^{89}Zr-Df-IAB2M Minibody Imaging In Patients With Prostate Cancer: Biodistribution, Kinetics, Lesion Uptake And Organ Dosimetry

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Memorial Sloan Kettering Cancer Center

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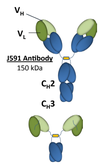
Anti PSMA Minibody: IAB2M



The minibody ("Mb"), IAB2M is an optimally engineered 80 kDa anti PSMA humanized Mb dimer in which each monomer is composed of an single chain variable fragment, scFv (V_H-V_L) linked to only the C_H3 domain.

^{89}Zr-Df-IAB2M, is the anti-PSMA Mb conjugated with desferrioxamine (Df) and radiolabeled with ^{89}Zr for imaging Prostate cancer.

Imaging advantages:
Faster clearance; high T/BG ratio by 48 h and earlier imaging compared to full antibody

Objectives

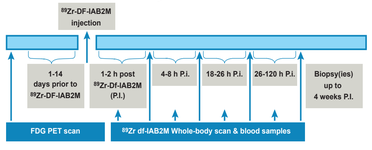
- **Primary Endpoints**
  - To determine the safety, pharmacokinetics (PK) and biodistribution of ^{89}Zr-Df-IAB2M PET imaging
  - To determine the ability of ^{89}Zr-Df-IAB2M PET imaging to detect known sites of disease
- **Secondary Endpoints**
  - Biopsy correlation of the ^{89}Zr-Df-IAB2M PET image lesions
  - To compare FDG PET with ^{89}Zr-Df-IAB2M PET tumor uptake

Subject Inclusion Criteria

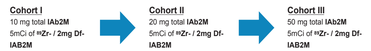
- Histologically confirmed prostate cancer
- Patients with progressive disease by Imaging or biochemical progression
- Measurable disease by CT, bone scan, or MRI that are consistent with disease
- KPS 60 or higher

Patient Demographics		
Characteristic (n = 18)	No. (%)	Median (Range)
Age, years		68 (54-86)
Gleason score		7 (6-9)
KPS, %		90 (70-90)
Disease Stage		
Castration-Resistant Metastatic	9 (50%)	
Non-Castrate Metastatic	9 (50%)	
PSA, ng/mL		14.7 (0.2-153.2)

Study Schema



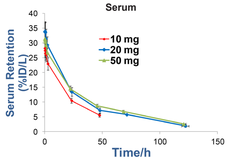
Dose Escalation Schema

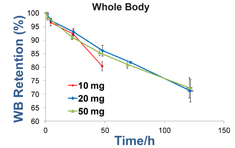


Methods

- **Administration:**
  - Total of 10/20/50 mg of IAB2M minibody
  - 5mCi of ^{89}Zr in 1-3mg of IAB2M minibody injected over 5-10 minutes.
- **Serial blood samples:** Pre-injection, 5, 15, 30, 60, and 120 to 240 minutes PI, and a sample at each subsequent day of imaging
- **Whole body counts:** Pre and post void; repeat at each subsequent time point.
- **Scans:** 10 mA CT scans on ¾ imaging and 80 mA CT scan on day 3 (48hr); acquisition 5-7 min/FOV

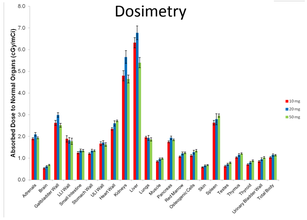
Results: Clearance of ^{89}Zr-Df-IAB2M



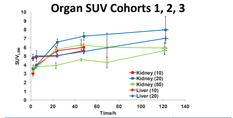


Pharmacokinetics

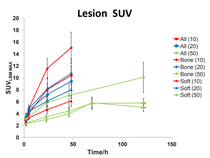
	Cohort I mean (range)	Cohort II mean (range)	Cohort III mean (range)
Blood Clearance (h) **Effective** $T_{1/2\alpha}$:	3 .3 (1.2 – 5.7)	5.1(1.9 – 8.0)	6.0(2.2 – 8.9)
$T_{1/2\beta}$:	20 (17-27)	23(19-27)	28(25-32)
Blood Clearance (h) **Biologic** $T_{1/2\alpha}$:	3.4(1.2 – 6.2)	5.5 (2.0 – 8.9)	6.6(2.2 – 10.1)
$T_{1/2\beta}$:	28 (22-41)	32(24-41)	45(36-55)
Whole Body Clearance (h)**effective**	52(47 – 60)	58(53 – 65)	60(57 – 67)
Whole Body Clearance (h) **Biological**	166(119 – 257)	241(165 – 365)	267(211 – 450)
AUC (%ID h/L)	797± 216	1059 ± 307	1257 ± 130
Clearance (L/h)	0.133±0.034	0.103±0.038	0.080 ± 0.009



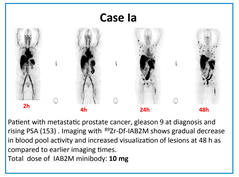
Estimated Absorbed Dose (cGy/mCi) Mean ± SD			
	Cohort-I	Cohort-II	Cohort-III
Liver	6.3 ± 0.9	6.8 ± 1.2	5.4 ± 0.9
Kidney	4.8 ± 0.9	5.7 ± 1.1	4.6 ± 0.7
Red Marrow	1.07 ± 0.13	1.22 ± 0.25	1.25 ± 0.13
Effective Dose (rem/mCi)	1.48 ± 0.19	1.59 ± 0.28	1.52 ± 0.15



(SUV) 48 hrs			
	Cohort I	Cohort II	Cohort III
Liver	5.6 ± 0.6	5.5 ± 0.6	4.6 ± 0.4
Kidney	6.0 ± 1.0	7.2 ±1.1	6.3 ±1.5

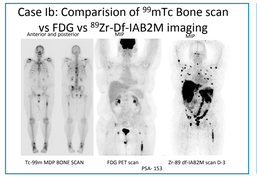


Case Ia

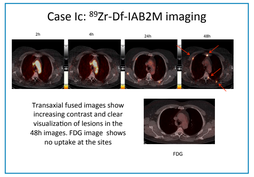


Patient with metastatic prostate cancer, gleason 9 at diagnosis and rising PSA (153) . Imaging with ^{89}Zr-Df-IAB2M shows gradual decrease in blood pool activity and increased visualization of lesions at 48 h as compared to earlier imaging times.
Total dose of IAB2M minibody: **10 mg**

Case Ib: Comparison of ^{99}mTc Bone scan vs FDG vs ^{89}Zr-Df-IAB2M imaging

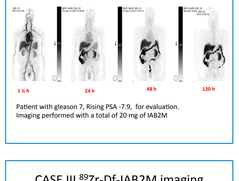


Case Ic: ^{89}Zr-Df-IAB2M imaging



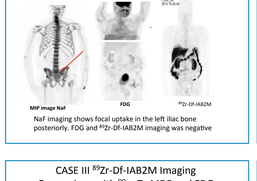
Transaxial fused images show increasing contrast and clear visualization of lesions in the 48h images. FDG image shows no uptake at the sites

Case II: ^{89}Zr-Df-IAB2M Projection Images



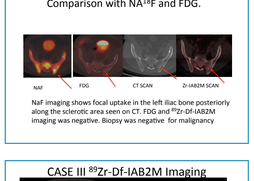
Patient with gleason 7, Rising PSA -7-9, for evaluation.
Imaging performed with a total of 20 mg of IAB2M

Case II - ^{89}Zr-Df-IAB2M imaging: Negative scan



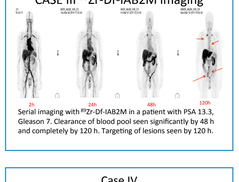
NaF imaging shows focal uptake in the left iliac bone posteriorly. FDG and ^{89}Zr-df-IAB2M imaging was negative

Case II ^{89}Zr-Df-IAB2M imaging: Negative scan Comparison with NA^{18}F and FDG.



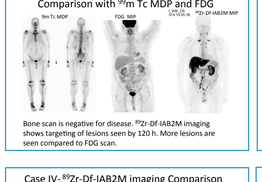
NaF imaging shows focal uptake in the left iliac bone posteriorly along the sclerotic area seen on CT. FDG and ^{89}Zr-Df-IAB2M imaging was negative. Biopsy was negative for malignancy

CASE III ^{89}Zr-Df-IAB2M imaging



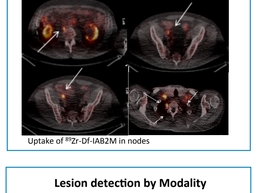
Serial imaging with ^{89}Zr-Df-IAB2M in a patient with PSA 13.3, Gleason 7. Clearance of blood pool seen significantly by 48 h and completely by 120 h. Targeting of lesions seen by 120 h.

CASE III ^{89}Zr-Df-IAB2M Imaging Comparison with ^{99}m Tc MDP and FDG



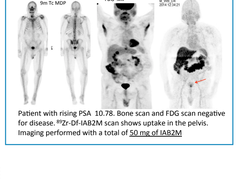
Bone scan is negative for disease. ^{89}Zr-Df-IAB2M imaging shows targeting of lesions seen by 120 h. More lesions are seen compared to FDG scan.

CASE III ^{89}Zr-Df-IAB2M Imaging



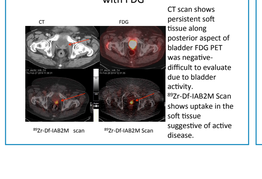
Uptake of ^{89}Zr-Df-IAB2M in nodes

Case IV



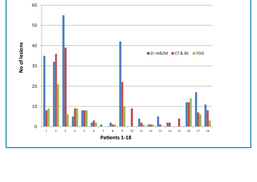
Patient with rising PSA 10.78. Bone scan and FDG scan negative for disease. ^{89}Zr-Df-IAB2M scan shows uptake in the pelvis. Imaging performed with a total of 50 mg of IAB2M

Case IV- ^{89}Zr-Df-IAB2M imaging Comparison with FDG



CT scan shows persistent soft tissue along posterior aspect of bladder FDG PET was negative- difficult to evaluate due to bladder activity. ^{89}Zr-Df-IAB2M Scan shows uptake in the soft tissue suggestive of active disease.

Lesion detection by Modality



SUVLBM (mean± SD(Range)	Cohort I 48h	Cohort II 48h	Cohort III 48 h	Cohort III 72-120 h
Bone	15.1 ± 9.4 (9.3-42.1) N = 13	10.7 ± 7.5 (2.5-19.6) N = 9	7.0 ± 3.8 (2.9-10.3) N= 3	8.5 ± 3.7 (5.4 -12.6) N =3
Soft Tissue	6.1 ± 3.3 (2.7-14.6) N = 14	8.0 ± 3.9 (1.6-12.8) N=8	3.9 ± 2.0 (0.7- 8.2) N=17	5.2 ± 2.2 (1.5-9.4) N=17

Imaging/Biopsy Concordance (5 Bone and 8 Soft-Tissue Biopsies)

Imaging Results	FDG +	FDG -	^{89}Zr-Df-IAB2M +	^{89}Zr-Df-IAB2M -
Biopsy +	9	2	11	0
Biopsy -	0	2	1	1
Concordance	11/13 (85%)		12/13 (92%)	

Results (2)

- Bone or soft tissue/node lesions seen in 17/18 patients
  - 1 pt with negative scan had bone lesion on NaF-Neg on path
- Bone lesions: Seen in 9 pts by ^{89}Zr-Df-IAB2M imaging (Bone scan + in 9 pts and FDG + in 6 pts). 2 pt showed bone uptake otherwise not prior known.
  - 1 pt with conventional imaging (CI) + ^{89}Zr-Df-IAB2M was negative on pathology
  - At least one or more lesions seen in 7 pts (5 with >5 lesions) for bone disease
- Nodal/soft tissue lesions seen in 14 pts (CI + in 13 pts)
  - 1 pt was CI + ^{89}Zr-Df-IAB2M - ; 2 patients were CI – ^{89}Zr-Df-IAB2M+

Conclusions

- Favorable kinetics and distribution with minimal differences at the higher minibody dose
- Lesion detection seen at all minibody dose levels
- Lesions detection with high contrast possible at 48 h P.i.
- ^{89}Zr-Df-IAB2M imaging shows targeting of both bone and soft tissue lesions.
- ^{89}Zr-Df-IAB2M imaging in larger patient population is underway

References

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