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Associations between quantitative baseline 68Ga-PSMA-11 PET parameters and 177Lu-PSMA-617 efficacy in the PSMAfore study

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Background

In the phase 3 PSMAfore study, [¹⁷⁷Lu]Lu-PSMA-617 (¹⁷⁷Lu-PSMA-617) prolonged rPFS versus change of androgen receptor pathway inhibitor (ARPI) in taxane-naïve adults with PSMA-positive (PSMA+) mCRPC and disease progression once on prior ARPI. We assessed associations between baseline quantitative PSMA PET parameters and efficacy outcomes.

Methods

PSMA+ mCRPC was defined as ≥1 PSMA+ lesion and no exclusionary PSMA-negative lesions on centrally read baseline [⁶⁸Ga]Ga-PSMA-11 PET/CT scans. Extracted quantitative parameters included whole-body mean standardized uptake value (SUV_{mean}) and PSMA+ tumor volume (TV). Efficacy outcome associations were assessed *post hoc* at the third interim analysis (data cut off 27 Feb 2024).

Results

Baseline PET/CT scans met quality requirements for this analysis in 455/468 randomized patients. Quantitative parameters were balanced between the study arms. In Cox proportional hazard models, higher SUV_{mean} was associated with improved rPFS, ORR, PSA response and OS in the ¹⁷⁷Lu-PSMA-617 arm but not the ARPI change arm. There was no optimal SUV_{mean} cutpoint for better vs worse rPFS or OS. Lower PSMA+ TV was associated with improved rPFS and OS in both arms, and PSA response in the ARPI change arm. In Kaplan-Meier analyses, patients in the ¹⁷⁷Lu-PSMA-617 arm with SUV_{mean} ≥ median had longer rPFS than those with SUV_{mean} < median (Table). OS was confounded by high crossover (57%) from ARPI change to ¹⁷⁷Lu-PSMA-617. In the ¹⁷⁷Lu-PSMA-617 arm, OS was longer among those with SUV_{mean} ≥ median (Table). In other subgroup analyses, patients with soft tissue only disease had higher SUV_{mean} and lower PSMA+ TV than those with bone disease, and appeared to have longer rPFS and OS when treated with ¹⁷⁷Lu-PSMA-617. Table: 2390P

SUV _{mean}	¹⁷⁷ Lu-PSMA-617 N = 234		ARPI change N = 234	
	< median ^a	≥ median ^a	< median ^b	≥ median ^b
<i>rPFS</i>				
Events, n/n	81/114	68/114	91/113	88/114
Median, months	7.5	17.1	5.5	5.7
HR (95% CI) ^c	0.91 (0.88, 0.95) NS			
<i>OS^d</i>				
Events, n/n	66/114	36/114	61/113	48/114
Median, months	17.2	29.6	19.6	25.1

SUV _{mean}	¹⁷⁷ Lu-PSMA-617 N = 234		ARPI change N = 234	
	< median ^a	≥ median ^a	< median ^b	≥ median ^b
HR (95% CI) ^c	0.86 (0.81, 0.92) NS			
PSMA+ TV	< median ^e	≥ median ^e	< median ^f ≥ median ^f	
<i>rPFS</i>				
Events, n/n	63/114	86/114	84/113	95/114
Median, months	14.6	7.9	6.1	3.7
HR (95% CI) ^c	1.56 (1.17, 2.07) 8.54 (3.69, 19.76)			
<i>OS^d</i>				
Events, n/n	30/114	72/114	40/113	69/114
Median, months	29.6	16.3	26.5	18.1
HR (95% CI) ^c	1.72 (1.32, 2.24) 2.22 (1.76, 2.80)			

^a8.7 ^b8.3 ^cAbove or below median within arm ^dIntent to treat, unadjusted for crossover ^e117.4 mL ^f107.7mL

Conclusions

In patients receiving ¹⁷⁷Lu-PSMA-617, higher SUV_{mean} was associated with better outcomes, with no optimal cutpoints. Higher PSMA+ TV was associated with worse outcomes regardless of treatment.

Clinical trial identification

ClinicalTrials.gov identifier: NCT04689828.

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Legal entity responsible for the study

Novartis.

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Disclosure

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