Bone metastases: Biology, treatment & palliation
Revisione Posters & Oral Abstracts

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Abstr #225

Predictive value of bone scan index using computer-aided diagnosis system for bone scans in patients receiving first-line hormone therapy for metastatic hormone-sensitive prostate cancer

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Introduction

Purpose: To evaluate the predictive value of bone scan index (BSI) using a computer-aided diagnosis system for patients receiving first-line hormone therapy for metastatic hormone-sensitive prostate cancer (mHSPC).

Materials and Methods: We identified 287 patients with bone metastasis (mHSPC) who received first-line hormone therapy (Table 1). Bone scan index (BSI) was calculated using computer-aided diagnosis system (CAD) software (BONEVAT, Fujifilm Medical Co., Ltd., Tokyo, Japan). The BSI was calculated as the sum of the maximum intensity of each lesion divided by the total body mass. The cutoff point for the BSI was set at 10.0.

Results: Among the 287 patients, the BSI was >10.0 in 145 patients (50.5%). The median PSA level at the start of hormone therapy was 17.5 ng/mL (range, 0.2-182 ng/mL). The median age was 72 years (range, 57-89 years). The median duration of hormone therapy was 14 months (range, 1-54 months). The median BSI was 10.0 (range, 1.0-29.0). The median PSA level at the start of hormone therapy was 17.5 ng/mL (range, 0.2-182 ng/mL). The median age was 72 years (range, 57-89 years). The median duration of hormone therapy was 14 months (range, 1-54 months). The median BSI was 10.0 (range, 1.0-29.0).

Conclusions: The BSI was a useful predictor of response to first-line hormone therapy in patients with mHSPC. The BSI was >10.0 in 145 patients (50.5%). The median PSA level at the start of hormone therapy was 17.5 ng/mL (range, 0.2-182 ng/mL). The median age was 72 years (range, 57-89 years). The median duration of hormone therapy was 14 months (range, 1-54 months). The median BSI was 10.0 (range, 1.0-29.0).
What about BSI (Bone Score Index)?

- amount of bone metastasis / whole body skeletal mass
- not to decide specific hot spot is metastasis or not

∑ \[ \text{Area of Metastases} \times C \]  
\[ \text{Total Anatomical Area} \]

C = Anatomical Area Coefficient

✓ diagnostic guide  ✓ prognostic guide
What about BSI (Bone Score Index)?

Bone Scan Index: Prognostic use is one of the most important applications

Events (death, skeletal related events, etc)

- BSI<1: good prognosis
- 1-5: moderate prognosis
- >5: poor prognosis

✓ diagnostic guide
✓ prognostic guide
Predictive value of bone scan index using computer-aided diagnosis system for bone scans in patients receiving first-line hormone therapy for metastatic hormone-sensitive prostate cancer – Abstr #225

**CONCLUSIONS**

- Patients’ age, initial PSA, and bone scan index (BSI) were the significant predictive factors for first-line hormone therapy in patients with metastatic hormone-sensitive prostate cancer (mHSPC).
- BSI might be useful tool for risk stratification of patients with mHSPC under the first-line hormone therapy.
- These findings might support the decision-making of induction of early chemotherapy for mHSPC.
Automated Bone Scan Index as a Quantitative Imaging Biomarker in Metastatic Castration Resistant Prostate Cancer Patients being treated with Enzalutamide

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BACKGROUND
The Unmet Need: A fully quantitative imaging biomarker to standardize the evaluation of change in bone scan of patients with metastatic castration-resistant prostate cancer (mCRPC) patients.

Bone Scan Index: A quantitative analysis of bone scintigraphy - Bone Scan Index (BSI), developed by Memorial Sloan-Kettering Cancer Center (Imtiaz et al. JCR 1998). In subsequent years, the BSI was automated by EXIN Diagnosis AB.

RESULTS
A week correlation was observed between automated BSI and the respective blood test biomarkers. Table 2. At baseline, adding the automated BSI to the blood based model significantly improved the C-index, from 0.67 to 0.73 (p<0.05). The combined predictive model of percent PSA change and change in automated BSI (C-index 0.71) was observed to be significantly higher than that of percent PSA change alone, p<0.05.

OBJECTIVE
In the multi-center study, we assessed the discriminatory strength of the automated BSI in predicting overall survival (OS) in mCRPC patients being treated with enzalutamide.

METHODS
Patients: Eighty of the eligible mCRPC patients had their baseline bone scans available for automated BSI analysis. Sixty-two and Forty-two of the eighty mCRPC patients had available bone scans at week twelve and at twenty-four weeks of treatment follow-up, respectively.

Automated BSI Analysis: This upgradable EXIN Bone AB software (version 2.0), was used to analyze the retrospectively collected bone scans and to generate automated BSI.

CONCLUSION
- The change in automated BSI has an additive clinical value to the change in PSA in mCRPC patients being treated with enzalutamide.
- The analytically validated automated BSI is an independent and a strong predictor of OS in mCRPC patients.
- The data serve as the foundation for future prospective studies aimed to clinically validate automated BSI as an imaging biomarker in mCRPC patients.
Automated bone scan index as a quantitative imaging biomarker indicative of efficacy to enzalutamide in patients with metastatic castrate resistant prostate cancer (mCRPC) – Abstr #226

<table>
<thead>
<tr>
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<th>C-index</th>
<th>SE</th>
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<tr>
<td>A. Baseline Analysis *</td>
<td></td>
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<tr>
<td>BSI</td>
<td>0.71</td>
<td>0.03</td>
</tr>
<tr>
<td>PSA</td>
<td>0.65</td>
<td>0.03</td>
</tr>
<tr>
<td>ALP</td>
<td>0.67</td>
<td>0.03</td>
</tr>
<tr>
<td>HgB</td>
<td>0.26</td>
<td>0.03</td>
</tr>
<tr>
<td>PSA + ALP + HgB</td>
<td>0.67</td>
<td>0.03</td>
</tr>
<tr>
<td>BSI + PSA + ALP + HgB</td>
<td>0.72</td>
<td>0.03</td>
</tr>
<tr>
<td>B. Change (Δ) at week 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ BSI</td>
<td>0.75</td>
<td>0.05</td>
</tr>
<tr>
<td>Δ PSA</td>
<td>0.73</td>
<td>0.05</td>
</tr>
<tr>
<td>Δ PSA + Δ BSI</td>
<td>0.77</td>
<td>0.05</td>
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</table>

Auto-BSI and its change demonstrated independent and a strong association with OS in mCRPC pts being treated with enzalutamide.

The study serve as a foundation for prospective validation of auto-BSI as an imaging biomarker indicative of efficacy to enzalutamide.
Abstr #191

Integration of Bone Scan and Computerized Tomography to Assess Bone Metastasis in Metastatic Castration-resistant Prostate Cancer

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**Purpose**
- Assess the integration of serial changes in bone scan (BS) and computerized tomography (CT) findings and its potential association with overall survival (OS) in men with metastatic castration-resistant prostate cancer (mCRPC).

**Background**
- Progression of bone metastasis in mCRPC is currently assessed solely by BS.
- BS are not very reliable and limited in sensitivity and specificity.
- We assessed bone progression by integrating BS and CT findings.
- The association of this composite metric with OS was explored.

**Methods**
- Data were obtained from patients (pts) receiving docetaxel chemotherapy (O) or post-docetaxel androgenal (O).
- Pts with baseline and on therapy CT and BS within 90 days were eligible.
- CT and BS underwent central radiology review to assess for new lesions.
- Progressive disease (PD) was defined as ≥1 new lesion on either BS or CT.
- Cox proportional hazards regression was used to explore the potential prognostic ability of OS and therapy was a stratification factor throughout.

**Results: Association of combined BS or CT findings with OS**

**Summary of Results**
- 28 pts were evaluable; 18 received O and 10 received O
- The mean age was 71.4 years and median (95% CI) OS was 18.4 (9.7–35.4) months
- 4 pts (14.3%) had PD on both BS and CT
- 2 pts (7.1%) had PD on CT but not BS
- 3 pts (10.7%) had PD on BS but not CT
- Pts with PD on BS or CT had worse OS (HR=2.68, 95% CI=1.04–6.90, p=0.043) than those with no PD on either BS or CT
- Examining individual lesions, 4 pts had ≥1 new lesion on CT but not BS, and they had worse OS (HR=3.72, 1.01–13.66, p=0.048)
- No significant difference in OS was observed for 4 pts with new lesions on BS but not CT (HR=2.67, 0.58–12.32, p=0.21).

**Conclusion**
- This hypothesis-generating study suggests the integration of ≥1 new lesion on CT and/or BS within 90 days of initiating therapy in mCRPC may robustly capture bone progression and predict OS.
- This composite metric determined at a single time-point needs to be compared with current criteria, which advocate bone progression as ≥2 new lesions on BS and ≥2 new lesions in a repeat BS after 26 weeks.
Integration of bone scan (BS) and computerized tomography (CT) findings as an endpoint to assess bone metastasis in metastatic castration-resistant prostate cancer (mCRPC) – Abstr #191

Figure 4: OS based on PD on CT only, or BS only, or CT and BS vs no PD

- 4 pts (14.3%) had PD on both BS and CT
- 2 pts (7.1%) had PD on CT but not BS
- 3 pts (10.7%) had PD on BS but not CT
- Pts with PD on BS or CT had worse OS (HR=2.68, 95% CI=1.04-6.90, p=0.041) than those with no PD on either CT or BS
Bone tumor progression vs. scan “flare” in new lesions detected on early bone scans in patients with chemonaive metastatic castration resistant prostate cancer (mCRPC) treated with placebo or enzalutamide

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ABSTRACT

Background: To differentiate between bone metastasis progression versus “flare” in new lesions detected on early bone scans (<12 weeks), 2 additional lesions on a confirmatory scan (6-8 weeks) are proposed. This reduces the risk of misinterpreting “flare” as progression in responding patients. Independent central review (ICR) of scans from placebo (PL)-controlled trials can help evaluate the role of confirmatory scans as PL should neither delay progression nor affect “flare”.

Methods: The ICR datasets from 3 randomized PL-controlled trials of enzalutamide (ENZ) in pts with chemotherapy-naive mCRPC were examined. Pts with 2-2 new lesions on Week 6 bone scans who underwent confirmatory scans were analyzed. Scan “flare” was defined as unconfirmed progression associated with responses in PSA (>50% decline).

Results: Confirmed tumor progression on Week 2 bone scan occurred more in pts on PL than in pts on ENZ (57% vs. 14%). In pts with unconfirmed progression, scan “flare” occurred in 86% of pts on ENZ. Of the pts with unconfirmed progression who had PSA progression, nearly 60% progressed on follow-up scans.

Conclusion: The data from the large PL-controlled trial provide strong evidence for performing confirmatory bone scans to verify tumor progression early versus “flare” in new lesions on mCRPC. For pts with unconfirmed progression, early PSA progression appears associated with progression on follow-up scans. This can help differentiate between tumor progression secondary to PLC treatment and “flare” in initial assessments of the antitumor activity of an effective treatment.

REFERENCES

Tumor progression versus bone scan “flare” in new lesions detected on early bone scans in patients with chemo-naïve metastatic castration resistant prostate cancer (mCRPC) treated with placebo or enzalutamide—Abstr #305

Table 2. Confirmed vs. Unconfirmed Bone Tumor Progression

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<tr>
<th>Treatment Arm</th>
<th>Placebo</th>
<th>Enzalutamide</th>
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<tr>
<td>Pts with $\geq$ 2 new lesions at Week 9 Bone Scan Followed by Confirmatory Bone Scan*</td>
<td>293 (100%)</td>
<td>222 (100%)</td>
</tr>
<tr>
<td>Confirmed Bone Tumor Progression (with $\geq$ 2 additional new lesions)</td>
<td>167 (57%)</td>
<td>32 (14%)</td>
</tr>
<tr>
<td>Unconfirmed Bone Tumor Progression (without $\geq$ 2 additional new lesions)</td>
<td>126 (43%)</td>
<td>190 (86%)</td>
</tr>
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</table>

*Not including patients who had no confirmatory scans performed or reported.

Strong evidence for performing confirmatory bone scans to verify tumor progression in new lesions on early bone scans in mCRPC
Bone scintigraphy vs NAF PET/TC

- initial staging
- evaluation of suspected recurrence
- extend of disease

- MORE ACCURATE initial staging
- EARLIER evaluation of suspected recurrence
- MORE QUANTITATIVE MEASURE OF extend of disease
Quantitative total bone imaging (QTBI): an innovative tool that allows extraction of comprehensive functional information in all osseous metastases, as well as treatment response in individual lesions, using 18F-Sodium Fluoride (NaF) PET/CT.
Harmon S. et al - [18F]NaF PET/CT imaging biomarkers of progression-free survival in metastatic prostate cancer – Abstr #277

**Conclusions**

- With superior detection and response quantification abilities, NaF PET/CT provides an ideal platform for improved characterization and response assessment of metastatic bone disease.
- Several imaging metrics evaluated throughout the course of therapy provided strong correlation to PFS.
- There is indication that total functional burden of disease during treatment with taxane or AR-directed therapy is a strong predictor of PFS in patients with metastatic CRPC to bone.
- Change in number of lesions was predictive of treatment efficacy.
- This work supports ongoing development of NaF PET/CT based imaging biomarkers in mCRPC.
2016 Genitourinary Cancer Symposium

Is NaF PET/CT Ready to Replace Technetium for Clinical Care and Research?

Glenn Liu, MD
Associate Professor of Medicine and Medical Physics
Director, Genitourinary Oncology and Phase 1 Research Programs
University of Wisconsin Carbone Cancer Center
January 7, 2016