

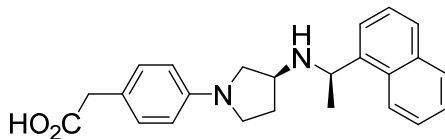
Discovery of Evocalcet, a Next Generation Calcium-Sensing Receptor Agonist for the Treatment of Hyperparathyroidism

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The calcium-sensing receptor (CaSR) is a G-protein coupled receptor (GPCR), which senses extracellular calcium ion and regulates PTH (parathyroid hormone) secretion on parathyroid gland cells. Cinacalcet hydrochloride, a CaSR agonist is widely used for the oral treatment of secondary hyperparathyroidism in dialysis patients by decreasing the serum PTH, calcium and phosphate levels. However, it is also known that cinacalcet has several issues such as adverse effects on the gastrointestinal tract (e.g., nausea and vomiting) and potential drug-drug interactions by strong CYP2D6 inhibition.

We started the drug discovery efforts targeting CaSR agonists without the defects of cinacalcet, and it led the discovery of evocalcet. Evocalcet shows a strong PTH suppression in a rat model, and a better result than cinacalcet on gastric emptying tests in rats. Furthermore, evocalcet also has no remarkable direct CYPs inhibition including CYP2D6.

We will present and discuss the story of the discovery of evocalcet from exploring the SAR of cinacalcet in this session.



Evocalcet