COUR

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

Kelly C[1,2], Murray J[3], Leffler D[4], Bledsoe A[3], Smithson G[4], Podojil J[5], First R[5], Morris A[5], Boyne M[5], Elhofy A[5], Wu T[3] and Miller S[5,6]

[1]Beth Israel Deaconess Medical Center, Boston, MA, USA

[2]Harvard Medical School, Boston, MA, USA

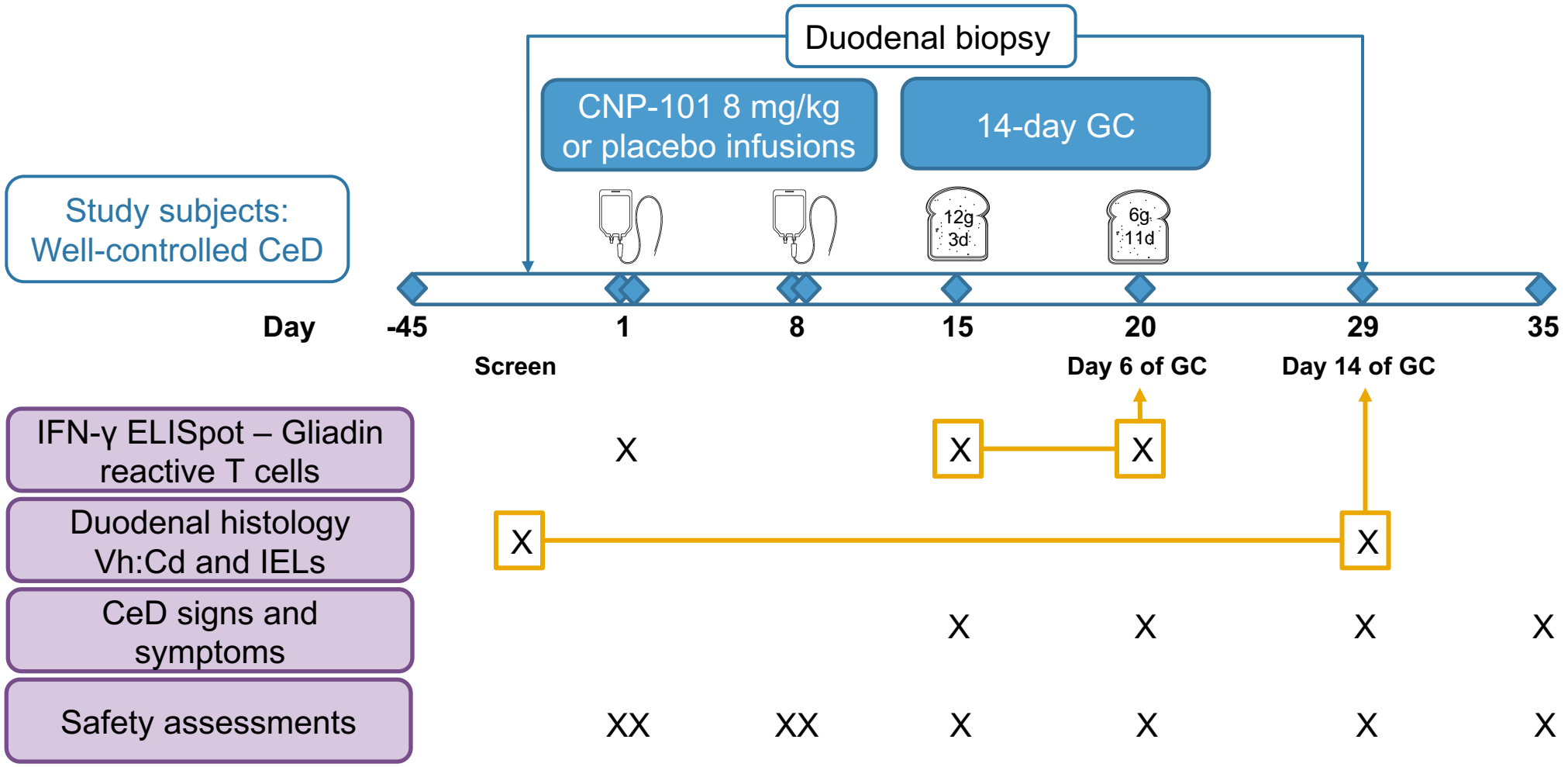
[3]Mayo Clinic, Rochester, MN, USA

[4]Takeda Pharmaceuticals International Co., Cambridge, MA, USA

[5]COUR Pharmaceuticals Development Co., Inc., Northbrook, IL, USA

[6]Feinberg School of Medicine, Chicago, IL, USA

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



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

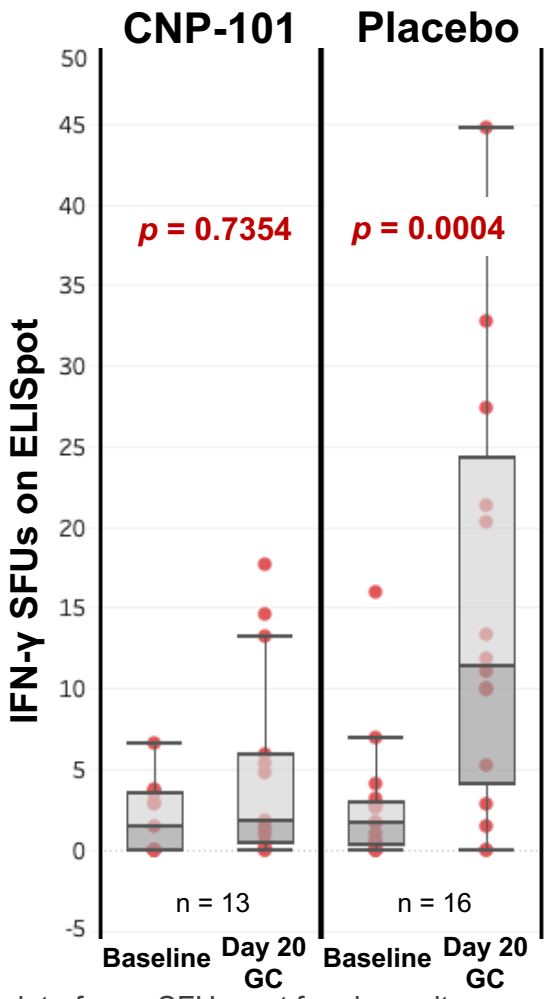
Phase 2a		
	CNP-101	Placebo
AE		
Nausea	81%	72%
Abdomen distention	56%	61%
Diarrhea	50%	50%
Headache	44%	17%
Abdominal pain	38%	28%
Vomiting	31%	33%
Fatigue	33%	50%
Back pain	31%	0%

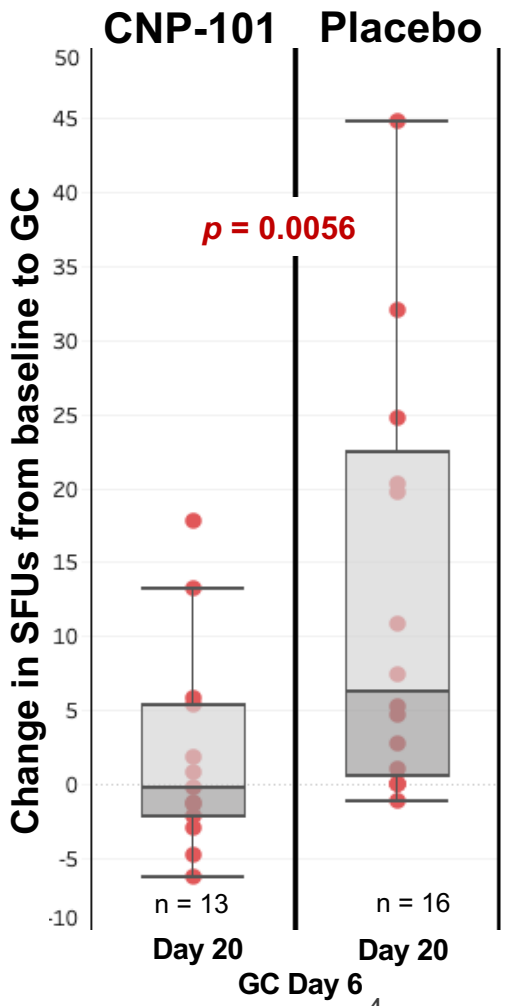
AE, adverse event; CNP, Cour Nanoparticle Platform; LFT, liver function test; SAE, serious adverse event

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



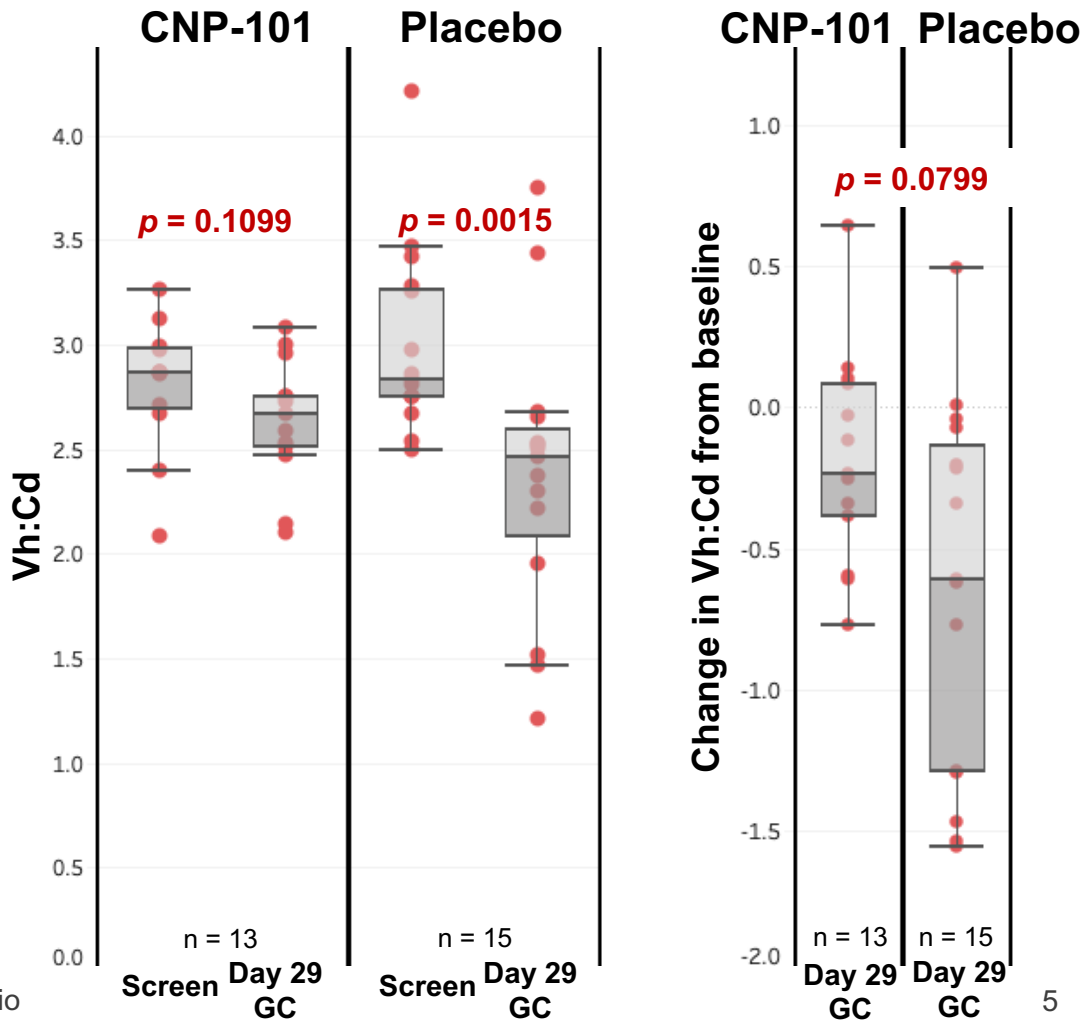


Baseline denotes Day 15 (or Day 1, if Day 15 sample inadequate)
~ One data point omitted for clarity SFU = 100
CNP, Cour Nanoparticle Platform; ELISpot, enzyme-linked immunospot; GC, gluten challenge; IFN, interferon; SFU, spot forming units

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

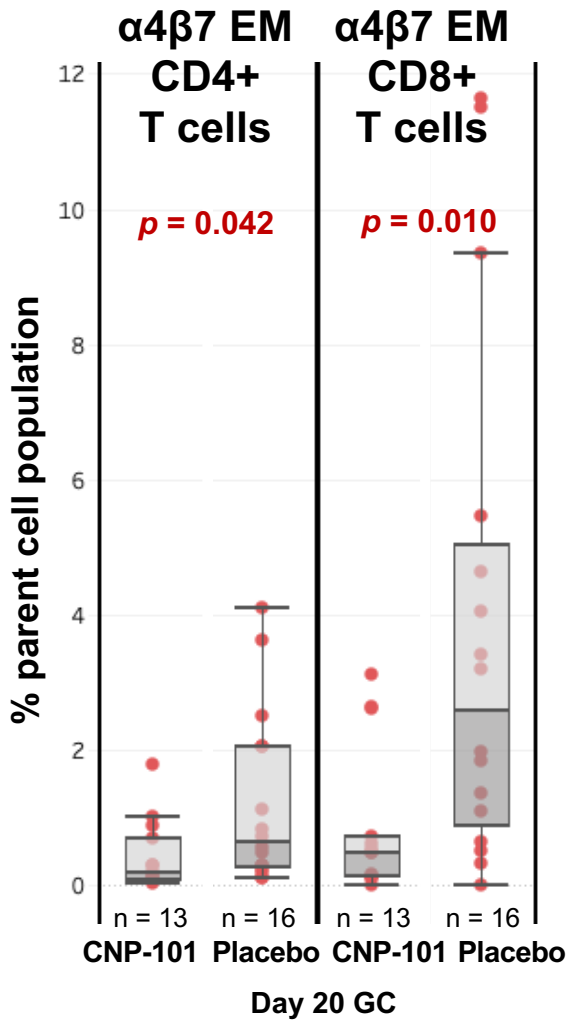
Secondary study objective:
To compare the change from baseline in the Vh:Cd following an oral GC in subjects treated with CNP-101 or placebo



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, Cour Nanoparticle Platform; EM, effector memory; GC, gluten challenge

Summary: CNP-101 prevents GC-induced immune activation in adults with CeD

- 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

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