Effect of Bisphosphonates and Denosumab on trabecular bone in children with Osteogenesis Imperfecta

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Conclusions

- **Osteogenesis imperfecta is a collagen related disease leading to low bone mass and increased fracture rate**
- **Neridronate treatment increases areal bone mineral density, but without correlation to fracture rate**
- **Trabecular Bone Score is promising to provide further information about the strength of cancellous bone by analyzing DXA scans**

Introduction and objective

Osteogenesis imperfecta (OI) is a hereditary connective tissue disorder due to mutations related to collagen type 1. Bone mass is relevant for determination of the severity of OI. Although bisphosphonate treatment is able to increase areal bone mineral density (aBMD) measured by DXA, there is no correlation to fracture rates.

The aim of this study was to analyze the Trabecular Bone Score (TBS) in children with OI, who were treated with bisphosphonates during the first year and with Denosumab (Dmab) during the second year.

Primary objective of the study: Evaluation of the trabecular bone score in pediatric patients with OI in respect to treatment monitoring.

Methods

3 DXA scans (GE lunar iDXA, lumbar spine) of 6 children (4 boys and 2 girls) with OI were performed at intervals of 12 months each. The first 2 scans were carried out during bisphosphonate treatment. The last was performed after 1 year of Dmab treatment.

Pseudo volumetric BMD (3D BMD) was calculated based on cylindrical model proposed by Kroeger et al., 1992. Pediatric TBS assessment was realized with a custom version of TBS iNsight (Med-Imaps SASU, France) that includes a dedicated soft tissue correction for pediatric subjects based on ex-vivo data and taking into account spine tissue thickness and acquisition mode. TBS, areal BMD (aBMD) and 3D BMD variations at lumbar spine were expressed in % from baseline and normalized at 12 and 24 months.

Patients

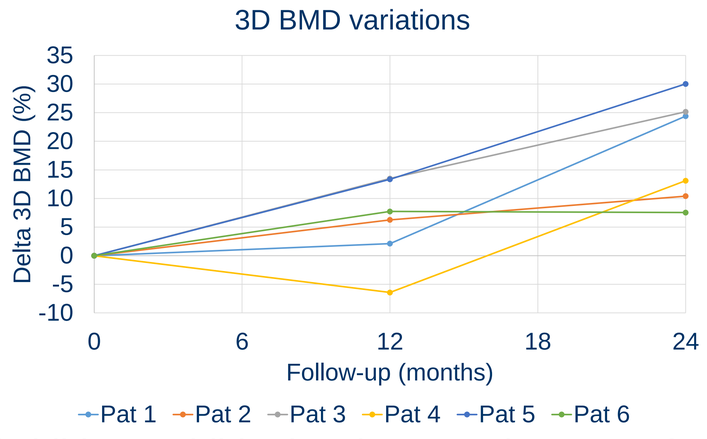
6 Children (4 boys and 2 girls) with a median age of 6.5 [3.9 - 9.3] years were followed 24 months.
Children characteristics at baseline are presented table below.

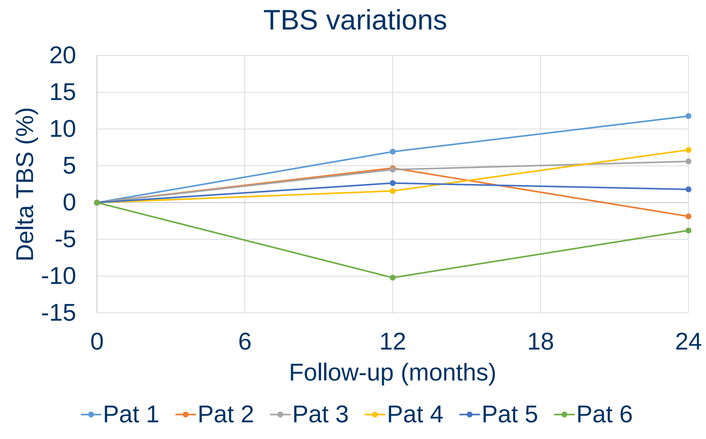
	Baseline
Gender (M/F)	(4/2)
Age (months)	6.5 (3.9-9.3)
Height (cm)	99.5 (86-124)
Height Z-score (SD)	-3.7(-9.4:-0.2)
Weight (Kg)	17.0 (10-24.3)
Weight Z-score (SD)	-1.8 (-3.5:-1.1)
TBS (-)	1.439±0.165
BMD (g/cm²)	0.486±0.145
3D BMD (g/cm³)	0.238±0.067

These children had lower height and weight for their age: -3.7 [-9.4:-0.2] SD, -1.8 [-3.5:-1.1] SD respectively.

Results

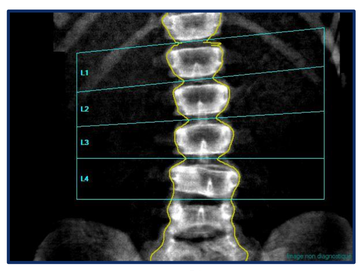
- At the end of the follow-up, height and weight remained stable in mean +0.03/-0.25 SD respectively
- Concerning the weight and height variations, those who exhibited a decrease at 12 months still exhibited a decrease at 24 month
- DXA assessment showed a mean increase in aBMD and 3D BMD of 8,9%/17,6% and 6.1%/18.4% after 12/24 months
- TBS exhibited a less marked increase of 1,7/3,4%.
- No correlations between TBS and DXA parameters have been observed



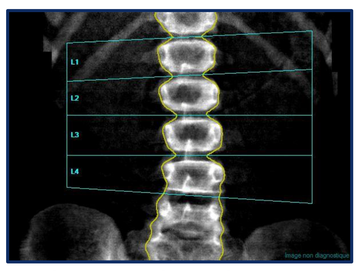


- All children exhibited an increase in terms of BMDs while 5/6 only in terms of TBS.
- The increase rate comparing 12 and 24 month between Denosumab and Bisphosphonates for 3D BMD and TBS is similar (about factor 2)

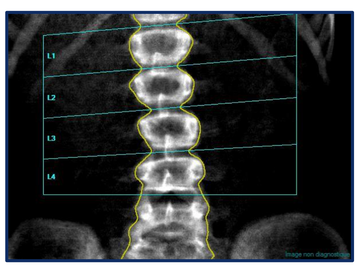
Example of 3D BMD and TBS variations discrepencies



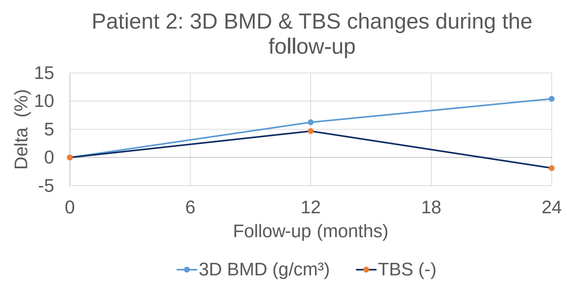
Baseline



After Bisphosphonates



After Denosumab



Patient n°2: Male, age 7.2 yrs

Discussion

- BMD and 3D BMD variations observed are consistent with those observed in the litterature for both bisphosphonates and Denosumab (Hoyer-Kuhn et al., 2016)
- The minimal increase of TBS demonstrates a stronger effect of antiresorptive drugs on cortical compared to trabecular bone.
- Main limitations of that study are the sample size, the imposibility to isolate the variation linked to the treatment from the natural variation due to children growth and that there are no normative data or reference values regarding micraoachitecture modification during growth in children.
- These first study shows a differenciated effect of these treatments on TBS and 3D BMD, which are consistent with those previously seen in adults.
- These promising results have to be strengthen by adding patients and checking bone markers.

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