The Osteoporosis Education Project

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working with nature to regenerate bone health

OsteOrganiCAL™ Pilot Study
Final Report

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The Fall of 2002, Dr. Susan Brown, Director of the Osteoporosis Education Project, initiated a pilot clinical study aimed at assessing the impact of OsteOrganiCAL™ supplementation on bone resorption and bone density in postmenopausal women. Twelve postmenopausal women were included in the study. The age of subjects ranged from 64 to 85.

Four of the study subjects were diagnosed with osteoporosis and eight with osteopenia. At the twelve week mark one subject was removed from the study because, through this research, it was discovered that she had Paget's bone disease. Thus, eleven women completed this year long study.

Below we provide our data on bone resorption and bone mineral density changes with OsteOrganiCAL™ use. In this report we will (a) present our research findings on changes in bone resorption and bone mineral density, and, (b) offer our discussion and analysis of this data.

Data Presentation: Changes in Bone Resorption With OsteOrganiCAL™ Use

In this study bone resorption, or bone breakdown, was measured by the Ostex International Urine NTx assay. The mean premenopausal score for the NTx bone resorption marker is 38 nMBCE/mM creatinine (or 38 NTx). It is held that the closer the NTx score of a postmenopausal is to 38, the more likely her bone is stable or increasing in density.

Bone resorption, or bone breakdown, was measured at three points during this study. It was measured at baseline, at twelve weeks, and at one year. In all cases bone resorption was measured twice, on two consecutive days and then averaged.

The research findings on the changes of bone resorption after twelve weeks use of OsteOrganiCAL™ were given in our mid-term report. Generally, there was a slight but consistent reduction in bone breakdown at twelve weeks. Appendix #1 presents the twelve week changes in bone resorption after twelve weeks use of OsteOrganiCAL™.

The NTx bone resorption marker was also measured at the end of the study. Table 1 below presents the data on changes of bone resorption from baseline to twelve months.

Table 1

OsteOrganiCAL™ Pilot Study
Changes in Bone Resorption at 52 weeks

Name	Individual Baseline Average NTx	Individual 52 weeks Average NTx	Individual 52 weeks Percent Change from Baseline
MB	81.5	58.5	-28.22%
SC	51.5	53.5	3.88%
RD	134.5	121.5	-9.67%
JD	63.5	79.5	25.20%
LD	56	49	-12.50%
AF	35.5	26	-26.76%
JG	38	43	13.16%
AR	170	131	-22.94%
CT	46.5	29	-37.63%
MES	21	28	33.33%
EW	80	101	26.25%

Discussion of Bone Resorption Marker Changes

The published literature suggests that high bone resorption markers well above the premenopausal mean indicate a strong likelihood of on-going bone loss. On the other hand, if the NTx marker of bone resorption decreases by 30% or more, or if it is reduced to the premenopausal range (38 or less), than studies suggest that the subject has likely halted bone loss.

In this study bone resorption markers were studied at baseline, twelve weeks and fifty-two weeks. The purposes of these measurements were to assess:

(1) If bone resorption significantly decreased at one year, and
(2) If one year changes in bone mineral density could be predicted from the twelve week changes in bone resorption.

Table #1 presents the data on bone resorption changes at 52 weeks as compared to baseline. Six subjects experienced a reduction in NTx marker of bone resorption. The ranges of NTx reduction was between -37.63% and -9.67%. Five subjects experienced an increase in NTx marker of bone resorption.

According to the NTx test results, only two subjects experienced a significant 30% or more change in NTx score. One had a 37.63% decrease in NTx and another a 33.33% increase in NTx. Thus, our NTx data does not suggest that OsteOrganiCAL™ use over the year was associated with a decrease in NTx score. This finding is intriguing for, as we shall see, the majority of subjects made some degree of gain in bone mineral density (BMD).

Theoretically we would expect to see such increases in BMD associated with decreases in bone resorption. There are several possible explanations for this lack of correlation between bone resorption and bone mineral changes. Given our growing experience with the NTx bone resorption markers, I suspect that a lack of accuracy and lack of consistency of the bone resorption test is perhaps the best explanation for this unexpected result.

The second question we asked was if one year change in bone mineral density could be predicted from the twelve week change in bone resorption. Again the answer our research provides is negative. As detailed below, bone mineral density changes at one year could not be predicted from the twelve week changes in bone resorption.

Data Presentation: Changes in Bone Mineral Density With OsteOrganiCAL™ use

The second and major endpoint of this study was change in bone mineral density over the year. Tables 2 and 3 present the data on bone mineral density change of the spine and hip over the study year.

OsteOrganiCAL™ Pilot Study
Change in Total Hip and Spine Bone Mineral Density
Eleven Subjects With 52 Weeks Using OsteOrganiCAL™

Table 2

	AP Spine		
	Baseline	1 year	Percent Change
MB	Scoliosis - no spine measurement		
SC	0.851	0.850	-0.1%
RD	0.828	0.871	**5.1%**
JD	0.635	0.642	**1.0%**
LD	0.850	0.839	-1.2%
AF	0.798	0.813	**1.9%**
JG	0.835	0.868	**3.9%**
AR	0.898	0.900	**0.3%**
MES	0.764	0.786	**2.9%**
CT	0.792	0.804	**1.6%**
EW	0.903	0.921	**2.0%**

Group AP Spine Average Percent Change Over 12 Months	1.74%
Range of Change for Spine Bone Density	+5.1 to -1.2%

Table 3

	Total Hip		
	Baseline	1 year	Percent Change
MB	0.545	0.553	**1.4%**
SC	0.685	0.669	-2.3%
RD	0.773	0.754	-2.5%
JD	0.542	0.491	-9.4%
LD	0.798	0.796	-0.2%
AF	0.747	0.797	**6.8%**
JG	0.856	0.856	0.0%
AR	0.738	0.732	**0.4%**
MES	0.780	0.820	**5.1%**
CT	0.765	0.780	**2.1%**
EW	0.643	0.665	**3.4%**

Group Total Hip Average Percent Change	0.44%
Range of Change for Hip Bone Density	+6.8 to -9.4%

Analysis in The Changes in Bone Mineral Density

Of the total eleven total study subjects, only two did not experience some degree of BMD gain of either the spine or hip.

- Eight of the ten study subjects to have spinal bone density measurements gained density in the spine, to one degree or another. Two lost BMD in the spine, to one degree or another.
- Six of the eleven study subjects gained bone mineral density in the hip, to one degree or another. Four lost BMD in the hip, to one degree or another.

The range of gain in bone mineral density in the spine was between 1.0% and 5.1%. The range of gain in bone mineral density in the hip was between .4% and 6.8%. As easily noted, five women (45%) experienced very substantial bone mineral density gains. The gains made by these five women were uncommon for a natural, non hormonal or non-drug bone therapy.

As a whole the group gained 1.74% in spinal bone mineral density and gained 0.44% in total hip bone density. These average group gains, while modest, are considerably better than that achieved with calcium alone. For decades research has suggested that calcium therapy is only able to slow the rate of bone loss in postmenopausal women. Calcium has not been held to build bone.

These current results, however, are similar to those of the calcium researcher Bess Dawson-Hughes and colleagues. Using 500 mg of calcium citrate malate and 700 IU of Vitamin D3 they found postmenopausal women averaged a gain of 2.12% in the spine and 0.50% n the hip (Dawson Hughes et al., N Eng J Med 1997, Sep 4; 337(10):701-2). Interestingly enough, Dawson Hughes and colleagues reported that although the changes in hip bone mineral density were small, the women using these doses of calcium and vitamin D suffered much fewer hip fractures than those using only placebo. Our study was not large enough, or long enough. to consider changes in fracture incidence. We suspect, however, that the OsteOrganiCAL™ formula will provide for a similar significant reduction in fracture incidence.

In this current study some of the changes in bone mineral density were small and insignificant. Overall, however, from a clinical perspective we consider that six of the eleven women, or 55% saw clinically important, positive results and experienced substantial improvements in bone mineral density.[*]

Curiously enough, two of the eleven study subjects gained in the spine but lost in the hip. One of these women, RD, was reported to experience a moderate 2.5% loss in the hip. The other, JD, was reported to experience a very significant hip density loss of 9.4%. To date, we have no explanation of this bone loss, but it was recommended that she consult her physician regarding this exceptionally high rate loss. Because JD's loss of hip bone was unusual and represents an outlier we also calculated the group's change in hip bone density excluding this subject. Table 4 presents this calculation. When considering average group change in hip BMD is probably most accurate to use

[*] We at the Osteoporosis Education Project are concerned with clinical significance. Those concerned with formal statistical significance are referred to Appendix #2.

Table 4 which excludes the outlier result of JD. Her hip bone loss was not typical and likely indicates uncommon metabolic problems

Table 4

Changes in Hip BMD
Baseline to 1 Year
Calculated Without the Unusual Outlier Score of Subject JD

	Total Hip		
	Baseline	1 year	Percent Change
MB	0.545	0.553	**1.4%**
SC	0.685	0.669	-2.3%
RD	0.773	0.754	-2.5%
LD	0.798	0.796	-0.2%
AF	0.747	0.797	**6.8%**
JG	0.856	0.856	0.0%
AR	0.738	0.732	**0.4%**
MES	0.780	0.820	**5.1%**
CT	0.765	0.780	**2.1%**
EW	0.643	0.665	**3.4%**

Group Total Hip Average Percent Change	1.42%
Range of Change for Hip Bone Density	+6.8 to -2.5%

Data Analysis: Correlation Between Change in Bone Resorption at Twelve Weeks and BMD Changes at One Year.

One of the questions we asked in this study was: "Can we predict one year changes in bone mineral density from short term (12 week) changes in the NTx bone resorption maker?".

Table 5 below presents the data on change in bone resorption at 12 weeks and change of BMD at one year. As is obvious, there is no direct, consistent correlation between bone resorption changes at 12 weeks and final BMD changes.

Our data does not support the notion that early change in bone resorption makers will predict longer term changes in BMD. Again, I suspect that the bone resorption marker tests as conducted were not

accurate enough or consistent enough to allow us to accurately detect individual bone resorption changes.

Table 5

Bone Resorption Changes (12 Weeks)
BMD Changes (1 Year)

Name	Individual Average Baseline Urine NTx	Individual 12 Weeks Average Urine NTx	Individual 12 Weeks Percent Change from Baseline	Percent Change In BMD Hip Baseline to 1 Year	Spine Percent Change
MB	81.5	47.5	**-41.72%**	**1.4%**	-2.1%
SC	51.5	40	-22.33%	-2.3%	-0.1%
RD	134.5	111.5	-17.10%	-2.5%	**5.1%**
JD	63.5	58	-8.66%	-9.4%	**1.0%**
LD	56	47.5	-15.18%	-0.2%	-1.2%
AF	35.5	28	-21.13%	**6.8%**	**1.9%**
JG	38	33.5	-11.84%	0.0%	**3.9%**
AR	170	145.5	-14.41%	**0.4%**	**0.3%**
MES	21	23.5	11.90%	**5.1%**	**2.9%**
CT	46.5	42	-9.68%	**2.1%**	**1.6%**
EW	80	82	2.50%	**3.4%**	**2.0%**

Statistical significant reduction in Urine NTx

Increase in BMD

Estimating The Effectiveness of OsteOrganiCAL™

The primary goal of this pilot study was to begin formal documentation of the bone building capacity of OsteOrganiCAL™. As with all small clinical trials, our ability to draw conclusions is limited by the reduced number of study participants (N 11).

Nonetheless, the following points can be made:

- Most participants experienced some degree of BMD gain in either the spine or hip. Only two participants failed to gain density in either the spine or hip.

- Five study subjects (45%) made exceptional gains which were much higher than those commonly seen with any type of non-drug therapy. Those who gained most BMD were as follows: subject RD gained 5.1% in the spine; AG gained 6.8% in the hip; MES gained 5.1% in the hip and 2.9% in the spine and EW gained 3.4% in the hip.

Summary Comments

We at the Osteoporosis Education Project realize that osteoporosis is a multi-causal disorder and that no one natural treatment will be effective in all people with low bone density. It is our mission to uncover promising natural approaches to bone building and to help the public understand the therapeutic potential of natural bone building products.

In this pilot clinical trial OsteOrganiCAL™ was shown to be an effective bone building agent for the majority of women in the study. Some women made exceptional gains in bone mineral density, other modest gains, and others simply stabilized their bone. Only two of the eleven study subjects did not gain some amount of bone density in either the hip or spine.

It is our conclusion that OsteOrganiCAL™ can be a strong bone building agent for a significant proportion of women with osteoporosis and osteopenia. As with other bone building agents, however, it seems wise that those interested in a using such a natural approach to bone building use the product, and then test for its effectiveness in her/his own case.

Our study would suggest that a year's trial will reveal the effectiveness of OsteOrganiCAL™ for any given woman or man, and that the odds are that the product will proven beneficial. Further, since the manufacturer of this product offers a true money back guarantee, it appears there is much to be gained and little to be lost from its use.

Appendix 1

Twelve Week Changes in Bone Resorption after Twelve Week use of OsteOrganiCAL™

		NTx Baseline			NTx 12 weeks			
		Test 1	Test 2		Test 3	Test 4		
	Name	Score	Score	Individual Average Baseline	Score	Score	Individual 12 weeks Average NTx	Individual 12 weeks Percent Change from Baseline
1	MB	83	80	81.5	47	48	47.5	-41.72%
2	SC	55	48	51.5	36	44	40	-22.33%
3	RD	136	133	134.5	90	133	111.5	-17.10%
4	JD	71	56	63.5	65	51	58	-8.66%
5	LD	54	58	56	41	54	47.5	-15.18%
6	AF	39	32	35.5	23	33	28	-21.13%
7	JG	36	40	38	36	31	33.5	-11.84%
8	AR	186	154	170	148	143	145.5	-14.41%
9	MES	23	19	21	20	27	23.5	11.90%
10	CT	38	55	46.5	42	42	42	-9.68%
11	EW	82	78	80	95	69	82	2.50%

Appendix #2

Comments on Formal Statistical Significance of BMD Changes

At the Osteoporosis Education Project we assessed this pilot study in terms of clinical outcome. We looked for increases in bone mineral density among the study participants, most of whom have tried other nutrient therapies and still had low bone density.

For those concerned with formal statistical analysis we would make the following comments.

In this study the issue of statistical significance involves two topics. One is the "coefficient of variation" (C.V.) of the DEXA machines. The other is a statistical test of confidence.

The DEXA bone density-measuring machine used in this study was the Hologic DEXA machine located at SUNY Upstate Medical Center in Syracuse, NY. From a technical point of view a 1% or more change in bone density of either the spine or hip is necessary to guarantee that the gain is real and not due to insensitivity of the DEXA bone density machine. Of the six women who gained in hip BMD all but one had greater than a 1% change in BMD. Of the eight subjects to gain in spinal BMD all but one had gains of 1% or more.

The second formal statistical criteria involves a calculation of statistical significance at the 95% confidence interval. This statistical calculation is provided by the Hologic DEXA machine software and requires a change in BMD that is somewhat more than three times the C.V. According to the Hologic calculations the BMD gains of four study subjects reached this level of statistical significance at the 95% confidence interval. One subject, according to this definition, lost a statistically significant amount of bone at to the 95% confidence interval level.