EXAMINING SKELETAL-RELATED EVENTS IN AUSTRALIAN MEN WITH CASTRATION-RESISTANT PROSTATE CANCER (CRPC)

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Background

Bone metastases are common in CRPC, occurring in over 90% of patients. They are associated with significant morbidity from skeletal-related events (SREs), which include pathological fractures, spinal cord compression and symptomatic bone lesions requiring radiotherapy or surgery. Bone-modifying agents (BMAs) reduce SRE rates. However, no survival benefit has been demonstrated and long-term use can lead to osteonecrosis of the jaw (ONJ). In Australia, BMA use is inconsistent and the optimal timing, schedule and duration remains unclear.

Discussion re-emerged following results presented at the ESMO 2018 congress, demonstrating the importance of BMAs even in the era of highly active life-prolonging therapies. Our study aimed to examine SRE rates and BMA use in Australian men with CRPC and bone metastases.

Methods

The electronic CRPC Australian Database (ePAD) prospectively collects real world data from multiple sites. Baseline characteristics, treatment and survival data on consecutive CRPC patients receiving systemic therapy are recorded by review of medical records.

Patients with bone metastases were identified and data from the ePAD registry, including 11 sites, were extracted. Descriptive statistics were used to examine BMA use, SRE rates and toxicity. Lines of systemic therapy were defined as life-prolonging treatment agents added to androgen deprivation and/or first-generation anti-androgen therapy.

Results

We identified 263 men with bone metastases who were receiving systemic therapy. After a median follow up of 17.2 months from development of CRPC, SREs were recorded in 80 men. In total, 125 men (48%) received BMAs with baseline characteristics presented in Table 1. BMA use was associated with younger age (p=0.009), but not performance status or PSA kinetics. Of those who received BMAs, 70% received denosumab at various schedules (Figure 1). The most common SREs were symptomatic bone lesions requiring intervention (69%). Importantly, more than half (52%) occurred prior to commencing systemic therapy for CRPC (Table 2).

Table 1: Patient and Disease Characteristics

Patient characteristic	BMA [N=125]	No BMA [N=138]	P-value
Median age at CRPC	71 years	74.5 years	0.009
ECOG			
0 - 1	118 (94%)	125 (91%)	0.35
≥ 2	7 (6%)	13 (9%)	
Visceral metastases			
Yes	13 (10%)	11 (8%)	0.53
No	112 (90%)	127 (92%)	
PSA Doubling Time			
≤ 3 months	70 (56%)	63 (46%)	0.20
> 3 months	31 (25%)	38 (28%)	
Unknown	24 (19%)	37 (27%)	
Hospital site			
Private	69 (55%)	76 (55%)	> 0.99
Public	56 (45%)	62 (45%)	

Figure 1: BMA Choice (inner circle) and Schedule (outer circle)

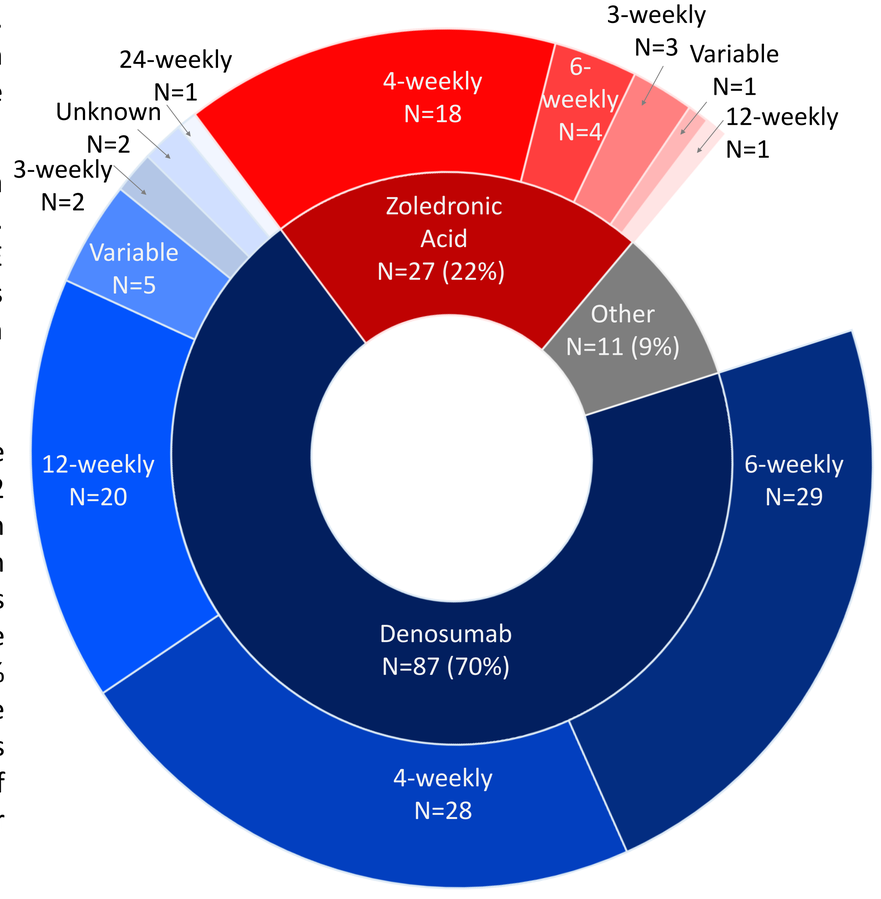
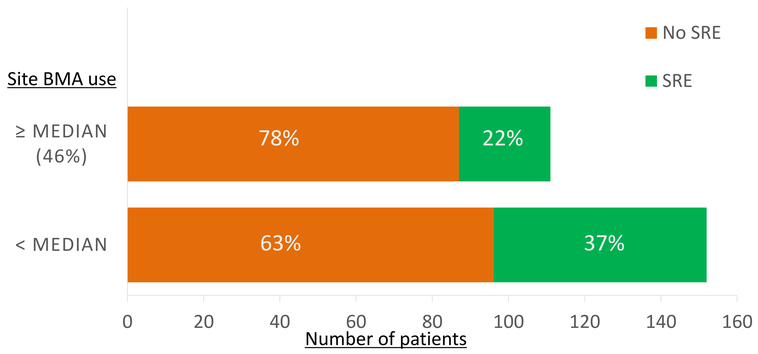


Table 2: Characteristics of First SRE

SRE Characteristic	Number of patients (%)
SRE type	
- Symptomatic bone lesion requiring RT or surgery	55 (69%)
- Clinically significant fracture	17 (21%)
- Cord compression	6 (8%)
- Other (hypercalcemia, not specified)	2 (3%)
SRE timing	
- Prior to systemic therapy	42 (52%)
- During first-line therapy	30 (38%)
- During second-line therapy or later	8 (10%)
Bone agent use	
- at time of SRE	16 (20%)
- after developing SRE	29 (36%)
- never received	35 (44%)

Patients treated at sites with lower BMA use had significantly higher SRE rates (p=0.01; Figure 2). BMA-related toxicity was reported in 4 patients (3%), with 1 case of documented ONJ (1%).

Figure 2: SRE occurrence in treatment sites with BMA use above and below the median rate of use



Conclusion

In our ePAD analysis SREs often occurred early in the disease trajectory, prior to the initiation of systemic therapy for CRPC. Few patients were receiving BMAs at time of first SRE. The low ONJ rate likely reflects the limitations of retrospective data collection and the modest follow up period. The higher SRE rate among patients treated at sites with lower BMA use supports the importance of considering earlier initiation of BMAs and systemic anti-cancer therapies to prevent SREs in men with CRPC.

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