ASX MEDIA RELEASE

29 November 2023

Clarity's theranostic prostate cancer trial progresses at the highest dose level cohort

HIGHLIGHTS

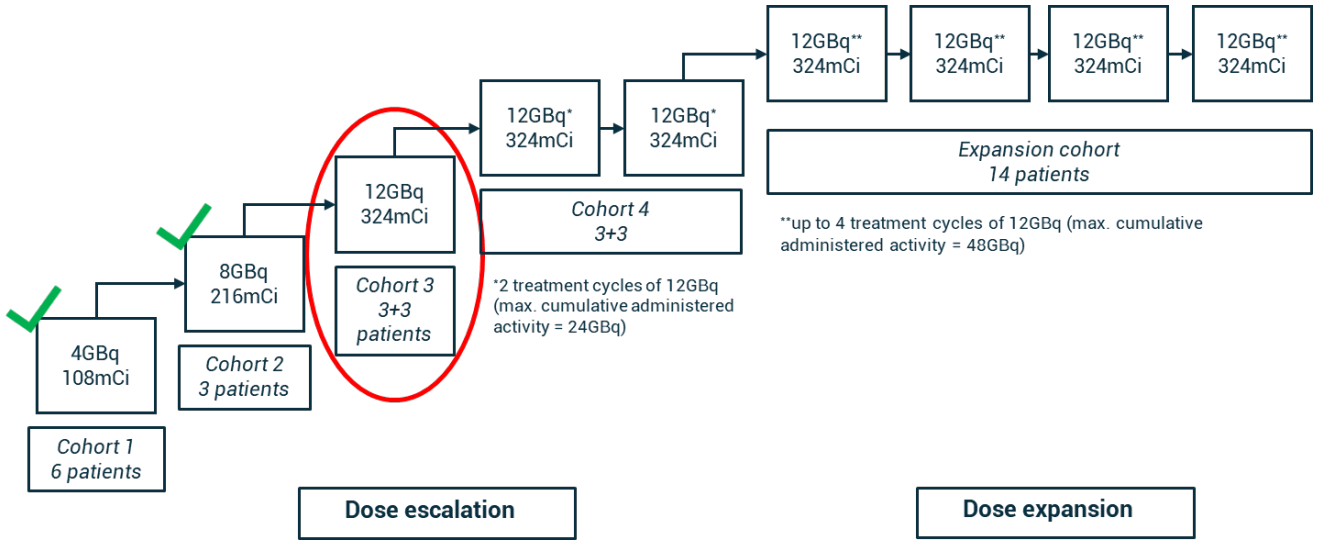
- Cohort 3 of the theranostic SECuRE trial investigating ^{64}Cu/^{67}Cu-SAR-bisPSMA in metastatic castrate-resistant prostate cancer (mCRPC) has enrolled and treated 3 participants who received therapy with ^{67}Cu-SAR-bisPSMA at the highest dose level of 12GBq.
- No dose limiting toxicities (DLTs) have been reported to date. Only one participant had one adverse event of Grade 1 reduction in neutrophil count and the participant fully recovered.
- The Safety Review Committee (SRC) has recommended that the trial continues with the additional 3 participants as planned in cohort 3.
- All 3 participants had been heavily pre-treated and failed a number of commercial and investigational therapies prior to treatment in the trial. Despite this, 2 of the 3 participants so far have shown a reduction in Prostate Specific Antigen (PSA) levels within weeks after a single cycle of 12GBq ^{67}Cu-SAR-bisPSMA.
- Recruitment has opened at clinical sites in the US for the additional 3 participants in cohort 3 for a single cycle of 12GBq of ^{67}Cu-SAR-bisPSMA.

Clarity Pharmaceuticals (ASX: CU6) ("Clarity"), a clinical stage radiopharmaceutical company with a mission to develop next-generation products that improve treatment outcomes for children and adults with cancer, is pleased to announce the successful completion of the first stage of cohort 3 of the Phase I/IIa theranostic trial, SECuRE, evaluating ^{64}Cu/^{67}Cu-SAR-bisPSMA in patients with mCRPC where 3 participants have been treated at the highest dose level of 12GBq of ^{67}Cu-SAR-bisPSMA. No adverse events were reported in relation to ^{64}Cu-SAR-bisPSMA. Only 1 adverse event was reported and related to the 12GBq cycle of ^{67}Cu-SAR-bisPSMA in 1 of the 3 participants, which was a grade 1 decrease in neutrophil count, and the patient has fully recovered. No ongoing adverse events and no DLTs have been reported and the SRC has recommended the trial progresses with the 3 additional participants as planned in cohort 3.

The SECuRE trial (NCT04868604)[1] is a Phase I/IIa theranostic trial for identification and treatment of Prostate-Specific Membrane Antigen (PSMA) expressing mCRPC using ^{64}Cu/^{67}Cu-SAR-bisPSMA. ^{64}Cu-SAR-bisPSMA is used to visualise PSMA expressing lesions and select candidates for subsequent ^{67}Cu-SAR-bisPSMA therapy. The trial is a multi-centre, single arm, dose escalation trial with a cohort expansion involving up to 44 patients in the US. The aim of the trial is to determine the safety and efficacy of ^{67}Cu-SAR-bisPSMA for the treatment of prostate cancer.

Cohort 3 of the trial has a 3+3 study design with the intent to gather and analyse data from the first 3 participants before progressing with an additional 3 participants. The initial data is very encouraging with no DLTs observed at the highest dose of ^{67}Cu-SAR-bisPSMA (12GBq) and the SRC, responsible for assessing safety of participants and overseeing the general progress of the trial, has assessed the data and recommended the trial continues.

SECuRE trial design



Cohort 3 is the last to assess single doses of ^{67}Cu-SAR-bisPSMA and will be followed by a multi-dose cohort, pending safety evaluation. The initial 3 participants in cohort 3 were heavily pre-treated prior to entering the trial, having received multiple lines of therapy including other investigational products, radioligand therapy and chemotherapy. They continue to be monitored by their physicians for safety and treatment response as per the trial protocol. All 3 participants in cohort 3 remain on the trial following their recent administration of 12GBq of ^{67}Cu-SAR-bisPSMA, with 2 demonstrating a PSA reduction within weeks of dosing, one of which is greater than 90% reduction and the second approximately 40% reduction to date.

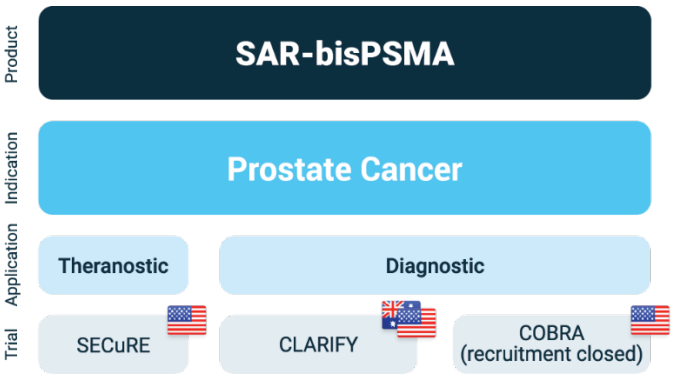
Clarity's Executive Chairperson, Dr Alan Taylor, commented, "We are excited by the PSA declines seen in almost all patients to date in cohorts 2 and 3 from just a single cycle. This result is also seen in patients that have been heavily pre-treated and have failed many other therapies that are either commercial or investigational. Moreover, the safety profile is very favorable and there have been no DLTs reported to date.

"SAR-bisPSMA was designed to be a best-in-class PSMA product as, unlike all other PSMA products in the market, it has dual targeting. The product was optimised to address the challenges of low uptake and retention in lesions that the first generation of PSMA products suffer from, and in both pre-clinical and clinical development to date we have observed two to three times the uptake of SAR-bisPSMA in lesions, followed by retention in lesions out to at least 96 hours. So far, the higher uptake and retention of product, coupled with the advantageous properties of copper-67, has shown quite impressive responses measured by PSA reductions in patients from single cycles of product to date.

"A number of patients from the SECuRE trial have either received, or will soon receive, additional doses of ^{67}Cu-SAR-bisPSMA under the US Food and Drug Administration's (FDA) Expanded Access Program (EAP). This demonstrates the initial clinical benefit observed in such patients after the administration of a single cycle of the product during the trial.

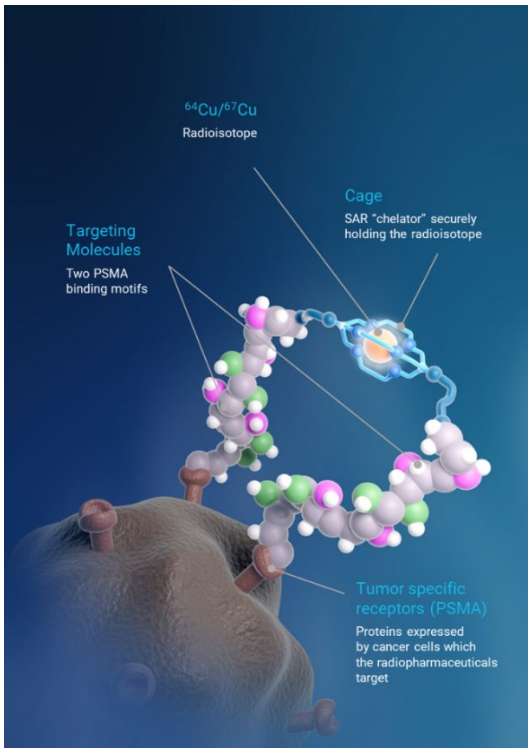
"As we have seen PSA reductions in the majority of patients after a single cycle of ^{67}Cu-SAR-bisPSMA across all dose levels, which is known to be an independent prognostic indicator of improved overall survival following radio-ligand therapy[2,3], we hope to achieve long-term and durable responses once we progress to the multi-dose cohorts of the trial. Furthermore, with commercial quantities of the ^{67}Cu radioisotope now being routinely produced domestically in the US, we see a clear path to commercialisation as we can resolve the supply and manufacturing issues which have plagued the commercial launch of first-generation products. We look forward to sharing more data along with any further updates from patients who may receive single or multiple cycles of ^{67}Cu-SAR-bisPSMA in our programs and bringing this product to the greater prostate cancer patient population," **said Dr Taylor.**

Overview of Clarity's SAR-bisPSMA clinical program



About SAR-bisPSMA

SAR-bisPSMA derives its name from the word "bis", which reflects a novel approach of connecting two PSMA-targeting agents to Clarity's proprietary sarcophagine (SAR) technology that securely holds copper isotopes inside a cage-like structure, called a chelator. Unlike other commercially available chelators, the SAR technology prevents copper leakage into the body. SAR-bisPSMA is a TCT that can be used with isotopes of copper-64 (Cu-64 or ^{64}Cu) for imaging and copper-67 (Cu-67 or ^{67}Cu) for therapy.



^{64}Cu-SAR-bisPSMA and ^{67}Cu-SAR-bisPSMA are unregistered products. Individual results may not represent the overall safety and efficacy of the products. The data outlined in this announcement has not been assessed by health authorities such as the US Food and Drug Administration (FDA). A clinical development program is currently underway to assess the efficacy and safety of these products. There is no guarantee that these products will become commercially available.

About Prostate Cancer

Prostate cancer is the second most common cancer diagnosed in men globally and the fifth leading cause of cancer death worldwide[4]. The American Cancer Institute estimates in 2023 there will be 288,300 new cases of prostate cancer in the US and around 34,700 deaths from the disease[5].

About Clarity Pharmaceuticals

Clarity is a clinical stage radiopharmaceutical company focused on the treatment of serious disease. The Company is a leader in innovative radiopharmaceuticals, developing targeted copper theranostics based on its SAR Technology Platform for the treatment of cancer in children and adults.

www.claritypharmaceuticals.com

References

1. ClinicalTrials.gov Identifier: NCT04868604, https://clinicaltrials.gov/ct2/show/NCT04868604
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4. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries, https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21660
5. American Cancer Society: Key Statistics for Prostate Cancer, https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html

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