <<Name of Institute>> where study will be performed.

If I wish to participate, I should sign below.

Date	Patient's Signature	Printed Name
Date	Person Obtaining Consent	Printed Name
Date	PI Consent	Printed Name

CONSENT/AUTHORIZATION
(Adult Patients Only)

I understand the information in this consent form. I have had a chance to read the consent form, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the doctor permission to begin treatment. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

SIGNATURE OF PATIENT	DATE

WITNESS TO CONSENT

I was present during the explanation of the treatment to be performed under **IND121922**

SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN TREATING DOCTOR)	DATE

[21]**PERSON OBTAINING CONSENT**

I have discussed this treatment with the patient[21] using language that is understandable and appropriate.

I believe that I have fully informed this patient of the nature of this treatment and its possible benefits and risks and that the patient understood this explanation.

SIGNATURE OF TREATING DOCTOR OR PERSON AUTHORIZED TO OBTAIN CONSENT	DATE

TRANSLATOR

I have translated the above informed consent form as written (without additions or subtractions) into _____ and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this patient.

NAME OF TRANSLATOR	SIGNATURE OF TRANSLATOR	DATE

☐ Please check here if the translator was a member of the treating doctor's team.
(If checked, a witness, other than the translator, must sign the witness line below.)

SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION (OTHER THAN TRANSLATOR, OR TREATING DOCTOR)	DATE