Effect of Phosphate and Vitamin D analogues of X-Linked Hypophosphatemia during growth on the development of osteoarticular lesions in the *Hyp* mouse model

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INTRODUCTION

✓ Mineralization defects and paradoxical mineralizing enthesopathies are hallmarks of X-linked Hypophosphatemia (XLH), a rare skeletal disease caused by inactivating mutations in the *PHEX* gene (Phosphate-regulating endopeptidase homolog, X-linked).

✓ The conventional medical treatment, which consists in oral phosphorus and active vitamin D analogue supplementation, aims at counteracting consequences of FGF23 excess and is commonly prescribed from early childhood to the end of growth[1], and sometimes through adulthood. Cartilaginous tissue complications in adults become a dominant feature in the clinical evolution of XLH[2].

✓ By using the *Hyp* mice, the murine model of XLH, we previously monitored the development of osteoarticular lesions through a 12 months follow up, identifying enthesopathies, calcifications and osteoarthritis. These lesions were already present at 3 months and significantly increased from 3 to 12 months.

AIM

✓ Here, we studied the effect of the current treatment (oral phosphorus and active vitamin D) of XLH on the development of skeletal manifestations. We compared the effect of the treatment when started early in life to that of treatment started in early adulthood.

METHODS

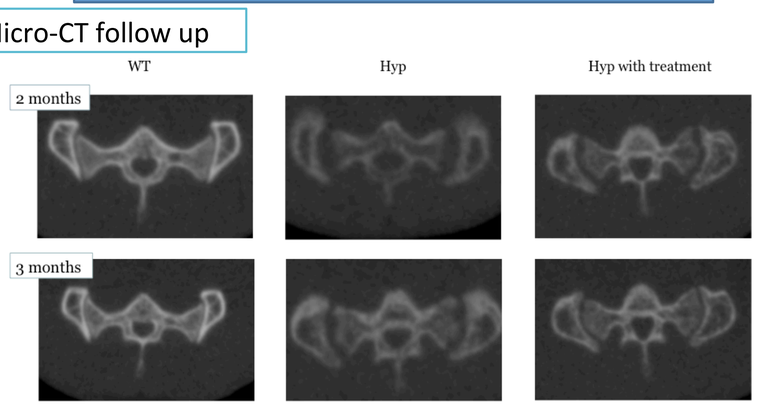
✓ *Hyp* mice were treated with oral phosphorus supplementation (1.93g/L in the water) and intraperitoneal calcitriol injections (0.175µg/kg) every other day and compared to non-treated *Hyp* mice and Wild Type (WT) mice (N = 6 per group).

✓ The treatment followed two different patterns: - **group 1**: from 2 months to 3 months to study the effect of the conventional treatment on osteoarticular lesions; **group 2**: from 3 weeks to 3 months to study the effect of long-term treatment started during growth.

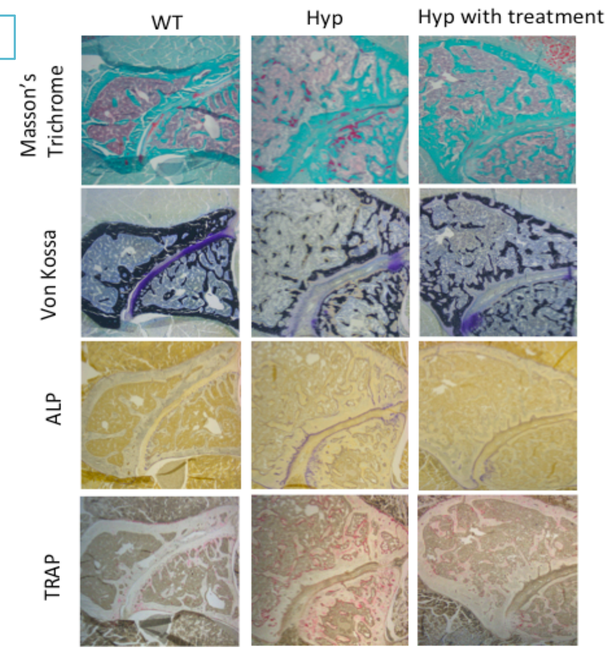
RESULTS

Group 1: treatment in early adulthood

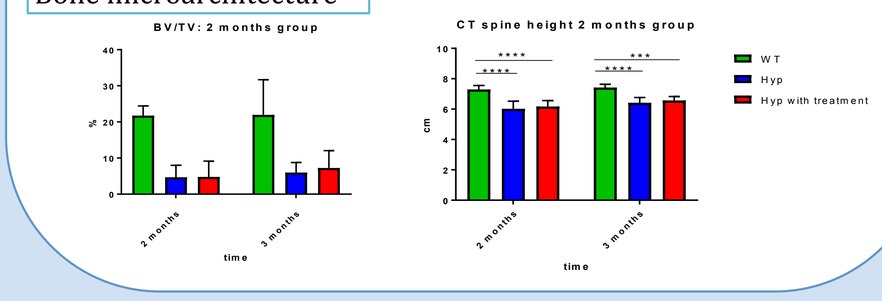
Micro-CT follow up



Histology

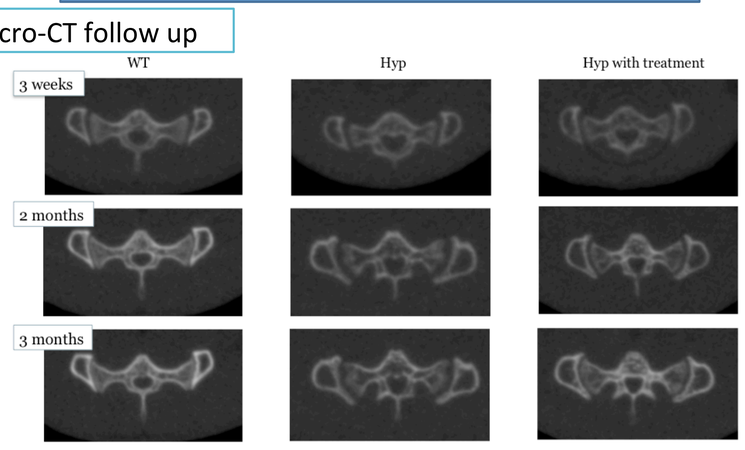


Bone microarchitecture

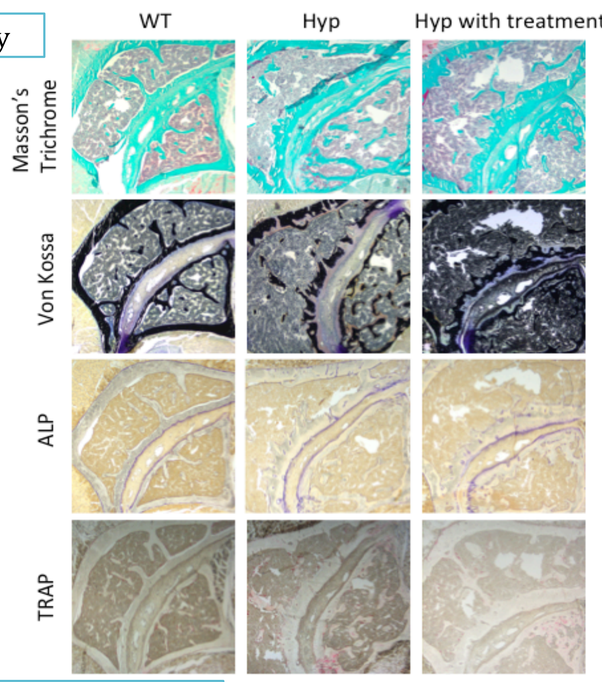


Group 2: long-term treatment

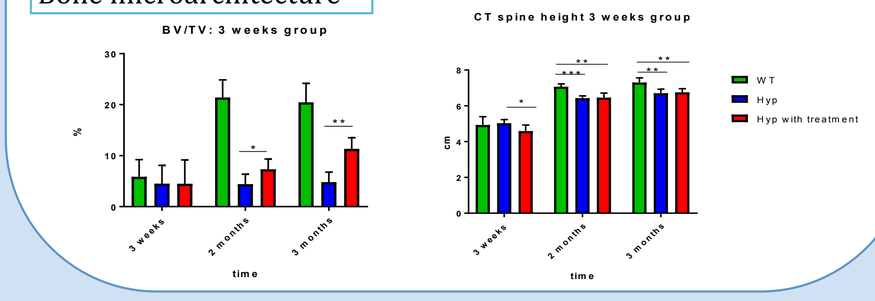
Micro-CT follow up



Histology



Bone microarchitecture



✓ Our work confirms that the conventional treatment given early in life improves osteoarticular lesions, bone mineralization and micro architecture, and fusion of growth plate (data not showed).

✓ We found no difference between untreated *Hyp* mice and mice treated only one month at the end of growth , suggesting that the treatment during adulthood should be administrated during a longer period to be efficient.

PERSPECTIVES

✓ Our findings highlight the **relevance of the *Hyp* murine model for preclinical studies** aiming to test new therapies on the development of osteoarticular lesions.

✓ Future studies should compare the effect of the new therapy based on the anti-FGF23 antibody to that of the conventional therapy.

REFERENCES

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2. Che *et al.*, Impaired quality of life in adults with X-linked hypophosphatemia and skeletal symptoms. *European Journal of Endocrinology*. 2016.

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