Clinical trial results:
Photodynamic diagnosis (PDD) in flexible cystoscopy – a randomized study with focus on significant recurrence

Summary

EudraCT number	2015-000436-15
Trial protocol	DK
Global end of trial date	14 December 2019

Results information

Result version number	v1 (current)
This version publication date	13 January 2021
First version publication date	13 January 2021
Summary attachment (see zip file)	DaBlaCa11 (DaBlaCa11.pdf)

Trial information

Trial identification

Sponsor protocol code	DD-study-3

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Blvd. 35, Aarhus N, Denmark, 8200
Public contact	Jørgen Bjerggaard Jensen, Aarhus Universitets Hospital, 0045 78452617, Bjerggaard@skejby.rm.dk
Scientific contact	Jørgen Bjerggaard Jensen, Aarhus Universitets Hospital, 0045 78452617, Bjerggaard@skejby.rm.dk

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	14 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2019
Global end of trial reached?	Yes
Global end of trial date	14 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The Hypothesis of this study is that the use of PDD in the outpatient clinic in patients with a high recurrence risk undergoing follow-up flexible cystoscopy will result in diagnosis of papillomas earlier than by the use of conventional flexible cystoscopy in white light. Thus, a higher number of tumours can be treated in the outpatient setting without the need for procedures in general anaesthesia. Furthermore, the number of follow-up cystoscopies can be reduced if PDD is used at the first cystoscopy following TURB.

Protection of trial subjects:

Trial Subjects in the intervention arm underwent instillation of Hexaminolevulinate (HAL) prior to the cystoscopy using local anesthesia (Lidocaine gel).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 696
Worldwide total number of subjects	696
EEA total number of subjects	696

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)	696

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

FVFS: Feb. 2016. LVLS: Dec. 2017

Pre-assignment

Screening details:

Pre-screened: 1130/ Excluded: 431
351 patients were allocated to the intervention group (flexible PDD), and 348 to the control group (flexible white light). Throughout the following 8 months after randomization, only 117 patients in the intervention group had at least 1 tumor recurrence compared to 143 patients in the control group

Pre-assignment period milestones

Number of subjects started	696
Number of subjects completed	696

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Intervention group (hexaminolevulinate was instilled in the bladder before flexible cystoscopy with PDD video cystoscope)

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

Dosage and administration details:

Hexvix 85 mg

Arm title	Control

Arm description:

Control group (white light flexible cystoscope), only.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Intervention	Control
Started	350	346
Completed	350	346

Baseline characteristics

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description:	
Intervention group (hexaminolevulinate was instilled in the bladder before flexible cystoscopy with PDD video cystoscope)	
Reporting group title	Control
Reporting group description:	
Control group (white light flexible cystoscope), only.	

Primary: Tumor recurrence within 8 months from the randomization

End point title	Tumor recurrence within 8 months from the randomization
End point description:	
Use of PDD in a routine surveillance cystoscopy first time after transurethral resection of bladder tumor for nonmuscle invasive bladder cancer reduces subsequent risk of tumor recurrence compared to WL cystoscopy alone.	
End point type	Primary
End point timeframe:	
Feb. 2016 - Dec. 2017	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	346		
Units: Numbers				
Risk of tumor recurrence	117	143		

Statistical analyses

Statistical analysis title	Analysis
Comparison groups	Control v Intervention
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.95

Variability estimate	Standard deviation
Dispersion value	0.05

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Feb. 2016 - Dec. 2017	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22

Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The trial subjects in both groups had to undergo the same procedure e.g. cystoscopy with expected post mikro/ makro haematuria when voiding the first 24 hours after the procedure. As for the intervention group who had to undergo catheterization prior to the cystoscopy post mikro/ makro haematuria is also expected.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported