Update on clinical research assessing CD8 immunoPET

Anna M. Wu, Ph.D.
Professor and Chair, Department of Immunology and Theranostics, DMRI
Co-Director, Center for Theranostics
Beckman Research Institute, City of Hope Medical Center

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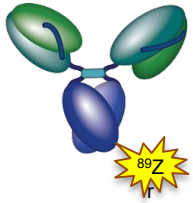
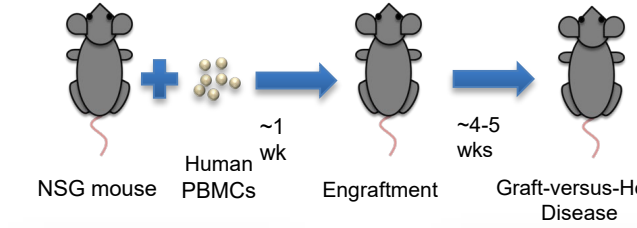
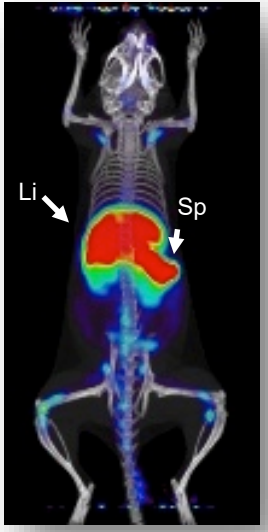
DISCLOSURE: Anna M. Wu is a Founder, Board Member, and consultant to ImaginAb, Inc.

Clinical imaging agent – IAB22M2C



- Humanized anti-human CD8 minibody; K_D = 0.4 nM
- Conjugated with DFO, labeled with Zr-89
- *In vitro* characterization showed no impact on proliferation, depletion, or cytokine release on normal human donor T cells
- *In vivo* studies in humanized mice showed no impact on T cell populations or cytokine release
- *In vivo* imaging in humanized mouse model

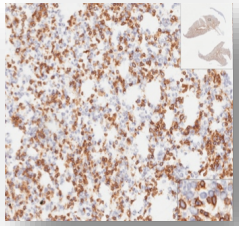




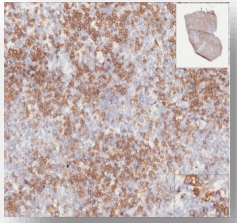
1 week Engraftment

4 weeks GVHD

huCD8 IHC



Lung



Spleen

T. Olafsen et al. abstract AACR 2016

MS submitted

CD8-targeted PET Imaging of Tumor Infiltrating T cells in Patients with Cancer: A Phase I First-in-Human Study of ^{89}Zr-Df-IAB22M2C, a Radiolabeled anti-CD8 Minibody

Michael D. Farwell, Raymond F. Gamache, Hasan Babazada, Matthew D. Hellmann, James J. Harding, Ron Korn, Alessandro Mascioni, William Le, Ian Wilson, Michael Gordon, Anna M. Wu, Gary A. Ulaner, Jedd D. Wolchok, and Michael A. Postow, and Neeta Pandit-Taskar

UPENN, MSKCC, Honor Health
Imaging Endpoints, ImaginAb

Study Design: Clinical imaging of CD8 T leukocytes using ^{89}Zr-IAB22M2C

- Solid malignancies with at least 1 RECIST measurable lesion on CT/MRI
- Eligible for/on checkpoint inhibitor therapy
- Open-label, non-randomized, 2 stage:
  - Protein dose escalation (6 patients: 3 mCi ^{89}Zr; 0.2, 0.5, 1, 1.5, 5, 10 mg protein)
  - Protein dose expansion (9 patients: 3 mCi ^{89}Zr; 0.5 or 1.5 mg protein)
- Serial imaging at 1-2 h; 6-8 h; 24 h; 48 h; 96-144 h
- Serial blood draws for pharmacokinetics
- Also assayed cytokines (baseline, 4h, 24 h) and ADA (anti-drug antibody) (baseline, 3-4 wk, 8-12 wk)

One patient had transient ADA (3-4 wk) which became undetectable by 8-12 wks

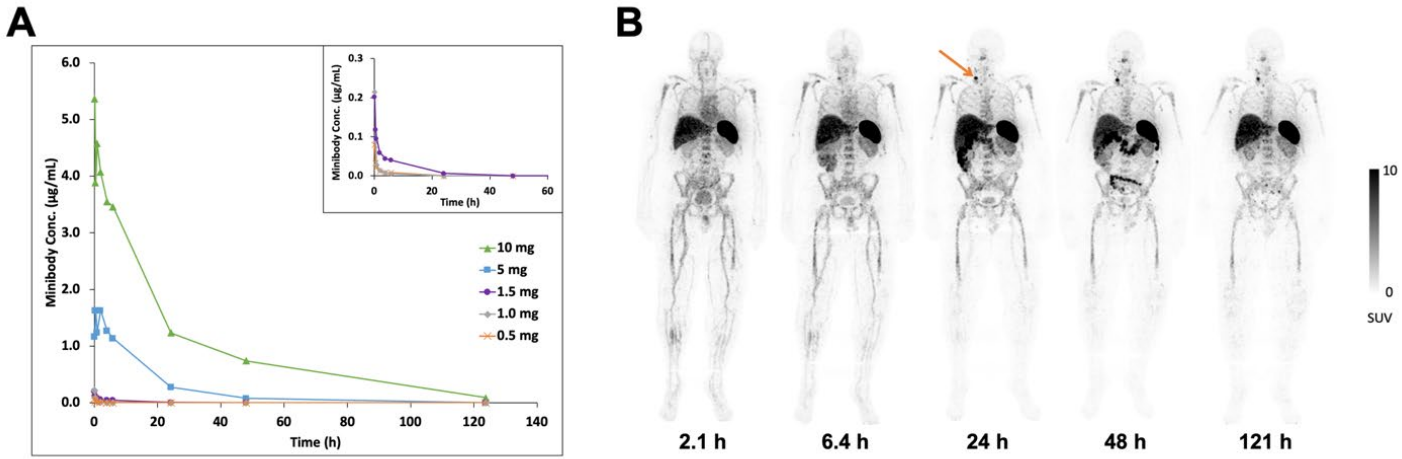
Stage 1 (first six patients) Pandit-Taskar et al. J. Nucl. Med. 61:512-519, 2020
Stage 2 (all 15 patients): M. Farwell et al., submitted

Clinical imaging of CD8 T leukocytes using ^{89}Zr-IAB22M2C

Table 1. Patient characteristics

Characteristic	All patients (n = 15)
Age, median years (range)	64 (30–81)
Sex, n (%)	
Male	9 (60)
Female	6 (40)
Tumor type, n (%)	
Melanoma	8 (53)
Non-small cell lung carcinoma	6 (40)
Hepatocellular carcinoma	1 (7)
Treatment profile at the time of imaging, n (%)	
On immunotherapy (<2 months)	3 (20)
On immunotherapy (>2 months)	5 (33)
On targeted therapy (1–6 months)	2 (13)
Discontinued prior treatment (>5 months)	2 (13)
Treatment naïve	3 (20)

Results: Pharmacokinetics



	$t_{1/2\alpha}$	Aα	$t_{1/2\beta}$	Aβ
0.5 mg (n=4)	0.33 ± 0.10 h	61.5%	14 ± 7.0 h	38.5%
1.5 mg (n=5)	0.38 ± 0.29 h	75.5%	6.4 + 3.4 h	24.5%

- Rapid, biexponential serum clearance
- Rapid localization to spleen, BM, LN
- Tumor uptake increases through 24 h

Results: Examples of negative lesions

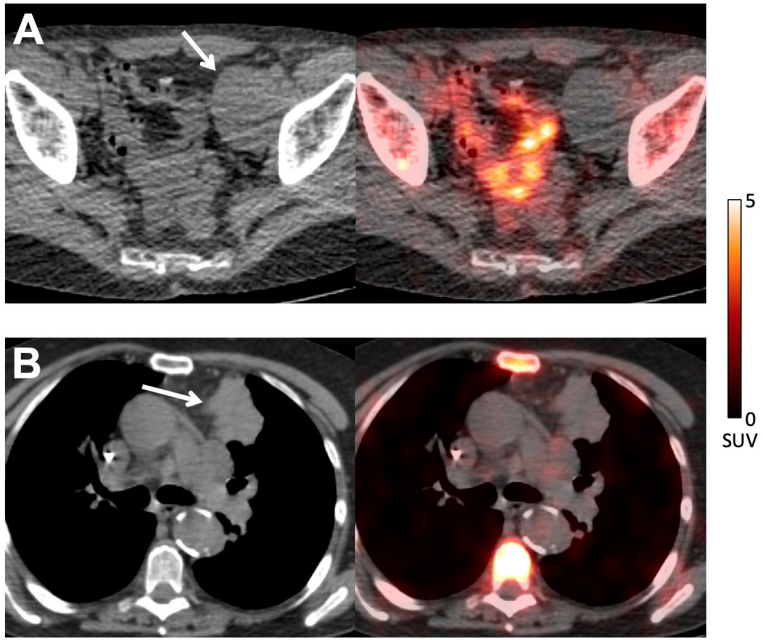


Figure S1. (A) CT and fused CD8 PET/CT images of a patient with metastatic melanoma on targeted therapy demonstrate a large nodal metastasis in the left pelvis (arrow) with tracer uptake at background. (B) CT and fused CD8 PET/CT images of a patient with non-small cell lung cancer prior to initiation of therapy demonstrate a large tumor lesion in the left lung (arrow) with tracer uptake at background.

Farwell et al., submitted

Results: Example of positive CD8 immunoPET

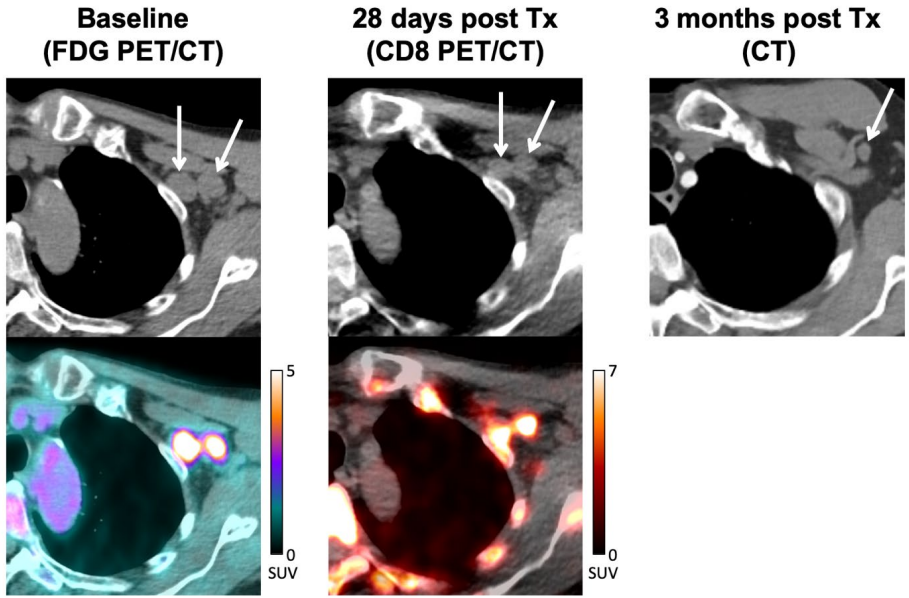


Figure 4. 71-year-old man with locally advanced stage III melanoma treated with pembrolizumab. Baseline CT and fused FDG PET/CT images (left) demonstrate two FDG avid metastases in the left axilla (SUV_{MAX} = 10.0, medial node; SUV_{MAX} = 7.6, lateral node). CT and fused CD8 PET/CT images (middle) performed 28 days after starting immunotherapy demonstrate increased tracer activity in both metastases (SUV_{MAX} = 11.7, medial node; SUV_{MAX} = 12.3, lateral node), suggestive of tumor infiltration by CD8+ T cells. Follow-up imaging with contrast-enhanced CT (right) demonstrated a complete response to therapy.

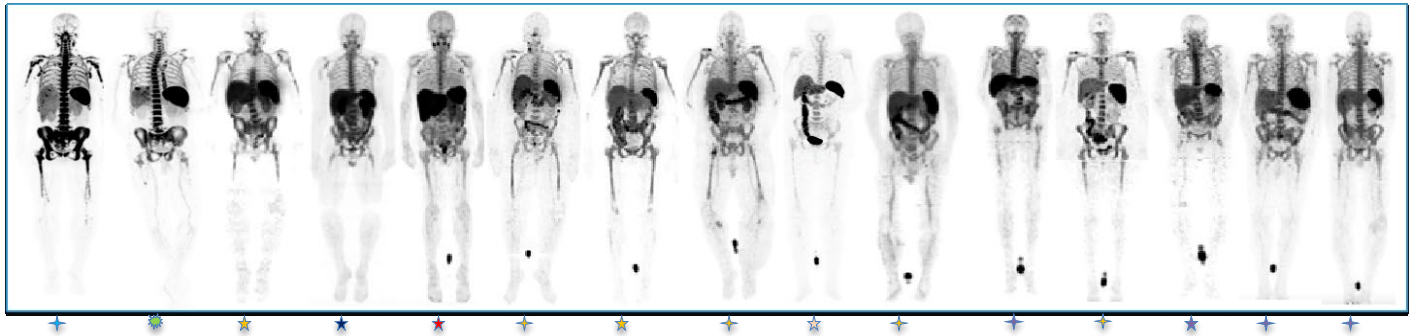
Follow-up: Complete response, 2.3+ years

Farwell et al., submitted

Phase I Summary

Imaging conclusions:

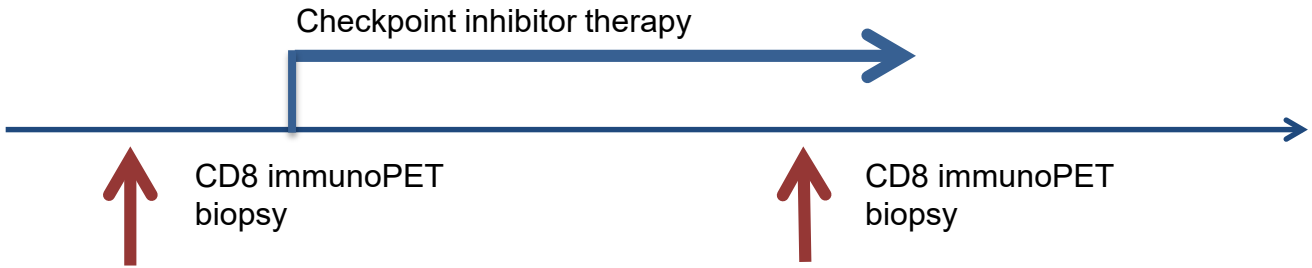
- Rapid clearance; excretion primarily hepatobiliary
- Uptake in T-cell rich tissues (spleen, BM, LN)
- No/low uptake in normal organs (muscle, heart, brain, lungs)
- Tumor uptake variable (SUV_{MAX} up to >20) and seen in 10/15 (67%) patients
- Protein dose range with favorable biodistribution: 0.5-1.5 mg
- Most favorable imaging time: 24 hrs, although tumors seen as early as 1-2 hrs



Gordon et al. SITC 2018; Farwell et al. submitted.

Phase II Pre-treatment/On-treatment study (NCT03802123)

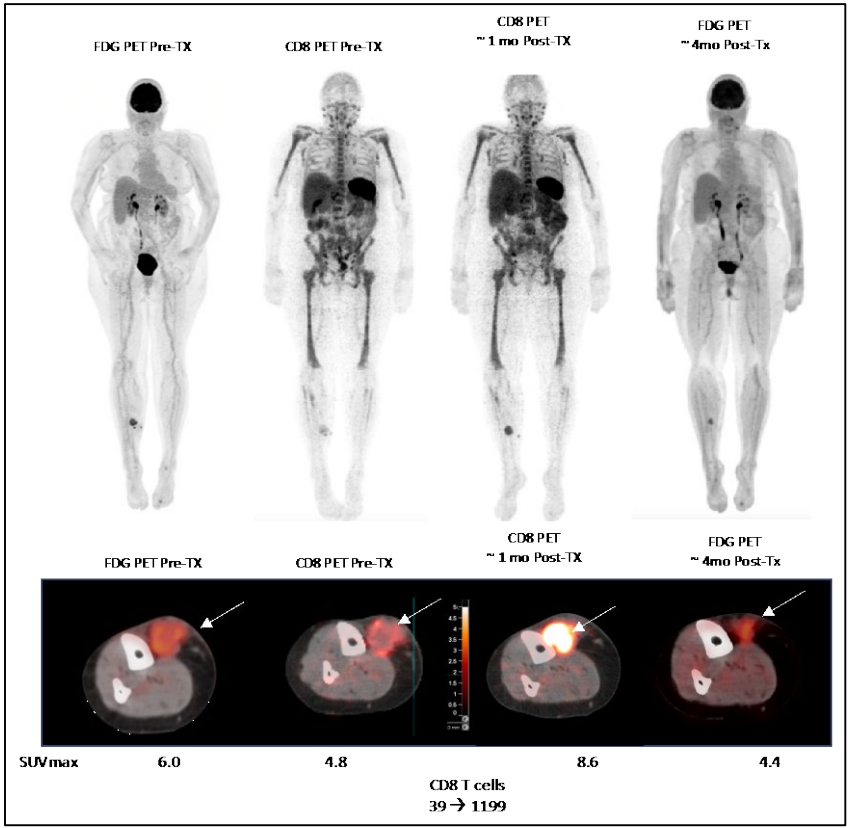
- Patients with metastatic solid tumors, initiating checkpoint inhibitor therapy
  - Pre-treatment (baseline) CD8 PET scan and biopsy (3 mCi* /1.5 mg; 24 h)
  - Initiate immunotherapy (ipi/nivo/pembro standard of care)
  - On-treatment CD8 PET scan and biopsy (4-5 weeks after therapy initiation)
- Goals
  - Safety of repeat dosing and imaging
  - Correlation of CD8 PET with CD8 IHC
  - Correlation with RECIST and outcome
- Multi-center trial, ongoing with ~ 10 sites active; ~ 30 patients enrolled



*Amended to reduce activity to 1 mCi/1.5 mg

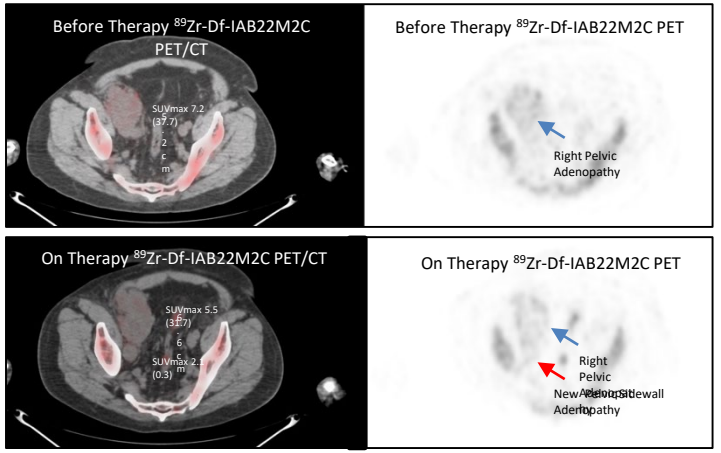
Phase II Examples

RECIST 1.1. Response



Early (1 mo) CD8 immunoPET correlated with response (4 mo)

RECIST 1.1 Progression

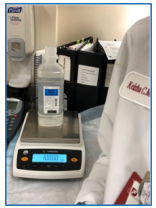


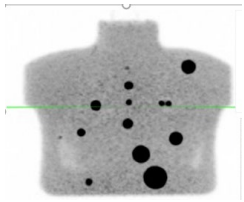
Lack of change of CD8 signal from baseline to 1 mo post-treatment

Courtesy ImaginAb, Inc.

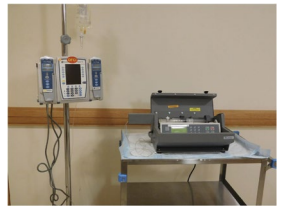
CD8 immunoPET Logistics

- PET scanner validation (SNMMI/Nuclear Medicine Clinical Trial Group) includes calibration of dose calibrator and shipment of calibrated Zr-89-filled phantom. Multiple manufacturers/scanners supported. NMCTG will send specific acquisition and reconstruction parameters back to the site.
- 16 sites validated in US; 9 sites in Canada/UK/EU/Australia
- Manufacturing and dose supply from 2 sites in US: MSKCC (NY) and Optimal Tracers (CA)
- Cloud-based product ordering platform, doses available M-F
- Doses shipped in lead shielding, thermally controlled and tracked









Point of Contact

William Le, VP Operations, Program Lead
Tel: +1.972.207.4209
Email: wle@imaginab.com

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