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Results from the phase Ib dose escalation of 212Pb-ADVC001 in PSMA-positive metastatic castration-resistant prostate cancer (mCRPC): The theraPb trial

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Background

ADVC001 is a novel PSMA-targeting radioligand therapy labelled with ^{212}Pb, an alpha-emitting payload, designed to potently kill prostate cancer cells while minimizing toxicity. We present first-in-human data of ^{212}Pb-ADVC001 in patients (pts) with mCRPC from the TheraPb trial (NCT05720130).

Methods

Open label, multi-centre interval 3+3 dose-escalation and expansion study in pts with progressive PSMA-avid (>liver) mCRPC previously treated with ≥1 androgen pathway inhibitor (ARPI) and ≥1 taxane unless unsuitable/declined. Primary endpoints are safety and defining the recommended phase 2 dose (RP2D). Escalating doses of 60–200 MBq were administered at prespecified schedules every 6 (Cohort 1), 4 (Cohorts 2a, 3a, 4a) or 2 weeks (optional Cohorts b) for up to 6 cycles.

Results

As of 9 May 2025 cut-off, dose escalation is complete with 16 pts enrolled. Median age was 75 years (range 61–88y), median PSA at baseline (BL) was 53 ng/mL; 69% had ≥1 prior taxane, and all had ≥1 prior ARPI. There were no Gr ≥3 treatment-related adverse events (TRAE; 97% Gr 1, 3% Gr 2). Most common TRAEs were dry mouth (75% overall; 69% Gr 1 >7 days; one pt had transient and reversible Gr 2), Gr 1/2 nausea (50%) and Gr 1 fatigue (44%). Patient-reported outcomes were consistent with AEs. There was no myelosuppression or renal impairment. There were no dose-limiting toxicities and no Gr 4/5 AEs. Two pts discontinued treatment in Cohort 1 (60 MBq) due to progressive disease. Treatment exposure and PSA response in pts receiving ≥120 MBq are shown in Table. A PSA decease ≥50% occurred in 75% of pts receiving ≥120 MBq and this corresponded with decreased PSMA-avid tumour volume on PET; 44% of responders had a BL SUVmean <10.Table: 2388P

Exposure and PSA responses in the 120 MBq, 160 MBq and 200 MBq Cohorts at cut-off

Parameter	≥120 MBq Cohorts n = 12 pts
Previous systemic therapy regimens (excluding ADT and 1st generation AR antagonists)	1 or 2: 6 pts (50%)≥3: 6 pts (50%)
^{212}Pb-ADVC001 cycles administered, by cohort*treatment complete, 6 cycles/pt‡treatment ongoing, up to 6 cycles/pt	Cohort 2a, 120 MBq Q4W: 18 (3 pts)*Cohort 3a, 160 MBq Q4W: 18 (3 pts)*Cohort 4a, 200 MBq Q4W: 10 (3 pts)‡Cohort 3b, 160 MBq Q2W: 12 (3 pts)‡
Premature treatment discontinuation or dose modification	0 pts
Best PSA response (decrease from baseline)	n pts (%)
PSA ≥50%	9 (75%)
PSA ≥80%	5 (42%)
PSA ≥90%	3 (25%)

Conclusions

^{212}Pb-ADVC001 has a favourable safety profile with promising anti-tumour activity at doses of 120–200 MBq. Updated safety and efficacy data, including Q2W cohorts, will be presented at the meeting and will inform the RP2D for the planned phase 2a.

Clinical trial identification

NCT05720130.

Legal entity responsible for the study

AdvanCell Pty Ltd.

Funding

AdvanCell Pty Ltd.

Disclosure

A.R. Hansen: Financial Interests, Institutional, Local PI: AdvanCell Ltd Pty, Aveo, BMS, Full-Life, Janssen, MSD, Roche, SEAGEN, Tyra BioSciences; Financial Interests, Institutional, Advisory Board: AdvanCell Ltd Pty, Fusion; Financial Interests, Personal, Advisory Board: Full-Life, Janssen, MSD, MOMA Therapeutics, Astellas, Bayer, Eisai; Financial Interests, Personal, Invited Speaker: Janssen, MSD, Astellas. D.A. Pattison: Financial Interests, Personal, Advisory Board: Ipsen; Financial Interests, Personal, Speaker, Consultant, Advisor: Eisai; Financial Interests, Institutional, Local PI: AdvanCell Ltd Pty. P. Santoro: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. M. Crumbaker: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. M. Baronet: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. S. Rose: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. A.A. Adamovich: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd; Financial Interests, Personal, Leadership Role: AdvanCell Pty Ltd. S. Puttick: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. T. Kryza: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. K. Kuan: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. A. Karmann: Financial Interests, Personal, Full or part-time Employment: AdvanCell Pty Ltd. D.K. Wyld: Financial Interests, Institutional, Local PI: AdvanCell Pty Ltd. All other authors have declared no conflicts of interest.