SECuRE: A dose escalation/expansion study to assess the anti-tumor efficacy of ^{67}Cu-SAR-bisPSMA in patients with metastatic castrate-resistant prostate cancer

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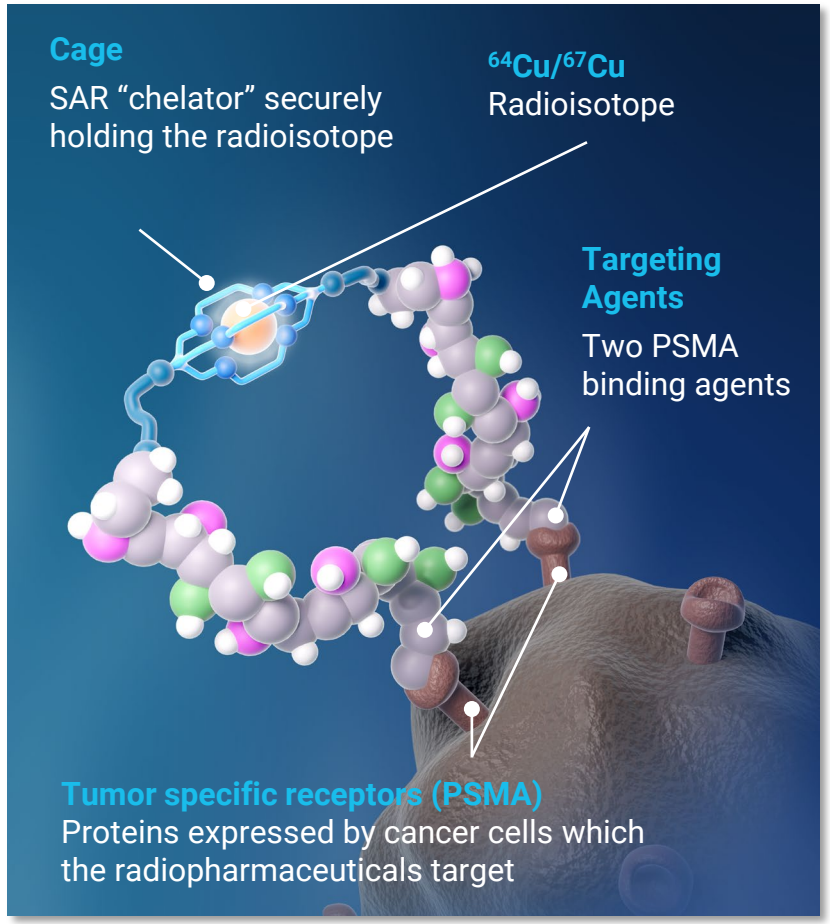
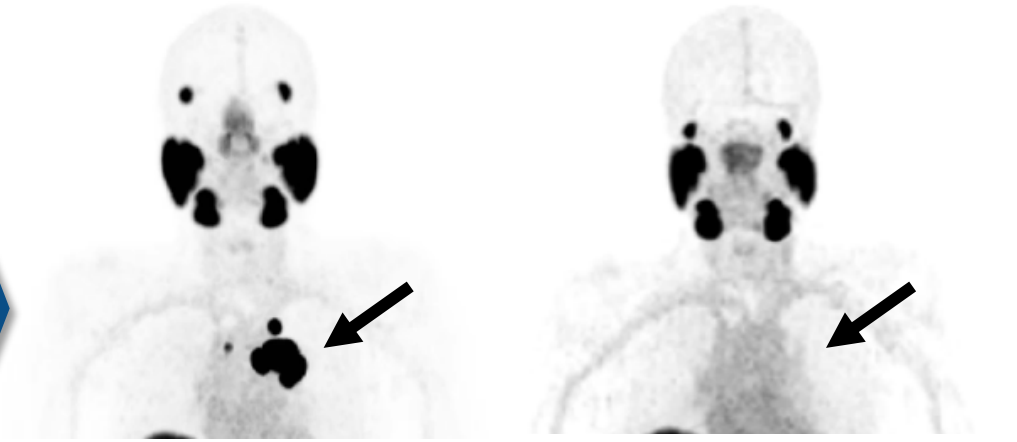
Background: characteristics of SAR-bisPSMA may offer advantages compared to single-target PSMA agents



- **2-3x higher tumour uptake with bisPSMA[1]**

Complete response with ^{67}Cu-SAR-bisPSMA (2 cycles of 8 GBq, multi-dose under EAP)[2]



Screening	Post-treatment

^{64}Cu-SAR-bisPSMA PET - MIP

- Complete anatomical response (CT; RECIST)
- Complete molecular response (PET)
- Undetectable PSA (47.2 ng/mL at baseline)

Case report, images on the right. 74-year-old male with Gleason 9 (5+4) metastatic castrate-resistant prostate cancer (diagnosed in 2017). Previous treatments included androgen deprivation therapy, Taxotere, abiraterone, enzalutamide and a clinical trial with a PARP inhibitor. Images show reduction in lesion uptake of ^{64}Cu-SAR-bisPSMA after two doses of ^{67}Cu-SAR-bisPSMA (no uptake in last follow-up). Local RECIST v1.1 assessment: complete response. No adverse events were reported as related to ^{64}Cu-SAR-bisPSMA. Adverse events related to ^{67}Cu-SAR-bisPSMA included dry mouth, altered taste and thrombocytopenia (all Grade 1, improved), fatigue (Grade 2, resolved), anaemia (Grade 3, improved to Grade 2). EAP: Expanded Access Program. PSA limit of detection: 0.05 ng/mL. Images shown: maximum intensity projection. **References**: 1. Lengyelova & Emmett et al. ASCO. 2023. 2. Nordquist. 35th Annual International Prostate Cancer Update. 2024. Data on file.

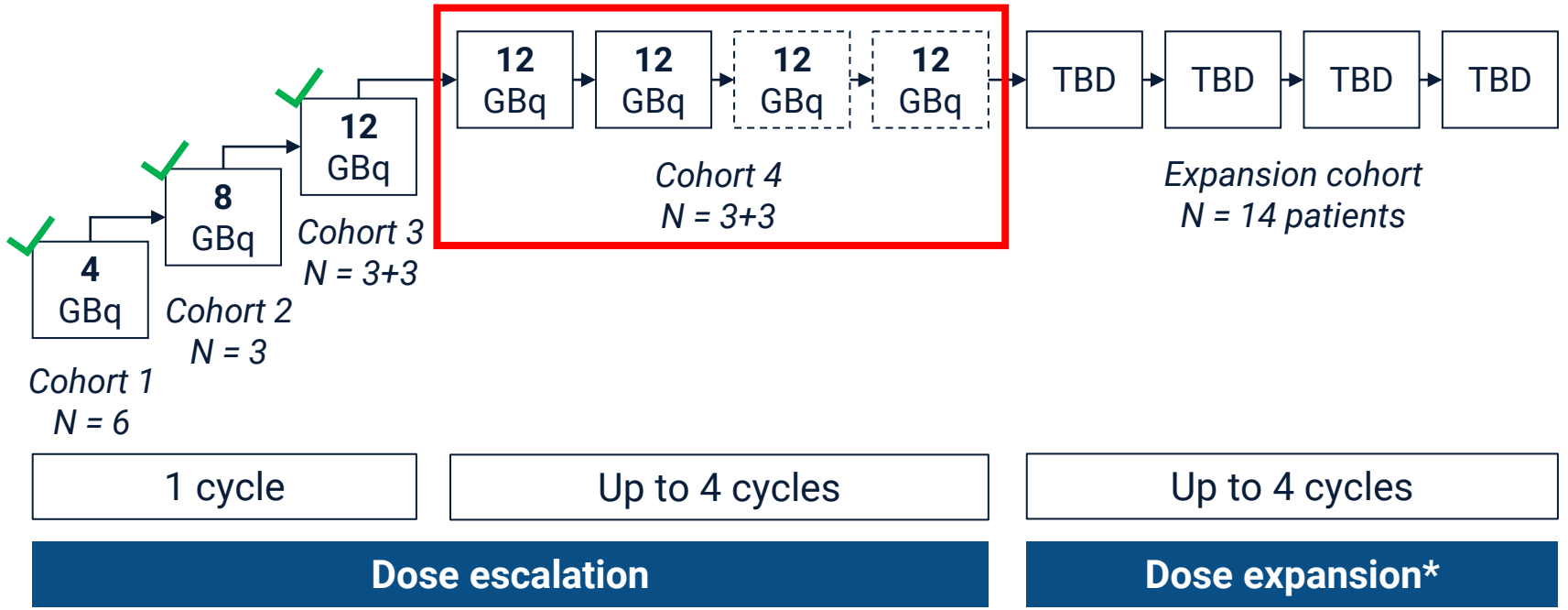
SECuRE Study Design and Status

Patient population:

- Participants with progressive mCRPC despite prior ADT and at least one ARPI (pre- or post-chemotherapy)[1]

Maximum dose being investigated:

- 12 GBq (>50% higher than the approved dose of Pluvicto®)[2]



Primary objectives include:

- To investigate the safety and tolerability of $^{64}Cu/Cu^{67}$-SAR-bisPSMA
- To investigate the anti-tumour efficacy of ^{67}Cu-SAR-bisPSMA (PSA and radiographic response)

At the time of this presentation, no dose limiting toxicities have been observed in cohorts 1, 2 and 3. In the United States, 5 sites are active. Additional sites in the United States and Australia are currently in start-up.

Dosimetry Phase not shown. Cohorts 1, 2 and 3 completed. Cohort 4 is currently recruiting (red box). Patients in cohort 4 will receive 2 doses of ^{67}Cu-SAR-bisPSMA (12 GBq) according to the current study protocol. A protocol amendment is underway to allow 2 additional doses of ^{67}Cu-SAR-bisPSMA in cohort 4. A Safety Review Committee meeting will take place after 3 and 6 participants receive the first 2 doses in this cohort (minimum period of 6 weeks for safety follow-up). Doses for each cohort: cohort 1, 4 GBq (108 mCi, single dose); cohort 2, 8 GBq (216 mCi, single dose); cohort 3, 12 GBq (324 mCi, single dose); cohort 4, 12 GBq (324 mCi, multi-dose). *Dose level of the expansion cohort will be determined based on safety review from Cohort 4 (TBD: to be determined). 1. Additional eligibility criteria apply NCT04868604. 2. Pluvicto FDA Approved Product Information.

Conclusions

- Characteristics of SAR-bisPSMA, including the double PSMA binding moiety in ^{64}Cu-SAR-bisPSMA (imaging) and ^{67}Cu-SAR-bisPSMA (therapy), may offer advantages compared to currently used single-target PSMA agents
- Preliminary data from mCRPC patients who received multiple doses of ^{67}Cu-SAR-bisPSMA through the Food and Drug Administration Expanded Access Program show encouraging efficacy signals with a favorable safety profile
- The SECuRE study aims to investigate the safety and anti-tumor effect of ^{67}Cu-SAR-bisPSMA in patients with mCRPC (up to 4 cycles)
- No dose limiting toxicities have been observed in the first 3 cohorts of the study
- Results of the SECuRE study will inform the design of a registrational phase 3 study using ^{67}Cu-SAR-bisPSMA to treat patients with mCRPC