VALUE OF BONE RESORPTION MARKERS TO PREDICT SKELETAL RELATED EVENTS AND RESPONSE TO BISPHOSPHONATE THERAPY IN PATIENTS WITH BONE METASTASES

(A PROSPECTIVE RANDOMIZED STUDY)

THESIS
Submitted in fulfilment of
MD Degree in Clinical Oncology

BY

Nermine Shawki Kamal

(MBBCH, MSC Radiation Oncology, Cairo University)

Supervised by

Prof. Dr.Wafaa El Metenawy

Professor of Radiation and cancer biology
Cairo University

Prof. Hamdy Abdel Azim

Professor of Clinical Oncology
Faculty of Medicine
Cairo University

Prof. Emad Hamada

Professor of Clinical Oncology
Faculty of Medicine
Cairo University

Department of Clinical Oncology & Nuclear Medicine
Kasr El Aini Faculty of Medicine
Cairo University
2009

ABSTRACT

The prospective analysis of urinary N-telopeptides, collagen break down products type I (NTX), in patients with metastatic bone disease revealed a positive relation between NTX level and risk of Skeletal related events (SREs). Normalization of NTX level at 3 months decreases the rate of serious types of SREs (pathological fractures and cord compression). Zoledronic acid decreases the rate of one or more SREs by four times in patients with elevated NTX levels compared to no Zoledronic acid.

Key words : metastatic bone disease; bone markers; N-telopeptides; NTX; Skeletal related event; SRE.

ACKNOWLEDGEMENT

I would like to express my deepest gratitude and thanks to Professor Wafaa el Metenawy, Prof of Radiobiology, Kasr El Aini Faculty of Medicine, Cairo University, for her supervision, great support and collaboration during this work.

Words cannot express my profound gratitude and appreciation to my dearest professor and mentor Prof. Hamdy A Azim, Prof of Clinical Oncology, Kasr El Aini Faculty of Medicine, Cairo University, for his continuous guidance, encouragement, valuable advice and dedicated time. I will always be indebted to him for his great support at all times.

I extend my thanks and gratitude to Professor Emad Hamada, Prof of Clinical Oncology, Kasr El Aini Faculty of Medicine, Cairo University, for his valuable supervision, guidance and continuous encouragement and support throughout this work.

A special thanks to Professor Hanna Attia, Prof of Clinical Oncology, Kasr El Aini Faculty of Medicine, Cairo University, for her help and encouragement in this work.

Thanks and gratitude for Mme Adila, technician in the Nemrock Laboratory, for her great help, efforts and collaboration in the study.

A special thanks to my dearest colleagues, nurses and staff at Cairo Oncology Centre for their great support and help in the fulfilment of this work.

I would also like to thank all my professors and colleagues in Nemrock and Bmt unit for their help and support.

Last but not least, my gratitude is beyond expression to my husband, my family, and my dear friends for their moral support throughout this work.

CONTENTS

List of Figures in Results section

List of Tables

Tables in Review of literature

Tables in Result Section

List of Figures

Figures in Review of literature

Results

Results

Table (7) NTX level (nmol/mmolcr) according to origin of metastases

NTX level	Breast	Prostate	Myeloma	P value
median	83	79	70	
minimum	14.5	19	14	
maximum	1904	300	300	0.27

Table 7.No statistical significance between the NTX level at baseline when sub-grouping the patients according to the origin of metastases (p=0.27).

Table 8. Distribution of baseline pain score among the groups

	GROUPS								Total
	A		B1		B2		C		
BPI Score	No	%	No	%	No	%	No	%	
Mild (0-5)	0		5	(25)	12	(44.4)	20	(66.7)	37
Moderate (6-9)	0		15	(75)	15	(55.6)	10	(33.3)	40
Severe (10)	23	(100)	0		0		0		23
	23	(100)	20	(100)	27	(100)	30	(100)	100

Results

Table 9. Relationship between Pain score and Baseline NTX level

NTX level (nmol/mmolcr)	Pain Score			Total no.	P value
	Mild (0-5)	Moderate (6-9)	Severe (10)		
≤ 50	18 (58%)	10 (32%)	0 (0%)	28	
51-100	13 (41%)	15 (47%)	4 (12%)	32	
>100	6 (15%)	15 (37%)	19 (48%)	40	
	37	40	23	100	<0.001*

*Statistically significant correlation between level of NTX and pain score at baseline rs=0.451, p<0.001.

Table 10. Distribution of percentages of 1st SREs among the groups

Groups	No of cases	% SRE at 2yrs	Median months	P value
Total	100	53.2	20	
A	23	56.6	15	
B1	20	52.0	13	
B2	27	59.7	20	
C	30	46.6	36	0.120

Results

Table 11. Time to 1st SRE in relation to NTX levels

NTX	No. of cases	% SRE at 2 yrs	Median months	P-value
<50 nmol/mmolcr	30	46.6	36	
>50 nmol/mmolcr	70	55.3	20	0.017

Table 12 Percentage of 1st SRE in relation to ZOL

Zometa	No. of cases	% SRE at 2yrs	Median month	P-value
No	57	53.0	20	
Yes	43	54.8	15	0.154

Table 13. Percentage and time to SRE according to origin of disease

Group	No. of cases	% SRE at 2 yrs	Median time to SRE	P value
Multiple myloma	7	0	11	
Breast cancer	76	52.9	27	
Prostate cancer	17	36.4	12	0.150

Results

Table 14. Evaluable patients at 3 months with SRE

Groups	Number of evaluable patients at 3 months*	Number of Patients with SRE throughout the study	No. of Patients with 1st SRE at 3 months
A	21/23 (91%)	14/21 (67%)	8/21 (38%)
B1	16/20 (80%)	6 /16 (38%)	0/16 (0%)
B2	18/27 (67%)	9 /18 (50%)	4/18 (22%)
C	24/30 (80%)	10/24 (42%)	1/24 (4%)
total	79/100* (79%)	39/79 (49%)	12/79 (15%)

* 8 patients were lost to follow up before months 3, 13 patients died at 3 months due to dominant visceral disease or progressive brain metastases.