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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

[68Ga]Ga-FF58

Trial Indication(s)

Relapsed or refractory glioblastoma multiple (r/r GBM), breast cancer (BC) that has metastasized to the brain, pancreatic ductal adenocarcinoma (PDAC) and gastroesophageal adenocarcinoma (GEA)

Protocol Number

CAAA504A12101

Protocol Title

Phase I, open-label, multicenter study to evaluate the imaging performance, safety, biodistribution and dosimetry of [68Ga]Ga-FF58 in adult patients with selected solid tumors expected to overexpress αvβ3 and αvβ5 integrins.

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1

Study Start/End Dates

Study Start Date: October 14, 2021 (Actual)

Primary Completion Date: June 18, 2024 (Actual)

Study Completion Date: July 01, 2024 (Actual)

Reason for Termination (If applicable)

On 06-Jun-2024, the sponsor (Novartis) made a decision to halt further enrollment of patients to the CAAA504A12101 study for business reasons.

No patient was enrolled in the dosimetry sub-group. The expansion part of the study was not opened.

Study Design/Methodology

This was a first in human (FIH) study of [^{68}Ga]Ga-FF58 to characterize the imaging properties, safety, biodistribution, and dosimetry of [^{68}Ga]Ga-FF58 in adult patients with r/r GBM, breast cancer (BC) that had metastasized to the brain, gastroesophageal adenocarcinoma (GEA), or pancreatic ductal adenocarcinoma (PDAC) expected to overexpress αvβ3 and αvβ5 integrins.

Approximately 80 patients (male and female) were planned to be enrolled into the study in total, approximately 20 patients in each indication (GBM, BC that had metastasized to the brain, GEA, or PDAC). The study had planned an imaging characterization part in approximately 24 patients (six in each indication) and an expansion part in approximately 56 patients (approximately 14 in each indication). All patients enrolled in this study were planned to receive a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [^{68}Ga]Ga-FF58 and then undergo [^{68}Ga]Ga-FF58 positron emission tomography (PET) imaging at different timepoints on Day 1 as well as conventional imaging (high resolution computed tomography (CT) or magnetic resonance imaging (MRI)) jointly acquired or separately up to 24 hours before/after the [^{68}Ga]Ga-FF58 administration. The estimated study duration for each individual patient was approximately 44 days (including screening period of 28 days and 14 days of safety follow-up).

After completing enrollment and an initial assessment of the available safety data, biodistribution and [^{68}Ga]Ga-FF58 uptake in patients, a decision was to be made whether to begin enrollment into the expansion part of the study. The expansion part was planned to be opened only if uptake of [^{68}Ga]Ga-FF58 in tumor had been demonstrated in the imaging characterization part.

Both parts of the study (imaging characterization and expansion) were to include a dosimetry sub-group in which the distribution, pharmacokinetics (PK), radiation dosimetry, and absorbed doses in tissue and tumor were assessed and for which additional assessments were required.

The study was terminated early due to business reasons and not as a consequence of any safety concern. This decision has no impact on any other clinical trials involving [^{68}Ga]Ga-FF58.

No patients were enrolled into either the dosimetry sub-group of the imaging characterization part, or into the expansion part of the study at the time of study enrollment halt.

Centers

2 centers in 2 countries: France(1), Germany(1)

Objectives:

The primary objective of the trial was to characterize the imaging properties (tumor uptake and bio-distribution), feasibility of tumor assessment of [^{68}Ga]-GaFF58 and to estimate the optimal time point for imaging in patients with malignancies expected to overexpress αvβ3 and αvβ5 integrins.

The secondary objectives were:

- To assess the safety of a single imaging dose of [^{68}Ga]-GaFF58 administered as an intravenous bolus injection
- To assess the concordance between [^{68}Ga]-GaFF58 positive lesions and those seen in conventional imaging (CT or MRI)
- Dosimetry sub-group: To assess the PK of [^{68}Ga]-GaFF58 in selected organs and tumors

- Dosimetry sub-group: To assess the radiation dosimetry in selected organs and tumors

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

The study had one study drug of [^{68}Ga]Ga-FF58 solution for injection, administered as single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection.

Statistical Methods

Analysis sets:

The Full Analysis Set (FAS) and Safety Set comprised all patients who received the study drug.

Analysis of primary endpoint:

The FAS was used for analysis of the primary endpoints.

The biodistribution and the initial estimation of the optimal timepoint for imaging and tumor uptake, the number and location of lesions identified by PET, SUV values per lesion and SUVr of [^{68}Ga]Ga-FF58 were analyzed. The descriptive analyses of all these parameters allowed preliminary assessment of the imaging properties of [^{68}Ga]Ga-FF58 in patients with malignancies expected to overexpress αvβ3 and αvβ5 integrins.

All statistical analyses were descriptive in nature. Imaging parameters were provided by an imaging vendor. Most summaries were at lesion-level. Categorical data (e.g. visual assessment of positivity) was summarized as frequencies and percentages. For continuous data (e.g. standard uptake value (SUV), standard uptake value ratio (SUVr)), mean and standard deviation were presented.

Analysis of secondary endpoints:

Imaging endpoints:

The FAS was used for the analysis of imaging endpoints.

A summary table of the concordance assessment between [^{68}Ga]Ga-FF58 PET scan results versus conventional CT/ MRI imaging results could not be presented since the data from the latter were recorded as free-form text.

Safety endpoints:

Secondary safety endpoints included adverse events (AEs) and (SAEs). The AE data were descriptively summarized using frequencies and percentages for all AEs, deaths and SAEs. Summaries for AEs were displayed using the Safety Set. All summaries included AEs occurring during the on-treatment period (from date of [^{68}Ga]Ga-FF58 administration to 14 days after the date of [^{68}Ga]Ga-FF58 administration).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Signed informed consent must be obtained prior to participation in the study
- Patients with histologically or cytologically confirmed and documented r/r GBM that has progressed after prior radiation therapy and have not received prior bevacizumab OR patients with BC that has metastasized to the brain and who should have at least one newly diagnosed brain metastasis that has not been resected or irradiated, or has been irradiated and progressed OR patients with histologically or cytologically confirmed and documented locally advanced or metastatic GEA (i.e., adenocarcinoma of the stomach (intestinal subtype), esophagus, or gastroesophageal junction), either untreated or r/r after one or more lines of treatment OR patients with histologically or cytologically confirmed and documented locally advanced or metastatic PDAC, either untreated or r/r after one or more lines of treatment.

Exclusion Criteria:

- Creatinine clearance (calculated using Cockcroft-Gault formula) <40 mL/min.
- Platelet count of < 75 x 10^9/L.

- Hemoglobin < 9 g/dL.
- Unmanageable bladder outflow obstruction or urinary incontinence.
- QTcF > 480 msec on screening ECG or congenital long QT syndrome.
- Any condition that requires chronic treatment with anticoagulants or antiplatelet agents
- Patients with a known bleeding disorder
- Administration of a radiopharmaceutical within a period corresponding to 10 half-lives of the radionuclide used prior to injection of [^{68}Ga]-FF58.
- Pregnant women. Women who are breastfeeding must express and discard breast milk for 12 hours after [^{68}Ga]-FF58 administration and must also stop breast feeding during this same period. Males and females must abstain from sexual intercourse for 12 hours after [^{68}Ga]-FF58 administration.
- Total bilirubin > 1.5 x ULN (except for patients with Gilbert's syndrome who are excluded if total bilirubin > 3.0 x ULN) or direct bilirubin > 1.5 x ULN
- Alanine aminotransferase (ALT) > 3 x ULN, except for patients that have tumor involvement of the liver, who are excluded if ALT > 5 x ULN
- Aspartate aminotransferase (AST) > 3 x ULN, except for patients that have tumor involvement of the liver, who are excluded if AST > 5 x ULN

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Participant Flow Table

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Started	14
Completed	14
Not Completed	0

Baseline Characteristics

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants [units: participants]	14
Baseline Analysis Population Description	
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation	
	54.4±11.11

Age, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)	
18 - <65 years	12
65 - <85 years	2
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)	
Female	8
Male	6
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)	
White	11
Not reported	3
Study Specific Characteristic **Diagnosis of disease** (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)	
Glioblastoma multiforme	6
Brain metastasis from breast cancer	3
Gastroesophageal adenocarcinoma	3
Pancreatic ductal adenocarcinoma	2
Study Specific Characteristic **Primary site of cancer** (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)	

Brain	6
Breast	3
Esophagus	3
Pancreas-Body	1
Pancreas-Head	1

Primary Outcome Result(s)

Number of participants with PET-avid lesions

Description	Participants received a single dose of [68Ga]Ga-FF58 and then underwent [68Ga]Ga-FF58 positron emission tomography (PET) imaging at different timepoints on Day 1. Imaging evaluations were assessed centrally. This endpoint summarizes the number of participants for whom PET-avid lesions were detected on blinded read.
Time Frame	30 minutes, 1 hour, and 2 hours post-injection of [68Ga]Ga-FF58 on Day 1
Analysis Population Description	Participants who received [68Ga]Ga-FF58 and had evaluable PET scans.

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	13
Number of participants with PET-avid lesions (units: participants)	**Count of Participants (Percentage)**
	9 (69.23%)

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Number of lesions identified by PET

Description	Participants received a single dose of [68Ga]Ga-FF58 and then underwent [68Ga]Ga-FF58 PET imaging at different timepoints on Day 1. Imaging evaluations were assessed centrally. This endpoint summarizes the number of PET-avid lesions.
Time Frame	30 minutes, 1 hour, and 2 hours post-injection of [68Ga]Ga-FF58 on Day 1
Analysis Population Description	Participants who received [68Ga]Ga-FF58 and had PET-avid lesions.

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	9
Number of lesions identified by PET (units: lesions)	
	14

[^{68}Ga]Ga-FF58 SUVmean by lesion location

Description	SUVmean (mean standardized uptake value) is the average SUV of all the voxels within a lesion. It provides a measure of the overall uptake of the radioligand in that lesion. Participants may have more than 1 lesion per lesion location.
Time Frame	1 hour post-injection of [68Ga]Ga-FF58 (optimal imaging timepoint)
Analysis Population Description	Participants who received [68Ga]Ga-FF58 and had PET-avid lesions.

All patients

Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	9
[68Ga]Ga-FF58 SUVmean by lesion location (units: grams per milliliter (g/mL))	**Mean**
Adrenal Gland Left Lesion (n=1)	9.4
Bone Skull Calvaria Lesion (n=1)	2.3
Bone Soft Tissue Extraosseous Extension Lesion (n=1)	4.0
Brain Frontal Lobe Left Lesion (n=1)	0.7
Brain Frontal Lobe Right Lesion (n=1)	1.1
Brain Occipital Lobe Right Lesion (n=1)	2.3
Brain Parietal Lobe Left Lesion (n=1)	1.3
Brain Temporal Lobe Right Lesion (n=1)	0.9
Lymph Node Cervical Deep Middle Right (Level Iii) Lesion (n=1)	3.1
Lymph Node Post Cervical Right (Level V) Lesion (n=1)	4.7
Lymph Node Pretracheal Right Lesion (n=1)	2.1
Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1)	2.3
Lymph Node Subcarinal (7) Lesion (n=1)	2.2
Stomach Cardia Lesion (n=1)	7.7

[^{68}Ga]Ga-FF58 SUVmax by lesion location

Description	SUVmax (maximum standardized uptake value) represents the highest SUV found within a lesion. It focuses on the single voxel with the highest uptake, which can be indicative of the most active or aggressive part of a tumor. Participants may have more than 1 lesion per lesion location.
Time Frame	1 hour post-injection of [68Ga]Ga-FF58 (optimal imaging timepoint)

Analysis Population Description: Participants who received [68Ga]Ga-FF58 and had PET-avid lesions.

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	9
[68Ga]Ga-FF58 SUVmax by lesion location (units: grams per milliliter (g/mL))	**Mean**
Adrenal Gland Left Lesion (n=1)	16.5
Bone Skull Calvaria Lesion (n=1)	3.2
Bone Soft Tissue Extraosseous Extension Lesion (n=1)	8.9
Brain Frontal Lobe Left Lesion (n=1)	1.5
Brain Frontal Lobe Right Lesion (n=1)	1.8
Brain Occipital Lobe Right Lesion (n=1)	3.6
Brain Parietal Lobe Left Lesion (n=1)	2.4
Brain Temporal Lobe Right Lesion (n=1)	1.6
Lymph Node Cervical Deep Middle Right (Level Iii) Lesion (n=1)	4.2
Lymph Node Post Cervical Right (Level V) Lesion (n=1)	6.8
Lymph Node Pretracheal Right Lesion (n=1)	3.1
Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1)	3.2
Lymph Node Subcarinal (7) Lesion (n=1)	3.1
Stomach Cardia Lesion (n=1)	11.5

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[^{68}Ga]Ga-FF58 SUVrmean by indication, lesion location and reference region of interest

Description	SUVrmean (mean standardized uptake value ratio) is defined as SUVmean of lesion divided by SUVmean of different reference regions of interest (ROI). Participants may have more than 1 lesion per lesion location. Results are presented by indication (GBM: glioblastoma multiple, BC: breast cancer, PDAC: pancreatic ductal adenocarcinoma, GEA: gastroesophageal adenocarcinoma), lesion location and ROI.
Time Frame	1 hour post-injection of [68Ga]Ga-FF58 (optimal imaging timepoint)
Analysis Population Description	Participants who received [68Ga]Ga-FF58 and had at least 1 PET-avid lesion

	Aorta	Bladder	Brain hemisphere left	Brain hemisphere right	Choroid plexus	Eyes	Heart wall	Kidney left	Kidney right	Lacrimal gland	Left colon	Liver
Arm/Group Description	Reference region of interest (ROI): Aorta	Reference region of interest (ROI): Bladder	Reference region of interest (ROI): Brain hemisphere left	Reference region of interest (ROI): Brain hemisphere right	Reference region of interest (ROI): Choroid plexus	Reference region of interest (ROI): Eye	Reference region of interest (ROI): Heart wall	Reference region of interest (ROI): Kidney left	Reference region of interest (ROI): Kidney right	Reference region of interest (ROI): Lacrimal gland	Reference region of interest (ROI): Left colon	Reference region of interest (ROI): Liver
Number of Participants Analyzed [units: participants]	9	9	9	9	9	9	9	9	9	9	9	9
[68Ga]Ga-FF58 SUVrmean by indication, lesion location and reference region of interest	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**

(units: grams per milliliter (g/mL))												
GBM-Brain Frontal Lobe Left Lesion (n=1)	0.9	0.1	9.0	7.7	0.3	3.2	0.3	0.1	0.1	0.2	0.2	0.1
GBM-Brain Frontal Lobe Right Lesion (n=1)	1.3	0.3	10.5	7.2	0.4	7.0	0.5	0.1	0.1	0.5	0.7	0.1
GBM-Brain Temporal Lobe Right Lesion (n=1)	1.1	0.1	12.4	14.9	0.4	2.1	0.3	0.1	0.1	0.4	0.3	0.1
BC-Adrenal Gland Left Lesion (n=1)	16.3	1.3	90.0	167.1	3.7	24.8	3.0	1.2	1.0	4.4	4.8	1.0
BC-Brain Occipital Lobe Right Lesion (n=1)	2.6	0.3	24.3	23.2	0.8	3.4	0.7	0.2	0.2	0.7	0.5	0.3
BC-Brain Parietal Lobe Left Lesion (n=1)	1.5	0.1	21.8	13.4	0.6	2.7	0.5	0.2	0.2	0.6	0.4	0.2
BC-Lymph Node Cervical Deep Middle	5.4	0.4	30.0	55.7	1.2	8.3	1.0	0.4	0.3	1.5	1.6	0.3

Right (Level Iii) Lesion (n=1)												
BC-Lymph Node Post Cervical Right (Level V) Lesion (n=1)	8.2	0.6	45.4	84.2	1.9	12.5	1.5	0.6	0.5	2.2	2.4	0.5
PDAC-Bone Skull Calvaria Lesion (n=1)	6.5	0.6	19.8	44.5	3.9	7.1	1.1	0.4	0.4	1.9	1.9	0.3
PDAC-Bone Soft Tissue Extraosseous Extension Lesion (n=1)	11.1	1.0	33.7	75.8	6.7	12.2	1.9	0.7	0.7	3.3	3.3	0.5
GEA-Lymph Node Pretracheal Right Lesion (n=1 or 0)	6.4	0.5					0.9	0.2	0.2		0.3	0.4
GEA-Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1 or 0)	7.0	0.6					1.0	0.3	0.2		0.3	0.4
GEA-Lymph	6.6	0.5					1.0	0.2	0.2		0.3	0.4

Node Subcarinal (7) Lesion (n=1 or 0)												
GEA-Stomach Cardia Lesion (n=1)	17.5	1.1	93.6	129.1	4.9	13.1	2.8	1.1	1.0	4.6	4.8	1.1

	Lungs	**Muscle**	**Nasal Cavity**	**Pituitary gland**	**Right colon**	**Salivary gland**	**Small intestine**	**Spleen**	**Stomach**	**Thyroid gland**	**Vertebral bodies**
Arm/Group Description	Reference region of interest (ROI): Lungs	Reference region of interest (ROI): Muscle	Reference region of interest (ROI): Nasal Cavity	Reference region of interest (ROI): Pituitary gland	Reference region of interest (ROI): Right colon	Reference region of interest (ROI): Salivary gland	Reference region of interest (ROI): Small intestine	Reference region of interest (ROI): Spleen	Reference region of interest (ROI): Stomach	Reference region of interest (ROI): Thyroid gland	Reference region of interest (ROI): Vertebral bodies
Number of Participants Analyzed [units: participants]	9	9	9	9	9	9	9	9	9	9	9
[68Ga]Ga-FF58 SUVrmean by indication, lesion location and reference region of interest (units: grams per milliliter (g/mL))	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**
GBM-Brain Frontal Lobe	0.8	0.9	0.4	0.3	0.4	0.2	0.1	0.1	0.2	0.1	0.2

Left Lesion (n=1)											
GBM-Brain Frontal Lobe Right Lesion (n=1 or 0)	1.1	2.3	0.3	0.4	0.4		0.1	0.1	0.1	0.1	0.5
GBM-Brain Temporal Lobe Right Lesion (n=1)	1.1	1.8	0.5	0.4	0.5	0.3	0.1	0.1	0.1	0.1	0.3
BC-Adrenal Gland Left Lesion (n=1)	17.5	19.3	8.0	4.2	3.8	2.5	1.1	0.8	4.5	1.5	5.1
BC-Brain Occipital Lobe Right Lesion (n=1)	2.9	3.0	0.7	0.8	0.5	0.6	0.3	0.2	0.3	0.3	1.0
BC-Brain Parietal Lobe Left Lesion (n=1)	1.7	2.3	0.5	0.5	0.4	0.3	0.2	0.1	0.2	0.6	0.5
BC-Lymph Node Cervical Deep Middle Right (Level Iii) Lesion (n=1)	5.8	6.4	2.7	1.4	1.3	0.8	0.4	0.3	1.5	0.5	1.7
BC-Lymph Node Post Cervical Right (Level V) Lesion (n=1)	8.8	9.7	4.0	2.1	1.9	1.3	0.6	0.4	2.3	0.8	2.6
PDAC-Bone Skull	6.6	6.8	2.9	1.3	0.9	0.7	0.6	0.4	0.7	0.6	1.7

Calvaria Lesion (n=1)											
PDAC-Bone Soft Tissue Extraosseous Extension Lesion (n=1)	11.3	11.6	4.9	2.2	1.6	1.3	1.0	0.6	1.2	1.0	2.9
GEA-Lymph Node Pretracheal Right Lesion (n=1 or 0)	4.1	5.4			0.7	0.7	0.4	0.3	0.4	0.4	1.0
GEA-Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1 or 0)	4.4	5.8			0.8	0.8	0.4	0.3	0.4	0.4	1.1
GEA-Lymph Node Subcarinal (7) Lesion (n=1 or 0)	4.1	5.5			0.7	0.7	0.4	0.3	0.4	0.4	1.1
GEA-Stomach Cardia Lesion (n=1)	13.2	19.4	5.9	3.4	1.7	2.4	1.0	0.8	1.4	1.0	5.0

[^{68}Ga]Ga-FF58 SUVrmax by indication, lesion location and reference region of interest

Description	SUVrmax (maximum standardized uptake value ratio) is defined as SUVmax of lesion divided by SUVmax of different reference regions of interest (ROI). Participants may have more than 1 lesion per lesion location. Results are presented by indication (GBM: glioblastoma multiple, BC: breast cancer, PDAC: pancreatic ductal adenocarcinoma, GEA: gastroesophageal adenocarcinoma), lesion location and ROI.
Time Frame	1 hour post-injection of [68Ga]Ga-FF58 (optimal imaging timepoint)

Analysis Population Description: Participants who received [68Ga]Ga-FF58 and had at least 1 PET-avid lesion

	Aorta	Bladder	Brain hemisphere left	Brain hemisphere right	Choroid plexus	Eyes	Heart wall	Kidney left	Kidney right	Lacrimal gland	Left colon	Liver
Arm/Group Description	Reference region of interest (ROI): Aorta	Reference region of interest (ROI): Bladder	Reference region of interest (ROI): Brain hemisphere left	Reference region of interest (ROI): Brain hemisphere right	Reference region of interest (ROI): Choroid plexus	Reference region of interest (ROI): Eye	Reference region of interest (ROI): Heart wall	Reference region of interest (ROI): Kidney left	Reference region of interest (ROI): Kidney right	Reference region of interest (ROI): Lacrimal gland	Reference region of interest (ROI): Left colon	Reference region of interest (ROI): Liver
Number of Participants Analyzed [units: participants]	9	9	9	9	9	9	9	9	9	9	9	9
[68Ga]Ga-FF58 SUVrmax by indication, lesion location and reference region of interest (units: grams per milliliter (g/mL))	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**
GBM-Brain Frontal	2.0	0.3	20.5	17.4	0.6	7.2	0.6	0.1	0.1	0.6	0.4	0.2

Lobe Left Lesion (n=1)												
GBM-Brain Frontal Lobe Right Lesion (n=1)	2.1	0.5	16.8	11.5	0.7	11.1	0.8	0.2	0.2	0.7	1.0	0.2
GBM-Brain Temporal Lobe Right Lesion (n=1)	1.9	0.2	21.0	25.2	0.6	3.6	0.5	0.1	0.1	0.7	0.6	0.2
BC-Adrenal Gland Left Lesion (n=1)	28.6	2.2	158.5	294.3	6.5	43.6	5.3	2.1	1.8	7.7	8.4	1.8
BC-Brain Occipital Lobe Right Lesion (n=1)	4.1	0.4	38.1	36.2	1.3	5.3	1.1	0.4	0.4	1.2	0.8	0.4
BC-Brain Parietal Lobe Left Lesion (n=1)	2.8	0.1	40.2	24.6	1.1	5.1	0.9	0.3	0.3	1.0	0.7	0.4
BC-Lymph Node Cervical Deep Middle Right (Level Iii) Lesion (n=1)	7.3	0.6	40.4	74.9	1.7	11.1	1.3	0.5	0.5	2.0	2.1	0.5
BC-Lymph Node Post Cervical	11.8	0.9	65.5	121.5	2.7	18.0	2.2	0.9	0.7	3.2	3.5	0.7

Right (Level V) Lesion (n=1)												
PDAC-Bone Skull Calvaria Lesion (n=1)	9.0	0.8	27.3	61.3	5.4	9.9	1.6	0.6	0.5	2.7	2.7	0.4
PDAC-Bone Soft Tissue Extraosseous Extension Lesion (n=1)	24.8	2.1	75.3	169.3	14.9	27.2	4.3	1.5	1.5	7.4	7.4	1.1
GEA-Lymph Node Pretracheal Right Lesion (n=1 or 0)	9.2	0.7					1.3	0.3	0.3		0.4	0.5
GEA-Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1 or 0)	9.7	0.8					1.4	0.4	0.3		0.4	0.6
GEA-Lymph Node Subcarinal (7) Lesion (n=1 or 0)	9.4	0.8					1.4	0.3	0.3		0.4	0.5
GEA-Stomach	26.2	1.6	139.6	192.7	7.4	19.6	4.1	1.6	1.5	6.9	7.2	1.6

Cardia
Lesion
(n=1)

	Lungs	Muscle	Nasal Cavity	Pituitary gland	Right colon	Salivary gland	Small intestine	Spleen	Stomach	Thyroid gland	Vertebral bodies
Arm/Group Description	Reference region of interest (ROI): Lungs	Reference region of interest (ROI): Muscle	Reference region of interest (ROI): Nasal Cavity	Reference region of interest (ROI): Pituitary gland	Reference region of interest (ROI): Right colon	Reference region of interest (ROI): Salivary gland	Reference region of interest (ROI): Small intestine	Reference region of interest (ROI): Spleen	Reference region of interest (ROI): Stomach	Reference region of interest (ROI): Thyroid gland	Reference region of interest (ROI): Vertebral bodies
Number of Participants Analyzed [units: participants]	9	9	9	9	9	9	9	9	9	9	9
[68Ga]Ga-FF58 SUVrmax by indication, lesion location and reference region of interest (units: grams per milliliter (g/mL))	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**
GBM-Brain Frontal Lobe Left Lesion (n=1)	1.8	2.1	0.8	0.8	0.8	0.4	0.1	0.2	0.6	0.2	0.4
GBM-Brain Frontal Lobe Right Lesion (n=1 or 0)	1.8	3.6	0.4	0.7	0.6		0.2	0.2	0.2	0.2	0.8

GBM-Brain Temporal Lobe Right Lesion (n=1)	1.8	3.0	0.8	0.7	0.8	0.5	0.2	0.1	0.2	0.2	0.6
BC-Adrenal Gland Left Lesion (n=1)	30.8	34.0	14.1	7.4	6.7	4.4	2.0	1.5	7.9	2.7	8.9
BC-Brain Occipital Lobe Right Lesion (n=1)	4.5	4.7	1.1	1.2	0.8	0.9	0.4	0.4	0.5	0.5	1.6
BC-Brain Parietal Lobe Left Lesion (n=1)	3.2	4.1	1.0	0.9	0.7	0.5	0.3	0.2	0.3	1.0	0.9
BC-Lymph Node Cervical Deep Middle Right (Level Iii) Lesion (n=1)	7.8	8.7	3.6	1.9	1.7	1.1	0.5	0.4	2.0	0.7	2.3
BC-Lymph Node Post Cervical Right (Level V) Lesion (n=1)	12.7	14.1	5.8	3.1	2.8	1.8	0.8	0.6	3.3	1.1	3.7
PDAC-Bone Skull Calvaria Lesion (n=1)	9.1	9.3	3.9	1.8	1.3	1.0	0.8	0.5	1.0	0.8	2.3
PDAC-Bone Soft Tissue Extraosseous Extension Lesion (n=1)	25.2	25.8	10.9	4.9	3.5	2.8	2.2	1.3	2.7	2.2	6.5

GEA-Lymph Node Pretracheal Right Lesion (n=1 or 0)	5.8	7.7			1.0	1.0	0.5	0.4	0.6	0.6	1.5
GEA-Lymph Node Pulmonary Hilar Right (10r) Lesion (n=1 or 0)	6.1	8.1			1.1	1.1	0.6	0.4	0.6	0.6	1.6
GEA-Lymph Node Subcarinal (7) Lesion (n=1 or 0)	5.9	7.8			1.0	1.0	0.6	0.4	0.6	0.6	1.5
GEA-Stomach Cardia Lesion (n=1)	19.8	28.9	8.8	5.1	2.6	3.6	1.5	1.1	2.1	1.5	7.5

Secondary Outcome Result(s)

Number of participants with treatment-emergent AEs and SAEs

Description	Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (SAEs), including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.002. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE.
Time Frame	From single dose of [68Ga]Ga-FF58 on Day 1 up to Day 14
Analysis Population Description	Participants who received [68Ga]Ga-FF58

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	14
Number of participants with treatment-emergent AEs and SAEs (units: participants)	**Count of Participants (Percentage)**
AEs	2 (14.29%)
Treatment-related AEs	0 (%)
AEs with grade >=3	0 (%)
Treatment-related AEs with grade >=3	0 (%)
SAEs	0 (%)
Treatment-related SAEs	0 (%)
Fatal SAEs	0 (%)
Treatment-related fatal SAEs	0 (%)

Percentage lesions detected by conventional scans that were also detected by PET scan

Description	Static whole body [68Ga]Ga-FF58 PET scan was performed at 30 minutes, 1 hour, and 2 hours post-injection. A dedicated brain scan was additionally acquired at each time point in patients with brain lesions. Conventional imaging scans (high resolution computed tomography (CT) or magnetic resonance imaging (MRI)) were also acquired either as part of the [68Ga]Ga-FF58 PET scan (joint acquisition as PET/CT with high resolution CT or joint acquisition as PET/MRI with high resolution MRI) or separately up to 24 hours before or after [68Ga]Ga-FF58 administration. Imaging evaluations were assessed centrally according to the imaging review charter.
Time Frame	Up to 24 hours post-injection of [68Ga]Ga-FF58 on Day 1

Analysis Population Description	Participants who received [68Ga]Ga-FF58.

	All patients
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Number of Participants Analyzed [units: participants]	14
Percentage lesions detected by conventional scans that were also detected by PET scan (units: lesions)	NA[1]

[1] The concordance assessment between [68Ga]Ga-FF58 PET scan results versus conventional CT/MRI imaging results could not be presented since the data from the latter were recorded as free-form text.

Dosimetry sub-group: Area under the concentration-time curve (AUC) of [^{68}Ga]Ga-FF58 based on blood radioactivity data

Description	The [68Ga]-FF58 pharmacokinetic (PK) analysis was planned to be performed based on blood radioactivity concentration data, obtained by measuring, in gamma-counting equipment, the blood samples drawn at pre-defined time-points. AUC was planned to be determined by non-compartmental analysis.
Time Frame	Pre-dose, 0-5, 10 and 30 minutes, and 1, 2, 3-4 and 5 hours post-injection of [68Ga]Ga-FF58
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.

Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Area under the concentration-time curve (AUC) of [68Ga]Ga-FF58 based on blood radioactivity data (units:)	**()**

Dosimetry sub-group: Clearance (CL) of [^{68}Ga]Ga-FF58 based on blood radioactivity data

Description	The [68Ga]-FF58 PK analysis was planned to be performed based on blood radioactivity concentration data, obtained by measuring, in gamma-counting equipment, the blood samples drawn at pre-defined time-points. CL was planned to be determined by non-compartmental analysis.
Time Frame	Pre-dose, 0-5, 10 and 30 minutes, and 1, 2, 3-4 and 5 hours post-injection of [68Ga]Ga-FF58
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Clearance (CL) of [68Ga]Ga-FF58 based on blood radioactivity data (units:)	**()**

Dosimetry sub-group: Volume of distribution (Vz) of [^{68}Ga]Ga-FF58 based on blood radioactivity data

Description	The [68Ga]-FF58 PK analysis was planned to be performed based on blood radioactivity concentration data, obtained by measuring, in gamma-counting equipment, the blood samples drawn at pre-defined time-points. The volume of distribution (Vz) during the terminal elimination phase was planned to be determined by non-compartmental analysis.
Time Frame	Pre-dose, 0-5, 10 and 30 minutes, and 1, 2, 3-4 and 5 hours post-injection of [68Ga]Ga-FF58

Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Volume of distribution (Vz) of [68Ga]Ga-FF58 based on blood radioactivity data (units:)	()

Dosimetry sub-group: Elimination half-life (T1/2) of [^{68}Ga]Ga-FF58 based on blood radioactivity data

Description	The [68Ga]-FF58 PK analysis was planned to be performed based on blood radioactivity concentration data, obtained by measuring, in gamma-counting equipment, the blood samples drawn at pre-defined time-points. The elimination half-life (T1/2) was planned to be determined by non-compartmental analysis.
Time Frame	Pre-dose, 0-5, 10 and 30 minutes, and 1, 2, 3-4 and 5 hours post-injection of [68Ga]Ga-FF58
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0

Dosimetry sub-group: Elimination half-life (T1/2) of [68Ga]Ga-FF58 based on blood radioactivity data (units:)	()

Dosimetry sub-group: Urinary excretion of [^{68}Ga]-GaFF58

Description	The elimination of the compound in urine was planned to be evaluated based on urine radioactivity concentration data obtained by measuring in gamma counting equipment the urine sample obtained at pre-defined time intervals. Urine elimination data was planned to be expressed as a percentage of injected activity (%ID) in each specified time interval and also as cumulative %ID excreted up to the end of each time interval.
Time Frame	0 - 30 minutes, 30 minutes – 2 hours, 2 – 3 hours and 3 -5 hours post-injection of [68Ga]Ga-FF58
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Urinary excretion of [68Ga]-GaFF58 (units:)	()

Dosimetry sub-group: Absorbed radiation dose of [^{68}Ga]-GaFF58

Description	The absorbed dose in target organs was planned to be summarized with descriptive statistics.
Time Frame	[68Ga]-GaFF58 PET imaging acquired at Day 1
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Absorbed radiation dose of [68Ga]-GaFF58 (units:)	**()**

Dosimetry sub-group: Whole body effective dose of [^{68}Ga]-GaFF58

Description	The effective radiation dose was planned to be summarized with descriptive statistics.
Time Frame	[68Ga]-GaFF58 PET imaging acquired at Day 1
Analysis Population Description	Participants from the dosimetry sub-group who received [68Ga]Ga-FF58. No patients were enrolled into the dosimetry sub-group.

	Dosimetry sub-group
Arm/Group Description	Participants were planned to receive [68Ga]-GaFF58. No participants were enrolled into the dosimetry sub-group.
Number of Participants Analyzed [units: participants]	0
Dosimetry sub-group: Whole body effective dose of [68Ga]-GaFF58 (units:)	**()**

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Safety Results

Time Frame	From single dose of [68Ga]Ga-FF58 on Day 1 up to Day 14
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	All patients N = 14
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Total Number Affected	0
Total Number At Risk	14

Serious Adverse Events

Time Frame	From single dose of [68Ga]Ga-FF58 on Day 1 up to Day 14
Source Vocabulary for Table Default	MedDRA (27.0)

Collection Approach for Table Default	Systematic Assessment

No serious adverse events were reported.

Other (Not Including Serious) Adverse Events

Time Frame	From single dose of [68Ga]Ga-FF58 on Day 1 up to Day 14
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 0%

	All patients N = 14
Arm/Group Description	All patients who received a single dose of 3 MBq/kg/injection ±10%, with no less than 150 MBq and no more than 250 MBq/injection of [68Ga]-GaFF58
Total # Affected by any Other Adverse Event	2
Total # at Risk by any Other Adverse Event	14

Gastrointestinal disorders	
Abdominal discomfort	1 (7.14%)
Dyspepsia	1 (7.14%)
General disorders and administration site conditions	
Fatigue	1 (7.14%)
Nervous system disorders	
Amnesia	1 (7.14%)
Hypersomnia	1 (7.14%)
Psychiatric disorders	
Disorientation	1 (7.14%)
Renal and urinary disorders	
Urinary incontinence	1 (7.14%)

Conclusion:

[^{68}Ga]Ga-FF58 was evaluated in adult patients with r/r GBM, BC that had metastasized to the brain, GEA, and PDAC expected to overexpress αvβ3 and αvβ5 integrins. Static PET images were acquired at 30 min, 1 hour, and 2 hours post-injection to characterize [^{68}Ga]Ga-FF58 biodistribution and tumor uptake. The 1-hour post-dose timepoint was reported as the optimal imaging timepoint for both PET-avid brain and PET-avid body lesions in the majority of patients across indications.

[^{68}Ga]Ga-FF58 uptake was observed in the principal normal organs for all patients, and uptake in lesions was observed in 9 of the 13 evaluable patients. SUV values for lesions appeared to be lower than SUV values for normal organs, except for the brain hemispheres.

The intravenous administration of a single dose of [^{68}Ga]Ga-FF58 appears to be safe and no drug-related AEs were observed.

Date of Clinical Trial Report

5-Mar-2025