

THE LANCET Oncology

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Aft R, Naughton M, Trinkaus K, et al. Effect of zoledronic acid on disseminated tumour cells in women with locally advanced breast cancer: an open label, randomised, phase 2 trial. *Lancet Oncol* 2010; published online April 1. DOI:10.1016/S1470-2045(10)70054-1.

Web appendix for :

Effect of zoledronic acid on disseminated tumour cells in women with locally advanced breast cancer: an open label, randomised, phase 2 trial

Supplemental Table 1: Bone Turnover Markers Changes over Time According to Treatment Group

All Patients										
Marker	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean	% Change from baseline	P-value*	N	Mean	% Change from baseline	P-value*	
NTx (nmol/mol)	0	59	38.61			60	38.35			<0.0001
NTx	3	52	48.40	25.37	<0.0001	57	17.35	-54.76	<0.0001	
NTx	12	39	50.77	31.49	0.0474	41	17.46	-54.46	<0.0001	
Osteo (ng/ml)	0	58	11.38			60	12.24			<0.0001
Osteo	3	50	14.95	31.41	0.0007	57	9.57	-21.76	<0.0001	
Osteo	12	40	16.07	41.22	0.0012	42	7.74	-36.76	<0.0001	
BSAP (ug/L)	0	58	10.31			60	9.69			<0.0001
BSAP	3	51	10.44	1.25	0.7739	57	7.26	-25.05	<0.0001	
BSAP	12	40	13.60	31.90	0.0012	42	6.52	-32.75	<0.0001	
Premenopausal Patients										
Marker	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean	% Change from baseline	P-value*	N	Mean	% Change from baseline	P-value*	
NTx	0	33	36.12			31	39.39			<0.0001
NTx	3	30	48.90	35.38	<0.0001	30	17.37	-55.90	<0.0001	
NTx	12	21	46.62	29.07	0.1460	22	17.86	-54.66	<0.0001	
Osteo	0	32	10.98			31	11.27			<0.0001
Osteo	3	29	14.10	28.42	0.0013	30	8.75	-22.36	0.0019	
Osteo	12	21	15.03	36.89	0.0242	22	7.17	-36.38	<0.0001	
BSAP	0	32	9.31			31	8.91			<0.0001
BSAP	3	30	10.15	9.02	0.2162	30	7.10	-20.31	0.0025	
BSAP	12	21	13.77	47.91	0.0028	22	6.33	-28.96	<0.0001	
Postmenopausal Patients										
Marker	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean	% Change from baseline	P-value*	N	Mean	% Change from baseline	P-value*	
NTx	0	26	41.77			29	37.24			0.0009
NTx	3	22	47.73	14.27	0.2119	27	17.33	-53.46	<0.0001	
NTx	12	18	55.61	33.13	0.1887	19	17.00	-54.35	<0.0001	
Osteo	0	26	11.87			29	13.27			<0.0001
Osteo	3	21	16.13	35.89	0.0530	27	10.49	-20.95	0.0099	
Osteo	12	19	17.22	45.07	0.0222	20	8.36	-37.00	0.0068	
BSAP	0	26	11.53			29	10.53			<0.0001
BSAP	3	21	10.85	-5.90	0.4449	27	7.45	-29.25	0.0068	
BSAP	12	19	13.41	16.31	0.1416	20	6.73	-36.09	0.0008	

In premenopausal women, significant elevations were observed compared to baseline for NTx and osteocalcin at 3 months (both $p < 0.001$) and osteocalcin and BSAP at 12 months (both $p < 0.02$). In postmenopausal women, a significant elevation in osteocalcin was observed at 12 months ($p = 0.022$).

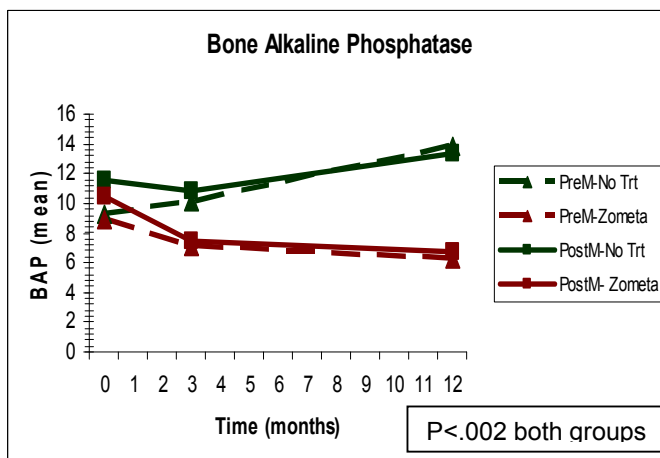
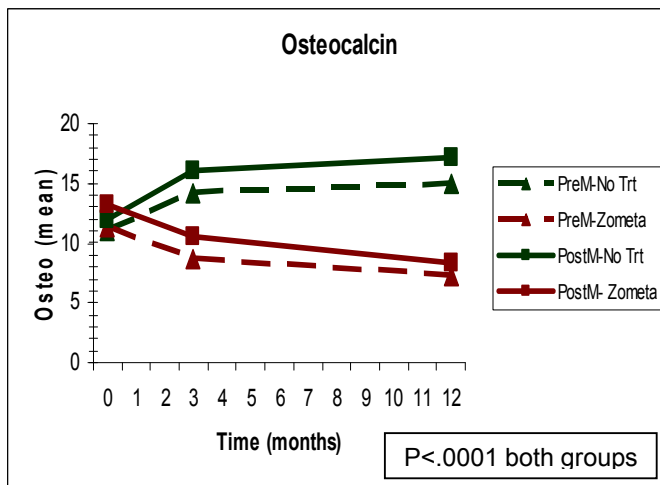
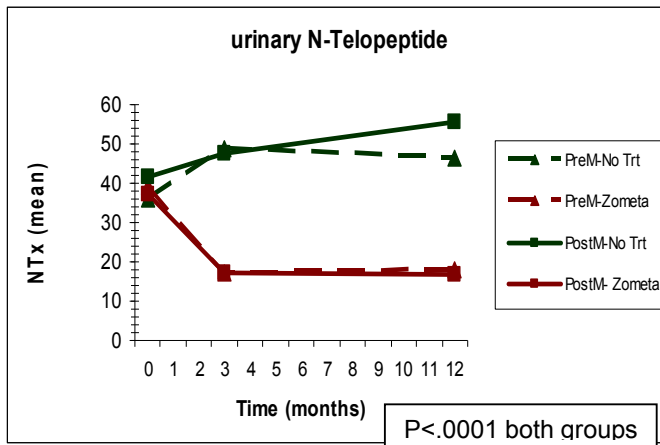
Supplemental Table 2. Bone Mineral Density Changes over Time According to Treatment Group

All Patients										
	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	
Hip	0	53	0.949			56	1.001			
	12	42	0.915	-3.53	0.0002	41	1.059	5.79	0.0275	<0.0001
Spine	0	52	1.041			56	1.084			
	12	42	0.995	-4.42	0.0054	41	1.109	2.31	0.5861	0.0519
Wrist	0	53	0.585			56	0.594			
	12	41	0.571	-1.41	0.0516	40	0.607	1.17	0.5157	0.0191
Premenopausal Patients										
	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	
Hip	0	29	0.966			30	1.043			
	12	22	0.929	-3.83	0.0051	20	1.142	9.49	0.0198	0.0003
Spine	0	23	1.087			30	1.165			
	12	22	1.011	-6.99	0.0001	20	1.202	3.16	0.8602	0.0185
Wrist	0	29	0.586			30	0.614			
	12	21	0.584	-0.20	0.0764	19	0.629	1.25	0.3453	0.3333
Post Menopausal										
	Time (months)	No ZA				ZA				P (Comparing %Change in ZA vs no ZA)
		N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	N	Mean (gm/cm ²)	% Change from Baseline	P* (t0 vs t12)	
Hip	0	24	0.927			26	0.953			
	12	20	0.900	-2.91	0.0009	21	0.979	2.73	0.4964	0.011
Spine	0	24	0.988			26	0.990			
	12	20	0.977	-1.11	0.5645	21	1.021	3.13	0.0066	0.5031
Wrist	0	24	0.583			26	0.571			
	12	20	0.557	-2.66	0.1813	21	0.588	1.67	0.1158	0.0439

Premenopausal women experienced a significant gain in bone density at the hip (p=0.0198) and postmenopausal women experienced a significant gain in the spine compared to baseline (p=0.0066).

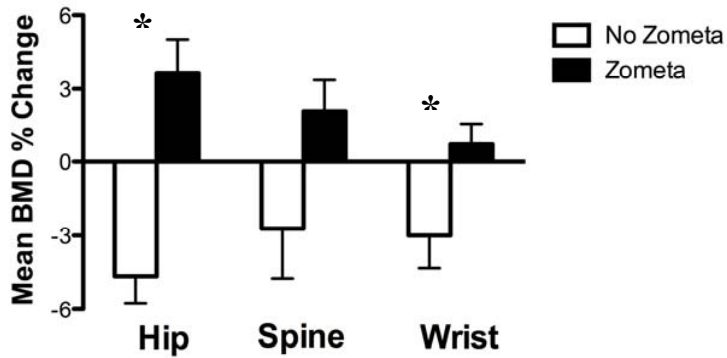
Supplemental Figure 1. Bone Turnover Markers by time according to menopausal status and treatment arm.

Standard error of the mean for bone turnover markers. P-values correspond to intra-group comparisons from baseline to 12 months.

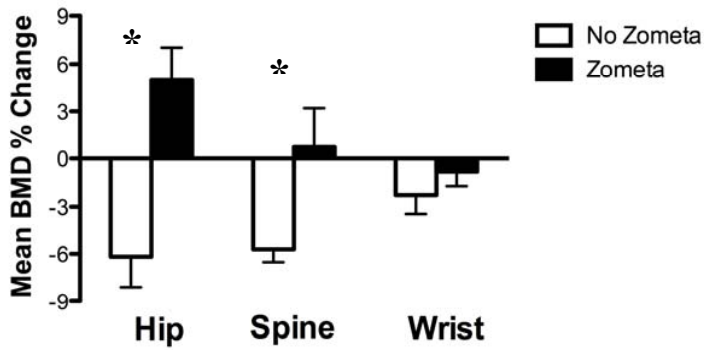


Supplemental Figure 2. Mean percent change in Bone Mineral Density at one year according to site, menopausal status, and treatment arm

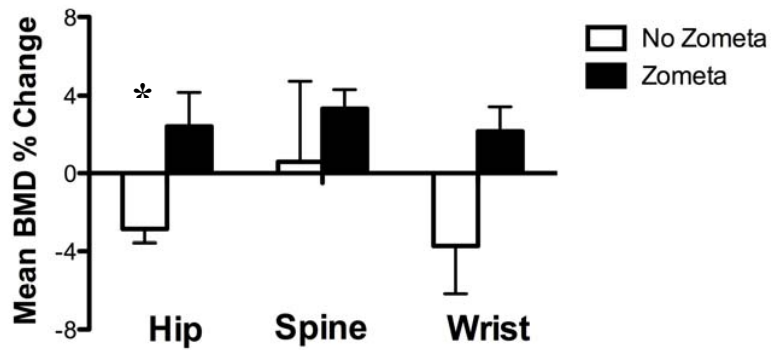
Standard error of the mean percent change in bone density at 12 months.



Premenopausal Patients



Postmenopausal Patients



* P=<0.05