SUN-101

Background: Achondroplasia (ACH) is the most common non-lethal skeletal dysplasia. Fibroblast growth factor receptor 3 (FGFR3) plays a crucial role in bone elongation, demonstrated by FGFR3 gain-of-function mutations in individuals with ACH and hypochondroplasia. Multiple therapeutic strategies have been considered for ACH, the most advanced is to employ an analog of C-type Natriuretic Peptide (CNP), which antagonizes the MAP kinase (MAPK) pathway. Here, we evaluated a therapeutic strategy that targets all pathways downstream of FGFR3 (e.g., STAT1), not just MAPK. We hypothesized that a very low dose of the oral selective FGFR1-3 tyrosine kinase inhibitor (TKI) infigratinib (BGJ398) would be able to improve defective bone elongation. We also hypothesized that infigratinib would have greater potency at lower concentrations in an ACH cell line than a CNP analog (e.g., vosoritide) given its effects on multiple downstream pathways. **Methods:** A mouse model (*Fgfr3*$^{Y367C/+}$) mimicking ACH was treated with subcutaneous injections of infigratinib daily (0.2 or 0.5 mg/kg/day) or intermittently (1 mg/kg, every 3 days) for a treatment duration of 15 days (PND1-15). *In vivo* results were compared with vehicle-treated mutant mice. TAN 4-18-chondrocytes, a human chondrocyte line expressing a heterozygous Y373C *FGFR3* mutation, were treated with multiple concentrations of infigratinib and vosoritide and MAPK levels were measured. **Results:** We observed a significant improvement of the upper (humerus +7%, ulna +11%) and lower (femur +11%, tibia +16%) limbs at 0.5 mg/kg/day, and improvement in the foramen magnum. The effect of infigratinib on bone elongation was reduced with a lower dose (0.2 mg/kg), confirming a dose-response relationship. With intermittent injections of infigratinib (1 mg/kg, every 3 days), gain of growth was significant for all the long bones (+7%) and the size of the foramen magnum was increased. Modification of the growth plate structure, displaying better organization, was also seen. In cell line data, compared with FGF18-treated TAN 4-18-chondrocytes, concentrations of 10^{-6}M to 10^{-10}M infigratinib led to statistically significant ($p<0.05$) improvements. With vosoritide treatment, a concentration of 10^{-4}M led to statistically significant improvements compared with FGF18-treated chondrocytes ($p<0.05$), although this was not seen at 10^{-5}M. **Conclusions:** Preclinical ACH mouse model data indicate that low, as well as intermittent, doses of infigratinib promote growth and can improve the foramen magnum. No apparent toxicity of infigratinib was observed, suggesting that TKI therapy has the potential to be a valuable and relevant option for children with ACH. Furthermore, cell line data indicate that infigratinib showed superior potency over a CNP analog, suggesting that inhibition of multiple FGFR3-related pathways vs MAPK inhibition alone may lead to increased efficacy.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Case Report: Malignant Pheochromocytoma

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SUN-939

Case Report: Malignant Pheochromocytoma

Introduction: The concept of malignancy for pheochromocytoma is complex and the best definition is the presence of metastases, according to WHO. Anatomopathological scoring systems are not effective in predicting metastases. Malignancy should be considered when tumors larger than 8cm (> 80g), paragangliomas (especially retroperitoneal), dopamine / methoxythyramine increase, Ki67> 6% and SDHB mutation. At 5 years, survival ranges from 50-69%. Metastases may appear 20-40 years after initial treatment of pheochromocytoma. We describe a case that metastasis was identified 33 years after pheochromocytoma excision

Case report: A 57-year-old female patient with a postoperative history of 33 years of right adrenal pheochromocytoma was discharged from the endocrinologist after 10 years of follow-up. At diagnosis 33 years ago, she had symptoms of hypertension with paroxysms and weight loss that disappeared after tumor removal. 2 years investigating weight loss with general practitioner without another celebratory. On physical examination, orthostatic hypotension was highlighted. Plasma methanephrine 0.8 nmol / L (VR <0.5) and plasma normetanephrine 1.8 nmol / L (VR <0.9), chromogranin A 5.7 nmol / L (VR <3 nmol / L) and clonidine test with 36.6% suppression of metanephrines, suggesting tumor recurrence. MRI localized recurrence of the adrenals and MIBG scintigraphy with I^{131} that showed, respectively, in the topography next to the paracaval and retroportal right diaphragmatic crura, isointense T1 and slightly hyperintense T2 at 1.8 cm and radiopharmaceutical hypercaptation in right adrenal topography. Genetic panel by NGS did not identify germline mutation in 22 pheochromocytoma-related genes. FDG PETCT was consistent with MRI and MIBG images. Gallium $PETCT^{68}$ DOTATOC detected the lesions already described, in addition to a lytic lesion in the left femoral intertrochanteric medulla. Anatomopathological approached abdominal lesion confirming pheochromocytoma metastasis in lymph node conglomerate. Currently has a negative methanephrine plasma, however chromogranin A 142 ng / mL (VR <93), and was chosen by the observant approach.

Conclusion: The case of the patient illustrates that pheochromocytoma should be followed indefinitely, as metastases may appear many years later and may present different aggressiveness potentials.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Ga-DOTATATE and Tumor Induced Osteomalacia: Finding the Culprit Lesion

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SAT-337

Introduction

Tumor-induced osteomalacia (TIO) is a very rare paraneoplastic disorder caused by tumors that produce fibroblast growth factor 23 (FGF23) resulting in phosphate