Abstract 77

Assessment of patient-reported outcomes (PROs) and longer-term adverse events (AEs) in phase I study of 225Ac-J591-PSMA for metastatic castration-resistant prostate cancer (mCRPC)

Jones T. Nauseef[1,2,3], Charlene Thomas[1], Benedict Ho[1], Juana Martinez Zuloaga[1], Brian D. Gonzalez[4], Michael Sun[1], A. Oliver Sartor[5], Sharon Singh[1], Mahelia Bissassar[1], Escarleth Fernandez[1], Angela Tan[1], Amie Patel[1], Muhammad Obaid Naiz[1], Shankar Vallabhajosula[1], Ana M. Molina[1,2,3], Cora N. Sternberg[1,2,3], David M. Nanus[1,2,3], Joseph Osborne[1,3], Neil H. Bander[1], Scott T. Tagawa[1,2,3]

Weill Cornell Medicine Hematology & Oncology

1-NewYork-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY; 2-Englander Institute for Precision Medicine, New York, NY, 3-Sandra and Edward Meyer Cancer Center, New York, NY; 4- Moffitt Cancer Center, Tampa, FL; 5-School of Medicine, Tulane Medical School, New Orleans, LA;

NewYork-Presbyterian

Background

Prostate Specific Membrane Antigen targeted radiotherapy (PSMA-TRT) allows exquisite delivery of ionizing radiation

The larger size of antibody-based PSMA-TRTs are less likely than small molecules to reach luminal PSMA on normal organs and prolong circulating times

We examined PROs and AEs from the dose-escalation and expansion cohorts of monoclonal antibody-potent alpha emitter PSMA TRT (^{225}Ac-J591)[1]

Methods

Men with mCRPC with PCWG3 progression, prior ARSI, prior chemotherapy (or ineligible) twere reated with single dose of ^{225}Ac-J591

Escalation (KBq/kg): 13.3, 26.7, 39.96, 53.2, 66.5, 80, 93.3
Expansion: 93.3 KBq/kg

1° outcome: DLT & MTD
2 ° outcomes: PROs, PFS, OS, PSA responses

PROs (BPI-SF, QOL, FACT-P) at baseline/12 weeks and AEs (CTCAE v5) and were evaluated including for associations with PSA response

Summary of PRO-evaluable cohort

Baseline Demographics (n=19)	
Age, median (range)	67.6 (52.9-85.0)
PSA, median (range)	112.8 (4.79-7168.4)
ECOG Performance Status	
0	3 (16)
1	13 (68)
2	3 (16)
Sites of Metastasis, n (%)	
Bone	18 (95)
Lymph Node	17 (90)
Liver	3 (16)
Lung	2 (11)
Prior Therapy, n (%)	
2+ potent AR inhibitors	13 (68)
Chemotherapy	9 (47)
Lu-PSMA TRT	7 (37)
Sipuleucel-T	4 (21)
PARP inhibitor	3 (16)
Radium-223	3 (16)

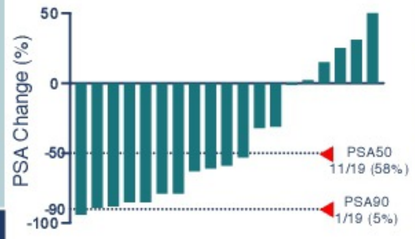
19 of 32 subjects completed pre- and post-treatment PRO data for analysis

Treatment Emergent AEs, n (%)	Gr 1	Gr 2	Gr 3/4
Xerostomia	10 (52)	0 (0)	0 (0)
Nausea	13 (68)	3 (16)	0 (0)
Pain	5 (26)	3 (16)	0 (0)
Fatigue	8 (42)	11 (58)	0 (0)
Anemia	4 (21)	4 (21)	0 (0)
Transaminitis	1 (5)	1 (5)	0 (0)
Thrombocytopenia	12 (63)	1 (5)	3 (16)
Neutropenia	2 (11)	1 (5)	1 (5)

1- NCT03276572

Results

Percent PSA decline is associated with decreased severity of pain

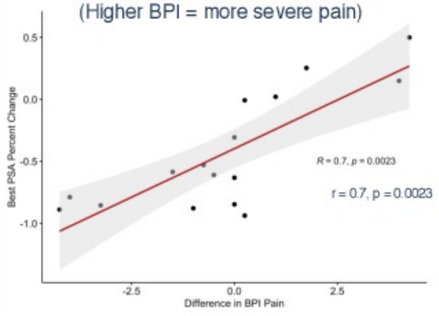


Maximum PSA responses of 50% or greater were observed in a majority of subjects

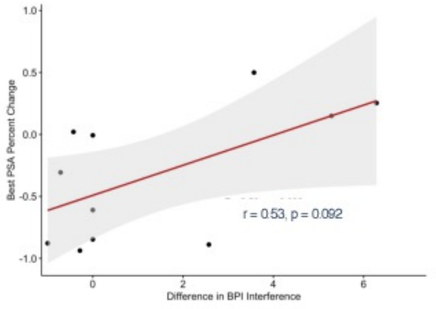
Yet, pain severity (p=0.8) and interference from pain (p=0.4) were unchanged at 12 weeks from baseline

PSA decline was associated with reduced BPI pain (r = 0.7, p = 0.0023) and a trend toward BPI interference severity (r = 0.53, p = 0.092)

PSA change and Change in BPI Pain
(Higher BPI = more severe pain)



PSA change and Change in BPI Interference



Characteristic	Baseline, N = 19[1]	Efficacy Visit, N = 19[1]	p-value[2]
Average BPI Pain Items	1.00 (0.38, 3.62)	1.00 (0.00, 3.12)	0.8
Average BPI Interference Items	0.86 (0.21, 5.71)	2.14 (0.00, 5.64)	0.4
Unknown	1	4	

[1] Median (IQR)
[2] Wilcoxon signed rank test with continuity correction

Overall FACT-P did not change with treatment

Despite every subject experiencing a treatment-emergent AE

Characteristic	Baseline, N = 19[1]	Efficacy Visit, N = 19[1]	p-value[2]
Physical Well-Being	11.0 (5.5, 15.2)	9.0 (7.0, 14.5)	0.8
Social/Family Well-Being	23.0 (21.0, 24.2)	23.0 (22.0, 24.0)	0.8
Emotional Well-Being	15.0 (10.0, 18.0)	10.0 (7.5, 13.0)	0.011
Functional Well-Being	20.0 (15.5, 24.5)	18.0 (14.5, 20.5)	0.3
Prostate Cancer Subscale	20 (16, 24)	20 (13, 26)	0.7
FACT-P Total Score	83 (76, 90)	81 (70, 92)	0.2

[1] Median (IQR)
[2] Wilcoxon signed rank test with continuity correction

Median emotional well-being was reduced in a clinically-meaningful degree

When stratified by AEs, only presence of xerostomia was associated with lower FACT-P scores after treatment

	No xerostomia	Xerostomia
Difference in FACT-P Total Score	-5 (-15, 0)	-13 (-14, -1)

Median (IQR)

Conclusions

- Pain and quality of life did not significantly change, on average, after treatment of mCRPC patients with ^{225}Ac-J591, despite prior evidence of treatment-emergent AEs
- Improved pain following treatment was associated with greater PSA decline, a trend warranting further investigation
- Small numbers limited testing additional subgroup associations
- Assessment of PROs is being pursued in additional follow up studies, including in "Fractionated and Multiple Dose ^{225}Ac-J591 for Progressive mCRPC" (NCT04506567)
- A PRO tool for PC patients receiving TRT is in development

Support

Grant support: Department of Defense, National Institutes of Health, and Prostate Cancer Foundation

Contact Information

jtn2001@med.cornell.edu @DrJonesNauseef