

Comparison Of ⁸⁹Zr-Df-IAB2M PET/CT To ¹¹¹In Capromab Pendetide SPECT/CT In The Detection Of Occult Prostate Cancer In Patients Undergoing Radical Prostatectomy (RP) In a Single Center Phase II Study

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Background

The detection of occult lymph node (LN) metastasis for prostate cancer (PC) in high risk (HR) patients is essential for proper staging and therapy. Conventional Imaging (CI) with CT/MRI and bone scan is insensitive for determining extracapsular spread of disease to locoregional and distant sites. Additional imaging with ¹¹¹In-Capromab Pendetide (CP; ProstaScint®), approved for detecting extracapsular disease in HRPC patients, lacks sufficient added sensitivity and specificity, which reinforces the need to develop better imaging agents for use prior to radical prostatectomy (RP). IAB2M is a novel anti-PSMA minibody (Mb) derived from a humanized J591 antibody that binds to the extracellular domain of PSMA. Interim data using ⁸⁹Zr-Df-IAB2M PET in 10 subjects reported previously¹ demonstrated promise over CP and CI. This poster provides summary results of 19 subjects from a single center phase II trial that compared ⁸⁹Zr-Df-IAB2M PET to CP in HRPC patients with negative CI. The findings from this study continue to demonstrate the advantage of ⁸⁹Zr-Df-IAB2M PET/CT over CP SPECT and CI for detecting lymph node metastasis using histopathology as the truth standard and lends support for further testing in a larger HRPC patient population.

Objectives

To compare the diagnostic performance of ⁸⁹Zr-Df-IAB2M PET/CT with CI and CP in the detection of extracapsular prostate cancer pre-prostatectomy as confirmed by tissue sampling.

Study Details

- The study protocol and informed consent were approved by a central IRB.
- 19 subjects with histologically confirmed PC scheduled to undergo RP with ≥ 15% associated risk of extracapsular disease by Briganti nomogram or Gleason score ≥ 9 were enrolled.
- All subjects underwent sequential ¹¹¹In-CP SPECT/CT (5mCi ¹¹¹In, whole body scans obtained 3 days p.i.) and ⁸⁹Zr-Df-IAB2M (2.5mCi, whole body scans obtained 2 days p.i.) up to 28 days prior to planned RP with standard lymph node dissection (SLND).
- ⁸⁹Zr-IAB2M PET, CP and CI scans were evaluated centrally by a single reader who was blinded to all clinical, laboratory and pathology information.
- Final scan performance was determined using histopathology as truth standard.
- There were 4 AEs reported in 3 subjects and none were thought to be drug related.

⁸⁹Zr-IAB2M Imaging Parameters

- ⁸⁹Zr-Df-IAB2M (manufactured and shipped from IBA, Somerset, NJ) was administered intravenously at 2.5mCi (+/- 10%) co-infused to yield a 10 mg total protein dose.
- Whole Body PET/CT were obtained at 48h (± 24h) on GE Discovery LS, 2D mode, set for ⁸⁹Zr positron (t_{1/2} = 78.4h, 897 keV, branching fraction = 0.227), iterative reconstruction, 6mm Gaussian filter, CT tube current 40mA.

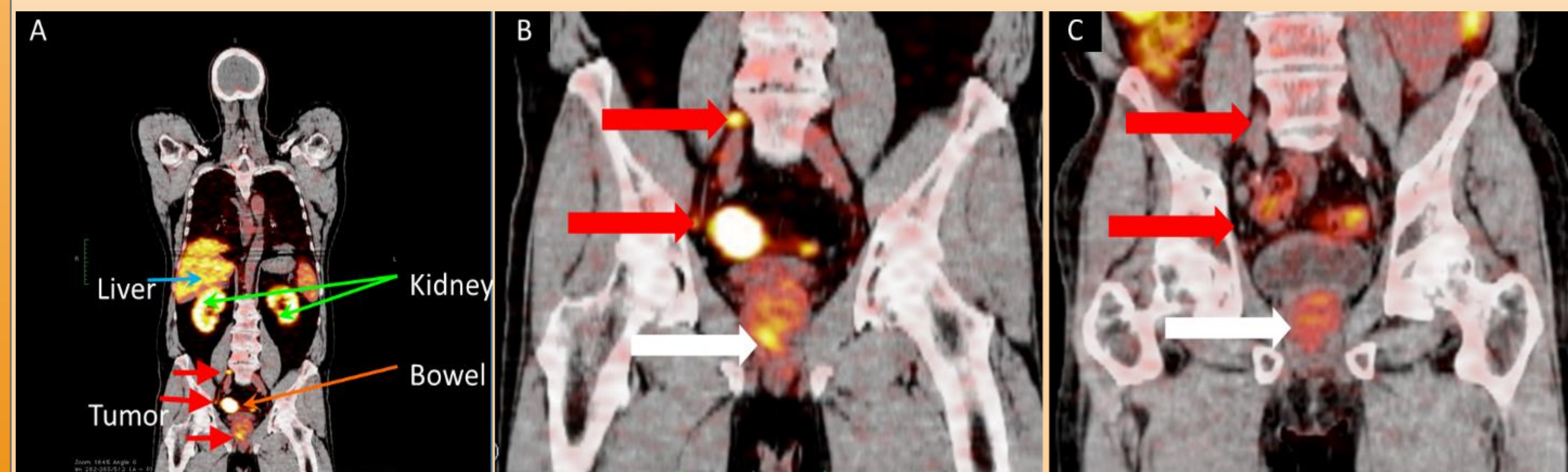
Results

Table 1: Final Demographics and Summary Results

Characteristics	No. (%) or Median (range)
Number of Scanned Subjects (n)	19
Age	65 (51-79)
PSA (ng/ml)	9.8 (3.3-110.5)
Gleason / Briganti Score	8 (7-9) / 0.35 (0.06-0.82)
Subjects with Regional LN Involvement	53% (10/19)
⁸⁹ Zr-Df-IAB2M Positive Scans In Subjects With Regional LN Involvement	50% (5/10)
¹¹¹ In-CP Positive Scans In Subjects With Regional LN Involvement	0% (0/10)
CI Positive Scans In Subjects With Regional LN Involvement	11% (1/9)
Lymph Node Positive Pathology Samples	22% (27/121)
PET Positive Lymph Nodes Short Axis Diameter on CI	6.5mm (4.8-17.7 mm)
PET Positive vs PET Negative SUVpeak (p-value) at 48h Time Point	5.2 vs 2.0 (p=0.04)
Subjects with ⁸⁹ Zr-Df-IAB2M Positive Prostate Gland Uptake	42% (8/19)

Table 2: Final Summary Performance For Occult Nodal Disease Per Subject

Parameter	⁸⁹ Zr-Df-IAB2M PET/CT n=19	¹¹¹ In-CP SPECT/CT n=19	CI (CT or MRI) n=18
Sensitivity	50% (5/10)	0% (0/10)	11% (1/9)
Specificity	78% (7/9)	100% (9/9)	89% (8/9)
Positive Predictive Value (PPV)	71% (5/7)	0% (0/0)	50% (1/2)
Negative Predictive Value (NPV)	58% (7/12)	47% (9/19)	50% (8/16)
Accuracy	63% (12/19)	47% (9/19)	50% (9/18)
Discordance Rate	37% (7/19)	53% (10/19)	50% (9/18)



Detection of prostate cancer metastasis in HR subjects. 66 y.o. Gleason 9, PSA 24.2 ng/ml and negative CI imaging studies. Panel A represents coronal whole body PET/CT scans 24 hours following ⁸⁹Zr-Df-IAB2M injection. Red arrow indicates increased uptake in a pathologically confirmed node and prostate gland. Normal physiologic activity in the liver, kidney and bowel is labeled. Panel B is a magnification view of panel A highlighting tumor uptake in normal size right pelvic lymph node (red arrows) and with the prostate gland (white arrow). Panel C is a magnification view from corresponding ¹¹¹In-CP scan showing no abnormal uptake in pelvic lymph nodes (red arrows) and prostate gland (white arrow).

Conclusions

- ⁸⁹Zr-Df-IAB2M PET/CT outperformed ¹¹¹In-CP SPECT/CT in direct head-to-head comparison in subjects with negative CI scans using histopathology as truth standard.
- ⁸⁹Zr-Df-IAB2M had a significantly higher PPV compared to ¹¹¹In-CP on a subject basis.
- SUV values were significantly higher in pathologically positive nodes compared to pathologically negative nodes suggesting that quantitative assessments may be helpful in distinguishing true positive from false positive uptake in the future.
- Though not a primary endpoint ⁸⁹Zr-Df-IAB2M PET/CT detected prostate gland disease in up to 42% of subjects
- Further testing in HRPC subjects is warranted.

References

- Gburek B, Woodruff A, Wyman B, Keppler J, Wu A, Masci P and Korn R. Head-to-Head Comparison of ⁸⁹Zr-Df-IAB2M PET/CT to ¹¹¹In Capromab Pendetide SPECT/CT Scans in the Detection of Occult Prostate Cancer in Patients Undergoing Radical Prostatectomy (RP) with Negative Conventional Imaging (CI) Studies. *World Mol Imaging Congress 2015; Honolulu, Hawaii*

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