Osteogenesis Imperfecta

Topalis Christos

ΝΟΣΟΚΟΜΕΙΟ
ΠΑΠΑΓΕΩΡΓΙΟΥ

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ACS Pharmacology & Translational Science

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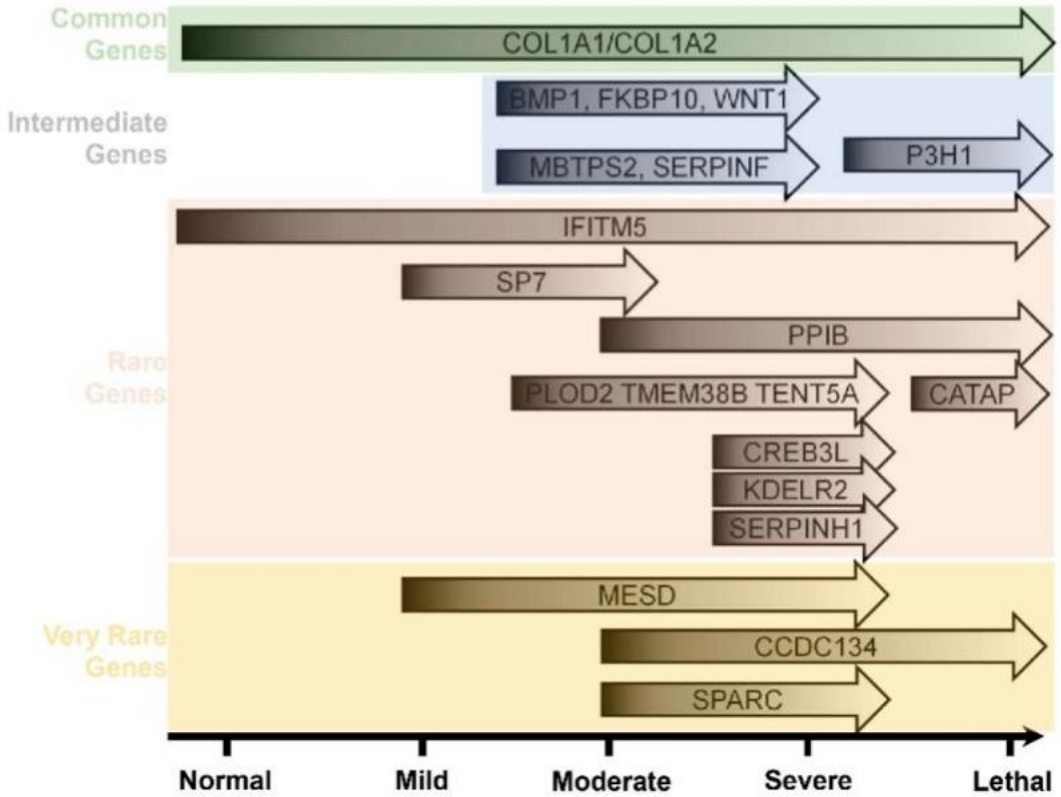
Emerging Landscape of Osteogenesis Imperfecta Pathogenesis and Therapeutic Approaches

Yu Sun,[#] Lin Li,[#] Jiajun Wang,[*] Huiting Liu,[*,#] and Hu Wang[*]



Mutated gene	OI type	Severity	Localization	Clinical characteristics
			Impairment of collagen synthesis and structure	
COL1A1 or COL1A2	I	Mild	Matrix	Normal stature, blue sclera, hearing loss, late onset
	II	Lethal		Perinatal lethality
	III	Severe		Severe progressive malformations
	IV	Mild to moderate		Moderately severe, white sclera, short stature, bone deformity
			Compromise bone mineralization	
IFITM5	V	Normal to severe	Plasma	Normal-to-severe skeletal deformities, endosteal ossification, radial dense bands and radial head dislocation, normal-to-blue sclera, sometimes hearing loss
SERPINF1	VI	Moderate to severe	Matrix	Moderate-to-severe skeletal deformity, the presence of osteoid, fish-scale appearance of lamellar bone pattern, childhood onset
			Abnormal collagen post-translation modification	
CRTAP	VII	Lethal	ER	Severe rhizomania with white sclera
P3H1	VIII	Severe to lethal	ER	Severe rhizomania with white sclera
PPIB	IX	Moderate to lethal	ER	Severe bone deformity with gray sclera
			Compromised collagen processing and cross-linking	
SERPINH1	X	Severe	ER-Golgi	Severe skeletal deformity, blue sclera, dentinogenesis imperfecta, skin abnormalities, inguinal hernia
FKBP10	XI	Moderate to severe	ER	Mild-to-severe skeletal deformity, normal-to-gray sclera, congenital contractures
BMP1	XII	Moderate to severe	Matrix	Mild-to-severe skeletal deformity, umbilical hernia
PLOD2	No type	Moderate to severe	ER	Moderate-to-severe skeletal deformities, progressive joint contractures
			Altered osteoblast differentiation and function	
SP7	XIII	Mild to moderate	Nucleus	Severe skeletal deformity, delayed tooth eruption, facial hypoplasia
TMEM38B	XIV	Moderate to severe	ER-Golgi	Severe bone deformity, normal-to-blue sclera
WNT1	XV	Moderate to severe	Matrix	Severe skeletal abnormalities, white sclera, possible neurological defects
MBTPS2	XVI	Moderate to severe	ER-Golgi	Moderate-to-severe skeletal deformity, light blue sclera, scoliosis, pectoral deformities
CREB3L1	XVII	Severe	ER-Golgi	Severe bone deformities
SPARC	XVIII	Moderate to severe	Matrix	Progressive severe bone fragility
			Other OI types	
TENT5A	XIX	Moderate to severe	Unknown	Congenital limb arch, wormy bone, blue sclera, severe osteoporosis, mineralization disorder
MESD	XX	Mild to severe	ER	Progressive deformity, early onset of osteoporosis
CCDC134	XXI	Moderate to lethal	ER-Golgi	Severe bone fragility, impaired mineralization
KDELR2	XXII	Severe	ER-Golgi	Progressive deformity, low bone density, bone fragility, short stature

Location	Phenotype	Inheritance	Phenotype OMIM no.	Gene/locus	Gene/locus OMIM no.	
17q21.33	Osteogenesis imperfecta, type I	AD	166200	*COL1A1*	120150	Mildest form. Fractures occur after birth. Blue sclerae, hearing loss, normal or near-normal stature.
7q21.3	Osteogenesis imperfecta, type II	AD	166210	*COL1A2*	120160	Most severe form. Lethal in perinatal period. Extreme bone fragility, multiple fractures, underdeveloped lungs.
7q21.3	Osteogenesis imperfecta, type III	AD	259420	*COL1A2*	120160	Severe form. Frequent fractures, bone deformities, short stature, blue sclerae, dental issues. Often wheelchair-bound.
7q21.3	Osteogenesis imperfecta, type IV	AD	166220	*COL1A2*	120160	Moderate severity. Fractures, short stature, normal sclerae, mild to moderate bone deformities.
11p15.5	Osteogenesis imperfecta, type V	AD	610967	*IFITM5*	614757	Hyperplastic callus formation, calcification of interosseous membranes, no dentinogenesis imperfecta, white sclerae.
17p13.3	Osteogenesis imperfecta, type VI	AR	613982	*SERPINF1*	172860	Progressive deforming OI. Hypermineralized bone. Often begins with fractures postnatally.
3p22.3	Osteogenesis imperfecta, type VII	AR	610682	*CRTAP*	605497	Moderate to severe OI. Short humerus and femur, coxa vara, white sclerae, rhizomelia.
1p34.2	Osteogenesis imperfecta, type VIII	AR	610915	*P3H1*	610339	Severe, often lethal. Extreme growth deficiency, under-mineralized bones, rib fractures, pulmonary complications.
15q22.31	Osteogenesis imperfecta, type IX	AR	259440	*PPIB*	123841	Severe to lethal OI. Progressive deforming with prenatal onset.
11q13.5	Osteogenesis imperfecta, type X	AR	613848	*SERPINH1*	600943	Moderate to severe OI. Collagen folding defect leading to brittle bones and frequent fractures.
17q21.2	Osteogenesis imperfecta, type XI	AR	610968	*FKBP10*	607063	Progressive deforming. Severe contractures of large joints, scoliosis, white sclerae, dentinogenesis imperfecta.
12q13.13	Osteogenesis imperfecta, type XII	AR	613849	*SP7*	606633	Moderate to severe OI. Bone deformities, frequent fractures, dental issues, short stature.
8p21.3	Osteogenesis imperfecta, type XIII	AR	614856	*BMP1*	112264	Severe OI. Fractures, deformities, short stature. Associated with abnormalities in bone matrix formation.
9q31.2	Osteogenesis imperfecta, type XIV	AR	615066	*TMEM38B*	611236	Progressive OI. Early onset fractures, bone deformity, short stature, white sclerae.
12q13.12	Osteogenesis imperfecta, type XV	AR	615220	*WNT1*	164820	Severe OI. Early onset, severe deformities, progressive bone fragility, dental problems.
11p11.2	Osteogenesis imperfecta, type XVI	AR	616229	*CREB3L1*	616215	Moderate to severe OI. Progressive deformities and fractures, white sclerae, and dental abnormalities.
5q33.1	Osteogenesis imperfecta, type XVII	AR	616507	*SPARC*	182120	Moderate to severe OI. Progressive skeletal deformities, white sclerae, fractures from birth.
6q14.1	Osteogenesis imperfecta, type XVIII	AR	617952	*TENT5A*	611357	Severe OI. Multiple fractures at birth, short stature, pulmonary complications, progressive deformities.
Xp22.12	Osteogenesis imperfecta, type XIX	XLR	301014	*MBTPS2*	300294	Severe OI with craniofacial anomalies. Blue sclerae, frequent fractures, short stature, dental issues.
15q25.1	Osteogenesis imperfecta, type XX	AR	618644	*MESD*	607783	Moderate to severe OI with delayed motor milestones, short stature, frequent fractures.
7p22.1	Osteogenesis imperfecta, type XXI	AR	619131	*KDELR2*	609024	Moderate OI with dentinogenesis imperfecta, delayed motor milestones, fractures, and short stature.
22q13.2	Osteogenesis imperfecta, type XXII	AR	619795	*CCDC13*	618788	Severe OI. Early onset fractures, white sclerae, significant deformities.
11q23.3	Osteogenesis imperfecta, type XXIII	AR	620639	*PHLDB1*	612834	Severe OI. Frequent fractures, bone deformities, short stature.

The Journal of Clinical Endocrinology & Metabolism, 2024, **109**, 1873–1882
https://doi.org/10.1210/clinem/dgae012
Advance access publication 5 January 2024
Clinical Research Article

Efficacy and Safety of Denosumab vs Zoledronic Acid in OI Adults: A Prospective, Open-Label, Randomized Study

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Pharmacotherapy studies are extremely rare in adult patients with OI. In this study, they prospectively evaluated the efficacy and safety of denosumab by comparing it head-to-head with zoledronic acid for the first time in a cohort of adult patients with OI

- This was a 12-month, prospective, randomized, open-label study.

- Adult patients with OI were randomized to receive either subcutaneous injections of 60 mg of denosumab (Prolia,Amgen Inc., USA) every 6 months or
  1 intravenous infusion of 5 mg of zoledronic acid (Aclasta, Novartis Pharmaceuticals, Switzerland).

- All patients were supplemented with 600 mg of calcium and 0.25 μg of calcitriol daily.

Areal BMD (aBMD) at the LS, femoral neck (FN), and total hip (TH) was measured at 0, 6, and 12 months of treatment

The trabecular bone score (TBS) was extracted from the DXA image

Fasting serum was collected at 8:00 to 10:00 AM at baseline and after 6 and 12 months of treatment.

Serum levels of β-C-terminal telopeptide of type 1 collagen (β-CTX, a bone resorption marker), 25-hydroxyvitamin D (25OHD), and intact parathyroid hormone (PTH) were measured

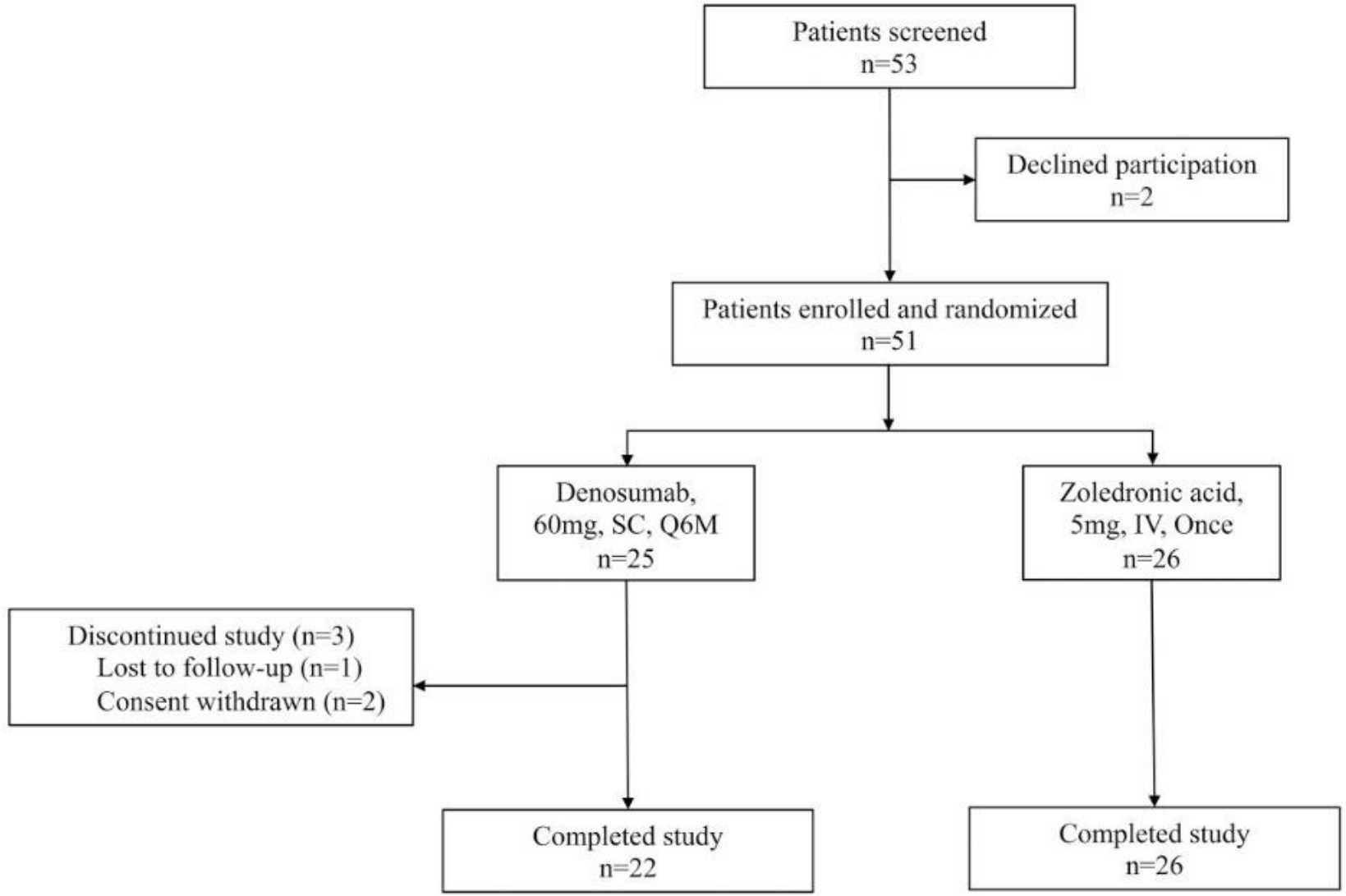
Serum levels of alkaline phosphatase (ALP, a bone formation marker), alanine aminotransferase (ALT), creatinine, albumin-adjusted calcium (Ca), and phosphate (P)

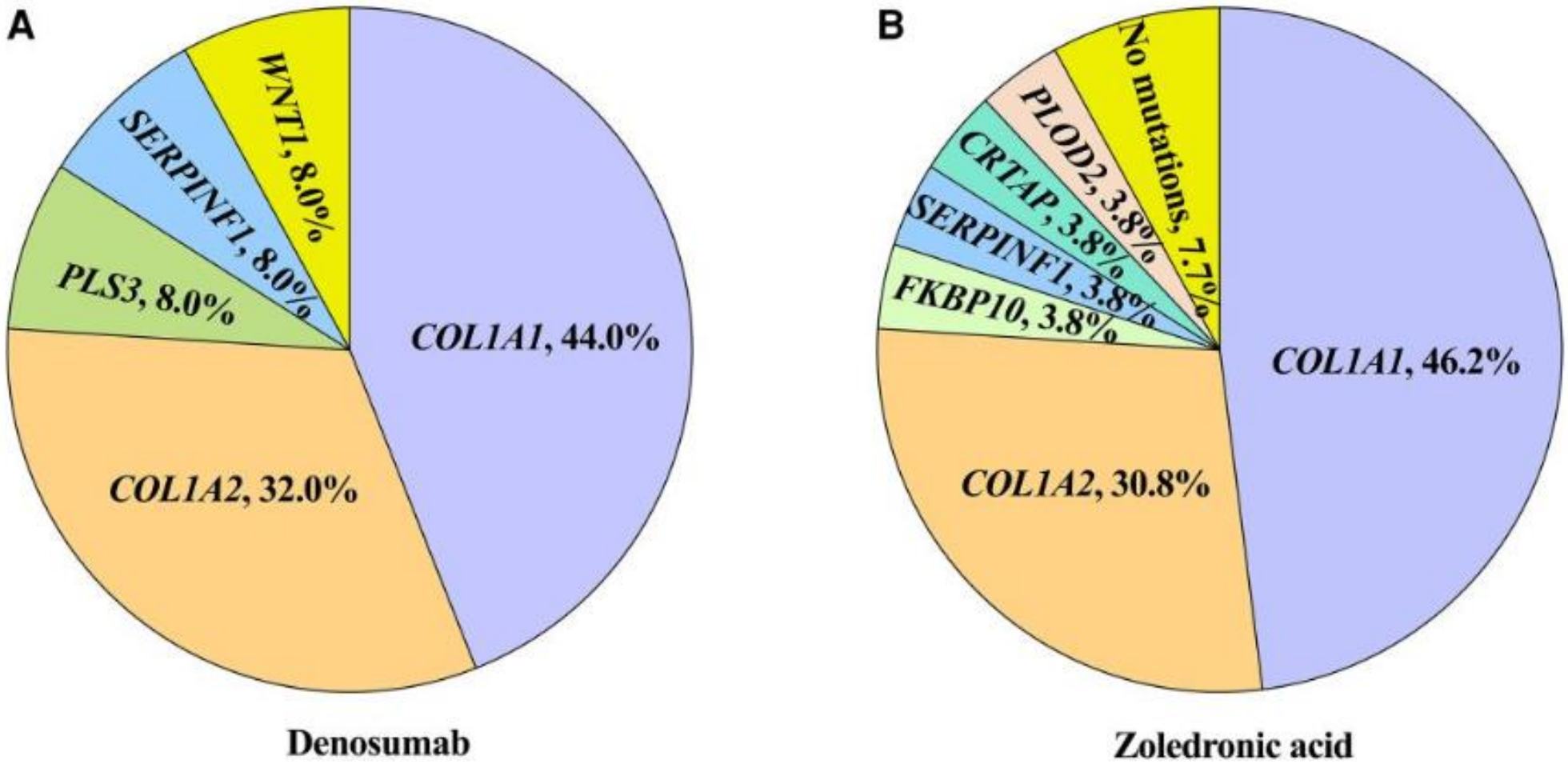
The primary efficacy endpoints were the changes in aBMD at the LS, FN, and TH from baseline to 6 and 12 months of treatment.

Secondary endpoints were the changes in the TBS, serum β-CTX, and ALP levels from baseline to 6 and 12 months of treatment.

Additional end points included the incidence of new fractures and changes in serum levels of Ca, P, PTH, and 25OHD during the treatment.

The changes in aBMD, TBS, and bone turnover biomarkers (BTMs) were evaluated in subgroups of patients with different inheritance patterns (AD or non-AD) and abnormalities of type I collagen (quantitative reduction or qualitative defect).


Patients screened
n=53
Declined participation
n=2
Patients enrolled and randomized
n=51
Denosumab,
60mg, SC, Q6M
n=25
Zoledronic acid,
5mg, IV, Once
n=26
Discontinued study (n=3)
Lost to follow-up (n=1)
Consent withdrawn (n=2)
Completed study
n=22
Completed study
n=26


A
WNT1, 8.0%
SERPINF1, 8.0%
PLS3, 8.0%
COL1A1, 44.0%
COL1A2, 32.0%
Denosumab
B
No mutations, 7.7%
PLOD2, 3.8%
CRTAP, 3.8%
SERPINF1, 3.8%
FKBP10, 3.8%
COL1A1, 46.2%
COL1A2, 30.8%
Zoledronic acid

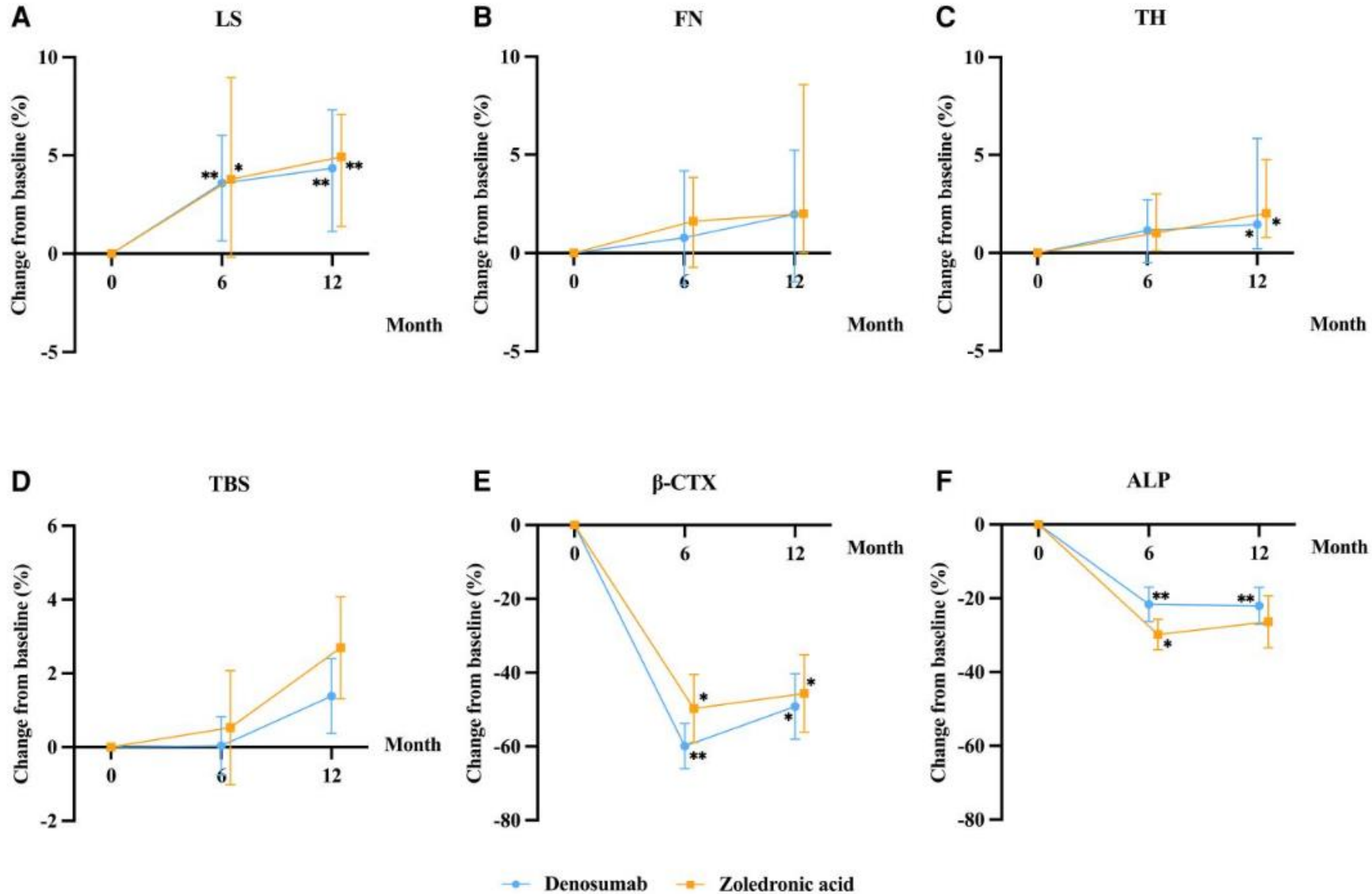


Figure 3. Percentage changes in aBMD, TBS, and BTMs after denosumab or zoledronic acid treatment. (A) Median percentage changes in aBMD at the LS during treatment. (B) Median percentage changes in aBMD at the FN during treatment. (C) Median percentage changes in aBMD at the TH during treatment. (D) Median percentage changes in the TBS during treatment. (E) Mean percentage changes in the serum levels of β-CTX during treatment. (F) Mean percentage changes in the serum levels of ALP during treatment. β-CTX, β-C-terminal telopeptide of type 1 collagen; aBMD, areal bone mineral density; ALP, alkaline phosphatase; BTM, bone turnover marker; FN, femoral neck; LS, lumbar spine; TBS, trabecular bone score; TH, total hip. Data are shown as the mean and standard error or median (IQR). $*P < .05$, $**P < .01$ vs baseline.

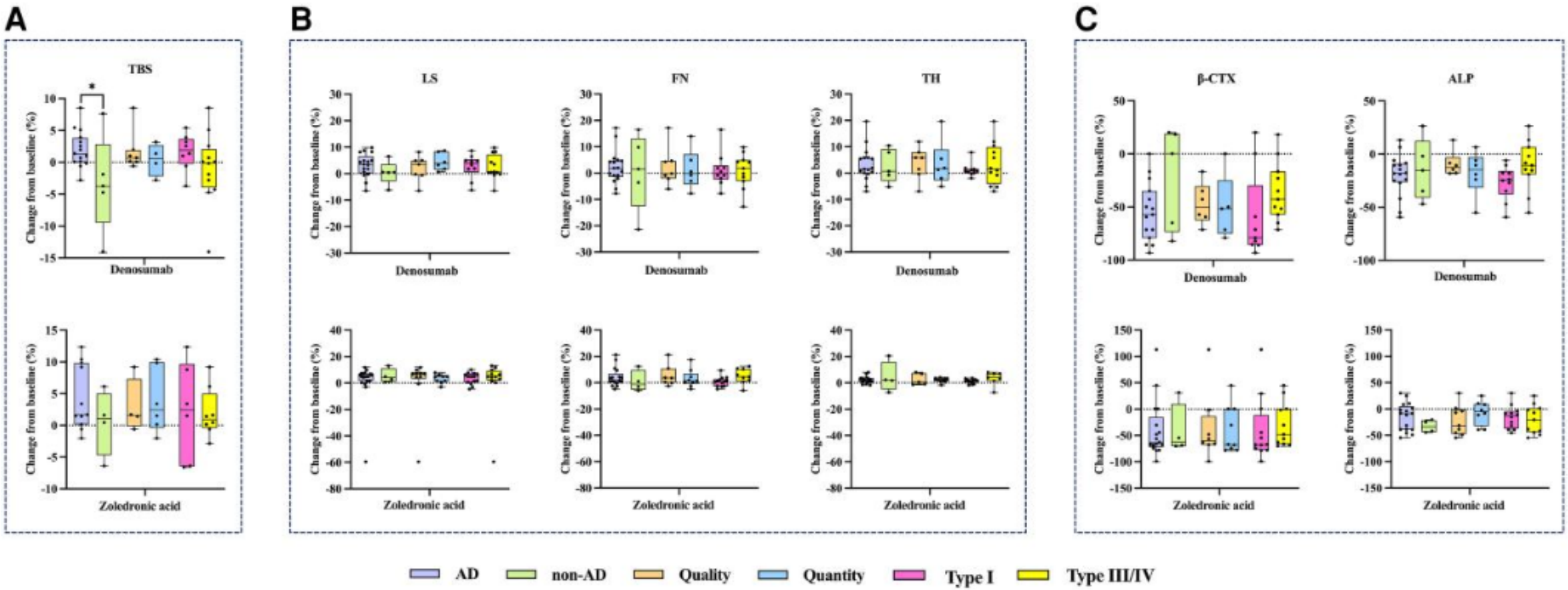


Figure 4. Correlation of pathogenic mutation or Sillence type and response to denosumab and zoledronic acid treatment. (A) Percentage changes in the TBS in patients with AD and non-AD inheritance, qualitative defects, and quantitative reductions in type I collagen, and type I and type III/IV after 12 months of denosumab and zoledronic acid treatment. (B) Percentage changes in aBMD at the LS, FN, and TH in patients with AD and non-AD inheritance, qualitative defects and quantitative reductions in type I collagen, and type I and type III/IV after 12 months of denosumab and zoledronic acid treatment. (C) Percentage changes in serum levels of β-CTX and ALP in patients with AD and non-AD inheritance, qualitative defects, and quantitative reductions in type I collagen, and type I and type III/IV after 12 months of denosumab and zoledronic acid treatment. β-CTX, β-C-terminal telopeptide of type 1 collagen; AD, autosomal dominant (inheritance); ALP, alkaline phosphatase; BMD, bone mineral density; FN, femoral neck; LS, lumbar spine; non-AD, autosomal recessive or X-linked (inheritance); OI, osteogenesis imperfecta; Quantity, quantitative reduction in type I collagen; Quality, qualitative defect of type I collagen; TBS, trabecular bone score; TH, total hip. $*P < .05$ AD vs non-AD.

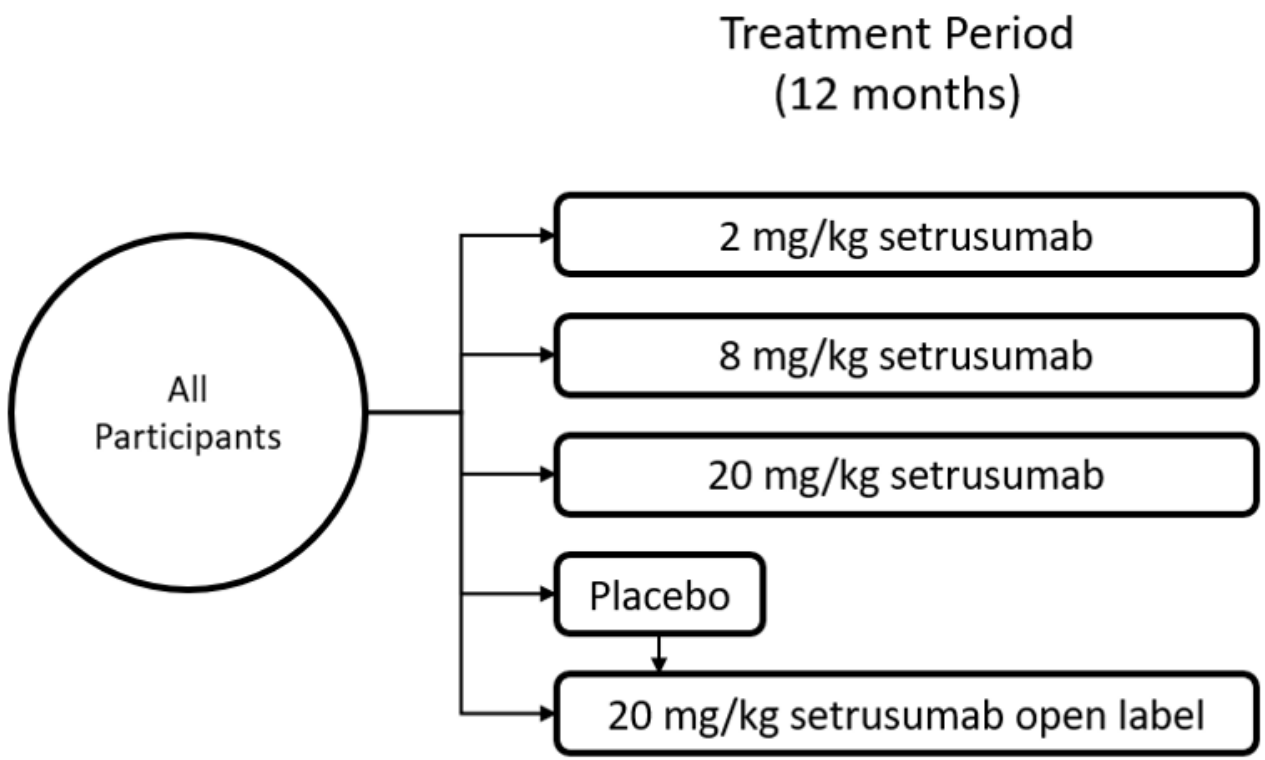
The efficacy of denosumab was similar to that of zoledronic acid, but denosumab treatment resulted in fewer AEs than zoledronic acid therapy during the study period.

Additionally, their findings indicated that patients with OI with AD inheritance may have a better response to denosumab treatment, as demonstrated by a significantly higher percentage increase in the TBS at 12 months.

Journal of Bone and Mineral Research, 2024, **39**, 1215–1228
https://doi.org/10.1093/jbmr/zjae112
Advance access publication: July 16, 2024
Clinical Trial

Setrusumab for the treatment of osteogenesis imperfecta: 12-month results from the phase 2b asteroid study

Francis H. Glorieux[1,*], Bente Langdahl[2,3], Roland Chapurlat[4], Suzanne Jan De Beur[5,†], Vernon Reid Sutton[6], Kenneth E.S. Poole[7], Kathryn M. Dahir[8], Eric S. Orwoll[9], Bettina M. Willie[10,11], Nicholas Mikolajewicz[10,11], Elizabeth Zimmermann[10,11], Seyedmahdi Hosseinitabatabaei[10,11], Michael S. Ominsky[12,†], Chris Saville[13], James Clancy[14], Alastair MacKinnon[14,†], Arun Mistry[14,†], Muhammad K. Javaid[15]


Treatment Period
(12 months)
All
Participants
2 mg/kg setrusumab
8 mg/kg setrusumab
20 mg/kg setrusumab
Placebo
20 mg/kg setrusumab open label

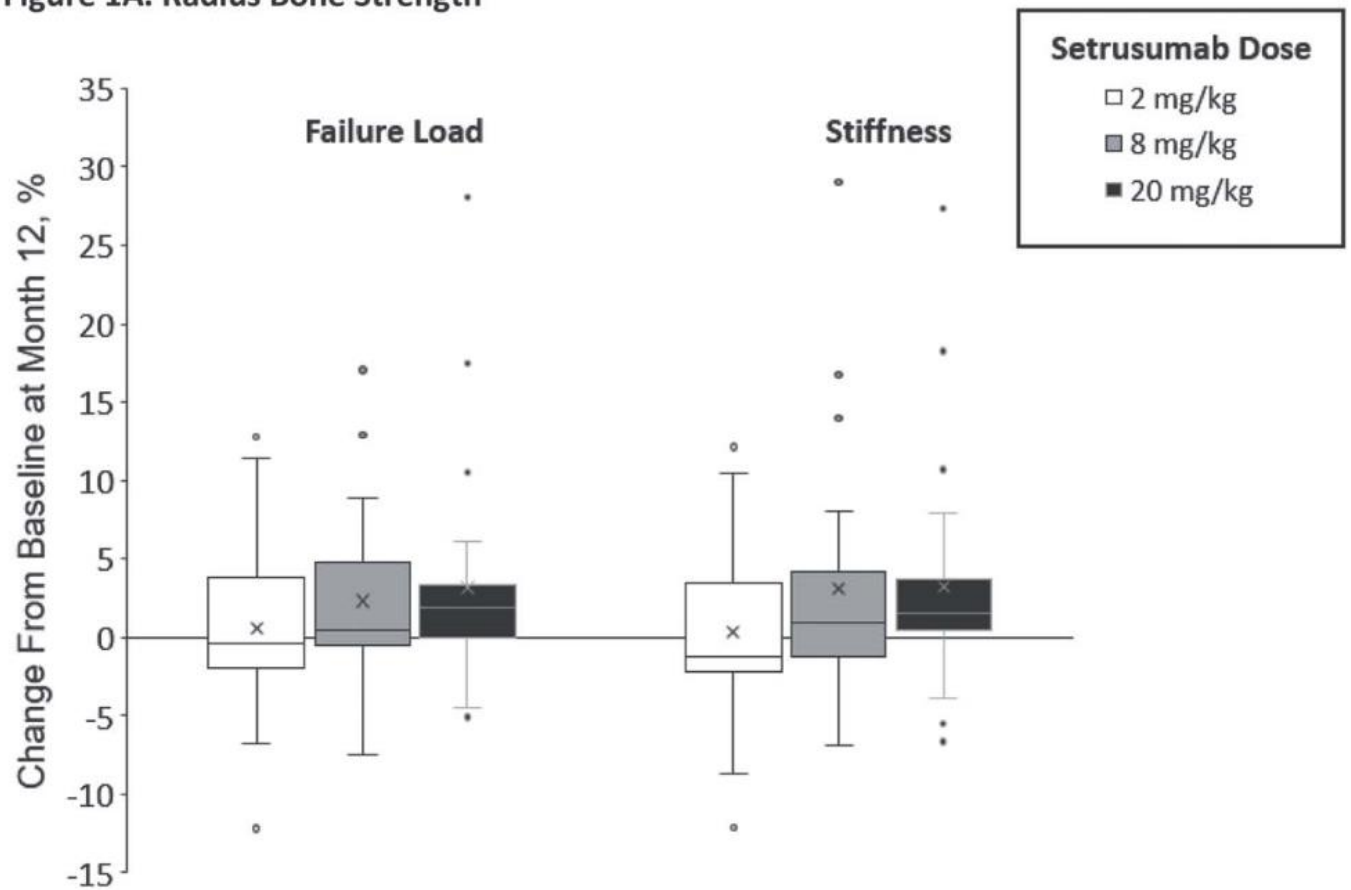
In a 21-week, open-label, phase 2a dose-escalation trial of setrusumab in adults with OI, a statistically significant increase in bone formation markers and LS aBMD occurred, while bone resorption markers decreased. In that study, participants receiving setrusumab through the highest dose of 20 mg/kg reported no adverse events attributed to treatment, and no treatment-related fractures were observed.

The phase 2b Asteroid trial is a parallel-group, dose-finding study of 3 doses of setrusumab over a 10-fold dose range, which was conducted to determine the dose of setrusumab that best improved bone parameters after 12 months of treatment.

Participants were eligible to participate in Asteroid if they had a
clinical diagnosis of OI type I, III, or IV
with a confirmed mutation in COL1A1/COL1A2,
were 18–74 yr of age,
and had experienced one or more nontraumatic long bone, rib,
hand/foot, and/or vertebral fractures within the previous 2 yr

(110 enrolled participants)

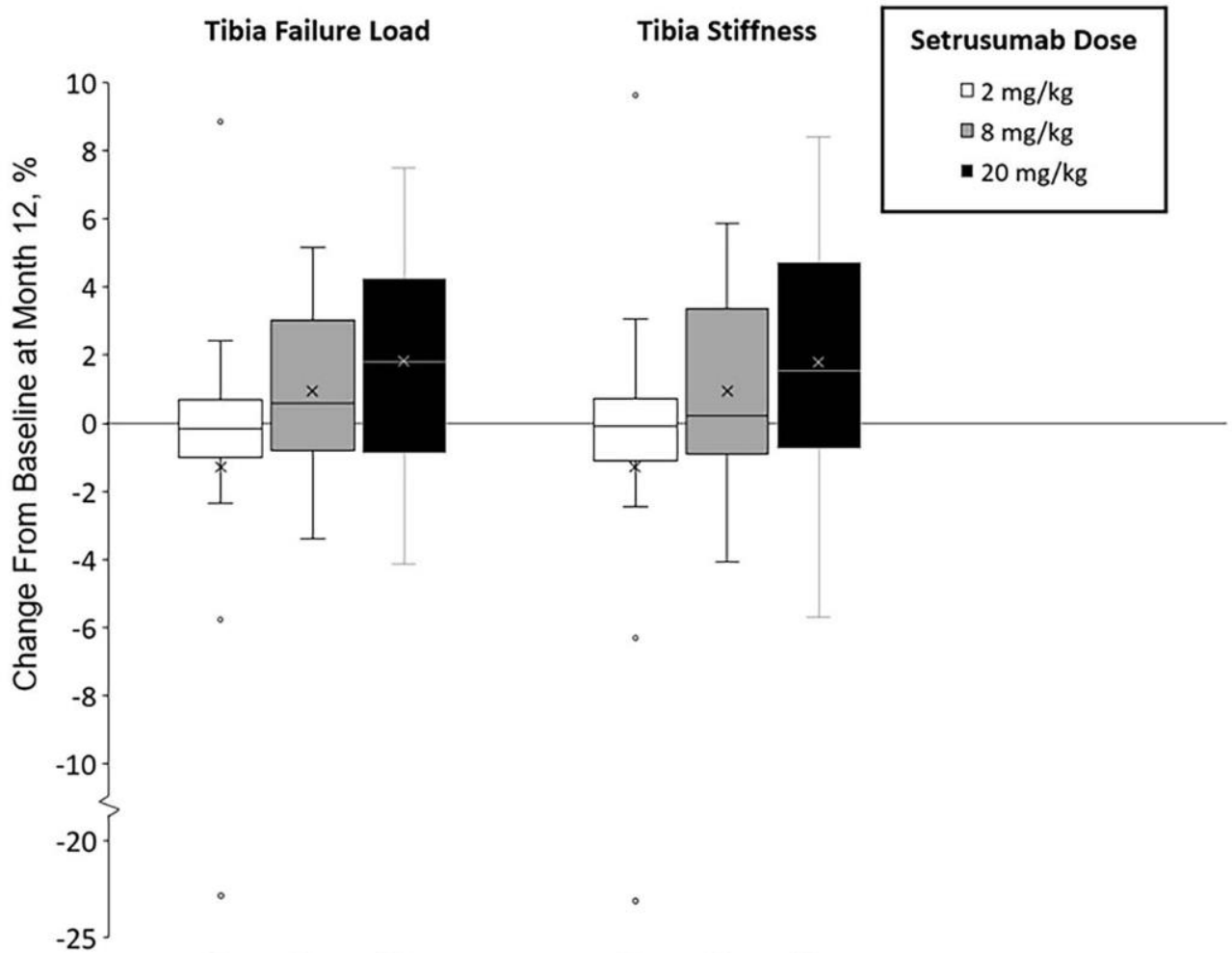
Figure 1A. Radius Bone Strength



	Failure Load			Stiffness		
n	25	22	28	25	22	28
Mean	0.57	2.33	3.17	0.37	3.06	3.19
p value	0.704	0.190	0.006	0.756	0.047	0.011

Error bars represent the minimum and maximum values, box edges represent 1st and 3rd quartiles, X = mean, horizontal bar = median.
p values vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates
ANCOVA, analysis of covariance; OI, osteogenesis imperfecta.

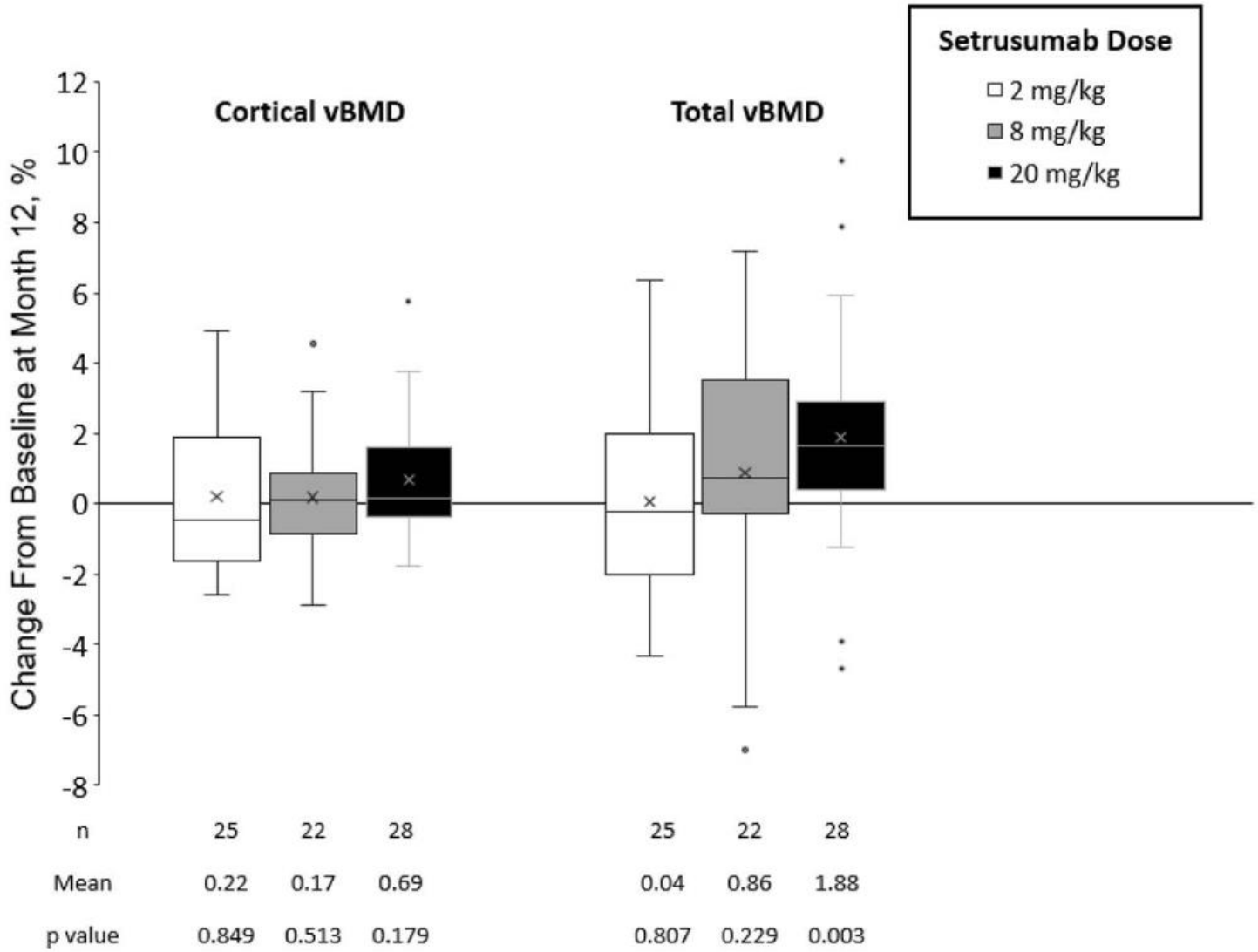
Figure 1B. Tibial Bone Strength



n	25	22	28	25	22	28
Mean	-1.30	0.95	1.82	-1.30	0.90	1.80
p value	0.232	0.245	0.086	0.291	0.224	0.031

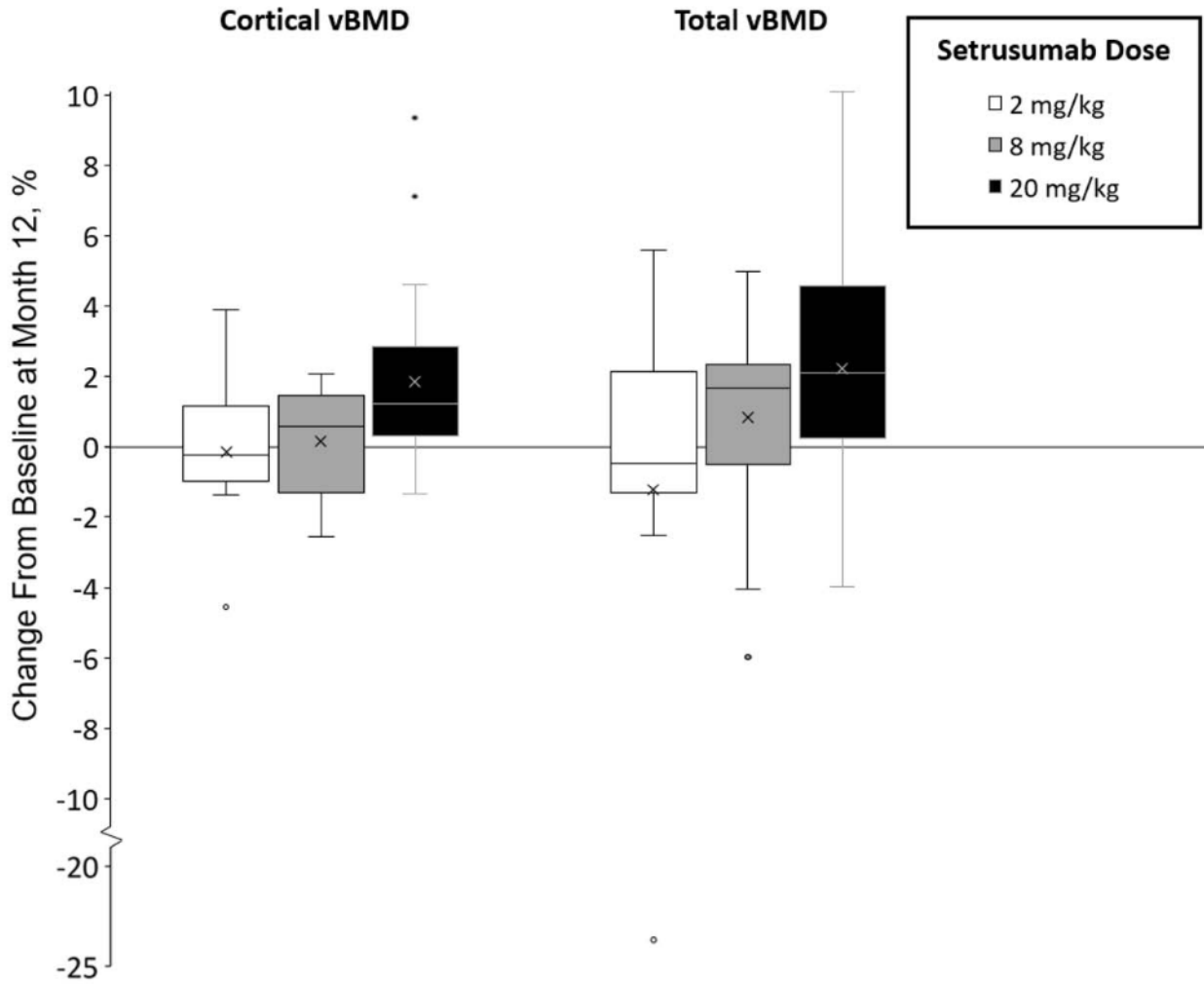
Error bars represent the minimum and maximum values, box edges represent 1st and 3rd quartiles, X = mean, horizontal bar = median.
p values vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates
ANCOVA, analysis of covariance; OI, osteogenesis imperfecta.

Figure 2A. Radius vBMD



Error bars represent the minimum and maximum values, box edges represent 1st and 3rd quartiles, X = mean, horizontal bar = median.
p values vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates
ANCOVA, analysis of covariance; OI, osteogenesis imperfecta.

Figure 2B. Tibial vBMD

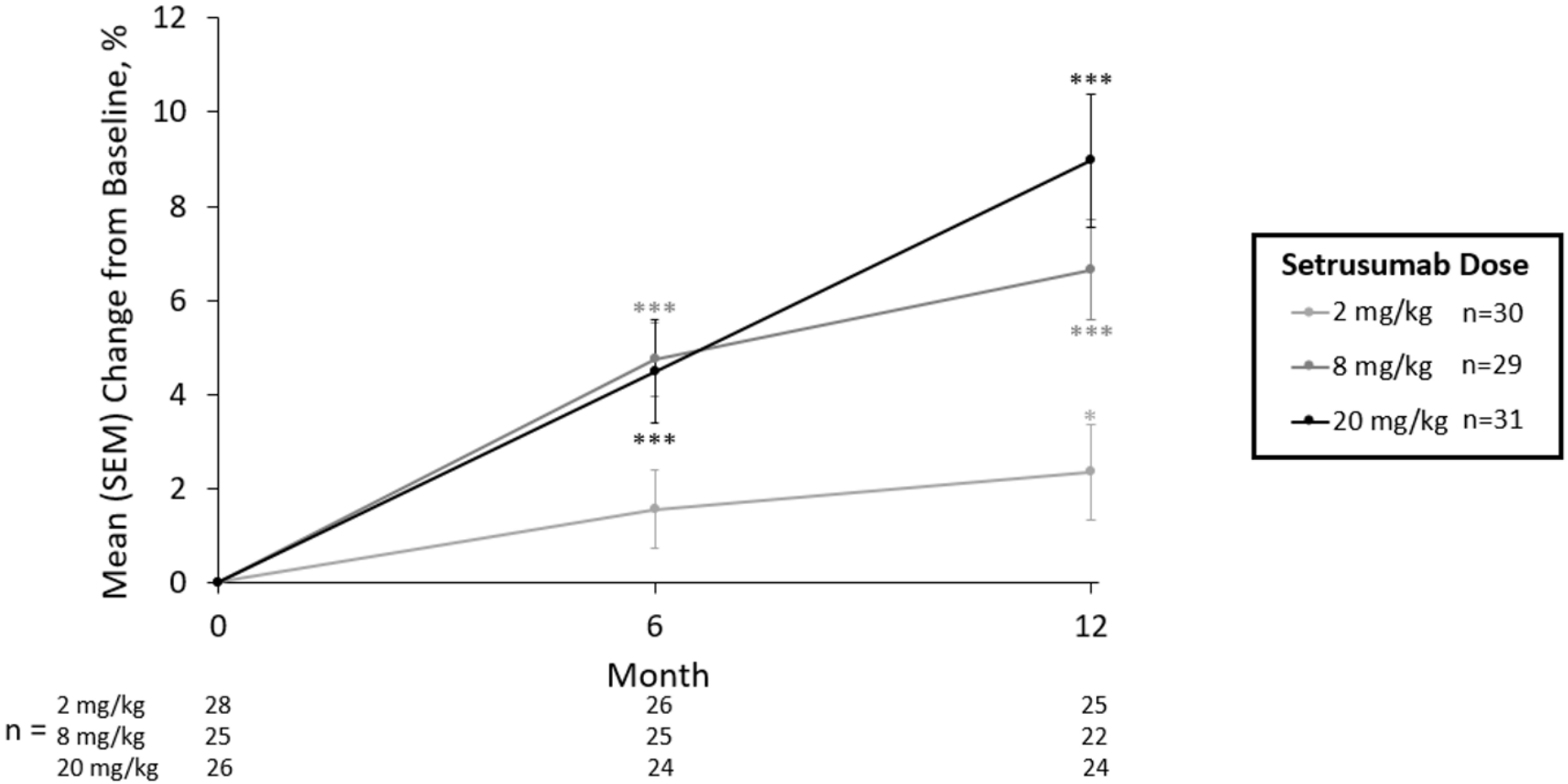


	Cortical vBMD			Total vBMD		
n	15	17	24	15	17	24
Mean	-0.15	0.17	1.85	-1.21	0.86	2.25
p value	0.685	0.482	<0.001	0.387	0.346	0.020

Error bars represent the minimum and maximum values, box edges represent 1st and 3rd quartiles, X = mean, horizontal bar = median.
p values vs baseline based on an ANCOVA model with baseline values, treatment group and OI type as covariates
ANCOVA, analysis of covariance; OI, osteogenesis imperfecta.

Supplementary Figure 3: Mean (SEM) Change from Baseline in Areal BMD by DXA of the lumbar spine (A), total hip (B), femoral neck (C), and total body excluding head (D)

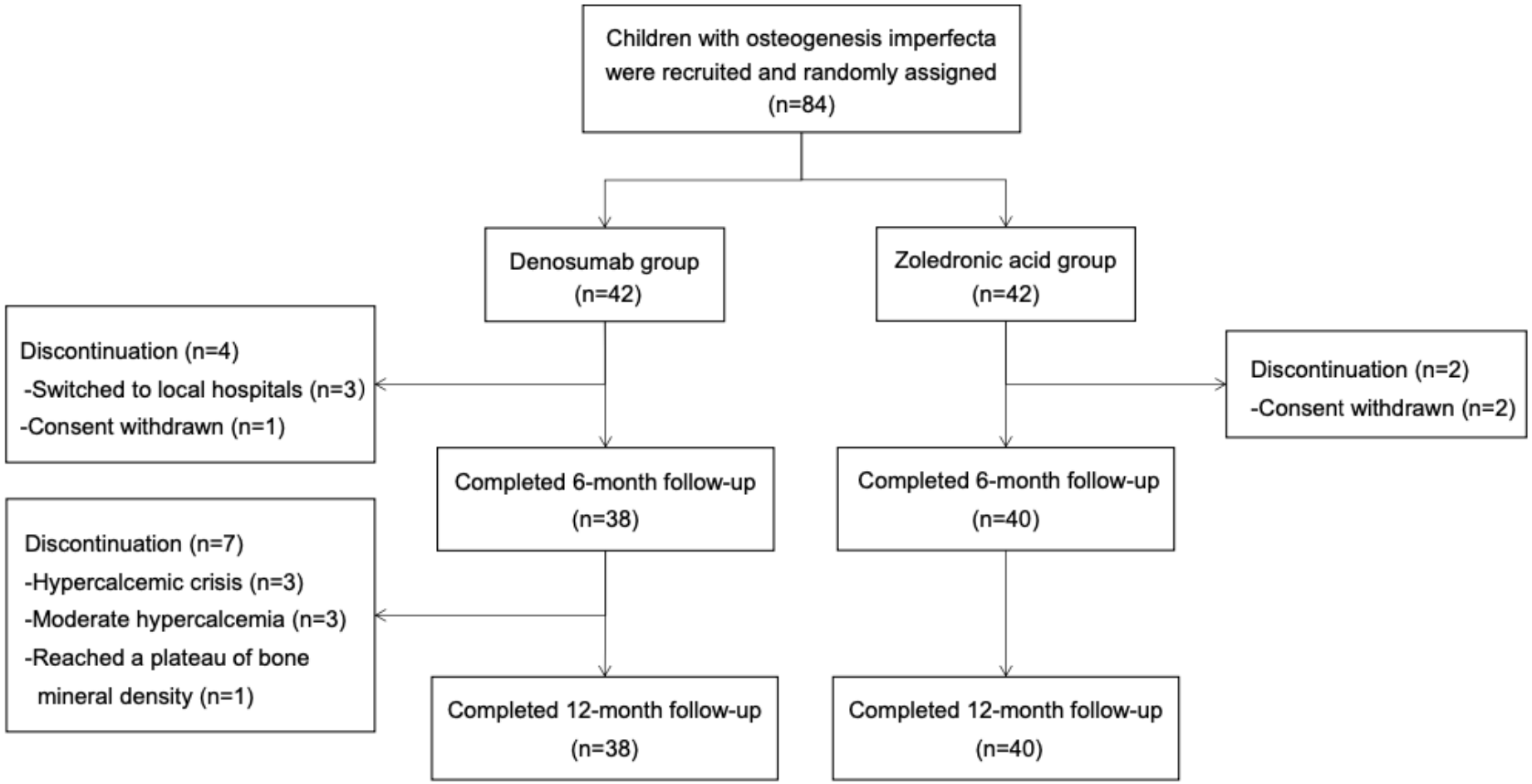
Supplementary Figure 3A: Lumbar Spine



The Journal of Clinical Endocrinology & Metabolism, 2024, **109**, 1827–1836
https://doi.org/10.1210/clinem/dgad732
Advance access publication 10 January 2024
Clinical Research Article

Safety and Efficacy of Denosumab in Children With Osteogenesis Imperfecta—the First Prospective Comparative Study

Jiayi Liu,[1] Xiaoyun Lin,[1] Lei Sun,[1] Qian Zhang,[1] Yan Jiang,[1] Ou Wang,[1] Xiaoping Xing,[1] Weibo Xia,[1] and Mei Li[1]


Children with osteogenesis imperfecta were recruited and randomly assigned (n=84)
Denosumab group (n=42)
Zoledronic acid group (n=42)
Discontinuation (n=4)
-Switched to local hospitals (n=3)
-Consent withdrawn (n=1)
Discontinuation (n=2)
-Consent withdrawn (n=2)
Completed 6-month follow-up (n=38)
Completed 6-month follow-up (n=40)
Discontinuation (n=7)
-Hypercalcemic crisis (n=3)
-Moderate hypercalcemia (n=3)
-Reached a plateau of bone mineral density (n=1)
Completed 12-month follow-up (n=38)
Completed 12-month follow-up (n=40)

The study was designed as a 1-year, open-label, randomized controlled study.

After baseline examinations and screening by endocrinology department, children or adolescents with OI were randomized to receive denosumab 30 mg or 60 mg subcutaneous injection every 6 months or ZOL 2.5 mg or 5 mg intravenous infusion once.

Children over 5 years old were given denosumab at a dose of 60 mg every 6 months, and those under 5 years old received a half dose of denosumab (30 mg every 6 months).

ZOL was administered at a dose of 5 mg (in children with a body weight >25 kg) or 2.5 mg (in children with a body weight ≤25 kg) once a year.

The primary endpoints were the changes in BMD at the LS, FN and total hip during the treatment.
The secondary endpoints were the changes in serum concentrations of calcium and bone turnover biomarkers, the incidence of new fractures, and the changes in spinal morphometry

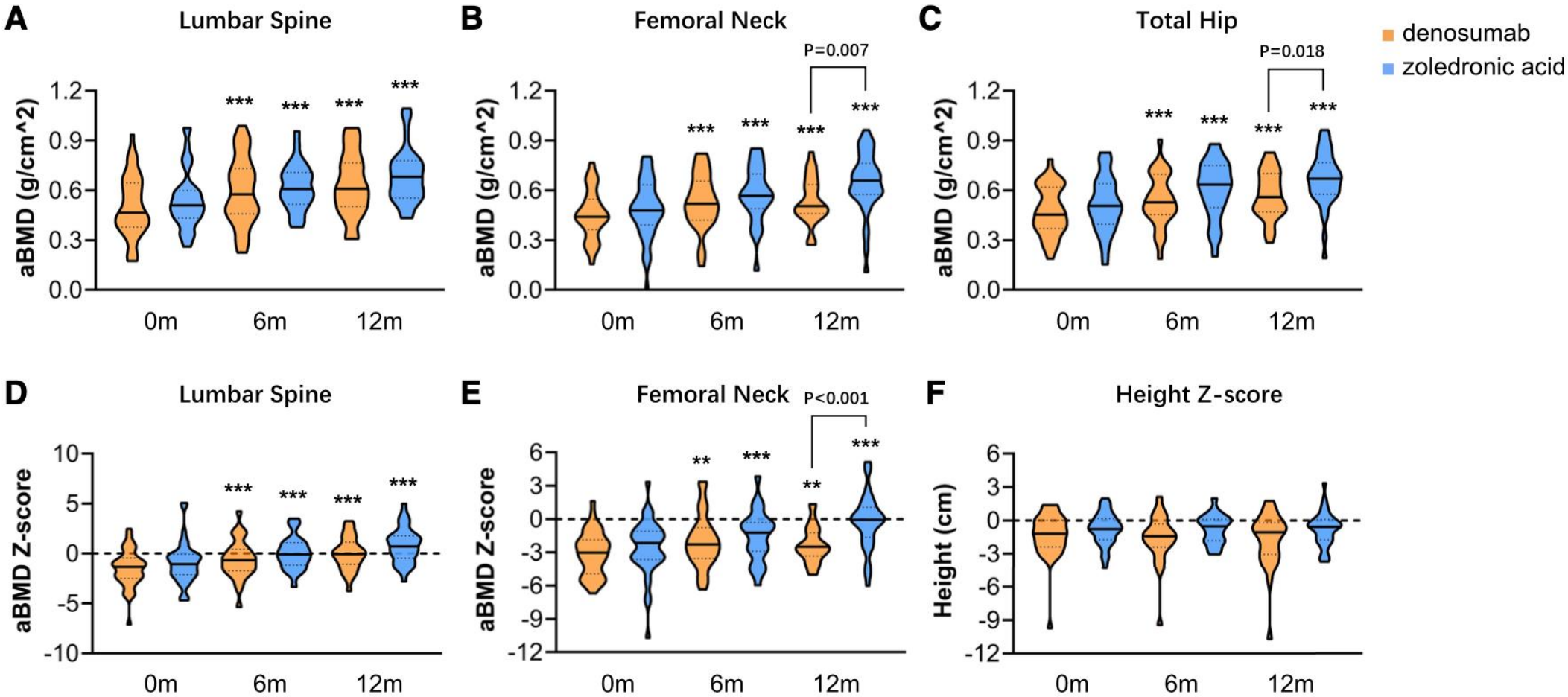


Figure 2. Changes in the areal bone mineral density (aBMD), Z-score, and height Z-score after denosumab or zoledronic acid treatment. A, Changes in aBMD at the lumbar spine. B, Changes in aBMD at the femoral neck. C, Changes in aBMD at the total hip. D, Changes in aBMD Z-score at the lumbar spine. E, Changes in aBMD Z-score at the femoral neck. F, Changes in height Z-score. A-F, Are presented as violin plots with median (solid line) and interquartile range (IQR, dotted line). $^{**}P < .01$, $^{***}P < .001$ vs baseline. m, month.

Osteoporosis International
https://doi.org/10.1007/s00198-025-07423-2

ORIGINAL ARTICLE

TBS as a complementary tool for assessing vertebral fractures and spinal deformity in children and adolescents with osteogenesis imperfecta

Jiayi Liu[1] · Yi Zhang[2] · Wei Yu[2] · Lei Sun[1] · Jing Hu[1] · Yan Jiang[1] · Ou Wang[1] · Xiaoping Xing[1] · Weibo Xia[1] · Mei Li[1]

Characteristic	OI type I ($n=70$)	OI type III ($n=33$)	OI type IV ($n=43$)	Total ($n=153$)	P-value	Reference
Age (years) (mean ± SD)	10.05 ± 3.47	10.86 ± 4.05	9.83 ± 3.22	10.18 ± 3.53	0.434	
Sex (male/female)	44/26	22/11	34/9	102/51	0.191	
Age of onset (years) (median (IQR))	3 (2, 6)	1.4 (0.3, 2.0)	3.0 (2.0, 6.0)	2.7 (1.5, 6)	< 0.001	
Previous fracture times (median (IQR))	3 (2, 4)	6 (4, 15)	4 (3, 6)	4 (3, 6)	< 0.001	
Annual fracture rate (median (IQR))	0.32 (0.24, 0.46)	0.60 (0.31, 1.21)	0.45 (0.30, 0.66)	0.38 (0.27, 0.65)	< 0.001	
Patients with vertebral fractures (n (%))	28 (40.0)	20 (60.6)	19 (44.2)	69 (45.1)	0.142	
Height (cm) [a] (mean ± SD)	136.3 ± 21.9	126.4 ± 20.5	132.3 ± 18.5	134.5 ± 19.5	0.099	
Height Z-score (mean ± SD)	− 0.206 ± 1.612	− 3.836 ± 4.463	− 1.283 ± 1.745	− 1.079 ± 2.825	< 0.001	
Weight (kg) [a] (mean ± SD)	36.4 ± 15.6	31.7 ± 12.6	34.2 ± 14.3	35.6 ± 14.17	0.341	
Weight Z-score (mean ± SD)	0.737 ± 1.931	− 1.256 ± 1.967	− 0.006 ± 1.233	0.018 ± 1.878	0.001	
BMI (kg/m^2) (mean ± SD)	18.9 ± 3.5	19.3 ± 5.1	19.0 ± 3.9	19.0 ± 4.0	0.883	
Ca (mmol/L) (mean ± SD)	2.44 ± 0.10	2.44 ± 0.10	2.44 ± 0.11	2.44 ± 0.12	0.987	2.13 ~ 2.70
P (mmol/L) (mean ± SD)	1.68 ± 0.19	1.65 ± 0.17	1.65 ± 0.22	1.64 ± 0.25	0.665	1.29 ~ 1.94
ALP (U/L) (mean ± SD)	296 ± 90	272 ± 88	302 ± 85	281 ± 94	0.332	58 ~ 400
β-CTX (ng/ml) (mean ± SD)	1.038 ± 0.432	0.875 ± 0.437	0.958 ± 0.409	0.942 ± 0.441	0.094	0.40 ~ 3.30
Lumbar spine aBMD (g/cm^2)[b] (mean ± SD)	0.607 ± 0.182	0.481 ± 0.201	0.493 ± 0.168	0.566 ± 0.201	< 0.001	
Z-score of lumbar spine aBMD (mean ± SD)	− 0.865 ± 2.064	− 2.653 ± 1.965	− 1.613 ± 2.009	− 1.498 ± 2.131	< 0.001	> − 2.0
Z-score of lumbar spine $aBMD_{HAZ}$ (mean ± SD)	− 0.629 ± 1.855	− 1.128 ± 2.091	− 1.098 ± 1.981	− 0.839 ± 1.913	0.406	
Femoral neck aBMD (g/cm^2)[b] (mean ± SD)	0.547 ± 0.142	0.406 ± 0.214	0.448 ± 0.165	0.504 ± 0.179	< 0.001	
Z-score of femoral neck aBMD (mean ± SD)	− 2.379 ± 1.489	− 4.562 ± 2.654	− 3.740 ± 2.004	− 2.795 ± 2.018	< 0.001	> − 2.0
Total hip aBMD (g/cm^2) (mean ± SD)	0.543 ± 0.143	0.462 ± 0.227	0.491 ± 0.166	0.528 ± 0.179	0.068	
TBS (median (IQR)) [c]	1.336 (1.234, 1.390)	1.266 (1.092,1.376)	1.294 (1.156, 1.380)	1.321 (1.206, 1.390)	0.159	
TBS Z-score (mean ± SD)	− 1.127 ± 1.377	− 1.758 ± 1.551	− 1.479 ± 1.802	− 1.249 ± 1.653	0.158	> − 2.0
SDI (median (IQR))	0 (0, 7)	6 (0, 15)	1 (0, 9)	1 (0, 10)	0.041	

OI osteogenesis imperfecta, *BMI* body mass index, *Ca* calcium, *P* phosphate, *ALP* alkaline phosphatase, *β-CTX* β-isomerized carboxy-telopeptide of type I, *aBMD* areal bone mineral density, *HAZ* height-for-age Z-score, *TBS* trabecular bone score, *IQR* interquartile range, *SD* standard deviation

P-value was obtained using one-way ANOVA for data with a normal distribution or using Kruskal–Wallis test for data with a non-normal distribution. Values were given as number (proportion), mean ± SD or median (IQR)

[a]The reference ranges for height and weight of different ages were based on standardized growth charts for Chinese children and adolescents (31)

[b]The reference range of aBMD was based on a cross-sectional study in healthy Chinese children and adolescents (23)

[c]The reference range of TBS was based on a cross-sectional study in healthy children and adolescents (26)

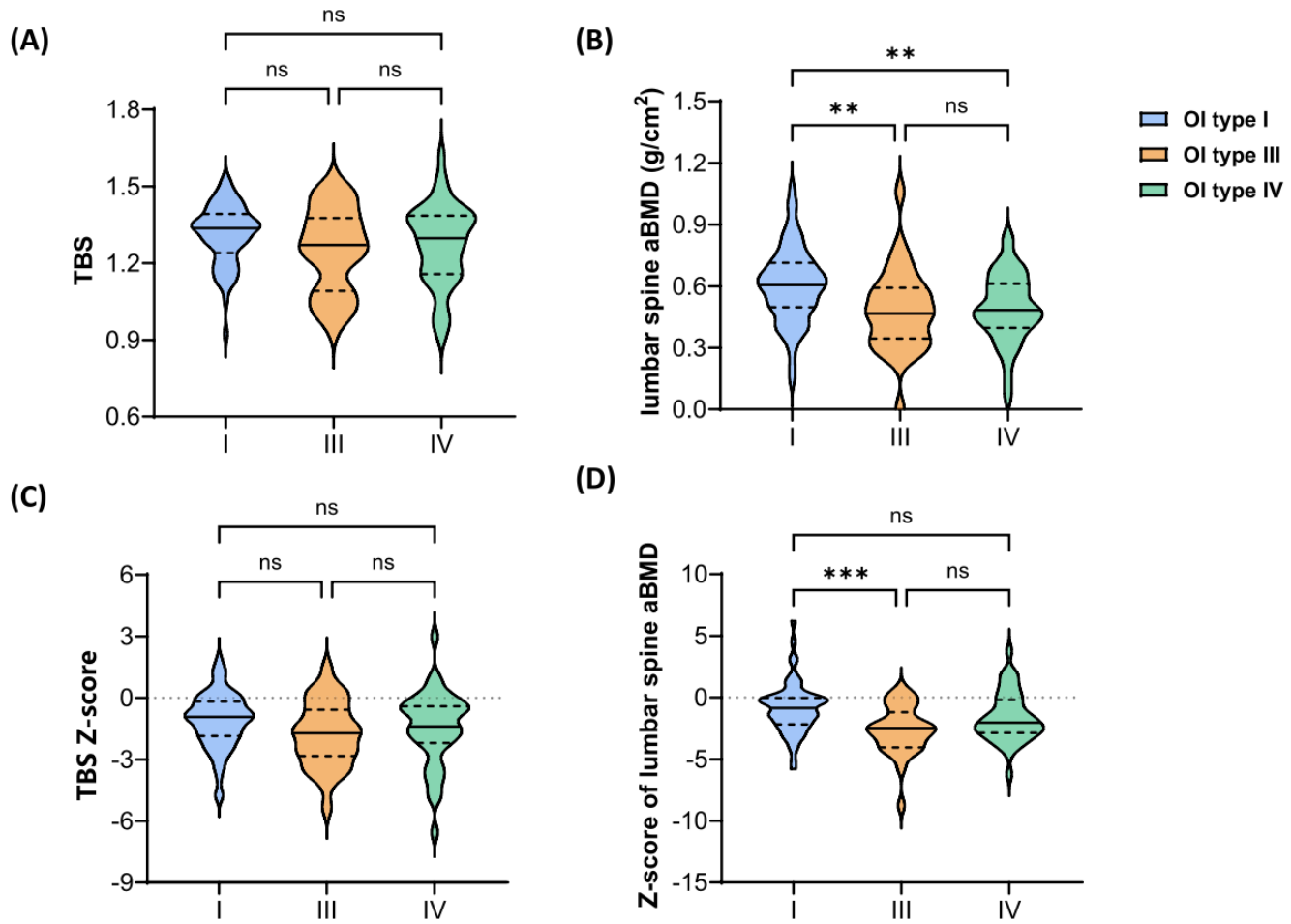


Fig. 1 Comparison of TBS, TBS Z-score, lumbar spine aBMD, and its Z-score in OI patients with different clinical classifications. **A** Comparison of TBS among patients classified by OI clinical type. **B** Comparison of lumbar spine aBMD among patients classified by OI clinical type. **C** Comparison of TBS Z-score among patients classified by OI clinical type. **D** Comparison of lumbar spine aBMD Z-score among patients classified by OI clinical type. Statistical analysis was performed using one-way ANOVA for normally distributed data and Kruskal–Wallis test for non-normally distributed data. Data were presented as violin plots with median (solid line) and interquartile range (IQR, dotted line). TBS, trabecular bone score; aBMD, areal bone mineral density; OI, osteogenesis imperfecta. $*P<0.05$, $**P<0.01$, $***P<0.001$

TBS values in patients with OI were lower than those in normal children and adolescents. However, the differences in TBS and its Z-score among patients with OI type I, III, and IV were not significant

The differences in lumbar spine aBMD and its Z-score among patients with OI type I, III, and IV were significant (both $P < 0.001$)

It was observed a negative correlation between the TBS Z-score and the age of patients with OI, which remained significant after adjusting for confounding factors. This result implied that pediatric patients with OI experienced a gradual degradation of bone microarchitecture assessed by TBS, resulting in a widening gap between them and their peers

In this study, 35% of patients with OI and VCFs did not show osteoporosis according to their aBMD measured by DXA. It was found that among patients without densitometric osteoporosis, the TBS Z-score had higher accuracy than the Z-score of lumbar spine aBMD in discriminating VCFs

Yuan *et al. BMC Musculoskeletal Disorders* (2024) 25:478
https://doi.org/10.1186/s12891-024-07596-7

BMC Musculoskeletal Disorders

RESEARCH Open Access

Low muscle density in children with osteogenesis imperfecta using opportunistic low-dose chest CT: a case-control study

Bone disorders can affect the muscles in different ways, for example, TGFbeta signaling appears to be increased in OI, and release of TGFbeta from bone can decrease muscle mass

Adults with OI had lower lean mass, muscle size, and muscle density compared to healthy controls and presented with markedly impaired muscle function

At the mid-T4 level, thoracic and back (pectoralis, intercostalis, paraspinals, serratus, latissimus dorsi) muscles were measured.
At the mid-T10 level, thoracic and back (latissimus dorsi, intercostalis, serratus, paraspinals, trapezius) muscles were measured

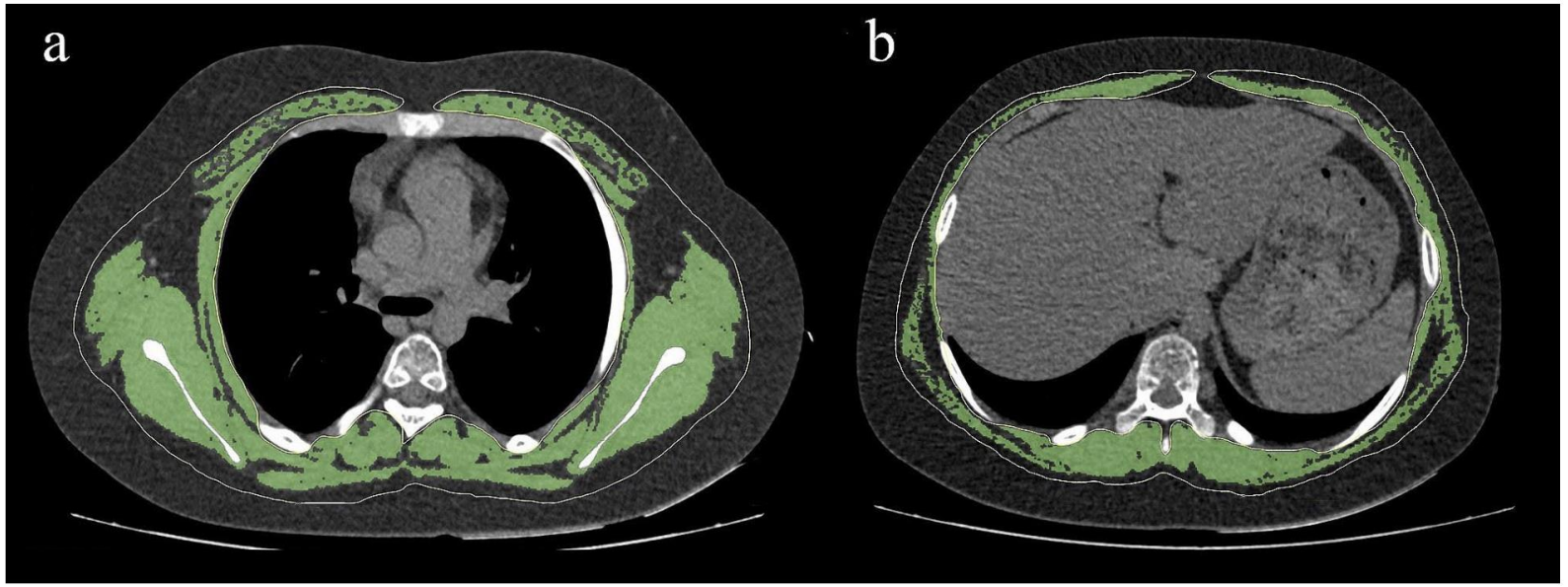


Fig. 1 Measurement of cross–sectional area and mean CT values of the trunk muscles. Measurement of cross–sectional area and mean CT values of the trunk muscles at the level of the mid-T4 (**a**). Measurement of cross–sectional area and mean CT values of the trunk muscles at the level of the mid-T10 (**b**)

Table 2 Differences between OI patients and controls

	OI ($n=20$)	Controls ($n=40$)	p Value
Gender			0.63
Male	15(0.750)	30(0.750)	
Female	5(0.250)	10(0.250)	
Age	9.1 ± 3.3	9.7 ± 3.0	0.47
Weight (kg)	38.4 ± 24.1	43.7 ± 18.8	0.35
Height (cm)	131.7 ± 26.8	144.6 ± 19.0	0.04
BMI (kg/m^2)	19.8 ± 4.6	20.0 ± 4.9	0.91
Muscle parameters measured by the fixed thresholds			
T4 muscle size (cm^2)	93.1 ± 33.4	108.9 ± 34.2	0.09
T4 muscle density (HU)	41.2 ± 5.5	48.0 ± 4.7	< 0.01
T10 muscle size (cm^2)	41.7 ± 15.5	51.0 ± 18.9	0.06
T10 muscle density (HU)	37.3 ± 6.8	45.9 ± 6.2	< 0.01
Muscle parameters measured by the Gaussian mixture model			
T4 muscle size (cm^2)	110.9 ± 18.4	127.2 ± 36.8	0.03
T4 muscle density (HU)	44.6 ± 7.3	51.3 ± 4.3	< 0.01
T10 muscle size (cm^2)	72.6 ± 16.4	88.0 ± 23.8	0.01
T10 muscle density (HU)	41.6 ± 10.4	50.3 ± 6.3	< 0.01

Note: OI, osteogenesis imperfecta; BMI, body mass index; T4, thoracic vertebra; T10, thoracic vertebra

Osteoporosis International (2024) 35:1303–1304
https://doi.org/10.1007/s00198-024-07089-2

LETTER TO THE EDITOR

Beneficial effects of romosozumab on bone mineral density and trabecular bone score assessed by dual-energy X-ray absorptiometry in a family with osteogenesis imperfecta

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Table 1 BMD and TBS in patients before and during romosozumab treatment

Patient Age/sex	Time course	BMD (g/cm^2)	TBS	TBS T-score	TBS Z-score
Proband 48 y.o/male	Before	0.496	1.179	−2.3	−1.5
	6 M	0.521	1.175	−2.3	−1.5
	12 M	0.578	1.224	−1.9	−1.1
Mother 72 y.o/female	Before	0.824	1.260	−3.3	0.6
	12 M	0.957	1.355	−1.9	2.0
Sister 44 y.o/female	Before	0.713	1.286	−2.9	−2.4

Romosozumab 210 mg was administered subcutaneously once a month for 1 year. BMD of the lumbar spine (vertebrae L1–L4) was measured with DXA (Discovery WI, Hologic Inc., Marlborough, MA, USA). TBS values of the same lumbar vertebrae were determined based on DXA images using dedicated analysis software iNsight (Version 3.03) before, 6 and 12 months after romosozumab treatment

BMD bone mineral density, *TBS* trabecular bone score, *DXA* dual-energy X-ray absorptiometry