Leukopenia as a Risk Factor for Osteonecrosis of the Jaw in Metastatic Prostate Cancer Receiving Zoledronic Acid and Docetaxel

Introduction and Objective: The use of bisphosphonates (BPs) is associated with osteonecrosis of the jaw (ONJ). Chemotherapeutic agents including docetaxel (TAX) may increase the risk of ONJ, especially when administered concomitantly with BPs. The aim of this study was to determine whether TAX could increase the risk of ONJ in patients with prostatic adenocarcinoma (PC) receiving zoledronic acid (ZA), one of BPs that have been used in cancer patients.

Materials and Methods: The medical records of 111 PC patients receiving ZA between September 2006 and March 2011 at our institutions were reviewed to assess the incidence and risk factors for ONJ.

Results: Nine patients (8.1%) developed ONJ during a median follow-up of 14.5 months. Univariate analysis revealed that TAX chemotherapy (p=0.037, Hazard ratio (HR) 6.611), tooth extraction during ZA therapy (p<0.001, HR 11.254), and high PSA level (p=0.019, HR 8.008) at the start of ZA were predictive factors. Multivariate analysis showed that TAX chemotherapy (p=0.011, HR 56.35) and tooth extraction (p=0.039, HR 7.471) remained as independent predictors. Among those receiving TAX chemotherapy, multivariate analysis identified tooth extraction (p=0.009) and nadir WBC counts less than 1,000/μL during TAX chemotherapy (p=0.030) as the independent risk factors.

Conclusions: Multivariate analysis detected tooth extraction and nadir WBC counts less than 1,000/μL as the risk factors for ONJ in metastatic prostate cancer treated with ZA and TAX combination therapy, underscoring the significance of leucopenia in the development of ONJ.

[illegible]	Yes	6	0.773 (0.111 – 5.524)	0.805	0.102 (0.001 – 7.561)	0.298
Smoking	No	44	Referent	0.263		
	Yes	11	<0.001 (0.037 – 2.460)			
Tooth extraction (within 6 months)	No	50	Referent	<0.001*	Referent	0.009*
	Yes	6	10.747(10.940 – >100.0)		15.974 (1.990 – >100.0)	
Dentures use	No	29	Referent	0.425	Referent	0.916
	Yes	27	1.753 (0.431 – 7.362)		0.889 (0.099 – 7.983)	
Extent of disease, grades 1, 2		34	Referent	0.311		
grades 3, 4		20	0.365 (0.090 – 2.153)			
Visceral metastasis	No	53	Referent	0.732		
	Yes	3	<0.001 (0.001 – >100.0)			
PSA=<27.6 ng/ml (median)		24	Referent	0.004*	Referent	0.165
PSA>27.6 ng/ml		32	10.976 (1.921 – 34.062)		25.737 (0.263 – >100.0)	
Elevation of ALP (>360 IU/L)	No	32	Referent	[illegible]		
	Yes	24	0.376 (0.088 – 2.225)			
Anemia (hemoglobin<13.8 g/dL)	No	5	Referent	0.192		
	Yes	51	>100.0 (0.529 – 23.894)			
Analgesics use	No	34	Referent	0.526	Referent	0.790
	Yes	22	0.533 (0.093 – 3.378)		0.706 (0.054 – 9.163)	
Steroid use	No	5	Referent	0.351	Referent	0.075
	Yes	51	0.389 (0.010 – 5.229)		35.790 (0.697 – >100.0)	
Number of ZA administration =<5		26	Referent	0.815		
>5		30	1.203 (0.248 – 5.878)			
Nadir WBC<1000	No	48	Referent	0.08	Referent	0.03*
	Yes	8	3.230 (0.800 – 39.386)		0.080 (0.008 – 0.785)	

*, p<0.05; ZA=zoledronic acid; CI=confidence interval; ALP=alkaline phosphatase; TAX=docetaxel