Efficacy of combined treatment with alendronate (ALN) and eldecalcitol, a new active vitamin D analog, compared to that of concomitant ALN, vitamin D plus calcium treatment in Japanese patients with primary osteoporosis (e-ADVANCED Study)

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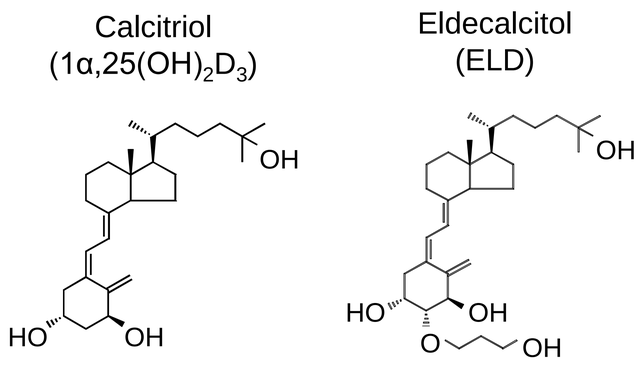
Introduction

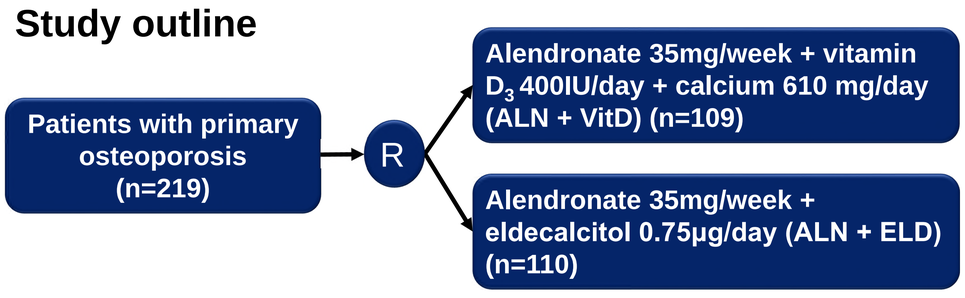
- Eldecalcitol (ELD) is an analog of calcitriol ($1\alpha,25(OH)_2D_3$) and has higher binding to serum vitamin D (VitD) binding protein, lower binding to VitD receptor, and resistance to metabolic degradation via 24-hydroxylation due to hydroxypropyloxy group at 2β position (Fig.1).
- ELD stimulates intestinal calcium (Ca) intake, increases lumbar spine (L) bone mineral density (BMD), and reduces bone turnover markers (BTMs) compared to placebo.
- ELD increases L-BMD by 3-4% in one year and reduces BTMs by 30-40% in patient with osteoporosis compared to placebo.
- Alendronate (ALN) increases BMD and suppresses BTMs. Serum Ca slightly decreases during the ALN treatment due to the reduction of Ca efflux from the bone. In order to enhance the efficacy of ALN treatment, and to prevent negative Ca balance in the body, vitamin D and Ca supplementation is recommended for elderly patient with osteoporosis.
- In this study, we compared the clinical efficacy and safety of ELD to those of vitamin D and calcium supplementation in patients with primary osteoporosis treated with ALN.

Fig. 1 Chemical structures of calcitriol and eldecalcitol



Methods

Study outline



Subjects:	219 primary osteoporosis patients (60 -90 yrs old)
Design:	Randomized open-labeled trial
Treatment period:	48 weeks
Primary endpoint:	L2-L4 L-BMD
Secondary endpoints:	Total hip BMD, bone turnover markers
Other endpoint:	Femoral neck (FN)-BMD
Safety:	Adverse events, serum calcium, urinary calcium

Table 1 Baseline characteristics of enrolled patients

		ALN + ELD group (n=110)	ALN + VitD group (n=109)
Age (years)		71.5 ± 7.3	71.6 ± 6.6
Gender (female/male)		109/1	105/4
Height (cm)		150.0 ± 5.9	149.8 ± 6.3
BMI (kg/m^2)		22.3 ± 3.1	21.7 ± 2.9
Prevalent vertebral fractures	0	54 (50.9%)	37 (36.6%)
	1	34 (32.1%)	41 (40.6%)
	≥2	16 (15.1%)	21 (20.8%)
L-BMD (mg/cm^2)		653 ± 77	655 ± 90
Total hip BMD (mg/cm^2)		666 ± 82	659 ± 95
FN-BMD (mg/cm^2)		518 ± 70	518 ± 84
Serum Ca (mg/dL)		9.43± 0.32	9.46 ± 0.34
Urinary Ca (mg/dL GF)		0.099 ± 0.073	0.103 ± 0.067
BAP (U/L)		19.6 ± 7.6	18.6 ± 7.4
Urinary NTX (nmol BCE/mmol Cr)		68.2 ± 27.3	70.0 ± 30.2
25(OH)D (ng/mL)		18.7 ± 6.2	19.2 ± 6.7
1,25(OH)$_2$D (pg/mL)		62.4 ± 26.8	58.6 ± 25.7
intact-PTH (pg/mL)		50.4 ± 17.6	50.8 ± 15.2

Data: Mean ± SD

Results

Fig. 2 Bone Mineral Density (BMD) change form baseline

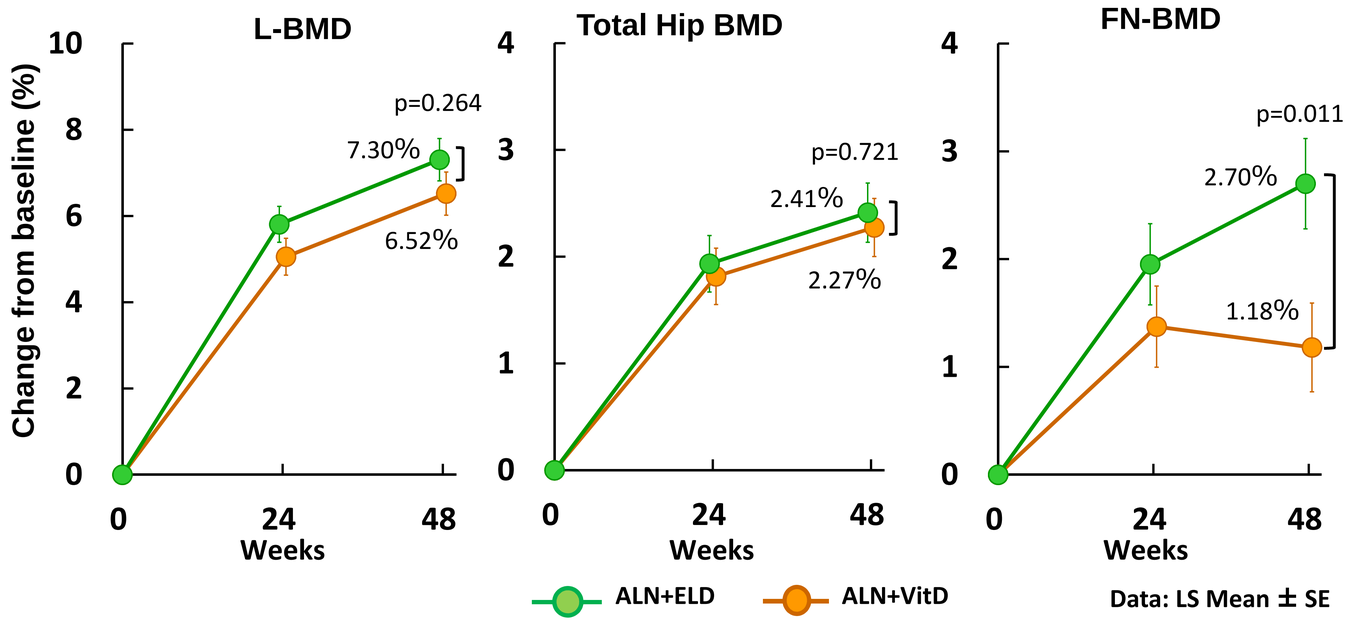


Fig. 3 Bone Turnover Markers (BTMs) change from baseline

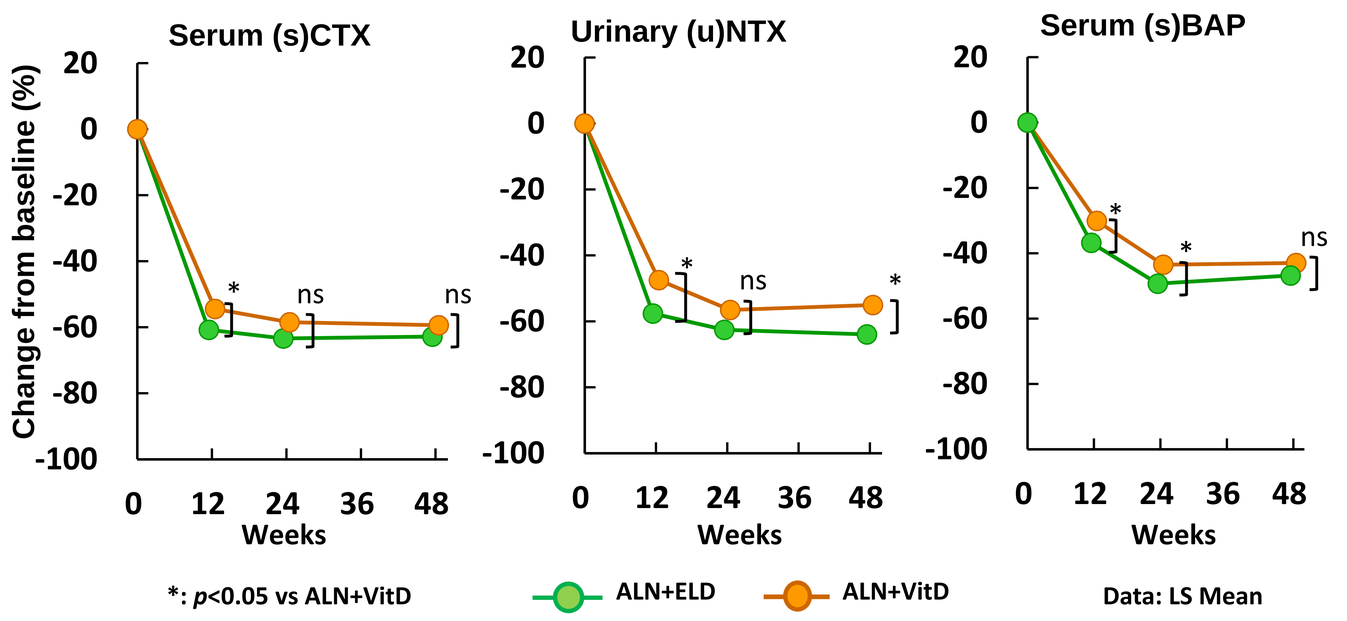
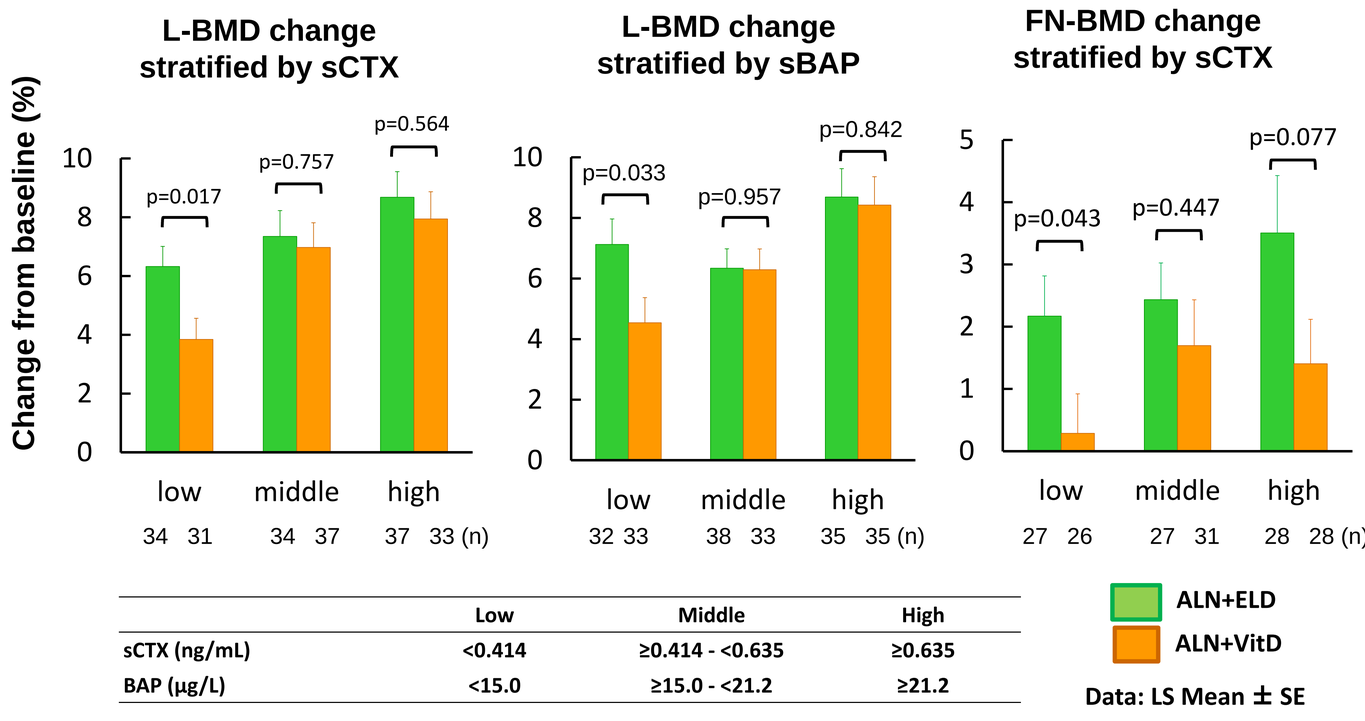


Fig. 4 BMD change stratified by baseline BTMs



	Low	Middle	High
sCTX (ng/mL)	<0.414	≥0.414 - <0.635	≥0.635
BAP (μg/L)	<15.0	≥15.0 - <21.2	≥21.2

Summary & Conclusion

- L-BMD, total hip BMD and FN-BMD increased from baseline in both group.
- Inter-group differences of L-BMD and total hip BMD values at 48 weeks were not significant.
- The increase of FN-BMD at 48 weeks was larger in the ALN+ELD group than the ALN+VitD group.
- Reductions of the BTMs at 12 weeks were greater in the ALN+ELD group than the ALN+VitD group.
- The increase in L-BMD correlated with the baseline levels of the BTMs in the ALN+VitD group, whereas, L-BMD increased regardless of baseline BTMs in the ALN+ELD group. Similarly, the increases of the FN-BMD in patients with lower baseline sCTX level was larger in the ALN+ELD group than the other group.
- The safety profile did not differ between the two groups (data not shown).
- Conclusion: Combination treatment of ALN plus ELD was more effective in reducing the BTMs and increasing the L-BMD and FN-BMD than ALN treatment with vitamin D3 and calcium, especially in the patients with low baseline BTMs levels.

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