Clinical trial results:
A Phase 3, Multicenter, Prospective, Randomized, Open label Study for Intraoperative Ureter(s) Visualization When Using ASP5354 with Near infrared Fluorescence (NIR-F) Imaging in Participants Undergoing Minimally Invasive and Open Abdominopelvic Surgeries

Summary

EudraCT number	2025-000122-33
Trial protocol	Outside EU/EEA
Global end of trial date	16 January 2025

Results information

Result version number	v1
This version publication date	31 July 2025
First version publication date	31 July 2025

Trial information

Trial identification

Sponsor protocol code	5354-CL-0301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05754333
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development, Inc
Sponsor organisation address	Northbrook, IL, United States, 60062
Public contact	Clinical Transparency, Astellas Pharma Global Development Inc., 847/224 8008887704, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Transparency, Astellas Pharma Global Development Inc, 847/224 8008887704, astellas.resultsdisclosure@astellas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-003099-PIP01-21
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was the investigator’s blinded conspicuity assessment of the ureter at the first time point for adults with normal renal function or mild renal impairment.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2023
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 107
Worldwide total number of subjects	107
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	14
Adults (18-64 years)	59
From 65 to 84 years	33

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Adults with normal renal function (NRF), mild renal impairment(MRI) [estimated glomerular filtration rate (eGFR)≥ 60 milliliter/minute (mL/min)], adults with moderate or severe renal impairment (SRI) [eGFR≥ 15 to < 60 mL/min] and adolescents with NRF or MRI [eGFR ≥ 60mL/min]) were enrolled in study. There were no participants enrolled with SRI.

Pre-assignment

Screening details:

Participants who met inclusion criteria and none of the exclusion criteria were enrolled in the study. Randomization was stratified by type of surgery :gynecological abdominopelvic

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Adult(Normal/Mild):White Light/near-infraredfluorescence

Arm description:

Pudexacianinium (3 milligrams [mg]) was administered as a single intravenous (IV) dose approximately 30 minutes (min) before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. White Light (WL) and near-infrared fluorescence (NIR-F) were used to recognize/identify the ureter.

Arm type	Experimental
Investigational medicinal product name	Pudexacianinium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

single IV 3 mg dose

Arm title	Adult(Normal/Mild):White Light only

Arm description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL was used to recognize/identify the ureter.

Arm type	Experimental
Investigational medicinal product name	Pudexacianinium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

single IV 3 mg dose

Arm title	Adult (Moderate):White Light/near-infraredfluorescence

Arm description:

Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Arm type	Experimental
Investigational medicinal product name	Pudexacianinium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

single IV 3 mg dose

Arm title	Adolescent(Normal/Mild):White Light/near-infraredfluorescence

Arm description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Arm type	Experimental
Investigational medicinal product name	Pudexacianinium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

single IV 3 mg dose

Number of subjects in period 1	Adult(Normal/Mild): White Light/near-infraredfluorescence	Adult(Normal/Mild): White Light only	Adult (Moderate):White Light/near-
Started	72	13	8
Participants did not receive study drug	2 [1]	0 [2]	0 [3]
Completed	67	12	8
Not completed	5	1	0
Lost to follow-up	2	1	-
miscellaneous	3	-	-

Number of subjects in period 1	Adolescent(Normal/Mild):White Light/near-infraredfluorescence
Started	14
Participants did not receive study drug	0 [4]
Completed	13
Not completed	1
Lost to follow-up	1
miscellaneous	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Two participants did not receive the study drug.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All participants in this arm received the study drug.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All participants in this arm received the study drug.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: All participants in this arm received the study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Adult(Normal/Mild):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3 milligrams [mg]) was administered as a single intravenous (IV) dose approximately 30 minutes (min) before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. White Light (WL) and near-infrared fluorescence (NIR-F) were used to recognize/identify the ureter.	
Reporting group title	Adult(Normal/Mild):White Light only
Reporting group description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL was used to recognize/identify the ureter.	
Reporting group title	Adult (Moderate):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter.	
Reporting group title	Adolescent(Normal/Mild):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.	

Reporting group values	Adult(Normal/Mild): White Light/near-infraredfluorescence	Adult(Normal/Mild): White Light only	Adult (Moderate):White Light/near-
Number of subjects	72	13	8
Age categorical Units: Subjects			
Age Units: years			
arithmetic mean	54.5	52.2	70.3
standard deviation	± 14.9	± 21.6	± 8.6
Sex Units: Participants			
Female	49	10	6
Male	23	3	2
Race Units: Subjects			
Asian	5	0	1
Black or African American	9	2	0
Not Reported	5	0	0
White	53	11	7
Ethnicity Units: Subjects			
HISPANIC OR LATINO	11	1	2
NOT HISPANIC OR LATINO	59	12	6
NOT REPORTED	2	0	0
Type of Surgery (Gynecological & Other-			

Abdominopelvic) Units: Subjects			
GYNECOLOGICAL	15	2	0
Other-Abdominopelvic	57	11	8

Reporting group values	Adolescent(Normal/ Mild):White Light/near-infraredfluorescence	Total	
Number of subjects	14	107	
Age categorical Units: Subjects			

Age Units: years			
arithmetic mean	14.4		
standard deviation	± 1.7	-	
Sex Units: Participants			
Female	8	73	
Male	6	34	
Race Units: Subjects			
Asian	1	7	
Black or African American	1	12	
Not Reported	0	5	
White	12	83	
Ethnicity Units: Subjects			
HISPANIC OR LATINO	4	18	
NOT HISPANIC OR LATINO	10	87	
NOT REPORTED	0	2	
Type of Surgery (Gynecological & Other-Abdominopelvic) Units: Subjects			
GYNECOLOGICAL	7	24	
Other-Abdominopelvic	7	83	

End points reporting groups

Reporting group title	Adult(Normal/Mild):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3 milligrams [mg]) was administered as a single intravenous (IV) dose approximately 30 minutes (min) before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. White Light (WL) and near-infrared fluorescence (NIR-F) were used to recognize/identify the ureter.	
Reporting group title	Adult(Normal/Mild):White Light only
Reporting group description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL was used to recognize/identify the ureter.	
Reporting group title	Adult (Moderate):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter.	
Reporting group title	Adolescent(Normal/Mild):White Light/near-infraredfluorescence
Reporting group description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.	
Subject analysis set title	Adult (Normal/Mild): WL/NIR-F (Only WL)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter. WL was reported for this arm.	
Subject analysis set title	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter. NIR-F was reported for this arm.	
Subject analysis set title	Adolescent (Normal/Mild): WL/NIR-F (Only WL)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only WL was reported for this arm.	
Subject analysis set title	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only NIR-F was reported for this arm.	
Subject analysis set title	Adult (Moderate): WL/NIR-F (Only WL)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only WL was reported for this arm.	
Subject analysis set title	Adult (Moderate): WL/NIR-F (Only NIR-F)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only NIR-F was reported for this arm.

Subject analysis set title	All Participants: WL/NIR-F (Only WL)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult and adolescent participants with normal renal function or mild or moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only WL was reported for this arm.

Subject analysis set title	All Participants: WL/NIR-F (Only NIR-F)
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult and adolescent participants with normal renal function or mild or moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter. Only NIR-F was reported for this arm.

Subject analysis set title	Adult(Normal/Mild):WL/NIR-F
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Subject analysis set title	Adult(Normal/Mild):White Light only
Subject analysis set type	Safety analysis

Subject analysis set description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL was used to recognize/identify the ureter.

Subject analysis set title	All Participants: White Light+near-infrared fluorescence
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult and adolescent participants with normal renal function or mild or moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Subject analysis set title	Adult (Moderate):White Light/Near-infraredfluorescence
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3mg) was administered as a single IV dose approximately 30min before ureter visualization, onDay 1 in adult participants with moderate renal impairment. WL and NIR-F were used torecognize/identifythe ureter.

Subject analysis set title	Adolescent(Normal/Mild):White Light/Near-infraredfluorescence
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F wereused torecognize/identifythe ureter.

Primary: Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Normal/Mild): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Normal/Mild): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores fromone ureter. Intent to Treat (ITT): All participants in the adult

normal/mild (eGFR) cohort randomized to WL/NIR-F.

End point type	Primary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)	2.7 (± 1.5)	4.3 (± 1.2)		

Statistical analyses

Statistical analysis title	statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	paired t Test
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult(Normal/Mild): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult(Normal/Mild): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. ITT with available data was analyzed. 99999

denotes not applicable (NA) as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 450, 480 minutes

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n= 72,72)	2.7 (± 1.5)	4.3 (± 1.2)		
60 minutes (n== 0,50)	99999 (± 99999)	4.3 (± 1.2)		
90 minutes (n= 0,45)	99999 (± 99999)	4.2 (± 1.1)		
120 minutes (n= 0,33)	99999 (± 99999)	4.2 (± 1.1)		
150 minutes (n= 0,23)	99999 (± 99999)	3.8 (± 1.4)		
180 minutes (n= 0,17)	99999 (± 99999)	3.8 (± 1.3)		
210 minutes (n= 0,9)	99999 (± 99999)	3.9 (± 1.7)		
240 minutes (n= 0,3)	99999 (± 99999)	4.7 (± 0.6)		
270 minutes (n= 0,4)	99999 (± 99999)	4.5 (± 1.0)		
300 minutes (n= 0,2)	99999 (± 99999)	5.0 (± 0.0)		
330 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
450 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
480 minutes (n= 0,2)	99999 (± 99999)	4.0 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Sign test
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Normal/Mild):WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Normal/Mild):WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. ITT population. 99999 denotes NA as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n=72,0)	2.7 (± 1.5)	99999 (± 99999)		
End of surgery (Day 1) (n= 0,72)	99999 (± 99999)	4.0 (± 1.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:	
Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.	
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	paired t Test
Parameter estimate	Mean difference (final values)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: Quantification of ureter conspicuity for WL and NIR-F illumination modes [Adult (Normal/Mild): WL/NIR-F]

End point title	Quantification of ureter conspicuity for WL and NIR-F illumination modes [Adult (Normal/Mild): WL/NIR-F]
End point description:	
Ureter conspicuity was quantified by image analysis measuring the color contrast when pudexacianinium chloride was present in the ureter. Contrast enhancement factor (CEF) was a measure of the degree to which color contrast was enhanced in areas in which study drug fluorescence signal was present when compared to areas in which study drug fluorescence signal was absent. Overall average data of each time point from first dose up to end of surgery was reported. ITT.	
End point type	Secondary
End point timeframe:	
From first dose every 30 minutes thereafter up to end of surgery (Day 1)	

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: ratio				
arithmetic mean (standard deviation)	1.08 (± 0.15)	2.38 (± 1.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adolescent (Normal/Mild): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adolescent (Normal/Mild): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Modified Intent to Treat (mITT): All adolescent participants in the WL/NIR-F arm. 99999 denotes Not applicable (NA).

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)	3.5 (± 1.5)	4.4 (± 1.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[1]
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[1] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adolescent(Normal/Mild): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adolescent(Normal/Mild): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT in adolescents with available data was analyzed. 99999 denotes NA, as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210 minutes

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n=14,14)	3.5 (± 1.5)	4.4 (± 1.2)		
60 minutes (n= 0,11)	99999 (± 99999)	4.5 (± 0.5)		
90 minutes (n= 0,4)	99999 (± 99999)	4.5 (± 0.6)		
120 minutes (n= 0, 1)	99999 (± 99999)	5.0 (± 99999)		
150 minutes (n= 0, 1)	99999 (± 99999)	4.0 (± 99999)		
180 minutes (n= 0, 1)	99999 (± 99999)	4.0 (± 99999)		
210 minutes (n= 0, 1)	99999 (± 99999)	2.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statitical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[2]
Parameter estimate	Mean difference (final values)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[2] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adolescent(Normal/Mild): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adolescent(Normal/Mild): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores fromone ureter. mIIT in adolescents. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n= 14,0)	3.5 (± 1.5)	99999 (± 99999)		
End of surgery (Day 1) (n= 0,14)	99999 (± 99999)	4.4 (± 0.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[3] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Moderate): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Moderate): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mIIT in adults with moderate eGFR in the WL/NIR-F arm. 99999 denotes NA.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				
arithmetic mean (standard deviation)	1.4 (± 0.7)	2.9 (± 1.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[4] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult(Moderate): WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult(Moderate): WL/NIR-F]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT in adults with moderate eGFR with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180 minutes

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n= 8,8)	14 (± 0.7)	2.9 (± 1.1)		
60 minutes (n= 0,5)	99999 (± 99999)	4.2 (± 1.1)		
90 minutes (n= 0,5)	99999 (± 99999)	3.2 (± 1.6)		
120 minutes (n= 0,5)	99999 (± 99999)	3.8 (± 1.1)		
150 minutes (n= 0,3)	99999 (± 99999)	2.7 (± 1.5)		
180 minutes (n= 0,1)	99999 (± 99999)	2.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.	
Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[5]
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[5] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Moderate):WL/NIR-F]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Moderate):WL/NIR-F]
End point description:	
Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT in adults with moderate eGFR. 99999 denotes NA, as no participants were evaluable.	
End point type	Secondary
End point timeframe:	
WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)	

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				

arithmetic mean (standard deviation)				
30 minutes (n=8,0)	14 (± 0.7)	99999 (± 99999)		
End of surgery (Day1) (n= 0,8)	99999 (± 99999)	2.9 (± 1.5)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[6] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [All participants]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [All participants]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT for any cohorts in WL/NIR-F arm. 99999 denotes NA.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)	2.7 (± 1.6)	4.2 (± 1.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[7] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [All participants]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [All participants]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT for all cohorts in WL/NIR-F arm with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 450, 480 minutes

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n= 94,94)	2.7 (± 1.6)	4.2 (± 1.2)		
60 minutes (n= 0,66)	99999 (± 99999)	4.3 (± 1.3)		
90 minutes (n= 0,54)	99999 (± 99999)	4.1 (± 1.1)		
120 minutes (n= 0,39)	99999 (± 99999)	4.2 (± 1.1)		
150 minutes (n= 0,27)	99999 (± 99999)	3.7 (± 1.4)		
180 minutes (n= 0,19)	99999 (± 99999)	3.7 (± 1.3)		
210 minutes (n= 0,10)	99999 (± 99999)	3.7 (± 1.7)		
240 minutes (n= 0,3)	99999 (± 99999)	4.7 (± 0.6)		
270 minutes (n= 0,4)	99999 (± 99999)	4.5 (± 1.0)		
300 minutes (n= 0,2)	99999 (± 9999)	5.0 (± 0.0)		
330 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
450 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
480 minutes (n= 0,2)	99999 (± 99999)	4.0 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.	
Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[8] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [All participants]

End point title	Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [All participants]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. mITT for all cohorts in WL/NIR-F arm. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)				
30 minutes (n= 94,0)	2.7 (± 1.6)	99999 (± 99999)		
End of surgery (Day 1) (n= 0,94)	99999 (± 99999)	4.0 (± 1.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[9]
Parameter estimate	Mean difference (final values)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[9] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Percentage of participants with an average index ureter conspicuity under NIR-F at least 2,3 or 4 point higher than the average index ureter conspicuity under WL over all time points [All Participants]

End point title	Percentage of participants with an average index ureter conspicuity under NIR-F at least 2,3 or 4 point higher than the average index ureter conspicuity under WL over all time points [All Participants]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Mean data from first dose and every 30 minutes thereafter up to end of surgery was evaluated and reported. mITT for all cohorts in WL/NIR-F arm.

End point type	Secondary

End point timeframe:

From first dose every 30 minute thereafter up to end of surgery (Day 1)

End point values	All Participants: White Light+near-infrared fluorescence			
Subject group type	Subject analysis set			
Number of subjects analysed	94			
Units: percentage of participants				
number (not applicable)				
2 points higher	40.4			
3 points higher	20.2			
4 points higher	2.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with an average index ureter conspicuity under NIR-F at least 1 point higher than the average index ureter conspicuity under WL over all time points [All Participants]

End point title	Percentage of participants with an average index ureter conspicuity under NIR-F at least 1 point higher than the average index ureter conspicuity under WL over all time points [All Participants]

End point description:

Ureter conspicuity was scored individually for each illumination mode using a 5-Point Likert Scale, ranging from1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident),4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Mean data from first dose and every 30 minutes thereafter up to end of surgery was evaluated and reported. mITT for all cohorts in WL/NIR-F arm.

End point type	Secondary

End point timeframe:

From first dose every 30 minute thereafter up to end of surgery (Day 1)

End point values	All Participants: White Light+near-infrared fluorescence			
Subject group type	Subject analysis set			
Number of subjects analysed	94			
Units: percentage of participants				
number (not applicable)	67.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Blinded Independent Central Reviewer (BICR) Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes (Adult (Normal/Mild): WL/NIR-F) and Concordance correlation coefficient (CCC) between Investigator and BICR reader

End point title	Blinded Independent Central Reviewer (BICR) Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes (Adult (Normal/Mild): WL/NIR-F) and Concordance correlation coefficient (CCC) between Investigator and BICR reader

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Concordance correlation coefficient (CCC) measures the agreement between investigator and BICR reader for the value difference between WL + NIR-F at 30 min timepoint. Results were reported for Reader 2, Reader 3 and Reader 4. Descriptive data for Investigator Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes is reported in Outcome measure #1. ITT.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2	1.5 (± 0.9)	3.4 (± 1.4)		

Reader 3	2.1 (± 1.3)	3.2 (± 1.3)		
Reader 4	2.0 (± 1.1)	4.3 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1,For reader 2
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	2.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[10] - Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Statistical analysis title	Statistical analysis 2, CCC, Reader 2
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	correlation coefficient
Point estimate	0.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.011
upper limit	0.431

Notes:

[11] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 3, For reader 3
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[12] - Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Statistical analysis title	Statistical analysis 3, CCC, Reader 3
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	correlation coefficient
Point estimate	0.053
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.181
upper limit	0.282

Notes:

[13] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis, For reader 4
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	2.6
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[14] - Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Statistical analysis title	Statistical analysis 6, CCC, Reader 4
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[15]
Parameter estimate	correlation coefficient
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.464

Notes:

[15] - It quantifies the degree of concordance between two measurements

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult (Normal/Mild): WL/NIR-F] and CCC between Investigator and BICR reader

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult (Normal/Mild): WL/NIR-F] and CCC between Investigator and BICR reader

End point description:

BICR's conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient(sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. CCC was concordance correlation coefficient, & it measured agreement between investigator and BICR reader for value difference between WL at 30-min timepoint & average of all NIR-F time points. Result were reported for Reader 2, Reader 3 and Reader 4. Descriptive data for Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints was reported in Outcome measure #2. ITT with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 450, 480 minutes

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2, 30 minutes (n= 72,72) Reader 2, 60 minutes (n= 0,45)	1.5 (± 0.9) 99999 (± 99999)	3.4 (± 1.4) 3.5 (± 1.3)		

Reader 2, 90 minutes (n= 0,39)	99999 (± 99999)	3.2 (± 1.4)		
Reader 2, 120 minutes (n= 0,29)	99999 (± 99999)	3.1 (± 1.4)		
Reader 2, 150 minutes (n= 0,20)	99999 (± 99999)	3.3 (± 1.5)		
Reader 2, 180 minutes (n= 0,15)	99999 (± 99999)	3.3 (± 1.5)		
Reader 2, 210 minutes (n=0,7)	99999 (± 99999)	3.4 (± 1.4)		
Reader 2, 240 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
Reader 2, 270 minutes (n= 0,4)	99999 (± 99999)	3.3 (± 2.1)		
Reader 2, 300 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
Reader 2, 330 minutes (n=0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 2, 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 2, 480 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
Reader 3, 30 minutes (n= 72,72)	2.1 (± 1.3)	3.2 (± 1.3)		
Reader 3, 60 minutes (n= 0,45)	99999 (± 99999)	3.5 (± 1.3)		
Reader 3, 90 minutes (n= 0,39)	99999 (± 99999)	3.5 (± 1.3)		
Reader 3, 120 minutes (n= 0,29)	99999 (± 99999)	3.4 (± 1.3)		
Reader 3, 150 minutes (n= 0,20)	99999 (± 99999)	3.4 (± 1.3)		
Reader 3, 180 minutes (n= 0,15)	99999 (± 99999)	3.5 (± 1.5)		
Reader 3, 210 minutes (n= 0,7)	99999 (± 99999)	3.6 (± 1.4)		
Reader 3, 240 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 3, 270 minutes (n= 0,4)	99999 (± 99999)	3.8 (± 1.9)		
Reader 3, 300 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 3, 330 minutes (n= 0,1)	99999 (± 99999)	2.0 (± 9999)		
Reader 3, 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 3, 480 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 9999)		
Reader 4, 30 minutes (n= 72,72)	2.0 (± 1.1)	4.3 (± 1.4)		
Reader 4, 60 minutes (n= 0,45)	99999 (± 99999)	4.4 (± 1.3)		
Reader 4, 90 minutes (n= 0,39)	99999 (± 99999)	4.5 (± 1.0)		
Reader 4, 120 minutes (n= 0,29)	99999 (± 99999)	4.4 (± 0.9)		
Reader 4, 150 minutes (n= 0,20)	99999 (± 99999)	4.7 (± 0.7)		
Reader 4, 180 minutes (n= 0,15)	99999 (± 99999)	4.3 (± 1.0)		
Reader 4, 210 minutes (n= 0,7)	99999 (± 99999)	4.3 (± 1.1)		
Reader 4, 240 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		

Reader 4, 270 minutes (n= 0,4)	99999 (± 99999)	4.0 (± 1.4)		
Reader 4, 300 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4, 330 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4, 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 4, 480 minutes (n=0,1)	99999 (± 99999)	2.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2
Statistical analysis description:	
Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.	
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Sign test
Parameter estimate	Mean difference (final values)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	Statistical analysis 6, CCC reader 4
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[16]
Parameter estimate	correlation coefficient
Point estimate	0.245
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.014
upper limit	0.451

Notes:

[16] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 4, CCC Reader 3
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[17]
Parameter estimate	correlation coefficient
Point estimate	0.043
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.191
upper limit	0.272

Notes:

[17] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 5 For reader 4
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.001
Method	Sign test
Parameter estimate	Mean difference (final values)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	2.5
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[18] - Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Statistical analysis title	Statistical analysis 2,CCC, Reader 2
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	correlation coefficient
Point estimate	0.219

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.013
upper limit	0.429

Notes:

[19] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 3, For reader 3
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.001
Method	Sign test
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[20] - Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adolescent (Normal/Mild): WL/NIR-F

End point title	BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adolescent (Normal/Mild): WL/NIR-F

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). Allparticipants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader4. mITT in adolescents. 99999 denotes NA.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)				

Reader 2	2.1 (± 1.2)	3.9 (± 1.3)		
Reader 3	2.9 (± 1.4)	4.1 (± 1.0)		
Reader 4	3.4 (± 1.4)	4.8 (± 0.6)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[21]
Parameter estimate	Mean difference (final values)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[21] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[22]
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[22] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2 For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[23]
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[23] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adolescent(Normal/Mild): WL/NIR-F]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adolescent(Normal/Mild): WL/NIR-F]

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader 4. mITT in adolescents with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes(+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210 minutes

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 14,14)	2.1 (± 1.2)	3.9 (± 1.3)		
Reader 2: 60 minutes (n= 0,10)	99999 (± 99999)	3.4 (± 1.2)		
Reader 2: 90 minutes (n= 0,4)	99999 (± 99999)	3.8 (± 1.3)		
Reader 2: 120 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
Reader 2: 150 minutes (n=0,1)	999999 (± 99999)	2.0 (± 99999)		

Reader 2: 180 minutes (n=0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 2: 210 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
Reader 3: 30 minutes (n= 14,14)	2.9 (± 1.4)	4.1 (± 1.0)		
Reader 3: 60 minutes (n= 0,10)	99999 (± 99999)	3.4 (± 1.0)		
Reader 3: 90 minutes (n= 0,4)	99999 (± 99999)	3.8 (± 1.0)		
Reader 3: 120 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 3: 150 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 3: 180 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 3: 210 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
Reader 4: 30 minutes (n= 14,14)	3.4 (± 1.3)	4.8 (± 0.6)		
Reader 4: 60 minutes (n= 0,10)	99999 (± 99999)	5.0 (± 0.0)		
Reader 4: 90 minutes (n= 0,4)	99999 (± 99999)	5.0 (± 0.0)		
Reader 4: 120 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 150 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 180 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 210 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[24]
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[24] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[25]
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[25] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[26]
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[26] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adolescent (Normal/Mild):WL/NIR-F]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adolescent (Normal/Mild):WL/NIR-F]

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader4. miTT in adolescents. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	Adolescent (Normal/Mild): WL/NIR-F (Only WL)	Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	14		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 14,0)	2.1 (± 1.2)	99999 (± 99999)		
Reader 2: End of surgery (Day 1) (n= 0,14)	99999 (± 99999)	3.4 (± 1.5)		
Reader 3: 30 minutes (n= 14,0)	2.9 (± 1.4)	99999 (± 99999)		
Reader 3: End of surgery (Day 1) (n= 0,14)	99999 (± 99999)	3.6 (± 1.3)		
Reader 4: 30 minutes (n= 14,0)	3.4 (± 1.3)	99999 (± 99999)		
Reader 4: End of surgery (Day 1) (n= 0,14)	99999 (± 99999)	4.8 (± 0.6)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[27]
Parameter estimate	Mean difference (final values)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[27] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[28]
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[28] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error

Statistical analysis title	Statistical analysis, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adolescent (Normal/Mild): WL/NIR-F (Only WL) v Adolescent (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority[29]
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[29] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Normal/Mild):WL/NIR-F] and CCC between Investigator and BICR reader

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Normal/Mild):WL/NIR-F] and CCC between Investigator and

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-PointLikert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3= sufficient(sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. CCC was concordance correlation coefficient, and it measures\d the agreement between investigator and BICR reader for the value difference between WL at 30-min timepoint and the end of surgery score under NIR-F. Results were

reported for Reader2, Reader 3 and Reader 4. Descriptive data for Investigator Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery is reported in Outcome measure #3. ITT. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	Adult (Normal/Mild): WL/NIR-F (Only WL)	Adult (Normal/Mild): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	72		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 72,0)	1.5 (± 0.9)	99999 (± 99999)		
Reader 2: End of surgery (Day 1) (n= 0,72)	99999 (± 99999)	3.0 (± 1.4)		
Reader 3: 30 minutes (n= 72,0)	2.1 (± 1.3)	99999 (± 99999)		
Reader 3: End of surgery (Day 1) (n= 0,72)	99999 (± 99999)	3.0 (± 1.4)		
Reader 4: 30 minutes (n= 72,0)	2.0 (± 1.2)	99999 (± 99999)		
Reader 4: End of surgery (Day 1) (n= 0,72)	99999 (± 99999)	4.0 (± 1.5)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[30] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 6, CCC, Reader 4
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[31]
Parameter estimate	correlation coefficient
Point estimate	0.297
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	0.495

Notes:

[31] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 4, CCC, Reader 3
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[32]
Parameter estimate	correlation coefficient
Point estimate	0.186
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.048
upper limit	0.4

Notes:

[32] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 5, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	2

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	2.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[33] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, CCC, Reader 2
Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	correlation coefficient
Point estimate	0.339
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.116
upper limit	0.529

Notes:

[34] - It quantifies the degree of concordance between two measurements

Statistical analysis title	Statistical analysis 3 For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Normal/Mild): WL/NIR-F (Only WL) v Adult (Normal/Mild): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	paired t test
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

Secondary: BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Moderate): WL/NIR-F]

End point title	BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [Adult (Moderate): WL/NIR-F]

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader4. mITT in adults with moderate eGFR. 99999 denotes NA.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2	1.3 (± 0.7)	2.4 (± 1.4)		
Reader 3	1.5 (± 0.5)	2.4 (± 1.1)		
Reader 4	2.0 (± 0.9)	4.1 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[35]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[35] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[36]
Parameter estimate	Mean difference (final values)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[36] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[37]
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[37] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult (Moderate):WL/NIR-F]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [Adult (Moderate):WL/NIR-F]

End point description:

BICR’s conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader4. mITT in adults with moderate eGFR with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180 minutes

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 8,8)	1.3 (± 0.7)	2.4 (± 1.4)		
Reader 2: 60 minutes (n= 0,2)	99999 (± 99999)	3.5 (± 2.1)		
Reader 2: 90 minutes (n= 0,4)	99999 (± 99999)	2.8 (± 1.5)		
Reader 2: 120 minutes (n= 0,4)	99999 (± 99999)	2.8 (± 1.7)		
Reader 2: 150 minutes (n= 0,3)	99999 (± 99999)	2.3 (± 0.6)		
Reader 2: 180 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
Reader 3: 30 minutes (n= 8,8)	1.5 (± 0.5)	2.4 (± 1.1)		
Reader 3: 60 minutes (n= 0,2)	99999 (± 99999)	3.5 (± 2.1)		
Reader 3: 90 minutes (n= 0,4)	99999 (± 99999)	2.8 (± 1.5)		
Reader 3: 120 minutes (n= 0,4)	99999 (± 99999)	3.0 (± 1.6)		
Reader 3: 150 minutes (n= 0,3)	99999 (± 99999)	2.3 (± 0.6)		
Reader 3 180 minutes (n= 0,1)	99999 (± 99999)	2.0 (± 99999)		
Reader 4: 30 minutes (n= 8,8)	2.0 (± 0.9)	4.1 (± 1.4)		
Reader 4: 60 minutes (n= 0,2)	99999 (± 99999)	4.5 (± 0.7)		
Reader 4: 90 minutes (n= 0,4)	99999 (± 99999)	5.0 (± 0.0)		
Reader 4: 120 minutes (n=0,4)	99999 (± 99999)	3.8 (± 1.5)		
Reader 4: 150 minutes (n= 0,3)	99999 (± 99999)	4.7 (± 0.6)		
Reader 4: 180 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate):

	WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[38]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[38] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[39]
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[39] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[40]
Parameter estimate	Mean difference (final values)
Point estimate	1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[40] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Moderate): WL/NIR-F]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [Adult (Moderate): WL/NIR-F]

End point description:

BICR's conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader4. mITT in adults with moderate eGFR. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	Adult (Moderate): WL/NIR-F (Only WL)	Adult (Moderate): WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	8	8		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 8,0)	1.3 (± 0.7)	99999 (± 99999)		
Reader 2: End of Surgery (Day 1) (n= 0,8)	99999 (± 99999)	2.3 (± 1.3)		
Reader 3: 30 minutes (n= 8,0)	1.5 (± 0.5)	99999 (± 99999)		
Reader 3: End of Surgery (Day 1) (n= 0,8)	99999 (± 99999)	2.6 (± 1.1)		
Reader 4: 30 minutes (n= 8,0)	2.0 (± 0.9)	99999 (± 99999)		
Reader 4: End of Surgery (Day 1) (n= 0,8)	99999 (± 99999)	4.0 (± 1.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[41]
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[41] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[42]
Parameter estimate	Mean difference (final values)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[42] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	Adult (Moderate): WL/NIR-F (Only WL) v Adult (Moderate): WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority[43]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[43] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [All Participants]

End point title	BICR Conspicuity Score Difference in Ureter Between WL and NIR-F at 30 minutes [All Participants]

End point description:

BICR's conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader 4. mITT for all cohorts in WL/NIR-F arm.

End point type	Secondary

End point timeframe:

30 minutes post dose (+/- 15 minutes)

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2	1.6 (± 0.9)	3.4 (± 1.4)		
Reader 3	2.1 (± 1.3)	3.3 (± 1.3)		
Reader 4	2.2 (± 1.2)	4.3 (± 1.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[44]
Parameter estimate	Mean difference (final values)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[44] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[45]
Parameter estimate	Mean difference (final values)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[45] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL scores and NIR-F scores at 30-min timepoint.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[46]
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999

Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[46] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [All Participants]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F an average of all timepoints [All Participants]

End point description:

BICR's conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader 4. mITT for all cohorts in WL/NIR-F arm with available data was analyzed. 99999 denotes NA as either no participants were evaluable or only 1 participant was evaluable, thus SD not reported.

End point type	Secondary

End point timeframe:

WL: 30 minutes (+/- 15 minutes); NIR-F: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 450, 480 minutes

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 94,94)	1.6 (± 0.9)	3.4 (± 1.4)		
Reader 2: 60 minutes (n= 0,57)	99999 (± 99999)	3.5 (± 1.3)		
Reader 2: 90 minutes (n= 0,47)	99999 (± 99999)	3.2 (± 1.4)		
Reader 2: 120 minutes (n= 0,34)	99999 (± 99999)	3.1 (± 1.4)		
Reader 2: 150 minutes (n= 0,24)	99999 (± 99999)	3.1 (± 1.4)		
Reader 2: 180 minutes (n= 0,17)	99999 (± 99999)	3.0 (± 1.4)		
Reader 2: 210 minutes (n= 0,8)	99999 (± 99999)	3.1 (± 1.6)		
Reader 2: 240 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
Reader 2: 270 minutes (n= 0,4)	99999 (± 99999)	3.3 (± 2.1)		
Reader 2: 300 minutes (n= 0,1)	99999 (± 99999)	4.0 (± 99999)		
Reader 2: 330 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 2: 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 2: 480 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		

Reader 3: 30 minutes (n= 94,94)	2.1 (± 1.3)	3.3 (± 1.3)		
Reader 3: 60 minutes (n= 0,57)	99999 (± 99999)	3.5 (± 1.2)		
Reader 3: 90 minutes (n= 0,47)	99999 (± 99999)	3.4 (± 1.3)		
Reader 3: 120 minutes (n= 0,34)	99999 (± 99999)	3.3 (± 1.3)		
Reader 3: 150 minutes (n= 0,24)	99999 (± 99999)	3.3 (± 1.4)		
Reader 3: 180 minutes (n= 0,17)	99999 (± 99999)	3.4 (± 1.4)		
Reader 3: 210 minutes (n= 0,8)	99999 (± 99999)	3.3 (± 1.6)		
Reader 3: 240 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 3: 270 minutes (n= 0,4)	99999 (± 99999)	3.8 (± 1.9)		
Reader 3: 300 minutes (n= 0,1)	99999 (± 99999)	3.0 (± 99999)		
Reader 3: 330 minutes (n= 0,1)	99999 (± 99999)	2.0 (± 99999)		
Reader 3: 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 3: 480 minutes (n= 0,1)	99999 (± 99999)	1.0 (± 99999)		
Reader 4: 30 minutes (n= 94,94)	2.2 (± 1.2)	4.4 (± 1.3)		
Reader 4: 60 minutes (n= 0,57)	99999 (± 99999)	4.5 (± 1.2)		
Reader 4: 90 minutes (n= 0,47)	99999 (± 99999)	4.6 (± 0.9)		
Reader 4: 120 minutes (n= 0,34)	99999 (± 99999)	4.4 (± 1.0)		
Reader 4: 150 minutes (n= 0,24)	99999 (± 99999)	4.7 (± 0.7)		
Reader 4: 180 minutes (n= 0,17)	99999 (± 99999)	4.3 (± 1.0)		
Reader 4: 210 minutes (n= 0,8)	99999 (± 99999)	4.1 (± 1.1)		
Reader 4: 240 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 270 minutes (n= 0,4)	99999 (± 99999)	4.0 (± 1.4)		
Reader 4: 300 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 330 minutes (n= 0,1)	99999 (± 99999)	5.0 (± 99999)		
Reader 4: 450 minutes (n= 0,0)	99999 (± 99999)	99999 (± 99999)		
Reader 4: 480 minutes (n= 0,1)	99999 (± 99999)	2.0 (± 99999)		

Statistical analyses

Statistical analysis title	Statistical analysis 1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants:

	WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[47]
Parameter estimate	Mean difference (final values)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[47] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[48]
Parameter estimate	Mean difference (final values)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[48] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between NIR-F scores at each time point and the 30-min WL score of the index ureter (left or right) for each participant.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[49]
Parameter estimate	Mean difference (final values)
Point estimate	1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[49] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [All Participants]

End point title	BICR Conspicuity Score Difference in Ureter Between WL at 30 minutes and NIR-F at end of Surgery [All Participants]

End point description:

BICR's conspicuity assessment of the ureter was scored individually for each illumination mode using a 5-Point Likert Scale ranging from 1 to 5 where 1= none (not self-evident), 2= poor (somewhat self-evident), 3=sufficient (sufficiently self-evident), 4= good (clearly self-evident), 5= excellent (extremely self-evident). All participants had conspicuity scores from one ureter. Results were reported for Reader 2, Reader 3 and Reader 4. mITT for all cohorts in WL/NIR-F arm. 99999 denotes NA, as no participants were evaluable.

End point type	Secondary

End point timeframe:

WL: 30 minute post dose (+/- 15 minutes); NIR-F: End of surgery (Day 1)

End point values	All Participants: WL/NIR-F (Only WL)	All Participants: WL/NIR-F (Only NIR-F)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	94	94		
Units: score on a scale				
arithmetic mean (standard deviation)				
Reader 2: 30 minutes (n= 94,0)	1.6 (± 0.9)	99999 (± 99999)		
Reader 2: End of surgery (Day 1) (n= 0,94)	99999 (± 99999)	3.0 (± 1.4)		
Reader 3: 30 minutes (n= 94,0)	2.1 (± 1.3)	99999 (± 99999)		
Reader 3: End of surgery (Day 1) (n= 0,94)	99999 (± 99999)	3.1 (± 1.4)		
Reader 4: 30 minutes (n= 94,0)	2.2 (± 1.2)	99999 (± 99999)		
Reader 4: End of surgery (Day 1) (n= 0,94)	99999 (± 99999)	4.1 (± 1.4)		

Statistical analyses

Statistical analysis title	Statistical analysis1, For reader 2

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time

point and the NIR-F score at the end of surgery across all participants.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[50]
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[50] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 3, For reader 4

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[51]
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[51] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Statistical analysis title	Statistical analysis 2, For reader 3

Statistical analysis description:

Mean Difference was calculated by averaging over the differences between WL score at 30-min time point and the NIR-F score at the end of surgery across all participants.

Comparison groups	All Participants: WL/NIR-F (Only WL) v All Participants: WL/NIR-F (Only NIR-F)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority[52]
Parameter estimate	Mean difference (final values)
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-99999
upper limit	99999
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[52] - SAP pre-specified that 95% Confidence Interval would not be analyzed for this endpoint, 2-Sides (-99999, 99999) was entered to remove validation error.

Secondary: Number of participants with Treatment Emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of participants with Treatment Emergent Adverse Events (TEAEs) and Serious TEAEs

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant administered an Investigational Product(IP) and which does not necessarily had a causal relationship with the treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding; abnormal laboratory test result or other safety assessment, symptom, or disease temporally associated with the use of IP whether considered related to the IP. A TEAE was defined as an AE with onset at any time from first dosing until the follow up period. AEs were considered serious (SAEs) if the AE resulted, in death, was life-threatening, resulted in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, resulted in congenital anomaly, or birth defect or required inpatient hospitalization or led to prolongation of hospitalization. SAF population

End point type	Secondary

End point timeframe:

From first dose up to 17 months and 15 days

End point values	Adult(Normal/Mild):White Light/near-infraredfluorescence	Adult(Normal/Mild):White Light only	Adult (Moderate):White Light/near-infraredfluorescence	Adolescent(Normal/Mild):White Light/near-infraredfluorescence
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	13	8	14
Units: participants				
number (not applicable)				
TEAE	28	8	1	7
Serious TEAE	8	4	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) of pudexacianinium chloride: Plasma Concentration

End point title	Pharmacokinetics (PK) of pudexacianinium chloride: Plasma Concentration

End point description:

Concentration of pudexacianinium chloride in plasma. Pharmacokinetic Analysis Set (PKAS): All participants in any cohort who received pudexacianinium chloride for which at least 1 plasma or urine concentration data was available with the time for dosing and sampling. PKAS with available data was analyzed. As planned SD was reported only if >=3 participants were evaluated for a specific timepoint. 99999 denotes NA as only 1 participant analyzed thus SD was not evaluable or less than 3 participants were evaluated and as planned SD was not evaluable.

End point type	Secondary

End point timeframe:

Day 1 Postdose: 10, 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 390, 360 minutes

End point values	Adult(Normal/ Mild):WL/NIR-F	Adult(Normal/ Mild):White Light only	Adult (Moderate):White Light/Near-infraredfluorescence	Adolescent(Normal/Mild):White Light/Near-infraredfluorescence
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	13	8	14
Units: nanogram/milliliters (ng/mL)				
arithmetic mean (standard deviation)				
10 minutes (n= 13,62,8,14)	411 (± 387)	366 (± 109)	426 (± 137)	410 (± 141)
30 minutes (n= 13,61,8,14)	185 (± 46.8)	197 (± 61.2)	267 (± 93.6)	244 (± 86.4)
60 minutes (n= 11,59,8,12,)	126 (± 36.1)	129 (± 34.4)	203 (± 56.8)	166 (± 50.1)
90 minutes (n= 7,30,5,9)	108 (± 34.6)	111 (± 40.5)	172 (± 42.3)	121 (± 46.1)
120 minutes (n= 8,45,6,8)	79.8 (± 30.3)	78.3 (± 37.1)	147 (± 44.7)	99.2 (± 26.8)
150 minutes (n= 3,21,4,2)	82.8 (± 29.0)	115 (± 37.3)	128 (± 25.1)	120 (± 99999)
180 minutes (n= 6,20,2,3)	61.9 (± 24.8)	59.2 (± 24.1)	128 (± 99999)	47.1 (± 17.5)
210 minutes (n= 2,5,1,0)	53.8 (± 16.0)	47.8 (± 99999)	97.6 (± 99999)	99999 (± 99999)
240 minutes (n= 1,5,0,0)	69.7 (± 28.5)	45.8 (± 99999)	99999 (± 99999)	99999 (± 99999)
270 minutes (n= 0,2,01)	42.4 (± 99999)	99999 (± 99999)	99999 (± 99999)	34.2 (± 99999)
300 minutes (n= 1,3,0,0)	51.1 (± 18.7)	30.9 (± 99999)	99999 (± 99999)	99999 (± 99999)
330 minutes (n= 0,1,0,0)	25.6 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
360 minutes (n= 0,1,0,0)	22.4 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
390 minutes (n= 0,2,0,0)	28.9 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: PK of pudexacianinium chloride: Urine Concentration

End point title	PK of pudexacianinium chloride: Urine Concentration

End point description:

Concentration of pudexacianinium chloride in urine. PKAS with available data was analyzed. As planned SD was reported only if >=3 participants were evaluated for a specific timepoint. 99999 denotes NA as

only 1 participant analyzed thus SD was not evaluable or less than 3 participants were evaluated and as planned SD was not evaluable.

End point type	Secondary

End point timeframe:

Day 1 Postdose: 0-10, 10-30, 30-60, 60-90, 90-120, 120-150, 150-180, 180-210, 210-240, 240-270, 270-300,300-330, 330-360, 360-390, 390-420, 420-450, 450-480 minutes

End point values	Adult(Normal/ Mild):WL/NIR-F	Adult(Normal/ Mild):White Light only	Adult (Moderate):White Light/Near-infraredfluorescence	Adolescent(Normal/Mild):White Light/Near-infraredfluorescence
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	11	8	13
Units: ng/mL				
arithmetic mean (standard deviation)				
0-10 minutes (n= 11,56,8,9)	235 (± 629)	1530 (± 4100)	80.4 (± 165)	9.98 (± 29.9)
10-30 minutes (n= 10,51,4,13)	10200 (± 15600)	4960 (± 6050)	7890 (± 3610)	14200 (± 15100)
30-60 minutes (n= 9,52,3,13)	19800 (± 20300)	18000 (± 18600)	10400 (± 6640)	25200 (± 22000)
60-90 minutes (n= 8,47,6,7)	20100 (± 21200)	16700 (± 18100)	25500 (± 17100)	41600 (± 41900)
90-120 minutes (n= 5,35,5,5)	14500 (± 9630)	17700 (± 13300)	25800 (± 37200)	49800 (± 62000)
120-150 minutes (n= 5,24,2,5)	10700 (± 6880)	20700 (± 8850)	17400 (± 99999)	25500 (± 16600)
150-180 minutes (n= 5,22,1,2)	9110 (± 6530)	17900 (± 7900)	18400 (± 99999)	19600 (± 99999)
180-210 minutes (n= 1,5,0,1)	8690 (± 6920)	6230 (± 99999)	99999 (± 99999)	10500 (± 99999)
210-240 minutes (n= 1,4,0,1)	5750 (± 2310)	5230 (± 99999)	99999 (± 99999)	6500 (± 99999)
240-270 minutes (n= 0,2,0,0)	5500 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
270-300 minutes (n= 0,3,0,0)	3690 (± 1600)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
300-330 minutes (n= 0,2,0,0)	4860 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
330-360 minutes (n= 0,3,0,0)	3630 (± 2680)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
360,390 minutes (n= 0,3,0,0)	2650 (± 1640)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
390-420 minutes (n= 0,3,0,0)	1570 (± 2400)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
420-450 minutes (n= 0,2,0,0)	3150 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
450-480 minutes (n= 0,1,0,0)	3070 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of pudexacianinium chloride excreted into urine (Ae)

End point title	Amount of pudexacianinium chloride excreted into urine (Ae)

End point description:

PKAS with available data was analyzed. As planned SD was reported only if >=3 participants were evaluated for a specific timepoint. 99999 denotes NA as only 1 participant analyzed thus SD was not evaluable or less than 3 participants were evaluated and as planned SD was not evaluable.

End point type	Secondary

End point timeframe:

Day 1 Postdose: 0-10, 10-30, 30-60, 60-90, 90-120, 120-150, 150-180, 180-210, 210-240, 240-270, 270-300,300-330, 330-360, 360-390, 390-420, 420-450, 450-480 minutes

End point values	Adult(Normal/ Mild):WL/NIR-F	Adult(Normal/ Mild):White Light only	Adult (Moderate):White Light/Near-infraredfluorescence	Adolescent(Normal/Mild):White Light/Near-infraredfluorescence
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	10	8	13
Units: milligrams				
arithmetic mean (standard deviation)				
0-10 minutes (n= 10,56,8,9)	0.0190 (± 0.0425)	0.0443 (± 0.0790)	0.000713 (± 0.0194)	0.000657 (± 0.00197)
10-30 minutes (n= 9,51,4,13)	0.164 (± 0.198)	0.0773 (± 0.122)	0.122 (± 0.0759)	0.245 (± 0.269)
30-60 minutes (n= 9,52,3,13)	0.274 (± 0.230)	0.375 (± 0.276)	0.175 (± 0.0305)	0.240 (± 0.258)
60-90 minutes (n= 8,48,6,7)	0.340 (± 0.232)	0.304 (± 0.290)	0.216 (± 0.160)	0.348 (± 0.417)
90-120 minutes (n= 5,36,5,5)	0.306 (± 0.199)	0.325 (± 0.261)	0.151 (± 0.0570)	0.578 (± 0.465)
120-150 minutes (n= 5,24,2,5)	0.203 (± 0.131)	0.301 (± 0.112)	0.0511 (± 99999)	0.256 (± 0.170)
150-180 minutes (n= 5,22,1,2)	0.143 (± 0.0859)	0.286 (± 0.289)	0.171 (± 99999)	0.450 (± 99999)
180-210 minutes (n= 1,5,0,1)	0.151 (± 0.0763)	0.147 (± 99999)	99999 (± 99999)	0.162 (± 99999)
210-240 minutes (n= 1,4,0,2)	0.0937 (± 0.0307)	0.175 (± 99999)	99999 (± 99999)	0.0702 (± 99999)
240-270 minutes (n= 0,2,0,0)	0.0803 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
270-300 minutes (n= 0,3,0,0)	0.0655 (± 0.0105)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
300-330 minutes (n= 0,2,0,0)	0.0582 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
330-360 minutes(n= 0,3,0,0)	0.0438 (± 0.0541)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
360-390 minutes (n= 0,3,0,0)	0.0808 (± 0.0412)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
390-420 minutes (n= 0,3,0,0)	0.0263 (± 0.0209)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
420-450 minutes(n= 0,2,0,0)	0.0835 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

450-480 minutes(n= 0,1,0,0)	0.0301 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of pudexacianinium chloride dose excreted into urine (Ae%)

End point title	Percentage of pudexacianinium chloride dose excreted into urine (Ae%)

End point description:

PKAS with available data was analyzed. As planned SD was reported only if >=3 participants were evaluated for a specific timepoint. 99999 denotes NA as only 1 participant analyzed thus SD was not evaluable or less than 3 participants were evaluated and as planned SD was not evaluable.

End point type	Secondary

End point timeframe:

Day 1 Postdose: 0-10, 10-30, 30-60, 60-90, 90-120, 120-150, 150-180, 180-210, 210-240, 240-270, 270-300,300-330, 330-360, 360-390, 390-420, 420-450, 450-480 minutes

End point values	Adult(Normal/ Mild):WL/NIR-F	Adult(Normal/ Mild):White Light only	Adult (Moderate):White Light/Near-infraredfluorescence	Adolescent(Normal/Mild):White Light/Near-infraredfluorescence
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	56	10	8	13
Units: percentage of drug excreted				
arithmetic mean (standard deviation)				
0-10 minutes (n= 10,56,8,9)	0.633 (± 1.42)	1.48 (± 2.63)	0.238 (± 0.646)	0.0219 (± 0.0657)
10-30 minutes (n=9,51,4,13)	5.46 (± 6.59)	2.58 (± 4.06)	4.06 (± 2.53)	8.18 (± 8.98)
30-60 minutes (n= 9,52,3,13)	9.15 (± 7.68)	12.5 (± 9.21)	5.83 (± 1.02)	7.99 (± 8.59)
60-90 minutes (n= 8,48,6,7)	11.3 (± 7.74)	10.1 (± 9.66)	7.20 (± 5.32)	11.6 (± 13.9)
90-120 minutes (n= 5,36,5,5)	10.2 (± 6.63)	10.8 (± 8.71)	5.03 (± 1.90)	19.3 (± 15.5)
120-150 minutes (n= 5,24,2,5)	6.77 (± 4.38)	10.0 (± 3.74)	1.70 (± 99999)	8.54 (± 5.68)
150-180 minutes (n= 5,22,1,2)	4.78 (± 2.86)	9.52 (± 9.62)	5.70 (± 99999)	15.0 (± 99999)
180-210 minutes (n= 1,5,0,1)	5.03 (± 2.54)	4.90 (± 99999)	99999 (± 99999)	5.39 (± 99999)
210-240 minutes (n= 1,4,0,1)	3.12 (± 1.02)	5.82 (± 99999)	99999 (± 99999)	2.34 (± 99999)
240-270 minutes (n= 0,2,0,0)	2.68 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
270-300 minutes (n= 0,3,0,0)	2.18 (± 0.351)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
300-330 minutes (n= 0,2,0,0)	1.94 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
330-360 minutes (n= 0,3,0,0)	1.46 (± 1.80)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

360,390 minutes (n= 0,3,0,0)	2.69 (± 1.37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
390-420 minutes (n= 0,3,0,0)	0.877 (± 0.697)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
420-450 minutes (n= 0,2,0,0)	2.78 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
450-480 minutes (n= 0,1,0,0)	1.00 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality (ACM): From randomization up to 17 months and 15 days
Adverse events: From first dose up to 17 months and 15 days

Adverse event reporting additional description:

ACM was analyzed for all randomized population.
Serious and Non serious adverse events: SAF

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v27.0

Reporting groups

Reporting group title	Adult (Normal/Mild): White Light/near-infrared fluorescence

Reporting group description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Reporting group title	Adolescent (Normal/Mild): WL/NIR-F

Reporting group description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adolescent participants with normal renal function or mild renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Reporting group title	Adult (Moderate): White Light/near-infrared fluorescence

Reporting group description:

Pudexacianinium (3mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with moderate renal impairment. WL and NIR-F were used to recognize/identify the ureter.

Reporting group title	Adult (Normal/Mild): White Light only

Reporting group description:

Pudexacianinium (3 mg) was administered as a single IV dose approximately 30 min before ureter visualization, on Day 1 in adult participants with normal renal function or mild renal impairment. WL was used to recognize/identify the ureter.

Serious adverse events	Adult (Normal/Mild): White Light/near-infrared fluorescence	Adolescent (Normal/Mild): WL/NIR-F	Adult (Moderate): White Light/near-infrared fluorescence
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 70 (11.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Postoperative ileus			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anastomotic leak			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic haematoma			

subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic haemorrhage			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis aspiration			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Adult (Normal/Mild): White Light only		
Total subjects affected by serious adverse events			

subjects affected / exposed	4 / 13 (30.77%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Postoperative ileus			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anastomotic leak			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic haematoma			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis aspiration			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract obstruction			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			

subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Adult (Normal/Mild): White Light/near-infrared fluorescence	Adolescent (Normal/Mild): WL/NIR-F	Adult (Moderate): White Light/near-infrared fluorescence
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 70 (15.71%)	7 / 14 (50.00%)	1 / 8 (12.50%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 70 (2.86%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	2 / 70 (2.86%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 70 (5.71%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Dilutional anaemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	3 / 70 (4.29%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	3	0	1
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	2 / 70 (2.86%)	5 / 14 (35.71%)	0 / 8 (0.00%)
occurrences (all)	2	5	0
Loss of bladder sensation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	0 / 70 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Adult (Normal/Mild): White Light only		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)		
occurrences (all)	0		
Dilutional anaemia			

subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0		
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all) Loss of bladder sensation subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1		
Infections and infestations Postoperative wound infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 0 / 13 (0.00%) 0 1 / 13 (7.69%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2023	• The protocol design is updated to include adult participants with moderate or severe renal impairment. Impacted language includes: • Primary and Key Secondary Objectives and endpoints • New additional secondary objective/endpoints are added • Primary estimands • Number of participants • Study Design Overview o Adult participants will now include a normal/mild eGFR cohort with randomization to the NIR-F/WL arm and a WL-only arm (investigator blinded), and a moderate/severe eGFR cohort with conspicuity assessed with NIR-F and WL at all time points o Adolescent cohort remains the same • Inclusion criterion no. 4 regarding eGFR criteria is updated • A new exclusion criterion is added for participants on hemodialysis, hemodiafiltration or peritoneal dialysis. • Assignment of study intervention • Statistical considerations • The eGFR formula for adolescents is changed to Schwartz formula. • Clarification for the timing of the first conspicuity assessment. Study design details for the investigator's selection of ureter(s) is updated.
02 October 2023	• Details for the addition of a blinded independent central review (BICR) are added. Notable updates include: new secondary objectives and endpoints, details on the timing and instructions on how to perform the new efficacy assessment and details on how the analysis of the secondary endpoints will be performed. • The number of participants in the moderate/severe eGFR cohort is increased from up to 7 to up to 10, with the total number of participants being updated from 104 to 107. • The rescreening language is updated.
04 April 2024	• Additional endpoints for the BICR additional secondary objective are added. The statistical analysis details for the new endpoints are added. • The visit window is updated from ± 5 days to ± 10 days. As a result, the anticipated duration of the study for each participant is updated from 5 to 43 days to 5 to 53 days. • The blood and urine sample collection schedule for pharmacokinetics is updated. The following language is updated in the key secondary endpoints: Descriptive statistics will be used to summarize the ureter conspicuity at the 30-min time point after ASP5354 administration with WL and the end of surgery time point with NIR-F. The same imputation algorithm described in the analysis of the first key secondary endpoint will be applied to the data prior to setting the end of surgery NIR-F value for each particiant.
24 October 2024	And other Non substantial amendments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported