CNP-101 Prevents Gluten Challenge Induced Immune Activation in Adults with Celiac Disease

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Phase 2a CNP-101 Proof-of-Concept study schematic

Study subjects: Well-controlled CeD

Day

-45 1 8 15 20 29 35

Screen 14-day GC

CNP-101 8 mg/kg or placebo infusions

Duodenal biopsy

Day 6 of GC

Day 14 of GC

Study subjects:
Well-controlled CeD

CeD, celiac disease; CNP, Cour Nanoparticle Platform; ELISpot, enzyme-linked immunospot; GC, Gluten Challenge; IEL, intraepithelial lymphocytes; IFN, interferon; PBMC, peripheral blood mononuclear cell; Vh: Cd, villus height to crypt depth ratio

Safety assessments

Duodenal histology Vh: Cd and IELs

CeD signs and symptoms

IFN-γ ELISpot – Gliadin reactive T cells

CeD, celiac disease; CNP, Cour Nanoparticle Platform; ELISpot, enzyme-linked immunospot; GC, Gluten Challenge; IEL, intraepithelial lymphocytes; IFN, interferon; PBMC, peripheral blood mononuclear cell; Vh: Cd, villus height to crypt depth ratio
CNP-101 was safe and well tolerated: results of Phase 2a studies

- No serious adverse events (SAEs)
- No clinically significant changes in vital signs, routine clinical laboratory results, liver function tests (LFTs), serum cytokines/chemokines and T cell proliferation
- Complement levels transiently raised in all patients, not associated with adverse events (AEs)
- Most AEs were mild and transient

<table>
<thead>
<tr>
<th>Phase 2a</th>
<th>CNP-101</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>AE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>81%</td>
<td>72%</td>
</tr>
<tr>
<td>Abdomen distention</td>
<td>56%</td>
<td>61%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Headache</td>
<td>44%</td>
<td>17%</td>
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<tr>
<td>Abdominal pain</td>
<td>38%</td>
<td>28%</td>
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<tr>
<td>Vomiting</td>
<td>31%</td>
<td>33%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>33%</td>
<td>50%</td>
</tr>
<tr>
<td>Back pain</td>
<td>31%</td>
<td>0%</td>
</tr>
</tbody>
</table>

AE, adverse event; CNP, Cour Nanoparticle Platform; LFT, liver function test; SAE, serious adverse event
CNP-101 met primary efficacy objective: reduced IFN-γ spot forming units response to gluten challenge

- IFN-γ spot forming units (SFUs) on enzyme-linked immunospot (ELISpot) correspond to gliadin-responsive T cells activated by gluten challenge (GC)
- The placebo group showed the expected, highly significant, increase in IFN-γ SFU during GC
- This GC-induced gliadin-dependant T cell response was substantially reduced by CNP-101 pre-treatment

Primary study objective:
To compare the increase from baseline in IFN-γ SFUs in a gliadin-specific ELISpot assay after an oral GC among patients treated with CNP-101 or placebo

Baseline denotes Day 15 (or Day 1, if Day 15 sample inadequate)
~ One data point omitted for clarity SFU = 100
CNP, Cour Nanoparticle Platform; ELISpot, enzyme-linked immunospot; GC, gluten challenge; IFN, interferon; SFU, spot forming units
CNP-101 pre-treatment effects on duodenal villus height to crypt depth ratio after GC

- Placebo group showed the expected, significant reduction in villus height to crypt depth ratio (Vh:Cd) during GC
- CNP-101 pre-treatment was associated with a reduced GC-induced Vh:Cd deterioration

Secondary study objective:
To compare the change from baseline in the Vh:Cd following an oral GC in subjects treated with CNP-101 or placebo

CNP, Cour Nanoparticle Platform; GC, gluten challenge; Vh:Cd, villus height to crypt depth ratio
CNP-101 pre-treatment reduces gut-homing α4β7 effector memory CD4+ and effector memory CD8+ circulating T cells during GC

- When compared to placebo, CNP-101 pre-treatment significantly reduced the circulation of activated α4β7 effector memory (EM) CD4+ and EM CD8+ T cells during GC.
- These activated α4β7 EM CD4+ and EM CD8+ T cells are gut homing and normally circulate to the intestine and participate in GC-induced intestinal inflammation.
CNP-101 gliadin nanoparticles are a novel approach to inducing tolerance to gluten in CeD

CNP-101 infusion met the primary study objective of preventing the expected activation of IFN-γ-producing gliadin-specific cells during GC

CNP-101 pre-treatment was associated with a trend towards a reduction in GC-induced Vh: Cd deterioration

CNP-101 gliadin nanoparticles also reduced circulating, gut-homing, EM CD4+ and EM CD8+ T cells during GC

To our knowledge, this is the first clinical trial to demonstrate induction of antigen specific immune tolerance in any autoimmune disease.