Clinical trial results:
Can 89Zr-atezolizumab PET scan identify patients with metastatic invasive lobular breast cancer who will respond to chemotherapy-immune checkpoint inhibition?

Summary

EudraCT number	2019-001197-28
Trial protocol	NL
Global end of trial date	01 May 2022

Results information

Result version number	v1 (current)
This version publication date	12 October 2022
First version publication date	12 October 2022

Trial information

Trial identification

Sponsor protocol code	201900180

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04222426
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Medical Centre Groningen
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands, 9713 GZ
Public contact	Department of Medical Oncology, University Medical Center Groningen, +31 503612821, c.p.schroder@umcg.nl
Scientific contact	Dr. C.P. Schröder, University Medical Center Groningen, +31 503612821, c.p.schroder@umcg.nl

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	01 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 May 2022
Global end of trial reached?	Yes
Global end of trial date	01 May 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the feasibility to detect a change in tumor PD-L1 expression on a 89Zr-atezolizumab PET scan, before and after two carboplatin induction treatments.

Protection of trial subjects:

89Zr-atezolizumab injection is safe, only one related low-grade adverse event (pruritus) has been noted in 1 out of 22 patients who completed the full imaging series of up to four 89Zr-atezolizumab PET scans. Whenever possible, to minimize the burden, intervention and patients'visits are preferably planned on the same day. If not possible, for this study, patients will make max. 3 extra visits to the hospital. Since 89Zr-atezolizumab is a radioactive compound, it will cause radiation burden to the patient.89Zr-atezolizumab PET implements a radiation burden of about 18 mSv for 37 MBq 89Zr-atezolizumab and 1.5 mSv for each low dose CT scan. For patients participating in the study, this implies a maximum additional radiation burden of 2 x (18 + 1.5) = 39 mSv. This additional radiation burden (moderate risk) is justifiable in this category of adult patients with metastatic cancer.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2019
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	Netherlands: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Due to the COVID pandemic inclusions were possibly slow. Due to the closure of the main study (GELATO) only 1 patient has been included in the study.

Pre-assignment

Screening details:

Due to the closure of the main study (GELATO) only 1 patient has been included in the study.

Period 1

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

Blinding implementation details:

not applicable.

Arms

Arm title	89Zr-atezolizumab PET scan

Arm description:

All patients will undergo two 89Zr-atezolizumab PET scans, one at baseline and one after two doses carboplatin induction treatment. The 89Zr-atezolizumab PET scan will be performed 4 days after tracer injection. Procedures within the ImaGelato study will be completed after the two 89Zr-atezolizumab PET scans, but patients will continue treatment with carboplatin combined with atezolizumab in the GELATO trial.

Arm type	Experimental
Investigational medicinal product name	[89Zr]-Atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Total of 37 MBq megabecquerel(s)

Number of subjects in period 1	89Zr-atezolizumab PET scan
Started	1
Completed	1

Baseline characteristics

Reporting groups

Reporting group title	89Zr-atezolizumab PET scan

Reporting group description:

All patients will undergo two 89Zr-atezolizumab PET scans, one at baseline and one after two doses carboplatin induction treatment. The 89Zr-atezolizumab PET scan will be performed 4 days after tracer injection. Procedures within the ImaGelato study will be completed after the two 89Zr-atezolizumab PET scans, but patients will continue treatment with carboplatin combined with atezolizumab in the GELATO trial.

Reporting group values	89Zr-atezolizumab PET scan	Total	
Number of subjects	1	1	
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	
Gender categorical Units: Subjects			
Female	1	1	

End points

End points reporting groups

Reporting group title	89Zr-atezolizumab PET scan

Reporting group description:

All patients will undergo two 89Zr-atezolizumab PET scans, one at baseline and one after two doses carboplatin induction treatment. The 89Zr-atezolizumab PET scan will be performed 4 days after tracer injection. Procedures within the ImaGelato study will be completed after the two 89Zr-atezolizumab PET scans, but patients will continue treatment with carboplatin combined with atezolizumab in the GELATO trial.

Primary: Change in tumor uptake between 89Zr-atezolizumab PET scan at baseline and after two carboplatin induction treatments, defined as decline or increase of standardized uptake value

End point title	Change in tumor uptake between 89Zr-atezolizumab PET scan at baseline and after two carboplatin induction treatments, defined as decline or increase of standardized uptake value[1]

End point description:

Change in tumor uptake between 89Zr-atezolizumab PET scan at baseline and after two carboplatin induction treatments, defined as decline or increase of standardized uptake value (SUV) of 30% or more, described as per lesion and per patient. For the two different time points we will calculate the SUV for all lesions and patients. Relative decrease or increase in SUV units between different time points will be calculated for all lesions and patients, and recorded as percentage of SUV decrease or increase.

End point type	Primary

End point timeframe:

2 years

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: descriptive statistics

End point values	89Zr-atezolizumab PET scan			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: SUV	1			

Statistical analyses

No statistical analyses for this end point

Secondary: The relation between standardized uptake value (SUV) on 89Zr-atezolizumab PET scan, to response to carboplatin-atezolizumab

End point title	The relation between standardized uptake value (SUV) on 89Zr-atezolizumab PET scan, to response to carboplatin-atezolizumab

End point description:

Relation of 89Zr-atezolizumab tumor uptake (at baseline, after carboplatin induction, and change between the two scans) per lesion and per patient with response to carboplatin-atezolizumab per lesion and per patient. For the 89Zr-atezolizumab PET scans, uptake will be quantified with SUV units for both time points.

End point type	Secondary

End point timeframe:

2 years

End point values	89Zr-atezolizumab PET scan			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: SUV	1			

Statistical analyses

No statistical analyses for this end point

Secondary: The relation of 89Zr-atezolizumab tumor uptake at baseline and after two courses of carboplatin, with tumor biopsy assessments

End point title	The relation of 89Zr-atezolizumab tumor uptake at baseline and after two courses of carboplatin, with tumor biopsy assessments

End point description:

Relation of 89Zr-atezolizumab tumor uptake at baseline and after carboplatin induction, with tumor biopsy assessments (for example PD-L1 immunohistochemistry (IHC)). We will investigate whether PD-L1 expression is associated with 89Zr-atezolizumab uptake. The relationship between tumor PD-L1 expression (measured in pre-treatment biopsy and induction treatment biopsy), and 89Zr-atezolizumab tumor uptake will be described.

End point type	Secondary

End point timeframe:

2 years

End point values	89Zr-atezolizumab PET scan			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: SUV	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

SAEs within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete initial report. All other SAEs within 15 days after sponsor has first knowledge.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Frequency threshold for reporting non-serious adverse events: 2 %

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: no adverse events observed

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

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

The main study, and thus this trial, has a slow inclusion known by criteria such as: no bone biopsies possible, measurable disease required, which certainly in this exceptional subpopulation of lobular breast cancer patients proved to be very severe

Notes: