USE OF BONE-MODIFYING AGENTS IN AUSTRALIAN MEN WITH CASTRATION-RESISTANT PROSTATE CANCER (CRPC)

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Background

Bone metastases occur in more than 90% of men with advanced prostate cancer, causing significant morbidity and mortality. Denosumab and zoledronic acid are bone-modifying agents (BMA), approved in Australia for men with CRPC and bone metastases.

However, pivotal studies evaluating BMA were conducted prior to the introduction of highly-active hormonal therapies and demonstrated reduction in skeletal-related events without survival benefit. Consequently, the use and scheduling of BMA varies widely across centres, with divergent opinions amongst clinicians and in current treatment guidelines.

Objective

We aimed to examine current prescribing patterns of BMA in men with CRPC and bone metastases, who are receiving systemic therapy.

Methods

The Electronic CRPC Australian Database (ePAD) was interrogated. Data from ten Australian sites were included at the time of analysis.

Information extracted included patient and disease characteristics, BMA choice and treatment schedule. Data were stratified by the presence of bone metastases and line of systemic therapy.

Results

Men with CRPC and bone metastases were included in the analysis. There were 190 men with bone metastases receiving first-line systemic therapy and 90 receiving second-line therapy. First-line therapy was defined as the systemic treatment commenced following progression on androgen deprivation therapy and/or first generation antiandrogen agents. The next subsequent systemic therapy was defined as second-line. Tables 1 and 2 describe BMA use during systemic therapy.

Table 1: Patient and Disease Characteristics

Patient characteristic	BMA [N=65]	No BMA [N=125]	P-value
Median age at CRPC	73.1 years	72.1 years	0.13
ECOG			
0 - 1	62 (95%)	115 (92%)	0.54
≥ 2	3 (5%)	10 (8%)	
Site of metastases			
Visceral	4 (6%)	14 (11%)	0.45
Lymph node	22 (34%)	45 (36%)	
Bone only	39 (60%)	66 (53%)	

After a median follow up of 16 months, the majority of patients receiving BMA (48 (74%) in first-line and 31 (70%) in second-line) remained on treatment. The most common treatment agent was denosumab (Figure 1), with a 6-weekly schedule used most frequently (Figure 2). During first-line therapy, BMA use was significantly higher in patients receiving docetaxel, compared to those treated with enzalutamide or abiraterone (Table 3).

Table 2: BMA use by hospital site

Site	First line BMA	Second line BMA
Total	65/190 (34%)	44/90 (49%)
Private	33/99 (33%)	25/50 (50%)
Public	32/91 (35%)	19/40 (48%)

Figure 1: BMA use during first- and second-line therapy

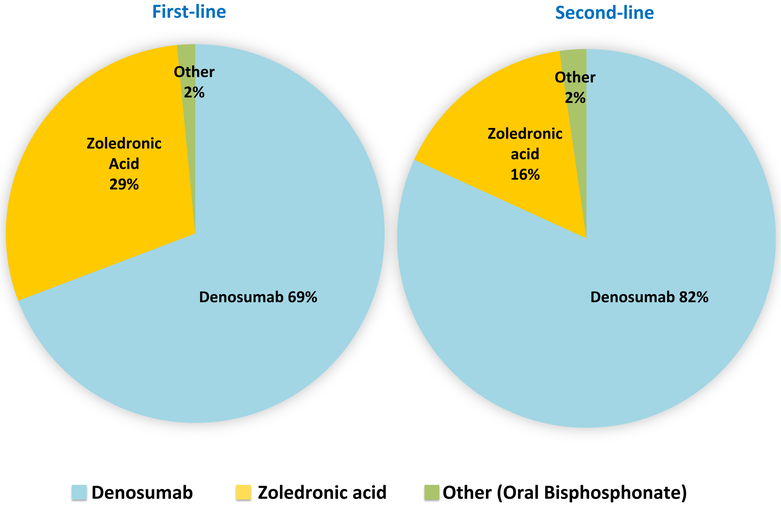

Figure 2: BMA schedules during first- and second-line therapy

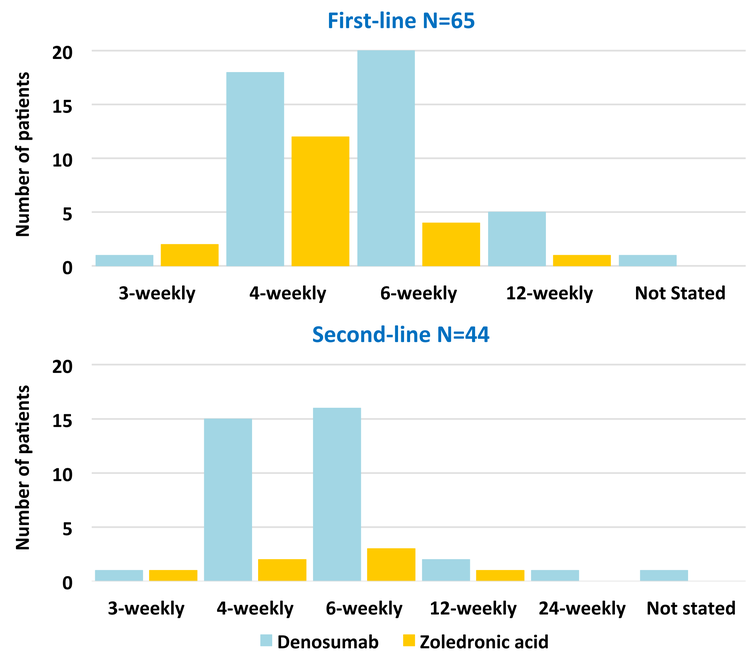

Table 3: BMA use by treatment agent

First-line therapy	BMA	No BMA	All	
Docetaxel	32 (54%)	27 (46%)	59	P = 0.0011
Abiraterone	9 (21%)	34 (79%)	43	
Enzalutamide	23 (31%)	52 (69%)	75	
Other	1 (8%)	12 (92%)	13	
Second-line therapy	**BMA**	**No BMA**	**All**	
Docetaxel	7 (35%)	13 (65%)	20	P= 0.500
Abiraterone	12 (52%)	11 (48%)	23	
Enzalutamide	17 (57%)	13 (43%)	30	
Cabazitaxel	6 (50%)	6 (50%)	12	
Other	2 (40%)	3 60%)	5	

Conclusion

Our results demonstrate a low rate of BMA use in Australian men with CRPC and bone metastases. The dominant 6-weekly treatment schedule is likely based on convenience, given the absence of efficacy data. Overall, these findings reflect the lack of robust evidence regarding BMA within the current treatment landscape.

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