Clinical trial results:
A Randomized, Controlled, Open-label Study of the Efficacy, Durability, and Safety of UGN-102 With or Without TURBT in Patients with Low Grade Intermediate Risk Non-Muscle Invasive Bladder Cancer (LG IR-NMIBC) (ATLAS)

Summary

EudraCT number	2020-003541-11
Trial protocol	EE BG LV PL
Global end of trial date	28 November 2023

Results information

Result version number	v1 (current)
This version publication date	23 May 2024
First version publication date	23 May 2024
Summary attachment (see zip file)	BL006_Clinical Study Report Synopsis (BL006_Clinical Study Report Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	BL006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04688931
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UroGen Pharma, Ltd.
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2023
Global end of trial reached?	Yes
Global end of trial date	28 November 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of UGN-102 with or without transurethral resection of bladder tumor (TURBT) versus TURBT alone with respect to disease-free survival (DFS) in patients with Low Grade Intermediate Risk Non-Muscle Invasive Bladder Cancer (LG IR-NMIBC).

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:
- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable laws and regulations

Background therapy: -

Evidence for comparator:

TURBT is the global standard of care for management of LG IR NMIBC and was designated the comparator because there is no accepted therapeutic alternative to treat this patient population.

Actual start date of recruitment	12 January 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Russian Federation: 91
Country: Number of subjects enrolled	Bulgaria: 63
Country: Number of subjects enrolled	Ukraine: 31
Country: Number of subjects enrolled	Georgia: 30
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Estonia: 18
Country: Number of subjects enrolled	Latvia: 16
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Poland: 2
Worldwide total number of subjects	282
EEA total number of subjects	99

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)	0
Adults (18-64 years)	114
From 65 to 84 years	162
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

Approximately 632 patients were planned to be enrolled. UroGen stopped study enrollment early after 282 patients were randomized (142 in the UGN102 ± TURBT arm and 140 in the TURBT alone arm).

Pre-assignment

Screening details:

Inclusion criteria: signed informed consent; ≥18 years old; LG NMIBC; negative voiding cytology for high-grade disease within 6 weeks of screening; intermediate risk disease (having 1-2 of the following: multiple tumors, solitary tumor >3 cm, recurrence); adequate organ/bone marrow function; no active UTI; agree to sex/contraception requirements.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	UGN-102 ± TURBT

Arm description:

UGN-102 ± TURBT arm underwent 6 weekly intravesical instillations of UGN-102 followed by TURBT at 3 months only if needed.

Arm type	Experimental
Investigational medicinal product name	mitomycin
Investigational medicinal product code	UGN-102
Other name	
Pharmaceutical forms	Powder and solvent for intravesical solution
Routes of administration	Intravesical use

Dosage and administration details:

The UGN-102 admixture for intravesical instillations contained mitomycin 75 mg in 56 mL admixture (1.33 mg/mL mitomycin). The UGN-102 admixture was prepared in advance of use by the pharmacy, up to 48 hours before administration. UGN-102 intravesical instillation was an outpatient procedure involving application of an anesthetic lubricant in the urethra, urethral catheterization using a flexible plastic catheter, and instillation of UGN-102 into the bladder over a period of approximately 1 to 2 minutes. The catheter stayed in place for approximately 15 minutes, after which it was removed, and the patient could continue activities of daily living.

Arm title	TURBT Alone

Arm description:

Participants in the TURBT Alone arm underwent TURBT only, followed by repeat TURBT at 3 months if needed.

Arm type	Active comparator
Investigational medicinal product name	transurethral resection of bladder tumor
Investigational medicinal product code	
Other name	TURBT
Pharmaceutical forms	Pharmaceutical dose form not applicable
Routes of administration	Other use

Dosage and administration details:

TURBT is the current standard of care for low-grade intermediate-risk non-muscle invasive bladder cancer (LG IR NMIBC).

Number of subjects in period 1	UGN-102 ± TURBT	TURBT Alone
Started	142	140
Completed	123	106
Not completed	19	34
Randomization error	3	-
Consent withdrawn by subject	5	16
Physician decision	3	5
Patient decision	-	1
Disease progression	-	2
Not eligible	1	3
Adverse event	4	1
Sponsor requirement	1	1
Lost to follow-up	1	3
New lesion, but biopsy could not be done	-	1
Independently applied to another medical center	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	UGN-102 ± TURBT
Reporting group description:	
UGN-102 ± TURBT arm underwent 6 weekly intravesical instillations of UGN-102 followed by TURBT at 3 months only if needed.	
Reporting group title	TURBT Alone
Reporting group description:	
Participants in the TURBT Alone arm underwent TURBT only, followed by repeat TURBT at 3 months if needed.	

Reporting group values	UGN-102 ± TURBT	TURBT Alone	Total
Number of subjects	142	140	282
Age categorical Units: Subjects			
< 65 years	51	63	114
≥ 65 to < 75 years	59	47	106
≥ 75 to < 85 years	29	27	56
≥ 85 years	3	3	6
Age continuous Units: years			
arithmetic mean	66.7	66.3	
standard deviation	± 10.59	± 10.50	-
Gender categorical Units: Subjects			
Female	37	47	84
Male	105	93	198
Race Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asian	1	1	2
Black or African American	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
White	140	139	279
Not reported	1	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	2	1	3
Not Hispanic or Latino	140	137	277
Not reported	0	2	2
BMI - Mean			
Body mass index (BMI) was taken from screening evaluations. Number of patients who reported BMI: UGN-102 ± TURBT arm = 138; TURBT Alone arm = 131.			
Units: kg/m2			
arithmetic mean	27.76	27.31	
standard deviation	± 5.005	± 4.666	-
BMI - Median Units: kg/m2			

median	26.85	26.69	
full range (min-max)	18.2 to 47.0	17.3 to 41.9	-

End points

End points reporting groups

Reporting group title	UGN-102 ± TURBT
Reporting group description:	
UGN-102 ± TURBT arm underwent 6 weekly intravesical instillations of UGN-102 followed by TURBT at 3 months only if needed.	
Reporting group title	TURBT Alone
Reporting group description:	
Participants in the TURBT Alone arm underwent TURBT only, followed by repeat TURBT at 3 months if needed.	

Primary: Disease-Free Survival (DFS)

End point title	Disease-Free Survival (DFS)

End point description:

DFS was defined as the time from randomization until the earliest date of any of the following events:
- Failure to be rendered free of local disease at the Month 3 assessment after the TURBT procedure.
- Recurrence of low-grade (LG) disease after the Month 3 assessment
- Progression to high-grade (HG) disease
- Death due to any cause

DFS was based on the ITT population.

Following early study enrollment closure to pursue an alternative development strategy for UGN-102, formal hypothesis testing was removed from the Statistical Analysis Plan assuming the study would be underpowered.

In the UGN-102 ± TURBT arm, 37 patients (26.1%) had DFS events, and 105 (73.9%) were censored. In the TURBT Alone arm, 55 patients (39.3%) had DFS events, and 85 (60.7%) were censored.

End point type	Primary

End point timeframe:

See endpoint description.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142[1]	140[2]		
Units: month				
median (confidence interval 95%)	9999 (9999 to 9999)	14.85 (8.94 to 9999)		

Notes:

[1] - 9999 = Value not estimable

[2] - 9999 = Value not estimable

Attachments (see zip file)	Kaplan-Meier Plot of Disease-Free Survival/KM Plot of DFS.pdf

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

HR was estimated using a stratified Cox regression model. Confidence intervals (CIs) were computed using the Brookmeyer-Crowley method.

Comparison groups	UGN-102 ± TURBT v TURBT Alone
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.68

Notes:

[3] - Descriptive

Secondary: Time to Recurrence (TTR)

End point title	Time to Recurrence (TTR)

End point description:

TTR was based on the ITT population. TTR analysis was the same as DFS, except death was not considered an event in the TTR analysis.

In the UGN-102 ± TURBT arm, 37 patients (26.1%) had events, and 105 (73.9%) were censored. In the TURBT Alone arm, 54 patients (38.6%) had events, and 86 (61.4%) were censored.

The Kaplan-Meier median TTR was not estimable (NE) in either arm.

End point type	Secondary

End point timeframe:

See endpoint description.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142[4]	140[5]		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9.03 to 9999)		

Notes:

[4] - 9999 = Value not estimable

[5] - 9999 = Value not estimable

Statistical analyses

Statistical analysis title	Hazard Ratio

Statistical analysis description:

HR was estimated using a stratified Cox regression model. CIs were computed using the Brookmeyer-Crowley method.

Comparison groups	UGN-102 ± TURBT v TURBT Alone

Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	other[6]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.7

Notes:

[6] - Descriptive

Secondary: Complete Response Rate (CRR) at Month 3 Assessment

End point title	Complete Response Rate (CRR) at Month 3 Assessment

End point description:

CRR was defined as the proportion of patients who achieved complete response at the Month 3 disease assessment. CRR was based on the ITT analysis set.

End point type	Secondary

End point timeframe:

CRR was measured 3 months after the start of treatment.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142[7]	140[8]		
Units: percent				
number (confidence interval 95%)	64.8 (56.3 to 72.6)	63.6 (55.0 to 71.5)		

Notes:

[7] - Patients with CR = 92
Patients with non-CR = 50
[8] - Patients with CR = 89
Patients with non-CR = 51

Statistical analyses

No statistical analyses for this end point

Secondary: Observed CRR at Scheduled Disease Assessment Time Points

End point title	Observed CRR at Scheduled Disease Assessment Time Points

End point description:

Observed CRR at scheduled disease assessment time points was defined as the proportion of patients who had CR at the Month 3 disease assessment and maintained CR up to that particular follow-up disease assessment. This endpoint was summarized for patients who achieved CR at the Month 3 Visit.

End point type	Secondary

End point timeframe:

Visit level CRR during follow-up was measured every 3 months until the end of study.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	89		
Units: percent				
number (confidence interval 95%)				
Month 6	92.4 (84.9 to 96.9)	71.9 (61.4 to 80.9)		
Month 9	80.4 (70.9 to 88.0)	62.9 (52.0 to 72.9)		
Month 12	75.0 (64.9 to 83.4)	57.3 (46.4 to 67.7)		
Month 15	71.7 (61.4 to 80.6)	55.1 (44.1 to 65.6)		
Month 18	34.8 (25.1 to 45.4)	25.8 (17.1 to 36.2)		
Month 21	7.6 (3.1 to 15.1)	4.5 (1.2 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time from first documented CR until the earliest date of recurrence of LG disease, progression to HG disease, or death due to any cause. This endpoint was summarized for CR patients at the Month 3 disease assessment.

DOR was based on the ITT population.

In the UGN-102 ± TURBT arm, 18 patients (19.6%) had DOR events, and 74 (80.4%) were censored. In the TURBT Alone arm, 24 patients (27.0%) had DOR events, and 65 (73.0%) were censored.

End point type	Secondary

End point timeframe:

See endpoint description.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92[9]	89[10]		
Units: month				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Notes:

[9] - 9999 = Value not estimable

[10] - 9999 = Value not estimable

Statistical analyses

Statistical analysis title	Hazard Ratio

Statistical analysis description:

HR was estimated using a stratified Cox regression model. CIs were computed using the Brookmeyer-Crowley method.

Comparison groups	UGN-102 ± TURBT v TURBT Alone
Number of subjects included in analysis	181
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.86

Notes:

[11] - Descriptive

Secondary: Patients Who Underwent TURBT for LG IR NMIBC by Month 3 Assessment

End point title	Patients Who Underwent TURBT for LG IR NMIBC by Month 3 Assessment

End point description:

Defined as the proportion of patients receiving a per protocol TURBT in each arm and the average number of per protocol TURBTs per patient in each arm in the Safety Analysis Set. Per protocol TURBTs were defined as the Day 1 TURBT for patients in the TURBT Alone arm and TURBT due to residual LG disease at the Month 3 disease assessment in either arm.

Presented here is the number of patients who underwent TURBT by the Month 3 assessment.

End point type	Secondary

End point timeframe:

Timeframe for this endpoint was 3 months after the start of treatment.

End point values	UGN-102 ± TURBT	TURBT Alone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138[12]	132[13]		
Units: percent				
number (not applicable)	17.4	100		

Notes:

[12] - Mean (SD) number of per protocol TURBT per patient = 0.2 (0.38)

[13] - Mean (SD) number of per protocol TURBT per patient = 1.1 (0.34)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from informed consent to the Month 6 Visit. After the Month 6 Visit, all SAEs (regardless of causality) and non-serious AEs assessed as related to UGN-102, TURBT, or study procedures were reported until the EOS Visit.

Adverse event reporting additional description:

Patient was counted once per system organ class or preferred term even if ≥1 event was reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	UGN-102 ± TURBT Arm - TEAEs

Reporting group description:

The values provided are for TEAEs. A TEAE in the UGN-102 ± TURBT arm was defined as an AE that occurred on or after the day of the first instillation of UGN-102, or a pre-treatment AE that worsened during the study.

TEAEs and serious TEAEs are taken from the Safety Analysis Set. For the UGN ± TURBT arm, the Safety Analysis Set includes all patients who received any dose of UGN-102.

Reporting group title	TURBT Alone Arm - TEAEs

Reporting group description:

The values provided are for TEAEs. A TEAE in the TURBT Alone arm was defined as an AE that occurred on or after the day of initial TURBT, or a pre-treatment AE that worsened during the study.

TEAEs and serious TEAEs are taken from the Safety Analysis Set. For the TURBT Alone arm, the Safety Analysis Set includes all patients who received at least one TURBT intervention.

Serious adverse events	UGN-102 ± TURBT Arm - TEAEs	TURBT Alone Arm - TEAEs	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 138 (8.70%)	7 / 132 (5.30%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung squamous cell carcinoma stage III			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Upper limb fracture			

subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 138 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 138 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 138 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 138 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 138 (0.00%)	1 / 132 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intestinal obstruction			

subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral stenosis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 138 (0.00%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 138 (2.90%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 132 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 138 (0.72%)	2 / 132 (1.52%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	UGN-102 ± TURBT Arm - TEAEs	TURBT Alone Arm - TEAEs	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 138 (73.91%)	62 / 132 (46.97%)	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 138 (4.35%)	2 / 132 (1.52%)	
occurrences (all)	14	2	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	8 / 138 (5.80%)	2 / 132 (1.52%)	
occurrences (all)	8	2	
Fatigue			
subjects affected / exposed	5 / 138 (3.62%)	0 / 132 (0.00%)	
occurrences (all)	6	0	
Pyrexia			
subjects affected / exposed	5 / 138 (3.62%)	0 / 132 (0.00%)	
occurrences (all)	5	0	
Gastrointestinal disorders			
Flatulence			
subjects affected / exposed	13 / 138 (9.42%)	4 / 132 (3.03%)	
occurrences (all)	19	4	
Abdominal distension			
subjects affected / exposed	6 / 138 (4.35%)	4 / 132 (3.03%)	
occurrences (all)	7	4	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	9 / 138 (6.52%)	4 / 132 (3.03%)	
occurrences (all)	9	4	
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	42 / 138 (30.43%)	6 / 132 (4.55%)	
occurrences (all)	66	6	
Micturition urgency			
subjects affected / exposed	25 / 138 (18.12%)	10 / 132 (7.58%)	
occurrences (all)	29	10	
Nocturia			
subjects affected / exposed	25 / 138 (18.12%)	9 / 132 (6.82%)	
occurrences (all)	30	10	
Pollakiuria			
subjects affected / exposed	22 / 138 (15.94%)	8 / 132 (6.06%)	
occurrences (all)	26	9	
Haematuria			
subjects affected / exposed	9 / 138 (6.52%)	5 / 132 (3.79%)	
occurrences (all)	11	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 138 (0.00%)	4 / 132 (3.03%)	
occurrences (all)	0	4	
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 138 (5.07%)	6 / 132 (4.55%)	
occurrences (all)	7	6	
Cystitis			
subjects affected / exposed	5 / 138 (3.62%)	5 / 132 (3.79%)	
occurrences (all)	9	5	
Urinary tract infection			
subjects affected / exposed	4 / 138 (2.90%)	5 / 132 (3.79%)	
occurrences (all)	4	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2021	• Added notification of early study enrollment closure (Sponsor pursuing an alternative development path for UGN-102 in patients with LG IR NMIBC.) • Clarified that NCR patients at the Month 3 Visit may have an alternative procedure to address residual disease if a formal TURBT is unnecessary. (Data from Study BL005 suggest some patients with NCR/disease recurrence may be managed with biopsy and/or fulguration.) • Revised statistical plans to reflect that the study is not powered to perform hypothesis testing or statistical comparison, and all analyses will be descriptive. (Smaller sample size due to early enrollment closure.) • Revised definitions of DFS and TTR to start from time of randomization for both CR and NCR patients at the Month 3 Visit. (Feedback from US FDA.) • Deleted exploratory endpoint of other resource utilization. (Reflect data being captured in the eCRF.) • Removed data review committee. (No interim analysis.) • Removed ET Visit from SOA and clarified that patients who discontinue the study should have an EOS Visit performed. (Logistical simplicity.) • Added COVID-19 to study risk assessment. (Feedback from Poland Office for Registration of Medicinal Products, Medical Devices and Biocidal Products.) • Clarified that hospitalization is not a study requirement. (Feedback from the Ministry of Healthcare of the Russian Federation.) • Clarified that access to treatment information by sponsor personnel will be restricted by role. (Maintain trial integrity.) • Clarified that patients with disease progression at the Month 3 Visit or subsequent follow-up visits will be considered to have completed the study at that time. (HG or muscle-invasive disease requires different care.) • Revised Section 8.2.2 and added new Appendix 1 (Guidance on Evaluation of Response). (Clarify evaluation of response at Month 3 Visit and follow-up visits.) • Deleted planned supportive analysis of primary endpoint based on propensity scores. (Feedback from FDA.)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Sponsor closed enrollment early to pursue alternative development strategy for UGN-102 in patients with LG IR-NMIBC. Study design followed patients up to 24 months after treatment start. Sponsor terminated study after last patient had 15 month Visit.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37548555