C30 DISCO: Diagnostic performance of ^{64}Cu-SARTATE compared to ^{68}Ga-DOTATATE in patients with known or suspected neuroendocrine tumors

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Background

- Imaging of somatostatin receptor 2 (SSTR2) expression using positron emission tomography/computed tomography (PET/CT) is now an established modality in the staging of patients with neuroendocrine tumours (NET) and in the selection of patients with gastroenteropancreatic-NET (GEP-NET) for peptide receptor radionuclide therapy[1].
- The use of ^{64}Cu as an imaging isotope may be advantageous over ^{68}Ga due to its longer half-life (12.7 h vs. 1 h) and its ability to be centrally manufactured. ^{64}Cu-SARTATE utilizes a proprietary chelator platform known as the sarcophagine (SAR) cage which tightly secures the isotope, preventing leakage (**Figure 1**).
- The pairing of ^{64}Cu with this SAR platform enables imaging at later timepoints and the potential to identify additional lesions due to increased uptake along with background washout, as compared to current standard of care SSTR2-targeted imaging agents.
- In a previous prospective Phase 1 study with 10 low- or intermediate-grade GEP-NET patients, ^{64}Cu-SARTATE was deemed safe and well tolerated, with high lesion uptake at 30 min, 1 h, 4 h and 24 h timepoints post-administration [2].
- DISCO was a prospective, multi-center, Phase II, single arm, non-randomized, blinded-data review study of ^{64}Cu-SARTATE in participants with known or suspected GEP–NETs. The primary objective of this study was to compare the diagnostic performance of ^{64}Cu-SARTATE PET/CT scans conducted at approximately 4 h and 20 h post-injection to the conventional ^{68}Ga-DOTATATE PET/CT on a per lesion basis.

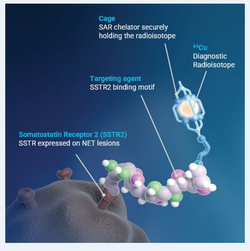


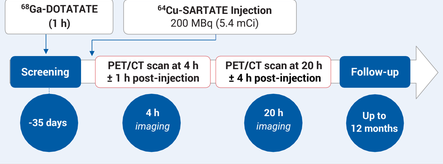
Figure 1. **^{64}Cu-SARTATE stylized structure**

Methods

Study Design

Key Eligibility Criteria

- Known diagnosis of GEP-NET or suspicion of GEP-NET based on axial imaging (CT and/or MRI and/or FDG) and/or biochemical evidence of NET
- Pre-study ^{68}Ga-DOTATATE PET/CT scan performed within 5 weeks of ^{64}Cu-SARTATE administration



Primary Objective	Key Primary Endpoint
To compare the diagnostic performance of ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE on a lesion basis	Sensitivity and specificity on the 4 h and 20 h ^{64}Cu-SARTATE PET/CT (SARTATE) compared to ^{68}Ga-DOTATATE (DOTATATE) PET/CT on a per-lesion basis for discordant findings per reader.
Key Secondary Objective	**Secondary Endpoints**
To investigate the safety and tolerability of ^{64}Cu-SARTATE	Report adverse clinical, biochemical or hematological events following ^{64}Cu-SARTATE administration.

PET assessment, discordant lesions & Standard of Truth (SOT). The SARTATE and DOTATATE PET/CT scans were interpreted by 2 independent, blinded, central readers. **Discordant lesions** were identified as those seen only on one of the comparative scans in the pair (either SARTATE or DOTATATE). These **discordant findings** were assessed against a composite SOT, which included histopathology and/or anatomical and/or functional imaging modalities (e.g. CT, MRI, bone scintigraphy, ^{18}F-FDG PET, ultrasound or follow-up ^{68}Ga-DOTATATE PET/CT), by an independent assessor. The final lesion status as True Positive (TP) or False Positive (FP) was determined based on the SOT results (positive or negative, respectively). Discordant lesion not verified as either positive or negative by SOT after the completion of the 12-month follow-up period were considered unverified and excluded from the analysis.

The rate of **False Negative (FN) and True Negative (TN) lesions** was then determined as follows:
- *1x TP discordant lesion on one scan = 1x FN lesion for the comparative scan*
- *1x FP discordant lesion on one scan = 1x TN lesion for the comparative scan*

Sensitivity and specificity were determined as follows:
- *Sensitivity for discordant lesions = (TP/(TP+FN))*
- *Specificity for discordant lesions = (TN/(TN+FP))*

Results

Participant flow and baseline disease characteristics

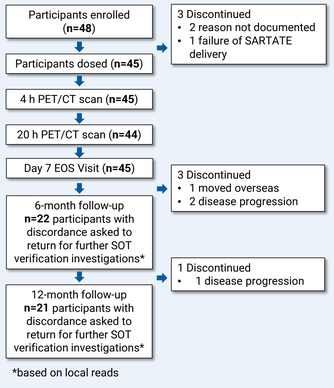


Figure 2. **Participant flow**

	All Participants (N=45)
Status of Tumor	
Known NETs	41 (91.1%)
Suspected NETs	4 (8.9%)
Tumor Type	
Functional	15 (33.3%)
Non-functional	26 (57.8%)
M Staging	
M0	14 (31.1%)
M1	27 (60.0%)
Tumor Stage	
Stage I	3 (6.7%)
Stage II	5 (11.1%)
Stage III	5 (11.1%)
Stage IV	27 (60.0%)
Tumor Grade	
G1	21 (46.7%)
G2	16 (35.6%)
G3	4 (8.9%)
Chromogranin A Level	
Normal	19 (42.2%)
High	26 (57.8%)

Table 1. **Participant Baseline Disease Characteristics**

^{64}Cu-SARTATE identified more lesions vs. ^{68}Ga-DOTATATE

4 h ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE (n=45)	Reader A		Reader B	
	4 h ^{64}Cu	^{68}Ga	4 h ^{64}Cu	^{68}Ga
Lesions detected	488	264	393	191
Discordant lesions	**237**	**14**	**215**	**15**
# Subjects with discordance*	**30**		**37**	

20 h ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE (n=44)	Reader A		Reader B	
	20 h ^{64}Cu	^{68}Ga	20 h ^{64}Cu	^{68}Ga
Lesions detected	488	265	393	186
Discordant lesions	**230**	**9**	**209**	**24**
# Subjects with discordance	**36**		**32**	

Table 2. **Summary of findings pertaining to lesion detection and determination of discordant lesions prior to SOT verification.** The number of lesions detected by ^{64}Cu-SARTATE was ~2x that detected by ^{68}Ga-DOTATATE. 209-237 lesions (range across readers) identified by ^{64}Cu-SARTATE were not observed with ^{68}Ga-DOTATATE, whereas only 9-24 lesions identified by ^{68}Ga-DOTATATE were not observed with ^{64}Cu-SARTATE.

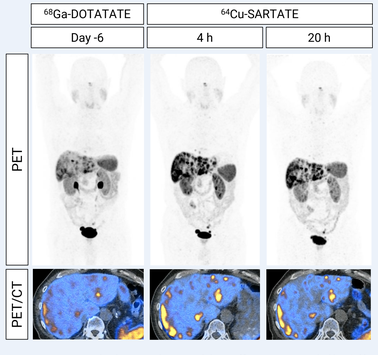


Figure 3. **Representative images of one participant.** ^{68}Ga-DOTATATE (left), 4 h ^{64}Cu-SARTATE (middle) and 20 h ^{64}Cu-SARTATE (right) images from PET scans (top row) and corresponding PET/CT fusion (bottom row). **Top row:** PET images show lesions detected by both tracers with more lesions identified by ^{64}Cu-SARTATE at both timepoints vs. ^{68}Ga-DOTATATE scan captured 6 days before 4 h ^{64}Cu-SARTATE. Images are shown as maximum intensity projections. **Bottom row:** Axial sections from PET/CT demonstrate higher liver lesion uptake with ^{64}Cu-SARTATE at both timepoints vs. ^{68}Ga-DOTATATE. Fused images are shown with consistent scaling for visual comparison.

^{64}Cu-SARTATE is more sensitive than ^{68}Ga-DOTATATE in detecting NET lesions

4 h ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE	Reader A (n=30)		Reader B (n=37)	
	4 h ^{64}Cu	**^{68}Ga**	**4 h ^{64}Cu**	**^{68}Ga**
Discordant lesions with SOT	132	8	104	7
Discordant lesions positive by SOT	130	6	103	6
Discordant lesions negative by SOT	2	2	1	1
Discordant lesions with no SOT	105	6	111	8
Sensitivity (%), 2-sided 95% CI	95.6 (88.9,98.3)	4.4 (1.7, 11.1)	94.5 (80.1,98.6)	5.5 (1.4, 19.9)
Specificity (%), 2-sided 95% CI	50 (3.1,96.9)	50 (3.1, 96.9)	NA*	NA*
P-value	<.001		<.001	

20 h ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE	Reader A (n=36)		Reader B (n=32)	
	20 h ^{64}Cu	**^{68}Ga**	**20 h ^{64}Cu**	**^{68}Ga**
Discordant lesions with SOT	120	6	100	10
Discordant lesions positive by SOT	117	6	99	7
Discordant lesions negative by SOT	3	0	1	3
Discordant lesions with no SOT	110	3	109	14
Sensitivity (%), 2-sided 95% CI	95.1 (65.1, 99.5)	4.9 (0.5, 34.9)	93.4 (81.4,97.9)	6.6 (2.1, 18.6)
Specificity (%), 2-sided 95% CI	NA*	NA*	75.0 (4.7, 99.5)	25.0 (0.5, 95.3)
P-value	<.001		<.001	

Table 3. **Sensitivity and specificity of discordant lesions for ^{64}Cu-SARTATE vs. ^{68}Ga-DOTATATE PET/CT per central reader at the 2 time points.** Sensitivity of ^{64}Cu-SARTATE = 1 – sensitivity of ^{68}Ga-DOTATATE; Specificity of ^{64}Cu-SARTATE = 1 – specificity of ^{68}Ga-DOTATATE. p-value is for the test of null hypothesis that sensitivity of ^{64}Cu-SARTATE equals 0.5. The cluster sampling method was used to calculate the corresponding variances and 95% CI between the ^{64}Cu-SARTATE and the ^{68}Ga-DOTATATE scans on a per-lesion basis per reader.
Of all the discordant lesions identified by ^{64}Cu-SARTATE as per Table 2, 99-130 lesions were verified as TP by SOT (across both timepoints and readers). The data show that ~95% of all TP discordant lesions were identified by ^{64}Cu-SARTATE. The numbers of TN and FP were very low amongst the discordant lesions. *Due to the very low number of discordant lesions deemed FP, per-lesion specificity could not be reliably estimated. SOT (Standard of Truth).

^{64}Cu-SARTATE was safe and well-tolerated

All Participants (N=45)	Participants (%)	Events	Severity	Duration
Participants with at least one **related** TEAE	7 (15.6%)	9		
Abnormal feces	1 (2.2%)	1	Mild	2 Days
Diarrhea	3 (6.7%)	3	All Mild	2 x 1 Day 1 x 15 Days
Feces discolored	1 (2.2%)	1	Mild	7 Days
Nausea	2 (4.4%)	2	All Mild	1 x 1 Day 1 x 3 Days
Chest discomfort	1 (2.2%)	1	Mild	1 Day
Rash	1 (2.2%)	1	Moderate	4 Days
Participants with at least one SAE	0 (0.0%)	0		
Participants with at least one TEAE leading to study discontinuation	0 (0.0%)	0		

Table 4. **Summary of related TEAEs.** 9 related TEAEs were observed in 7 participants with majority of these events being Grade 1 and resolving within a few days. No serious adverse events or TEAEs leading to study discontinuation were reported.

Conclusions

^{64}Cu-SARTATE was deemed safe and well-tolerated. In participants with known or suspected GEP-NETs, lesion detection by ^{64}Cu-SARTATE outperformed that of ^{68}Ga-DOTATATE. The improved diagnostic performance of ^{64}Cu-SARTATE has important clinical implications for the identification of GEP-NET lesions to inform different treatment pathways. A phase III study of ^{64}Cu-SARTATE in NETs is being planned to build on these results.

Corresponding author: Eva Lengyelova (Eva.Lengyelova@claritypharmaceuticals.com); ClinicalTrials.gov Identifier NCT04438304. This study is sponsored by Clarity Pharmaceuticals Ltd. **References**: 1. NCCN Guidelines (Neuroendocrine and Adrenal tumors) Version 2.2025; 2. Hicks RJ et al., J Nucl Med. 2019 Jun