Quantitative Imaging by Automated Bone Scan Index (BSI) as a Response Biomarker in Standard Clinical Care of Patients with Metastatic Castration Resistant Prostate Cancer (mCRPC) 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 mCRPC.

Prostate Cancer Working Group Criteria (PCWG2): The first semi-quantitative guideline to standardize the bone scan evaluation. Recent work published by Morris et al., (JCO, 2015) showed positive clinical association of PCWG2 guideline with overall survival.

Bone Scan Index: A quantitative analysis of bone scintigraphy – BSI, was developed by Memorial Sloan Kettering Cancer Center. In subsequent years, the BSI was automated by EXINI Diagnostics AB in collaboration with Memorial Sloan Kettering Cancer Center. In this registry study, we evaluated BSI to access response in mCRPC patients being treated with Enzalutamide.

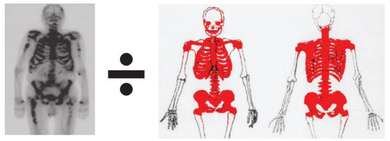

Fig 1. BSI expresses the tumor burden in bone as a percent of the total skeletal mass (Dennis et al., JCO, 2012)

Objective: Primary objective in this retrospective study was to evaluate the association of on-treatment change in BSI and PSA with overall survival (OS) in patients being treated with Enzalutamide.

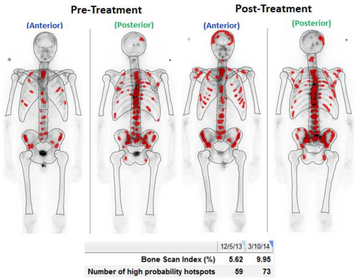

Fig 2. Automated BSI Calculation by EXINI bone^{BSI}

METHOD

Patients: Patients with mCRPC, at Skåne University Hospital, Sweden, who initiated treatment with FDA approved Enzalutamide after failing chemotherapy, were eligible for evaluation in this retrospective study. Patients with available bone scans, prior to treatment start, were included in the study and evaluated for automated BSI. Treatment follow-up bone scan available, preferably, after 12 weeks of treatment with Enzalutamide was evaluated for automated BSI.

Clinical, laboratory and survival data was collected from the computerized medical records. BSI was calculated using the EXINI bone^{BSI} software (EXINI Diagnostics AB, Lund, Sweden) . The retrospective registry study was approved by the Regional Ethical Review Board at Lund University, Sweden.

RESULTS

Thirty-five mCRPC patients, who initiated Enzalutamide treatment at Skåne University Hospital, were eligible for the BSI analysis. The demographic is listed below (Table 1). Follow-up scans for the BSI analysis were available from 24 patients. The average week interval between the baseline and follow-up bone scan was 12.4 weeks (IQR 10 – 14 weeks).

Table 1. Characteristics of patients enrolled in the study

Demographic	Median (range)
Age	70 (62 – 83)
Diagnosis PSA	34 (4.2 – 825)
Gleason Score	8 (7 – 10)
Dead (follow-up in wks)	16 (48 wks)

Prior Treatment	N=35 (%)
Primary	
Radiation	9 (26%)
Surgery	14 (40%)
Chemo	
Exposed to 1st line	35 (100%)

BSI at baseline, follow-up and BSI change from baseline to follow-up were all significantly associated with OS, while the PSA values were not (Table 2).

Table 2. OS was associated with BSI at both baseline and at follow-up as opposed to that of PSA

BSI & PSA as continuous variable	OS			
	N	HR	95% CI	P value
BSI at Baseline	35	1.29	1.06 – 1.39	<0.01
PSA at Baseline	35	1.00	0.99 – 1.00	0.566
BSI at Follow-up	24	1.39	1.08 – 1.59	<0.01
PSA at Follow-up	24	1.00	0.99 – 1.00	0.228
BSI Change	24	1.81	1.12 – 2.96	<0.05
PSA Change	24	1.00	0.99 – 1.00	0.756

Patients with increase in BSI from baseline to follow-up (n=13) showed a worse survival compared to patients with no change or decline in BSI during treatment (n=11) (Figure 3 and Table 3).

Fig 3. Kaplan Meier survival analysis

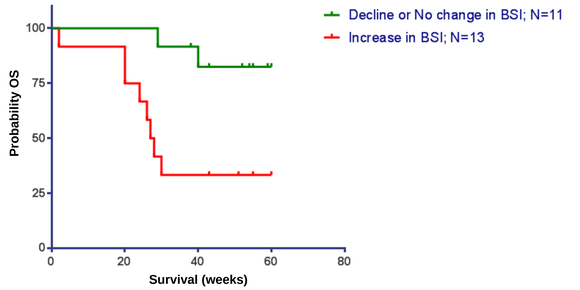

Table 3. Overall Survival vs. change in BSI post treatment with Enzalutamide; N=24

Time Point	BSI			
	N	Median OS (N)		P
		BSI increase;	BSI decrease or stable	
BL to FU1	24	27 wks (13)	Not reached (11)	<0.0001

CONCLUSION

BSI can standardize the fully quantitative analysis of on-treatment change in bone scan. In this retrospective registry study, we showed that automated BSI and its relative change were associated with overall survival in mCRPC patients receiving Enzalutamide as standard of care treatment.

FUTURE DIRECTION

The result deserves further validation, in controlled investigational studies, of BSI as a quantitative imaging biomarker indicative of efficacy response to second-line treatment in castrate resistant prostate cancer patients.

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