This research was originally published in JNM.
Emmett L et al. Interim results of a Phase I/II prospective dose escalation trial evaluating safety and efficacy of combination ^{177}Lu PSMA 617 and NOX66 in men with mCRPC post androgen signalling inhibition and 2 lines of taxane chemotherapy (LuPIN trial). J Nucl Med. 2019;60:465.

Interim results of a Phase I/II prospective dose escalation trial evaluating safety and efficacy of combination ^{177}Lu PSMA 617 and NOX66 in men with mCRPC post androgen signalling inhibition and 2 lines of taxane chemotherapy (LuPIN trial).

1. **Louise Emmett**[3],
2. **Megan Crumbaker**[3],
3. **Andrew Nguyen**[3],
4. **Bao Ho**[3],
5. **Charlotte Yin**[3],
6. **Noah Isheish**[3],
7. **Arun Azad**[1],
8. **John Violet**[2],
9. **Shikha Sharma**[3] **and**
10. **Anthony Joshua**[3]

+ Author Affiliations

1. [1]Oncology Monash University Melbourne Australia
2. [2]Radiation Oncology Peter MacCallum Cancer Centre Melbourne Australia
3. [3]390 Victoria St St Vincent's Hospital Sydney Australia

Abstract

465

Background: Despite treatment advances, metastatic castrate resistant prostate cancer (mCRPC) remains a lethal disease. Trials in ^{177}LuPSMA - 617 have demonstrated good efficacy and safety, but not all men respond to treatment, and treatment responses may be limited in duration. Idronoxil is an inhibitor of external NADH oxidase type 2 and has a variety of downstream pro-apoptotic actions including radio-sensitization. We present preliminary results of a phase 1/2 dose escalation trial of LuPSMA and NOX66 in men with heavily pre-treated mCRPC.

Methods: 16 men with mCRPC progressing despite docetaxel, cabazitaxel and either abiraterone or enzalutamide were enrolled. Imaging criteria included a PSMA PET/CT intensity SUV max >10 at all sites of measurable disease with no discordant disease on FDG PET/CT. Men required Hb >10ng/mL, Platelets >90 and GFR >40 mls/min. All men received up to 6 doses of ^{177} Lu-PSMA 617 at 6-weekly intervals; the first 8 men received 400mg idronoxil (suppository) daily cycle days 1-10. Following safety data review, the dose for patients 9-16 was escalated to 800mg idronoxil daily. All men received Dexamethasone 8mg on Day 1 and 4mg days 2,3.

Results: To date, all 16 men have received ≥2 doses and 4/16 (25%) 6 cycles. The treatment has been well tolerated. Adverse events (AEs) and PSA responses are summarized in the table below; 1/16 reported an SAE due to pneumonitis and continued on trial without NOX66. 3/16 (19%) have exited trial prematurely due to progressive disease

Conclusions: Combination LuPSMA-617 + NOX66 demonstrate encouraging early results. Based on these findings, particularly safety, recruitment for a phase II expansion cohort is underway.

	Cohort 1 (n=8)	Cohort 2 (n=8)	Overall
PSA response (>50%) reduction	5/8 (62.5%)	6/8 (75%)	11/16 (69%)
AEs ≥ grade II	4/8 (37.5%)	1/8 (12.5%)	5/16 (31%)
• Haematologic	3/8	-	
• Fatigue	3/8	1/8	
• Other (pneumonitis)	1/8	-	