ASX ANNOUNCEMENT

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DISCO topline results: ^{64}Cu-SARTATE is highly effective in detecting tumours in NET patients compared to SOC imaging. Phase III planning underway.

HIGHLIGHTS

- Topline data from Clarity's diagnostic Phase II trial, DISCO, confirms that ^{64}Cu-SARTATE is safe and highly effective compared to standard-of-care (SOC) imaging at detecting lesions in patients with neuroendocrine tumours (NETs).
- DISCO compared the diagnostic performance of ^{64}Cu-SARTATE at an average of 4 hours (between 3 to 5 hours) and 20 hours post-administration (same-day and next-day imaging, respectively) to ^{68}Ga-DOTATATE.
- ^{64}Cu-SARTATE lesion detection substantially outperformed that of ^{68}Ga-DOTATATE. ^{64}Cu-SARTATE detected 393 to 488 lesions, and ^{68}Ga-DOTATATE identified 186 to 265 lesions among 45 study participants across the readers.
- Out of all the lesions identified by the readers, 230-251 were deemed to be discordant (i.e. only present on one of the scans, ^{68}Ga-DOTATATE or ^{64}Cu-SARTATE positron emission tomography [PET] / computed tomography [CT]). Of these lesions, 93.5% (average across readers) were only detected on the ^{64}Cu-SARTATE PET/CT scans. The number of discordant lesions detected by ^{64}Cu-SARTATE on the same-day and next-day scans was comparable.
- Approximately half of all the discordant lesions had an available standard-of-truth (SOT), such as histopathology or conventional imaging. The identified discordant lesions yielded a lesion-level sensitivity of 93.4% to 95.6% (95% confidence interval [CI]: 65.1, 99.5) for ^{64}Cu-SARTATE (across both timepoints) and only 4.4% to 6.6% (95%CI: 0.5, 34.9) for ^{68}Ga-DOTATATE across both readers.
- ^{64}Cu-SARTATE was deemed safe and well tolerated. Only 7 (15.6%) participants experienced ^{64}Cu-SARTATE-related adverse events (AEs). No serious treatment-emergent AEs were observed in the study.
- Based on the exciting preliminary results of the DISCO trial, Clarity will commence next steps to conduct a registrational Phase III study of ^{64}Cu-SARTATE in NETs with the US Food and Drug Administration's (FDA) guidance.

Clarity Pharmaceuticals (ASX: CU6) ("Clarity" or "Company"), a clinical-stage radiopharmaceutical company with a mission to develop next-generation products that improve treatment outcomes for patients with cancer, is pleased to announce positive results from the diagnostic Phase II DISCO trial (NCT04438304)[1] with ^{64}Cu-SARTATE in patients with known or suspected NETs.

DISCO trial design

DISCO is a "**D**iagnostic **I**maging **S**tudy of ^{64}**CO**pper-SARTATE Using PET on Patients with Known or Suspected Neuroendocrine Tumours". It assessed the performance of Clarity's SARTATE imaging product as a potential new method to diagnose and manage NETs. The trial aimed to build on earlier clinical experience with ^{64}Cu-SARTATE in patients with NETs, which demonstrated that the diagnostic has excellent imaging characteristics and suggested that ^{64}Cu-SARTATE PET/CT provides comparable or superior lesion detection to ^{68}Ga-DOTATATE PET/CT in all patients, especially in the liver[2].

DISCO recruited participants with Gastroenteropancreatic NETs (GEP-NETs) across 4 sites in Australia, comparing the diagnostic performance of ^{64}Cu-SARTATE PET at an average of 4 hours (between 3 and 5 hours) and approximately 20 hours post-administration (same-day and next-day imaging, respectively) to the current SOC, ^{68}Ga-DOTATATE PET. Participants were required to have undergone a pre-study ^{68}Ga-DOTATATE PET/CT scan within 5 weeks, but not closer than 6 hours prior to the administration of ^{64}Cu-SARTATE as part of their routine clinical care.

The trial was initially designed to enrol up to 63 patients, based on the anticipated lesion-level discordance rate between ^{64}Cu-SARTATE and ^{68}Ga-DOTATATE PET. Following a pre-planned early analysis of the data collected during the study, the sample size was adjusted to 45 patients, allowing for an earlier enrolment completion.

Study participants were dosed with 200 MBq of ^{64}Cu-SARTATE. Both the ^{64}Cu-SARTATE and ^{68}Ga-DOTATATE PET/CT scans were reviewed by 2 blinded central readers. Participants were followed for up to 12 months to complete additional investigations (e.g. biopsy and conventional imaging) and obtain the SOT used to verify discordant findings between the scan pairs. The verification of discordant findings against the SOT evidence (as true- or false-positive findings) was completed by an independent central assessor, distinct from the central readers evaluating the ^{64}Cu-SARTATE and ^{68}Ga-DOTATATE scans. Lesion-level sensitivity was calculated for the discordant lesions between the scan pairs, with each true-positive discordant lesion on one scan considered a false-negative lesion on the other scan, and each false-positive discordant lesion on one scan considered a true-negative lesion on the other scan.

Topline results

The results indicate that lesion detection by ^{64}Cu-SARTATE (regardless of imaging timepoint) substantially outperformed that of ^{68}Ga-DOTATATE. ^{64}Cu-SARTATE detected 393 to 488 lesions, and ^{68}Ga-DOTATATE identified 186 to 265 lesions among 45 participants across the readers (**Figure 1**).

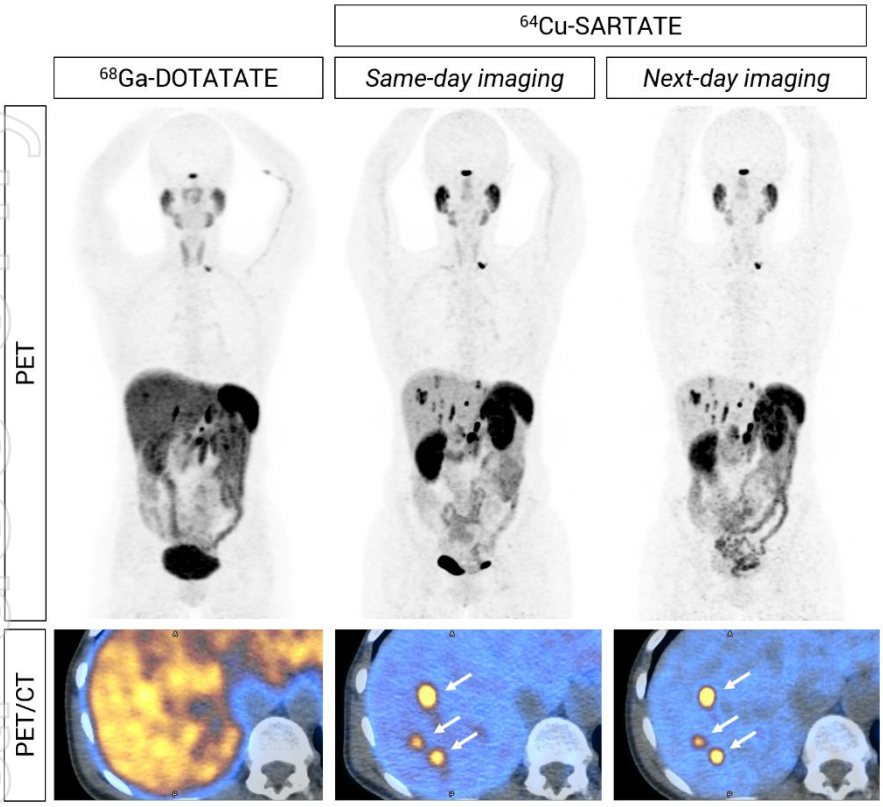

Figure 1: 59-year-old participant with functional NETs. ^{68}Ga-DOTATATE PET/CT was performed 26 days prior to the ^{64}Cu-SARTATE PET/CT (same-day imaging). **PET (top images):** top left image shows higher background on the ^{68}Ga-DOTATATE PET. Top centre and right PET images show multiple lesions detected by ^{64}Cu-SARTATE against a low background. Images are shown as maximum intensity projections. **PET/CT fusion (bottom images):** axial sections show intense liver uptake on the ^{68}Ga-DOTATATE PET/CT (bottom left), which limits the ability to distinguish lesions from the background, and 3 clearly defined lesions are visible on the ^{64}Cu-SARTATE PET/CT (arrows; bottom centre and right images, same-day and next-day imaging, respectively). Mean maximum standardised uptake value (SUVmax) of lesions shown in the ^{64}Cu-SARTATE PET/CT images: 16.1 and 16.5 on same-day and next-day imaging, respectively. Lesions in the liver have been verified as true-positive based on other scans, including diagnostic CT and magnetic resonance imaging (MRI). Fused images are shown with consistent scaling for visual comparison.

Out of all lesions identified by the readers, 230-251 were deemed to be discordant between ^{64}Cu-SARTATE and ^{68}Ga-DOTATATE PET/CT, with 93.5% (average across readers and imaging days) of these discordant lesions detected on the ^{64}Cu-SARTATE scans only. A previously completed Phase I study demonstrated a 1.7 fold increase (median of 6.70 vs. 3.92, p=0.002) in contrast (i.e. lesion-to-background ratio) for ^{64}Cu-SARTATE PET/CT performed at 4 hours post-administration compared to ^{68}Ga-DOTATATE PET/CT[2]. This improvement in contrast may explain the detection of additional lesions observed in the DISCO trial. The average SUVmax, representing the highest concentration of ^{64}Cu-SARTATE uptake in lesions, was notably high, ranging from 37.42 to 43.90 across both imaging days in the DISCO trial.

Approximately half of all discordant lesions had an available SOT, which yielded a lesion-level sensitivity of 93.4% to 95.6% (95%CI: 65.1, 99.5) for ^{64}Cu-SARTATE, including both timepoints, and only 4.4% to 6.6% (95%CI: 0.5, 34.9) for ^{68}Ga-DOTATATE.

^{64}Cu-SARTATE was deemed safe and well tolerated. Only 7 (15.6%) trial participants experienced ^{64}Cu-SARTATE-related AEs, the majority of which were mild (Grade 1) gastrointestinal events, commonly observed in NET patients, and typically resolved within 2 days of onset. No serious treatment-emergent AEs were observed in the study.

Based on the findings of the DISCO trial to date, Clarity will commence the next steps to conduct a registrational Phase III study of ^{64}Cu-SARTATE in NETs with the US FDA's guidance.

Clarity's Executive Chairperson, Dr Alan Taylor, commented, "We are very excited about the initial topline data from the DISCO trial as ^{64}Cu-SARTATE was confirmed to be safe and very effective in detecting NET lesions in patients with known or suspected disease. The DISCO trial demonstrates a significant advantage of our diagnostic over ^{68}Ga-DOTATATE. ^{64}Cu-SARTATE detected almost double the number of lesions compared to the SOC, and, where SOT was available, a very high lesion-level sensitivity of 93.4% - 95.6% in comparison to just 4.4% - 6.6% for ^{68}Ga-DOTATATE for these discordant findings. In addition to identifying more lesions with our product, lesions detected by ^{64}Cu-SARTATE also exhibited high uptake with low background on the PET scans, making it easier to identify those lesions by readers. Excellent lesion visualisation was also supported by substantial clearance from the liver. The favourable biodistribution of ^{64}Cu-SARTATE PET enabled high-contrast diagnostic imaging for up to approximately 24 hours post-injection (**Figure 1**), offering greater flexibility in the scheduling of PET/CT scans.

"In the DISCO trial, we continue to observe the substantial limitations of the current-generation of short half-life isotope products, what we call isotope-centric medicine. This is clearly illustrated by ^{68}Ga-DOTATATE with imaging timepoints solely dictated by the very short isotope half-life (approximately 1 hour for gallium-68) as opposed to good science and medicine. In contrast, ^{64}Cu-SARTATE highlights the extraordinary benefits of next-generation patient-centric medicine, where imaging is guided by the optimal timepoint to scan and detect lesions, focusing on the needs of the patients and their treating professionals.

"We believe that the flexibility of imaging with ^{64}Cu-SARTATE, in comparison to approximately 1 hour with ^{68}Ga-DOTATATE, plays an important role in the detection benefits seen in the DISCO study. We have known this for many years and have demonstrated these advantages of optimal timepoint imaging with different products in our Targeted Copper Theranostic (TCT) platform, including SARTATE. We have seen first-hand in a number of clinical trials that once radiopharmaceutical products are administered, they take time to find the lesion whilst also needing to clear from non-target organs, providing greater contrast. This is known as signal-to-noise ratio or, in our case, tumour-to-background ratio. Having greater contrast is especially important to identify smaller or more difficult to find cancers.

"The longer half-life of copper-64, combined with Clarity's proprietary SAR Technology, sets up a strong foundation for next-generation diagnostics, which could be unmatched in the radiopharmaceutical sector. In addition to clinical benefits, the opportunity for high-volume centralised manufacturing and broad, on-demand distribution of ready-to-use diagnostics translates into flexibility and reliability for patients and their treating staff, meaning that every patient with access to PET imaging, including those in underserved and broad geographic areas, may access improved cancer diagnostics.

"Patients with NETs are often misdiagnosed and experience delays in receiving the correct diagnosis, which may lead to disease progression and identification of their cancer at later stages. Visualising NET lesions earlier and more accurately may have a significant impact on patient outcomes as it equips clinicians with crucial information on disease burden, helping to determine an optimal treatment plan. As such, the SSTR2 imaging market is an important focus for Clarity. We estimate the NET diagnostic market in the US alone to be around 100,000 scans per year, growing to approximately 120,000 scans per year by 2029.

"Importantly, the positive results of the DISCO trial open broader opportunities for the development of ^{64}Cu-SARTATE in additional SSTR2-expressing malignancies beyond NETs, such as certain types of breast and lung

cancers, where unmet clinical needs remain high. We believe the SSTR2 market is set to grow substantially with a number of therapies in development for this target, which include large indications such as breast and lung cancers. Subject to the successful completion of these studies, we believe that the imaging market for ^{64}Cu-SARTATE could be as large, if not larger, than the very lucrative prostate cancer imaging market where radiopharmaceuticals currently dominate the diagnostic paradigm.

"We look forward to sharing additional data readouts from the trial and presenting the results at future international medical conferences. We plan to rapidly progress discussions with the FDA to initiate a diagnostic registrational Phase III study, as a first key step in expanding SARTATE into the theranostic field of NETs, as well as other SSTR2-expressing cancers, with the copper-64/copper-67 pair. If the findings from the DISCO trial are substantiated in a registrational Phase III study and lead to regulatory approval by the US FDA, ^{64}Cu-SARTATE may play an important role in improving diagnostic accuracy, lesion detection and staging of patients with NETs. These factors could improve clinical decision-making and treatment outcomes, potentially positioning ^{64}Cu-SARTATE as a best-in-class agent for the diagnosis of NETs."

About SARTATE

SARTATE is a next generation, highly targeted theranostic radiopharmaceutical. It is being developed for diagnosing, staging and subsequently treating cancers that express SSTR2, such as NETs. Like all Clarity products, the SARTATE product can be used with copper-64 (^{64}Cu) for imaging (^{64}Cu-SARTATE) or copper-67 (^{67}Cu) for therapy (^{67}Cu-SARTATE).

Disclaimer

^{64}Cu-SARTATE is an unregistered product. The safety and efficacy of ^{64}Cu-SARTATE has not been assessed by health authorities such as the US FDA or the Therapeutic Goods Administration (TGA). There is no guarantee that this product will become commercially available.

About NETs

NETs, also known as well-differentiated neuroendocrine neoplasms or carcinoids, represent a heterogeneous group of malignant transformations of cells of the diffuse neuroendocrine system[3]. They most commonly occur in the gastrointestinal tract (48%), lung (25%), and pancreas (9%), but may also originate in other areas, including the breast, prostate, thymus and skin[4]. NETs can either be benign or malignant, as well as non-functional and functional[5]. NETs traditionally have been considered uncommon; however, the incidence has been increasing as a worldwide phenomenon[6].

Overall, it is estimated that more than 20,000 people in the United States are diagnosed with a NET each year[7], and approximately 190,000 people are living with this diagnosis[8]. Patients with NETs present with subtle clinical symptoms, which can lead to a delay in diagnosis of more than 4 years[9]. As such, about 30-75% of NET patients have distant metastases at the time of diagnosis[10]. A 10-year relative survival rate for patients with metastatic GEP-NETs is 3–36%[11].

About Clarity Pharmaceuticals

Clarity is a clinical stage radiopharmaceutical company focused on the treatment of serious diseases. The Company is a leader in innovative radiopharmaceuticals, developing Targeted Copper Theranostics based on its SAR Technology Platform for the treatment of cancers.

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This announcement has been authorised for release by the Executive Chairperson.