



## Clinical trial results:

**An open-label, single-arm, rater-blinded, multicenter phase 1/2 study to assess safety and diagnostic accuracy and radiotherapeutic implications of pre-operative Ga-68-PSMA-11 PET/CT imaging in comparison to histopathology, in newly-diagnosed prostate cancer (PCA) patients at high risk for metastasis, scheduled for radical prostatectomy (RP) with extended pelvic lymph node dissection (EPLND).**

### Summary

EudraCT number	2016-001815-19
Trial protocol	DE AT
Global end of trial date	03 July 2020

### Results information

Result version number	v1 (current)
This version publication date	15 September 2022
First version publication date	15 September 2022
Summary attachment (see zip file)	Clinical Study Report (Synopsis) (Ga-68-PSMA-11_CSR Synopsis_v1.0_211129.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	Ga-68-PSMA-11
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03362359
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Deutsches Krebsforschungszentrum (DKFZ)
Sponsor organisation address	Im Neuenheimer Feld 280, Heidelberg, Germany, 69120
Public contact	Dr. Julia Ritzerfeld, Deutsches Krebsforschungszentrum (DKFZ) Clinical Trial Office (M130)  , +49 6221 42-1678, j.ritzerfeld@dkfz.de
Scientific contact	Dr Klaus Kopka, Helmholtz-Zentrum Dresden-Rossendorf, +49 351 260 2060, k.kopka@hzdr.de

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
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Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 July 2020
Global end of trial reached?	Yes
Global end of trial date	03 July 2020
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. To assess the ability of Ga-68-PSMA-11 PET/CT imaging to detect prostate cancer tissue within
  - a. the prostate gland on level of quadrant (or octant if possible) and
  - b. pelvic lymph node metastases on level of 8 defined sub-regions.
2. To assess the clinical safety of Ga-68-PSMA-11.

Protection of trial subjects:

To minimise irradiation of the urinary bladder, subjects will be encouraged to increase fluid intake and to void frequently through the first day after administration.

Background therapy:

All patients were scheduled for radical prostatectomy (RP) with extended pelvic lymph node dissection (EPLND).

Evidence for comparator:

no comparator used

Actual start date of recruitment	01 September 2017
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	Austria: 3
Country: Number of subjects enrolled	Germany: 169
Country: Number of subjects enrolled	Switzerland: 1
Worldwide total number of subjects	173
EEA total number of subjects	172

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	0
From 65 to 84 years	173
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited in 9 uro-oncological sites in Germany, Austria, and Switzerland, with access to a radiopharmaceutical laboratory, experienced to prepare 68Ga-labelled compounds, and high-quality PET/CT imaging.

### Pre-assignment

Screening details:

Histologically confirmed adenocarcinoma of the prostate. High risk for metastasis, defined by either:

- a. stadium cT3 according to TNM classification, or
- b. Gleason Score >7, or
- c. PSA >20 ng/mL.

Patient scheduled for radical prostatectomy (RP) with extended pelvic lymph node dissection (EPLND) according to current guidelines 7–60 days after

### Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor <sup>[1]</sup>

Blinding implementation details:

Histology analysis were made centrally by a single pathologist blind to imaging results. Conversely, PET/CT (PET/MR) images were analysed by two central readers plus a central adjudication reader blind to histology results.

### Arms

<b>Arm title</b>	Single arm study
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Arm description:

Study subjects were not divided into different arms i.e. single arm.

Arm type	Experimental
Investigational medicinal product name	68Ga-complex of Glu-NH-CO-NHLys-(Ahx)-HBED-CC
Investigational medicinal product code	Ga-68-PSMA-11
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Total dose (number and unit): ≤ 6 µg microgram(s)

Route of administration (relevant to the maximum dose): Intravenous use

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Investigator and subject were unblinded. Only entral assessments of pathology and image data were blinded to each other.

<b>Number of subjects in period 1</b>	Single arm study
Started	173
Completed	163
Not completed	10
Protocol deviation	10



## Baseline characteristics

### Reporting groups

Reporting group title	overall trial
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Reporting group description:

ddd

Reporting group values	overall trial	Total	
Number of subjects	173	173	
Age categorical			
The patients had a mean $\pm$ standard deviation (SD) age of 65.8 $\pm$ 8.0 years (Range 45–82 years).			
Units: Subjects			
Male adults of age 45–82 years	173	173	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	173	173	

## End points

### End points reporting groups

Reporting group title	Single arm study
Reporting group description: Study subjects were not divided into different arms i.e. single arm.	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description: All patients who were enrolled and were given a treatment number, irrespective of whether or not they received Ga-68-PSMA-11	
Subject analysis set title	Safety analysis
Subject analysis set type	Safety analysis
Subject analysis set description: All patients who received Ga-68-PSMA-11.	
Subject analysis set title	Image data set
Subject analysis set type	Per protocol
Subject analysis set description: Also called IDS (= image data set). All patients who: <ul style="list-style-type: none"><li>• had Ga-68-PSMA-11 PET image data with sufficient technical quality allowing to determine at least one of the imaging variables (see Section 9.5.8.1)</li><li>• underwent the planned RP / EPLND, and</li><li>• did not have major protocol deviations</li></ul>	
Subject analysis set title	Per protocol
Subject analysis set type	Per protocol
Subject analysis set description: All patients who had data available for the primary variable and did not have major protocol deviations (ICH E9).	

### Primary: Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in Detecting Prostate Cancer Tissue Within the Prostate Gland on Level of Patient

End point title	Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in Detecting Prostate Cancer Tissue Within the Prostate Gland on Level of Patient <sup>[1]</sup>
End point description: The ability of Ga-68-PSMA-11 PET/CT imaging to detect prostate cancer tissue within the prostate gland was performed per patient . Histopathology results were the reference for assessment.	
End point type	Primary
End point timeframe: overall trial	

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: We did not succeed at entering the data on statistics given in the CSR into the existing fields of this website

<b>End point values</b>	Image data set			
Subject group type	Subject analysis set			
Number of subjects analysed	139			
Units: TN;TP;FN;FP				
number (confidence interval 95%)				
Efficacy	0.971 (0.928 to 0.992)			

<b>Attachments (see zip file)</b>	14.2.1.1 Sensitivity, Specificity, PPV, NPV And Ac/Ga-68-PSMA-
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### Statistical analyses

No statistical analyses for this end point

### Primary: Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in Detecting Prostate Cancer Tissue Within the Prostate Gland on Level of Quadrant

End point title	Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in Detecting Prostate Cancer Tissue Within the Prostate Gland on Level of Quadrant <sup>[2]</sup>
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End point description:

The ability of Ga-68-PSMA-11 PET/CT imaging to detect prostate cancer tissue within the prostate gland was performed per quadrant of the prostate gland. Histopathology results were the reference for assessment

End point type	Primary
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End point timeframe:

overall trial

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: We did not succeed at entering the data on statistics given in the CSR into the existing fields of this website

<b>End point values</b>	Image data set			
Subject group type	Subject analysis set			
Number of subjects analysed	139			
Units: TN;TP;FN;FP				
number (confidence interval 95%)				
Efficacy	0.710 (0.670 to 0.750)			

<b>Attachments (see zip file)</b>	Detection of tracer uptake/Ga-68-PSMA-11_CSR_Table 14.2.5
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### Statistical analyses

No statistical analyses for this end point

### Primary: Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in detecting Prostate Cancer Tissue within Pelvic Lymph Node Metastases at the Level of 8



## defined Sub-regions

End point title	Sensitivity and Specificity of 68Ga-PSMA-11 PET/CT Imaging in detecting Prostate Cancer Tissue within Pelvic Lymph Node Metastases at the Level of 8 defined Sub-regions <sup>[3]</sup>
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End point description:

Sensitivity and specificity of Ga-68-PSMA-11 PET/CT imaging in detecting prostate cancer tissue within the pelvic lymph node metastases at the level of 8 defined sub-regions were evaluated. The evaluation was done at patient, gross-region (pelvic left/right) and sub-region level

End point type	Primary
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End point timeframe:

overall trial

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: We did not succeed at entering the data on statistics given in the CSR into the existing fields of this website

<b>End point values</b>	Image data set			
Subject group type	Subject analysis set			
Number of subjects analysed	139			
Units: TN;TP;FN;FP				
number (confidence interval 95%)				
Efficacy	0.345 (0.244 to 0.447)			

<b>Attachments (see zip file)</b>	pelvic lymph nodes/Ga-68-PSMA-11_CSR_Table 14.2.1_v1.
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## Statistical analyses

No statistical analyses for this end point

## Primary: Safety

End point title	Safety <sup>[4]</sup>
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End point description:

Quantity and Severity of Adverse Events

End point type	Primary
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End point timeframe:

day0-day7

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: We did not succeed at entering the data on statistics given in the CSR into the existing fields of this website

<b>End point values</b>	Safety analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	173			
Units: adverse events				
Safety	20			

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From treatment until day 7 (end of study)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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### Reporting groups

Reporting group title	overall trial
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Reporting group description:

A total of 173 patients received the study treatment within the stipulated dose range and were included in safety analysis.

Serious adverse events	overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 173 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 173 (8.09%)		
Investigations			
Alanine aminotransferase increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Aspartate aminotransferase increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Blood creatinine increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Blood glucose increased	Additional description: mild toxicity grade		

subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Blood urea increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Liver function test increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Monocyte count increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Neutrophil count increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
White blood cell count increased	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Cardiac disorders			
Sinus arrhythmia	Additional description: Moderate toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Tachycardia	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Atrial fibrillation	Additional description: mild toxicity grade		
subjects affected / exposed	3 / 173 (1.73%)		
occurrences (all)	3		
Nervous system disorders			
Headache	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Hypertonia	Additional description: mild toxicity grade		

subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle spasms	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		
Pain in extremity	Additional description: mild toxicity grade		
subjects affected / exposed	1 / 173 (0.58%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2017	<p>Only PSMA expression in lymph nodes and not in prostate to be analysed following a 2nd injection of Ga-68-PSMA-11</p> <ul style="list-style-type: none"><li>• Addition of an exclusion criterion of simultaneous participation in other clinical trials</li><li>• Increase in number of patients considering a 15% drop out rate</li><li>• Redefinition of negative histological result</li><li>• Change of study start dates</li><li>• Addition of an examination/evaluation</li><li>• Removal of categorising of AE assessment as optional</li><li>• Detailed information on pharmacovigilance system</li><li>• Correction of calculation error related to total volume of blood collected from each patient</li><li>• Update of monitoring process</li></ul>
05 July 2017	<ul style="list-style-type: none"><li>• Change of study dates</li><li>• Correction of radioactivity concentration of the study drug</li></ul>
22 March 2018	<ul style="list-style-type: none"><li>• Increase the number of days after start of the study for patients scheduled for RP with EPLND provided in the current guidelines in the inclusion criteria</li><li>• Increase the number of days in the inclusion criteria which the pelvic MRI or CT and 99mTc bone scintigraphy should be prior to inclusion</li><li>• Inclusion of a document name to improve clarity related to histological guidance</li><li>• Update of the contact person in the administrative structure (Histology reference laboratory)</li><li>• Update of the reference pathologist</li><li>• Inclusion of a document name related to histological guidance in sample shipment</li></ul>
30 September 2019	<ul style="list-style-type: none"><li>• Increase in the number of days after the start of the study for patients scheduled for RP with EPLND provided in the current guidelines in the inclusion criteria</li><li>• To let pelvic MRI or CT be used at the discretion of the investigators in preoperative PCA staging inclusion criteria</li><li>• Clarification that central readers to be used and that a central adjudication reader to be involved in case of ambiguous results</li><li>• Clarification that if surgery and sampling of tissue specimens is performed after the study as part of standard care, it is to be done between Day 7 (after EOS) and Day 60 after the start of the study.</li><li>• Extend the end of recruitment date</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported