

EFFECT OF THREE DOSES OF STRONTIUM MALONATE (NB S101) ON MARKERS OF BONE TURNOVER AND BONE MINERAL DENSITY: THE STRONG STUDY

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AIM

Strontium ranelate (Protelos®, Servier) reduces fracture risk and is approved in Europe for the treatment of postmenopausal osteoporosis. The exact mechanism whereby strontium salts act on bone is not fully understood. NB S101 (strontium malonate, Osteologix, Inc.), a once-daily tablet formulation of strontium malonate, was primarily evaluated for its effect on bone resorption in this Phase II study.

PATIENTS AND METHODS

A total of 289 postmenopausal women, age >50, with low BMD were randomized to 5 groups and treated for 12 wks. The primary endpoint was 12-wk % change in CTX-1 with 3 daily doses of NB S101 (0.75g, 1g or 2 g) vs placebo or Protelos (2g). 2° endpoints included: bone formation markers and spine and hip BMD.

RESULTS

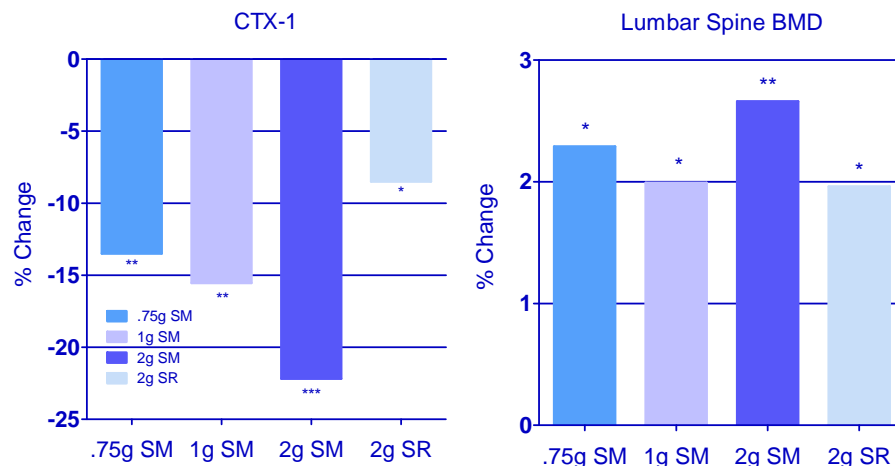
Baseline characteristics of the study groups did not differ. (Table 1) Table 2 shows the mean percent change over 12 wks as compared to placebo. NB S101 significantly reduced CTX-1 in all dose groups and achieved greater reductions in CTX-1 than Protelos, with the 2g NB S101 dose achieving significantly greater reductions ($p < 0.01$) in CTX-1 than Protelos. Adverse events included diarrhea, nausea, fatigue, back pain, headache, and muscle spasms. Potentially-related serious AEs with NB S101 included one event each of DVT, TIA, and allergic reaction. The frequency and types of AEs reported for patients with NB S101 at all three doses were comparable to those after treatment with the active comparator, Protelos.

Treatment		NB S101 0.75g n=57	NB S101 1.0g n=57	NB S101 2.0g n=58	Protelos® 2.0g n=56
Age	Mean(SD)	65.4 (8.0)	64.8 (7.7)	65.8 (8.0)	64.4 (8.6)
Race n (%)	Caucasian	56 (98.2)	56 (98.2)	58 (100)	56 (100)
	Asian	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)
Weight (kg)	Median	64.00	65.00	67.90	64.80
	Range	43.5-93.0	41.4-79.5	45.3-82.9	43.9-89.2
BMI (kg/m ²)	Median	24.50	24.90	26.95	24.85
	Range	17.4-30.5	17.3-29.7	18.6-30.9	17.5-30.4
BMD T-score	Median	-1.9	-1.9	-2.0	-1.9
	Range	-2.9- -1.0	-3.0- -1.0	-3.0- -1.0	-3.0- -1.0

Table 1: Baseline demographics of the study cohort. No parameter differed significantly between the groups at baseline.

CONCLUSIONS

All 3 doses of NB S101 were well-tolerated and significantly suppressed bone resorption while improving BMD. The results consistently show that NB S101 was safe and well tolerated and was effective on bone turnover and BMD in the short-term; it merits development as a treatment for postmenopausal osteoporosis.



Treatment		NB S101 0.75g n=57	NB S101 1.0g n=57	NB S101 2.0g n=58	Protelos® 2.0g n=56
Serum CTX-1	Mean % Δ	-13.48***	-15.54***	-22.17***	-8.50*
	Mean % Δ	-6.98*	-8.17*	-12.76***	-2.66
Serum BSAP	Mean % Δ	-3.57	-0.85	+7.19	+5.34
	Mean % Δ	+2.29*	+1.99*	+2.66**	+1.96*
Total Hip BMD	Mean % Δ	+1.48*	+1.82**	+1.67*	+2.02**

Table 2: Mean %Δ over 12 weeks vs. placebo (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$)