New and Future Therapies for Hypoparathyroidism

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Disclosures

- 100% NIH Funded
- No Commercial Interests
- Collaborator MGH Long-Acting PTH Drug Development Study
- Opinions are personal - not NIH
Treatment of Hypoparathyroidism – what do we need to consider?

- Blood levels of calcium
- Urine levels of calcium
- Effects on bone
- Effects on brain

Safety

Convenience

Cost
New Therapies

• PTH 1-34 s.q. injections
• PTH 1-84 s.q. injections
• PTH 1-34 pump

Future Therapies

• Calcilytics
• Long-acting PTH
• Gene therapy
• Transplant therapy
New Therapies: PTH 1-34 s.c. injection

Safety +

Convenience ↓

Cost $$$
New Therapies: PTH 1-84 s.c. injection

Safety ?

Convenience ↑

Cost $$
New Therapies: PTH 1-34 pump

Safety ?

Convenience ↓↓

Cost $$$
Future Therapies: Long-acting PTH

Safety ?

Convenience

Cost $$
Future Therapies: Calcilytics
Future Therapies: Calcilytics

• What is a calcilytic?
• A calcilytic is an antagonist of the calcium-sensing receptor
• AKA = “anti” calcium; tricks your parathyroid and kidney into thinking calcium is lower than it is:
  - if you have any parathyroid function, it will increase PTH
    • could potentially be VERY effective for autosomal dominant hypoparathyroidism (which is due to CSR mutations)
  - it will make the kidney hold on to calcium
    • could potentially be an “adjunct” to any treatment for hypoparathyroidism

Example: Ronacaleret manufactured by GlaxoSmithKline
Future Therapies: Calcilytics

Safety ?

Convenience ↑

Cost $$
Future Therapies: Gene Therapy

Human Parathyroid Hormone Is Secreted Primarily into the Bloodstream After Rat Parotid Gland Gene Transfer

Future Therapies: Gene Therapy

Safety ?

Convenience ↓

Cost $$$
Future Therapies: Transplant
Future Therapies: Transplant

Safety ?
Convenience ↓
Cost $$
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<th>Bones</th>
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<th>Safe</th>
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NIH Study

• Patient Advocacy Groups
  – Hypopara Assoc + Umbrella Groups
• Government Research
• Academic Research
• Legislative Efforts
• Industry
NIH Study

• PTH 1-34 titrated to blood calcium
• Primary endpoint: effect on bone
  – Bone biopsies at start and end of treatment
• Up to 5 years of treatment
• All testing and travel expenses paid for
• The BEST hypoparathyroidism doctors and nurses in the business! (opinion)
NIH – Skeletal Clinical Studies Unit Team

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Long-Acting PTH Drug Development Program