SNF472 – a potential novel calcification inhibitor in CKD-MBD

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Chronic Kidney Disease – Mineral Bone Disorder

Vascular calcification in CKD-MBD:

Loss of inhibitors
↓MGP
↓Ppi
↓OPN

Matrix vesicle release

Fetuin-A uptake

ECM modification and degradation

Lineage reprogramming
↑Runx2
↑ALP
↓SM22

Apoptosis

ECM Mineralization

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What is SNF472?

• Main component: myo-inositol hexaphosphate (IP6, phytate)
  • Natural nutritional ingredient
  • Potent modulator of calcification

• SNF472:
  • Modified IP6 salt, i.v. formulation
  • Being developed for:
    - Reducing of cardiovascular calcification in dialysis patients
    - Treatment of calciphylaxis

Methods: VSMC culture

- **VSMCs from rat aorta**
- **Cell culture**
  - Standard medium: DMEM / F12 + 10% FCS
- **Calcifying cells**
  - Pro-calcific medium: DMEM / F12 + 10% FCS + 3mM Ca and PO₄

**Treatment of calcifying VSMCs with:**
- SNF472
- STS

**Steps:**
1. Cell culture
2. Calcifying cells
3. TUNEL staining
4. Ca-assay
SNF472: Most Effective Dose Finding

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<th>5 days</th>
<th>Ca-Assay</th>
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<td>control</td>
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<tr>
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SNF472 vs STS: Most Effective Dose Finding

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5 days Ca-Assay
SNF472 vs STS: Most Effective Dose Finding

Calcium levels after 5 days SNF472 treatment

Calcium levels after 5 days STS treatment
STS472 vs STS: 
apoptosis rate after 7 days of treatment
Time dependency of SNF472 treatment

- Control
- CaPO
- CaPO + Ca+SNF
- CaPO + CaPO+SNF472
- CaPO + SNF472

0 3 5 7 10 days

Ca-assay
Time dependency of SNF472 treatment
Conclusions:

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<th>STS:</th>
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<td>- Reduces in vitro calcium deposition of rodent VSMCs in a pro-calcific milieu</td>
<td>- Also reduces in vitro calcium deposition of rodent VSMCs in a pro-calcific milieu</td>
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<td>- No significant increase of apoptosis (0.8%)</td>
<td>- Very high levels of apoptosis (77%)</td>
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These results are promising on the future use of SNF472 for the inhibition of cardiovascular calcification in CKD patients
Discussion:
Thank you

for your attention!