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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

68Ga]Ga-DOTA-TATE/AAA501

Trial Indication(s)

neuroendocrine neoplasms (NENs)

Protocol Number

CAAA501A11301

Protocol Title

A prospective, open-label, multi-center, single arm, phase III study of [68Ga]Ga-DOTA-TATE in the diagnosis of patients with neuroendocrine neoplasms (NENs) and healthy volunteers in Japan

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: March 21, 2024 (Actual)
Primary Completion Date: December 27, 2024 (Actual)
Study Completion Date: December 27, 2024 (Actual)

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Reason for Termination (If applicable)

Study Design/Methodology

This was a prospective, open-label, multi-center, single arm, phase III study to evaluate the diagnostic performance of [68Ga]Ga-DOTA-TATE PET/CT imaging compared with conventional imaging (CIM) as standard of truth in patients with NENs and healthy volunteers (HVs).

A total of 71 participants (48 patients with confirmed/suspected NENs and 23 HVs) were enrolled to ensure that at least 70 participants (47 patients with confirmed/suspected NENs and 23 HVs) were evaluable for the co-primary endpoints. All enrolled participants were administered [68Ga]Ga-DOTA-TATE and completed positron emission tomography (PET) / computed tomography (CT) scan.

The co-primary endpoints of the subject-level sensitivity and the subject-level specificity were assessed by comparing the central reading results of the [68Ga]Ga-DOTA-TATE PET/CT scan to the central reading results of CIM.

Centers

Japan(8)

Objectives:

Primary:

To evaluate the subject-level sensitivity of [68Ga]Ga-DOTA-TATE PET/CT imaging for NENs.

To evaluate the subject-level specificity of [68Ga]Ga-DOTA-TATE PET/CT imaging for NENs.

Secondary:

To evaluate subject-level positive predictive value (PPV) of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate subject-level negative predictive value (NPV) of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate subject-level accuracy of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate region-level sensitivity of [68Ga]Ga-DOTA-TATE PET/CT imaging for NENs.

To evaluate region-level specificity of [68Ga]Ga-DOTA-TATE PET/CT imaging for NENs.

To evaluate region-level positive predictive Value (PPV) of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate region-level negative predictive value (NPV) of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate region-level accuracy of [68Ga]Ga-DOTA-TATE PET/CT imaging.

To evaluate number of lesions detected by [68Ga]Ga-DOTA-TATE PET/CT imaging and each CIM at region-level.

To evaluate the impact of [68Ga]Ga-DOTA-TATE PET/CT imaging on treatment decision.

To evaluate inter-reader variability.

To evaluate safety and tolerability of [68Ga]Ga-DOTA-TATE.

To evaluate pharmacokinetics (PK) of [68Ga]Ga-DOTA-TATE.

To evaluate lesion-level concordance for sSomatostatin receptor (SSTR) between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology results.

Test Product (s), Dose(s), and Mode(s) of Administration

[68Ga]Ga-DOTA-TATE was administered intravenously at a single dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a total maximum dose of 200 MBq (5.4 mCi), and PET/CT imaging was acquired 40 to 90 minutes after the intravenous administration of [68Ga]Ga-DOTA-TATE.

Statistical Methods

Novartis performed the final data analysis using the SAS version 9.4 and R version 4.3.1.

The following analysis sets were used in the study:

- The Full Analysis Set (FAS) comprised all enrolled participants.
- The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have result of [68Ga]Ga-DOTA-TATE PET/CT imaging. If at least one central reader could not judge results for all CIM or [68Ga]Ga-DOTA-TATE PET/CT imaging due to imaging quality, the results were considered as "Not evaluable". Those participants were excluded from the EFF.
- The Safety Set comprised all participants who received any dose of [68Ga]Ga-DOTA-TATE.
- The Pharmacokinetic analysis set (PAS) included all participants who provided at least one evaluable PK concentration. A profile considered evaluable if participant received the study drug, and participant provided at least one primary PK parameter.

Analysis of the co-primary endpoints: Analysis of the co-primary endpoints were performed for the EFF.

The co-primary endpoints of the study were subject-level sensitivity and specificity.

Subject-level sensitivity was defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. True Positive (TP) participants) among conventional imaging (CIM) positive participants (i.e. TP or FN participants).

Subject-level specificity was defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. True Negative (TN) participants) among CIM negative participants (i.e. TN or FP participants).

Subject-level sensitivity and its 95% exact confidence interval (CI) were calculated based on the binomial distribution. The lower bound of the 95% exact CI for subject-level sensitivity required to be greater than 0.7 to attain the first co-primary objective.

Subject-level specificity and its 95% exact CI were calculated based on the binomial distribution. The lower bound of the 95% exact CI for subject-level specificity required to be greater than 0.6 to attain the second co-primary objective.

Analysis of the secondary endpoints: All efficacy analyses supporting secondary objectives were performed for the EFF.

Subject-level Positive predictive Value (PPV), Negative predictive value (NPV),, and accuracy were summarized respectively with corresponded exact 95% CI.

Region-level sensitivity, specificity, PPV, NPV, and accuracy were summarized respectively with corresponded exact 95% CI by regions. Region consists of liver, pancreas, gastrointestinal, lymph nodes and others.

Number of lesions detected by [68Ga]Ga-DOTA-TATE PET/CT imaging and by CIM were counted. Regarding [68Ga]Ga-DOTA-TATE PET/CT imaging, descriptive statistics of number of lesions for each of 3 central readers, and 3 readers' mean number of lesions were presented. Regarding CIM, descriptive statistics of number of lesions detected by [111In]In-Pentetreotide SPECT/CT and High Resolution CT with contrast (or MRI if CT with contrast was medically contraindicated) were presented, respectively.

Numbers and percentages of participants for each intended treatment plan collected from physicians at pre and post [68Ga]Ga-DOTA-TATE PET/CT imaging was summarized. Summary statistics of participants for the change of intended treatment plan and each combination of transition of intended treatment plan were also presented.

Inter-reader variability for [68Ga]Ga-DOTA-TATE PET/CT imaging was defined as agreement rate among reader determinations and was assessed by Fleiss' Kappa statistics. Inter-reader variability (%) and its 95% CI were presented. An additional table was presented to show the distribution of agreements with the number and percentage of scans agreed by two readers and of scans agreed by all three readers.

The lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among legions which were available, was calculated. The rate was defined as the proportion of lesions which were positive or negative on both local read of [68Ga]Ga-DOTA-TATE PET/CT imaging and local histopathology among lesions detected by local histopathology.

Safety analyses: For all safety analyses, the Safety set was used. All listings and tables were presented by population (i.e. patients with confirmed/suspected NENs and HVs). Safety summaries (tables, figures) included only data from the on-treatment period (from day of dosing of investigational drug to 8 days after dosing of investigational drug) except for baseline data which was also summarized where appropriate (e.g. change from baseline summaries). In addition, a separate summary for death including on treatment and post treatment deaths were provided.

PK analysis: All PK data analysis and PK summary statistics were performed for the PAS.

Descriptive summary statistics of [68Ga]Ga-DOTA-TATE blood concentration data were provided by participant, and sampling time point. Summary statistics included mean (arithmetic and geometric), standard deviation (SD), coefficient of variation (CV) (arithmetic and geometric), median, minimum, and maximum.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

1. Signed informed consent must have been obtained prior to participation in the study
2. Participants must have been adults >= 18 years of age
3. ECOG performance status 0-2
4. For patient with NENs only: Participants were to be confirmed NENs based on histopathology, imaging and other relevant examination, or with suspected NENs which localization could not have been confirmed by CIM
5. For HVs only: Male or female participant in good health condition as determined by no clinically significant findings from medical history, physical examination, vital signs, lab test and ECG
6. Women of childbearing potential must havehad a negative urine or blood pregnancy test.

Key Exclusion Criteria:

1. Inability to complete the needed investigational and conventional imaging due to any reason (severe claustrophobia, inability to lie still for the entire imaging time, etc.)
2. Any additional medical condition, serious intercurrent illness, concomitant cancer or other extenuating circumstance that, in the opinion of the Investigator, would indicate a significant risk to safety or impair study participation
3. Known allergy, hypersensitivity, or intolerance to [68Ga]Ga-DOTA-TATE and [111In]In-Pentetreotide
4. Therapeutic use of any somatostatin analogue except for the following washout period

• Short-acting analogs of somatostatin can be used up to 24 hours before injection of [68Ga]Ga-DOTA-TATE.

• Long-acting analogs of somatostatin can be used up to 28 days before injection of [68Ga]Ga-DOTA-TATE.

5. Prior administration of a radiopharmaceutical unless 10 or more half-lives have elapsed before injection of [68Ga]Ga-DOTA-TATE

6. Use of other investigational drugs within 30 days before screening

7. Participants who were pregnant.

8. Participants who were lactating.

Participant Flow Table

Overall Study

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers	Total
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	
Started	48	23	71
Completed	48	23	71
Not Completed	0	0	0

Baseline Characteristics

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers	Total

Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	
Number of Participants [units: participants]	48	23	71
Baseline Analysis Population Description			
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	23	10	33
Male	25	13	38
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
American Indian or Alaska Native	0	0	0
Asian	48	23	71
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Age Categorical (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			

<=18 years	0	0	0
Between 18 and 65 years	29	22	51
>=65 years	19	1	20

Primary Outcome Result(s)

Number of [68Ga]Ga-DOTA-TATE positive participants (TP participants) among CIM positive participants (TP or FN participants)

Description	Subject-level sensitivity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. TP participants) among CIM positive participants (i.e. TP or FN participants). • TP participants were those who showed at least one lesion based on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM by central read. • FN participants were those who did not show any lesions based on [68Ga]Ga-DOTA-TATE PET/CT imaging but showed at least one lesion based on CIM by central read. True Positive [TP] False Positive [FP] False Negative [FN] True Negative [TN]
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are CIM positive participants (TP or FN participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	46
Number of [68Ga]Ga-DOTA-TATE positive participants (TP participants) among CIM positive participants (TP or FN participants) (units: Participants)	**Count of Participants (Not Applicable)**

True Positive [TP]	40 (86.96%)
False Negative [FN]	6 (13.04%)

Number of [68Ga]Ga-DOTA-TATE negative participants (TN participants) among CIM negative participants (TN or FP participants)

Description	Subject-level specificity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. TN participants) among CIM negative participants (i.e. TN or FP participants). • TN participants were those who did not show any lesions based on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM by central read. • FP participants were those who showed at least one lesion based on [68Ga]Ga-DOTA-TATE PET/CT imaging but did not show any lesions based on CIM by central read. True Positive [TP] False Positive [FP] False Negative [FN] True Negative [TN]
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are CIM negative participants (TN or FP participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	25
Number of [68Ga]Ga-DOTA-TATE negative participants (TN participants) among CIM negative participants (TN or FP participants) (units: Participants)	**Count of Participants (Not Applicable)**
True Negative [TN]	23 (92%)
False Positive [FP]	2 (8%)

Subject-level sensitivity

Description	Subject-level sensitivity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. TP participants) among CIM positive participants (i.e. TP or FN participants). True Positive [TP] False Positive [FP] False Negative [FN] True Negative [TN] Sensitivity = TP / (TP + FN)
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are CIM positive participants (TP or FN participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	46
Subject-level sensitivity (units: Sensitivity (%))	**Number (95% Confidence Interval)**
	87.0 (73.74 to 95.06)

Subject-level Specificity

Description	Subject-level specificity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. TN participants) among CIM negative participants (i.e. TN or FP participants). True Positive [TP] False Positive [FP] False Negative [FN] True Negative [TN] Specificity = TN / (TN + FP).
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are CIM negative participants (TN or FP participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	25
Subject-level Specificity (units: Sensitivity (%))	**Number** **(95% Confidence Interval)**
	92.0 (73.97 to 99.02)

Secondary Outcome Result(s)

Number of participants who are positive on both [68Ga]Ga-DOTA-TATE PET/CT imagings and CIM (TP participants) among participants who are positive on [68Ga]Ga-DOTA TATE PET/CT imaging (TP or FP participants)

Description	Subject-level positive predictive values (PPV) is defined as the proportion of TP participants among [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. TP or FP participants).
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are positive on [68Ga]Ga-DOTA TATE PET/CT imaging (TP or FP participants).

	All participants

Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	42
Number of participants who are positive on both [68Ga]Ga-DOTA-TATE PET/CT imagings and CIM (TP participants) among participants who are positive on [68Ga]Ga-DOTA TATE PET/CT imaging (TP or FP participants) (units: Participants)	**Count of Participants (Not Applicable)**
True Positive [TP]	40 (95.24%)
False Positive [FP]	2 (4.76%)

Number of participants who are negative on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM (TN participants) among participants who are negative on [68Ga]Ga-DOTA-TATE PET/CT imaging (TN or FN participants)

Description	Subject-level NPV was defined as the proportion of TN participants among [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. TN or FN participants).
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are negative on [68Ga]Ga-DOTA-TATE PET/CT imaging (TN or FN participants).

Arm/Group Description	All participants Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	29

Number of participants who are negative on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM (TN participants) among participants who are negative on [68Ga]Ga-DOTA-TATE PET/CT imaging (TN or FN participants) (units: Participants)	**Count of Participants (Not Applicable)**
False Negative [FN]	6 (20.69%)
True Negative [TN]	23 (79.31%)

Subject-level PPV

Description	Subject-level positive predictive values (PPV) is defined as the proportion of TP participants among [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. TP or FP participants). PPV (Subject-level positive predictive values) = TP / (TP + FP)
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are [68Ga]Ga-DOTA-TATE PET/CT imaging positive participants (i.e. TP or FP participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	42
Subject-level PPV (units: PPV (%))	**Number (95% Confidence Interval)**
	95.2 (83.84 to 99.42)

Subject-level NPV

Description	Subject-level NPV was defined as the proportion of TN participants among [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. TN or FN participants). NPV (Subject-level negative predictive values) = TN / (TN + FN)
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact, and who are [68Ga]Ga-DOTA-TATE PET/CT imaging negative participants (i.e. TN or FN participants).

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	29
Subject-level NPV (units: NPV (%))	**Number (95% Confidence Interval)**
	79.3 (60.28 to 92.01)

Participants who have consistent results (i.e. TP or TN participants) among all participants assessed by [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM - Subject-level Accuracy

Description	Subject-level accuracy is defined as the proportion of TP and TN participants among all patients in the EFF (i.e. TP+TN+FP+FN participants). Accuracy = (TP + TN) / (TP + TN + FP + FN).
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Participants who have consistent results (i.e. TP or TN participants) among all participants assessed by [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM - Subject-level Accuracy (units: Accuracy (%))	**Number (95% Confidence Interval)**
	88.7 (79.00 to 95.01)

Region-level sensitivity

Description	Region-level sensitivity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging positive regions (TP regions) among CIM positive regions (i.e. TP or FN regions). (n=the number of participants with CIM positive) Sensitivity = TP / (TP + FN),
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level sensitivity (units: Sensitivity (%))	**Number (95% Confidence Interval)**

Liver	77.8 (60.85 to 89.88)
Pancreas	42.9 (17.66 to 71.14)
Gastrointestinal tract	0 (0 to 97.50)
Lymph nodes	75.0 (47.62 to 92.73)
Other	84.6 (54.55 to 98.08)

Region-level specificity

Description	Region-level specificity is defined as the proportion of [68Ga]Ga-DOTA-TATE PET/CT imaging negative regions (TN regions) among CIM negative regions (i.e. TN or FP regions). (n=the number of participants with CIM negative) Specificity = TN / (TN + FP),
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level specificity (units: Specificity(%))	**Number** **(95% Confidence Interval)**
Liver	97.1 (85.08 to 99.93)

Pancreas	89.5 (78.48 to 96.04)
Gastrointestinal tract	95.7 (87.98 to 99.11)
Lymph nodes	83.6 (71.20 to 92.23)
Other	94.8 (85.62 to 98.92)

Region-level positive predictive values (PPV)

Description	Region-level PPV is defined as the proportion of regions which are positive on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM (TP regions) among [68Ga]Ga-DOTA-TATE PET/CT imaging positive regions (i.e. TP or FP regions). (n=the number of participants with [68Ga]Ga-DOTA-TATE PET/CT imaging positive) Region-level positive predictive values (PPV) = TP / (TP +FP)
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level positive predictive values (PPV) (units: PPV (%))	**Number** **(95% Confidence Interval)**
Liver	96.6 (82.24 to 99.91)
Pancreas	50.0 (21.09 to 78.91)

Gastrointestinal tract	0 (0 to 70.76)
Lymph nodes	57.1 (34.02 to 78.18)
Other	78.6 (49.20 to 95.34)

Region-level negative predictive values (NPV)

Description	Region-level NPV is defined as the proportion of regions which are negative on both [68Ga]Ga- DOTA-TATE PET/CT imaging and CIM (TN regions) among [68Ga]Ga-DOTA-TATE PET/CT imaging negative regions (i.e. TN or FN regions). (n=the number of participants with [68Ga]Ga-DOTA-TATE PET/CT imaging negative) Region-level negative predictive values (NPV) = TN / (TN + FN)
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level negative predictive values (NPV) (units: NPV (%))	**Number** **(95% Confidence Interval)**
Liver	81.0 (65.88 to 91.40)
Pancreas	86.4 (75.02 to 93.96)
Gastrointestinal tract	98.5 (92.08 to 99.96)

Lymph nodes	92.0 (80.77 to 97.78)
Other	96.5 (87.89 to 99.57)

Region-level accuracy

Description	Region-level accuracy is defined as the proportion of regions which are CIM and [68Ga]Ga-DOTA-TATE PET/CT imaging positive (TP regions) or negative (TN regions) among regions detected by CIM and [68Ga]Ga-DOTA-TATE PET/CT imaging (i.e. TP+TN+FP+FN regions). Accuracy = (TP + TN) / (TP + TN + FP + FN).
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level accuracy (units: accuracy (%))	**Number** **(95% Confidence Interval)**
Liver	87.3 (77.30 to 94.04)
Pancreas	80.3 (69.14 to 88.78)
Gastrointestinal tract	94.4 (86.20 to 98.44)
Lymph nodes	81.7 (70.73 to 89.87)

Other	93.0 (84.33 to 97.67)

Region-level True Positive

Description	TP regions were the regions which showed at least one lesion based on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM by central read
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level True Positive (units: Participants)	**Count of Participants** **(Not Applicable)**
Liver	28 (39.44%)
Pancreas	6 (8.45%)
Gastrointestinal tract	0 (%)
Lymph nodes	12 (16.9%)
Other	11 (15.49%)

Region-level False Negative

Description	FN regions were the regions which did not show any lesions based on [68Ga]Ga-DOTA-TATE PET/CT imaging but show at least one lesion based on CIM by central read.
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level False Negative (units: Participants)	**Count of Participants (Not Applicable)**
Liver	8 (11.27%)
Pancreas	8 (11.27%)
Gastrointestinal tract	1 (1.41%)
Lymph nodes	4 (5.63%)
Other	2 (2.82%)

Region-level False Positive

Description	FP regions were the regions which showed at least one lesion based on [68Ga]Ga-DOTA-TATE PET/CT imaging but do not showed any lesion based on CIM by central read.

Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level False Positive (units: Participants)	**Count of Participants (Not Applicable)**
Liver	1 (1.41%)
Pancreas	6 (8.45%)
Gastrointestinal tract	3 (4.23%)
Lymph nodes	9 (12.68%)
Other	3 (4.23%)

Region-level True Negative

Description	TN regions were the regions which did not show any lesion based on both [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM by central read.
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Region-level True Negative (units: Participants)	**Count of Participants (Not Applicable)**
Liver	34 (47.89%)
Pancreas	51 (71.83%)
Gastrointestinal tract	67 (94.37%)
Lymph nodes	46 (64.79%)
Other	55 (77.46%)

Number of participants who underwent a change in intended treatment plan attributed to the [68Ga]Ga-DOTA-TATE PET/CT imaging as assessed by pre and post imaging questionnaires

Description	Numbers of participants for each intended treatment plan collected from physician at pre and post [68Ga]Ga-DOTA-TATE PET/CT imaging will be summarized.
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM, with a valid measurement without a protocol deviation with impact. Patients with confirmed/suspected NENs)

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	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	48	0
Number of participants who underwent a change in intended treatment plan attributed to the [68Ga]Ga-DOTA-TATE PET/CT imaging as assessed by pre and post imaging questionnaires (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Planned treatment of Chemotherapy - Before imaging	8 (16.67%)	(NaN%)
Planned treatment of Lutathera - Before imaging	14 (29.17%)	(NaN%)
Planned treatment of Observation/surveillance - Before imaging	6 (12.5%)	(NaN%)
Planned treatment of Radiation - Before imaging	0 (%)	(NaN%)
Planned treatment of Somatostatin Analog - Before imaging	15 (31.25%)	(NaN%)
Planned treatment of Surgery - Before imaging	5 (10.42%)	(NaN%)
Planned treatment of Other - Before imaging	2 (4.17%)	(NaN%)
Planned treatment of Chemotherapy - After imaging	6 (12.5%)	(NaN%)
Planned treatment of Lutathera - After imaging	17 (35.42%)	(NaN%)
Planned treatment of Observation/surveillance - After imaging	7 (14.58%)	(NaN%)

Planned treatment of Radiation - After imaging	2 (4.17%)	(NaN%)
Planned treatment of Somatostatin Analog - After imaging	15 (31.25%)	(NaN%)
Planned treatment of Surgery - After imaging	4 (8.33%)	(NaN%)
Planned treatment of Other - After imaging	2 (4.17%)	(NaN%)
Participants with no change in treatment plans - After imaging	30 (62.5%)	(NaN%)
- Chemotherapy - After imaging	4 (8.33%)	(NaN%)
- Chemotherapy, Somatostatin Analog - After imaging	2 (4.17%)	(NaN%)
- Lutathera -After imaging	10 (20.83%)	(NaN%)
-Observation/surveillance -After imaging	3 (6.25%)	(NaN%)
- Somatostatin Analog -After imaging	8 (16.67%)	(NaN%)
- Surgery -After imaging	2 (4.17%)	(NaN%)
- Other -After imaging	1 (2.08%)	(NaN%)
Participants with change in treatment plans	18 (37.5%)	(NaN%)
-Chemotherapy Before - Lutathera After	2 (4.17%)	(NaN%)
-Lutathera Before - Lutathera, Radiation After	1 (2.08%)	(NaN%)
- Lutathera Before - Lutathera, Surgery After	1 (2.08%)	(NaN%)

-Lutathera Before - Observation/surveillance After	1 (2.08%)	(NaN%)
- Lutathera Before - Radiation After	1 (2.08%)	(NaN%)
- Observation/surveillance Before - Lutathera After	1 (2.08%)	(NaN%)
- Observation/surveillance Before - Observation/surveillance After	1 (2.08%)	(NaN%)
- Observation/surveillance Before - Somatostatin Analog After	1 (2.08%)	(NaN%)
- Somatostatin Analog Before - Lutathera After	1 (2.08%)	(NaN%)
- Somatostatin Analog Before - Observation/surveillance After	1 (2.08%)	(NaN%)
- Somatostatin Analog Before - Somatostatin Analog After	3 (6.25%)	(NaN%)
- Surgery Before - Lutathera, Surgery After	1 (2.08%)	(NaN%)
-Surgery Before - Observation/surveillance After	1 (2.08%)	(NaN%)
- Surgery Before - Somatostatin Analog After	1 (2.08%)	(NaN%)
- Other Before - Other After	1 (2.08%)	(NaN%)

Inter-reader agreement on [68Ga]Ga-DOTA-TATE PET/CT imaging

Description	The assessment of [68Ga]Ga-DOTA-TATE PET/CT images set was compared among the 3 independent readers.
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants
Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Inter-reader agreement on [68Ga]Ga-DOTA-TATE PET/CT imaging (units: Participants)	**Count of Participants (Not Applicable)**
Central Reader 1 Positive	54 (76.06%)
Central Reader 2 Positive	42 (59.15%)
Central Reader 3 Positive	41 (57.75%)
Central Reader 1 Negative	17 (23.94%)
Central Reader 2 Negative	29 (40.85%)
Central Reader 3 Negative	30 (42.25%)

Inter-reader variability (%) on [68Ga]Ga-DOTA-TATE PET/CT imaging

Description	Inter-reader variability for [68Ga]Ga-DOTA-TATE PET/CT imaging is defined as agreement rate among reader determinations. As assessed by Fleiss' Kappa statistics. Inter-reader variability (%) and its normality 95% CI is presented.
Time Frame	Day 1
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	All participants

Arm/Group Description	Confirmed/suspected NENs + HVs. All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	71
Inter-reader variability (%) on [68Ga]Ga-DOTA-TATE PET/CT imaging (units: Inter-reader variability (%))	**Number** **(95% Confidence Interval)**
	65.2 (51.79 to 78.65)

Incidence of Treatment emergent adverse event (TEAE) within 8 days after [68Ga]Ga-DOTATATE administration

Description	An adverse event (AE) is any untoward medical occurrence (e.g., any occurrence of unfavorable and unintended sign(s), symptom(s) or medical condition, including abnormal laboratory findings, or worsening of any pre-existing sign(s), symptom(s) or medical condition) in a participant after providing written informed consent for participation in the study. Therefore, an AE may or may not be temporally or causally associated with the use of any treatment used in this study. This includes events reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative).
Time Frame	For treated pts: AEs are reported from the single dose of study treatment plus 8 days post treatment, up to a maximum timeframe of 9 days. For HV pts: AEs are reported from the study start plus 8 days, up to a maximum timeframe of 9 days.
Analysis Population Description	The Safety Set comprised all participants who received any dose of [68Ga]Ga-DOTA-TATE.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	48	23

Incidence of Treatment emergent adverse event (TEAE) within 8 days after [68Ga]Ga-DOTATATE administration (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Adverse events (AEs)	8 (16.67%)	2 (8.7%)
Adverse events - Treatment-related	1 (2.08%)	0 (%)
Serious Adverse events (SAEs)	2 (4.17%)	0 (%)
Serious Adverse events Treatment-related	0 (%)	0 (%)
Fatal SAEs	0 (%)	0 (%)
Fatal SAEs - Treatment-related	0 (%)	0 (%)
AEs requiring additional therapy	3 (6.25%)	0 (%)

Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time (AUCinf) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. AUC(0-inf) will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2

	(0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time (AUCinf) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: h*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	0.420 (25.5%)	

Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. AUClast will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Area under the serum concentration-time curve from time zero to the time of last quantifiable concentration (AUClast) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: h*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

0.304 (26.3%)

Observed maximum plasma concentration (Cmax) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. Cmax will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Observed maximum plasma concentration (Cmax) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	0.656 (30.7%)	

Time of maximum observed drug concentration occurrence (Tmax) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. Tmax will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)

Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Time of maximum observed drug concentration occurrence (Tmax) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: hour)	**Median (Full Range)**	**Median (Full Range)**
	0.0750 (0.0333 to 0.100)	

Terminal elimination half-life (T1/2) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. The half-live will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers

Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Terminal elimination half-life (T1/2) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: hour)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	1.77 (26.3%)	

Total systemic clearance for intravenous administration (CL) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. CL will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0

Total systemic clearance for intravenous administration (CL) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: L/h)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)
	26.0 (32.5%)	

Volume of distribution during the terminal phase following intravenous elimination (Vz) of [68Ga]Ga-DOTA-TATE [mass-based concentration]

Description	Venous whole blood samples will be collected for activity-based pharmacokinetics characterization. Vz will be listed and summarized using descriptive statistics.
Time Frame	Day 1 (5 min, 15 min, 30 min, 45 min, 60 min, 120 min, 180 min)
Analysis Population Description	PAS - pharmacokinetics analysis set - for treated participants with a valid measurement without a protocol deviation with impact. PK analysis was planned to be performed on a small subset of patients only, 6, and not healthy volunteers.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	6	0
Volume of distribution during the terminal phase following intravenous elimination (Vz) of [68Ga]Ga-DOTA-TATE [mass-based concentration] (units: L)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	66.2 (53.5%)	

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Lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among lesions that local histopathology result are available

Description	The lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among legions which is available, will be calculated. The rate is defined as the proportion of lesions which are positive or negative on both local read of [68Ga]Ga-DOTA-TATE PET/CT imaging and local histopathology among lesions detected by local histopathology.
Time Frame	Day 1 to Day 30
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	Healthy Volunteers
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	48	0
Lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among lesions that local histopathology result are available (units: Number of histopathology assessments)		
Total number of lesions with histopathology assessments	11	
Positive Result of SSTR by histopathology	8	
Negative Result of SSTR by histopathology	3	
Positive Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	11	
Negative Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	0	
+ Result of SSTR by histopathology - + Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	8	

+ Result of SSTR by histopathology & -Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	0
- Result of SSTR by histopathology & + Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	3
- Result of SSTR by histopathology & - Result of [68Ga]Ga-DOTA-TATE PET/CT imaging by local read	0
Lesions with concordant results	8

Lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among lesions that local histopathology result are available - concordance rate

Description	The lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among legions which is available, will be calculated. The rate is defined as the proportion of lesions which are positive or negative on both local read of [68Ga]Ga-DOTA-TATE PET/CT imaging and local histopathology among lesions detected by local histopathology.
Time Frame	Day 1 to Day 30
Analysis Population Description	The Efficacy Analysis Set (EFF) comprised all enrolled participants who were administered with [68Ga]Ga-DOTA-TATE. Patients with confirmed/suspected NENs had to have both results of [68Ga]Ga-DOTA-TATE PET/CT imaging and CIM. HVs had to have results of [68Ga]Ga-DOTA-TATE PET/CT imaging, with a valid measurement without a protocol deviation with impact.

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs	**Healthy Volunteers**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Number of Participants Analyzed [units: participants]	48	0
Lesion-level concordance rate for SSTR between [68Ga]Ga-DOTA-TATE PET/CT imaging local read and local histopathology result among lesions that local	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**

histopathology result are available - concordance rate (units: Concordance rate (%))	
Concordance rate (%)	72.7 (39.03 to 93.98)

Safety Results

Time Frame	Adverse events are reported from the single dose of study treatment plus 8 days post treatment, up to a maximum timeframe of 9 days.
Source Vocabulary for Table Default	MedDRA (27.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs N = 48	**Healthy Volunteers N = 23**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Total Number Affected	0	0
Total Number At Risk	48	23

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Serious Adverse Events

Time Frame	Adverse events are reported from the single dose of study treatment plus 8 days post treatment, up to a maximum timeframe of 9 days.
Source Vocabulary for Table Default	MedDRA (27.1)
Collection Approach for Table Default	Systematic Assessment

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs N = 48	**Healthy Volunteers N = 23**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Total # Affected by any Serious Adverse Event	2	0
Total # at Risk by any Serious Adverse Event	48	23
Gastrointestinal disorders		
Intra-abdominal haemorrhage	1 (2.08%)	0 (0.00%)
Vomiting	1 (2.08%)	0 (0.00%)

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Other (Not Including Serious) Adverse Events

Time Frame	Adverse events are reported from the single dose of study treatment plus 8 days post treatment, up to a maximum timeframe of 9 days.
Source Vocabulary for Table Default	MedDRA (27.1)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	0%

	[68Ga]Ga-DOTA-TATE / Confirmed/suspected NENs N = 48	**Healthy Volunteers N = 23**
Arm/Group Description	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)	All eligible participants received [68Ga]Ga-DOTA-TATE via intravenous injection at a dose of 2 MBq/kg (0.054 mCi/kg) of body weight up to a maximum total dose of 200 MBq (5.4 mCi)
Total # Affected by any Other Adverse Event	8	2
Total # at Risk by any Other Adverse Event	48	23
Blood and lymphatic system disorders		
Neutropenia	1 (2.08%)	0 (0.00%)
General disorders and administration site conditions		

Malaise	0 (0.00%)	1 (4.35%)
Pyrexia	1 (2.08%)	0 (0.00%)
Hepatobiliary disorders		
Liver disorder	1 (2.08%)	0 (0.00%)
Investigations		
Aspartate aminotransferase increased	1 (2.08%)	0 (0.00%)
Blood creatine phosphokinase increased	1 (2.08%)	0 (0.00%)
Electrocardiogram PR prolongation	1 (2.08%)	0 (0.00%)
Electrocardiogram QT prolonged	1 (2.08%)	0 (0.00%)
Electrocardiogram ST-T segment abnormal	1 (2.08%)	0 (0.00%)
Platelet count decreased	1 (2.08%)	0 (0.00%)
White blood cell count decreased	1 (2.08%)	0 (0.00%)
White blood cells urine positive	1 (2.08%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Tumour pain	1 (2.08%)	0 (0.00%)
Nervous system disorders		
Headache	1 (2.08%)	0 (0.00%)
Presyncope	0 (0.00%)	1 (4.35%)

Other Relevant Findings

Conclusion:

The results of study CAAA501A11301 were positive and met its two co-primary endpoints. This supports the imaging efficacy of [68Ga]Ga-DOTA-TATE PET/CT for the detection and localization of neuroendocrine neoplasms (NENs) in Japanese patients with NENs, thus confirming its diagnostic performance for NENs.

[68Ga]Ga-DOTA-TATE was found to be safe and well-tolerated in Japanese patients with NENs and in healthy volunteers (HVs).

Date of Clinical Trial Report

20 May 2025