CP101, an Investigational Oral Microbiome Therapeutic for the Prevention of Recurrent *C. difficile* Infection: A Combined Analysis of the PRISM3 (Randomized Placebo-Controlled) and PRISM-EXT (Open-Label) Trials

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Background

- Disruption of the microbiome is key to the pathogenesis of recurrent *Clostridioides difficile* infection (CDI).
- Placebo-controlled trials assessing microbiome therapeutics have demonstrated efficacy in recurrent CDI; however, long-term safety and efficacy data from rigorously conducted studies of microbiome therapies, including cumulative efficacy in those who received a second dose following a CDI recurrence, is limited.
- CP101 is an investigational orally-administered microbiome therapeutic designed to restore microbiome diversity and break the cycle of recurrent CDI.

Methods

- We conducted a combined post-hoc analysis of data from the PRISM3 placebo-controlled trial and the PRISM-EXT open label trial of CP101 for the prevention of recurrent CDI.
- PRISM3 enrolled participants older than 65 years with one CDI recurrence, or any age with two or more CDI recurrences. PRISM-EXT enrolled participants of any age with one or more CDI recurrences. PRISM-EXT included participants who rolled over from PRISM3 after an on-study CDI recurrence and direct entry participants who were not enrolled in PRISM3.
- In both trials, eligibility criteria included clinical symptoms, CDI diagnosis by guideline-recommended testing (PCR or toxin EIA), in addition to the initiation and clinical response to standard-of-care (SOC) antibiotics.
- In PRISM3, participants were randomized 1:1 to receive one-time oral administration of CP101 or placebo without bowel preparation, following SOC CDI antibiotics. In PRISM-EXT, participants received a one-time oral administration of CP101 without bowel preparation following SOC CDI antibiotics.
- The primary efficacy endpoint for both trials was the proportion of participants without CDI recurrence through 8 weeks post-treatment. In both studies, missing data through Week 8 (primary endpoint) was to be imputed as recurrence. Missing data through Week 24 (secondary endpoint) was imputed as no recurrence. Efficacy and safety were evaluated through 24 weeks.

Results

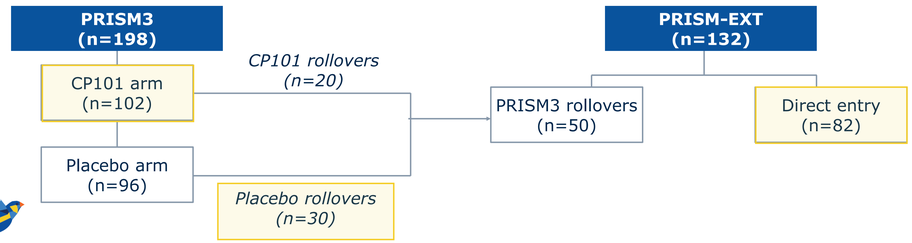
Clinical and demographic characteristics

	PRISM3	PRISM-EXT		
		PRISM3 Rollover		
	CP101 N=102	CP101 in PRISM3 N=20	Placebo in PRISM3 N=30	Direct Entry N=82
Age in years - median (range)	69.0 (19-97)	76.5 (63-94)	71.0 (30-94)	67.0 (18-95)
Female sex - n (%)	69 (68%)	17 (85%)	22 (73%)	60 (73%)
Charlson comorbidity index - mean (SD)	3.9 (2.9)	5.3 (2.5)	3.6 (2.6)	3.0 (2.2)
Recurrent CDI Category[1] - n (%)				
≤ 2 CDI episodes	28 (28%)	1 (5%)	2 (7%)	43 (52%)
≥ 3 CDI episodes	73 (72%)	19 (95%)	28 (93%)	39 (48%)
Positive CDI laboratory test at study entry - n (%)				
PCR-based testing (alone or in combination)[2]	64 (63%)	1 (5%)	0	39 (48%)
Toxin EIA-based testing (alone or in combination)[3]	36 (35%)	19 (95%)	30 (100%)	39 (48%)
Not reported	2 (2%)	0	0	4 (4%)
SOC CDI antibiotic at study entry - n (%)				
Oral vancomycin (alone or in combination)	87 (85%)	19 (95%)	25 (83%)	73 (89%)
Oral fidaxomicin (alone or in combination)	21 (21%)	2 (10%)	6 (20%)	16 (20%)
Oral metronidazole (alone or in combination)	2 (2%)	0	0	1 (1%)
Other	1 (1%)	0	0	0

Abbreviations: SD = standard deviation; CDI = C. difficile infection; PCR = polymerase chain reaction; EIA = enzyme immunoassay; GDH = glutamate dehydrogenase; SOC = standard of care

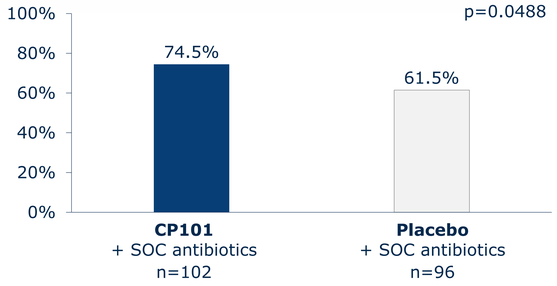
1. *Number of CDI episodes in the previous 6 to 12 months for PRISM3 participants and in the previous 6 months for PRISM-EXT participants*
2. *PCR based testing includes: PCR positive alone or in combination (e.g. GDH+/PCR+; GDH+/toxin EIA-/PCR+; PCR+/Toxin EIA-/without toxigenic culture)*
3. *Toxin EIA based testing includes: Toxin EIA positive alone or in combination (e.g. GDH+/Toxin EIA+; PCR+/Toxin EIA+; GDH+/PCR+/Toxin EIA+; PCR+/Toxin EIA-/toxigenic culture+)*

Across PRISM3 and PRISM-EXT, 214 unique participants received CP101



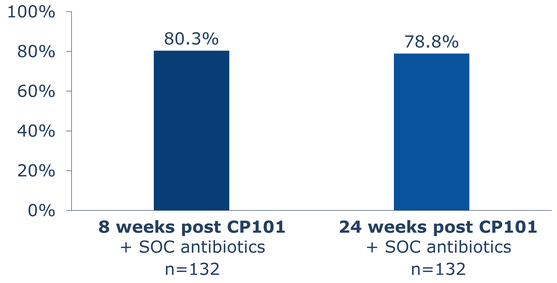
In PRISM3, a Phase II, RCT, CP101 achieved 33.8% relative risk reduction for CDI recurrence

Primary efficacy endpoint: Proportion without CDI recurrence through Week 8



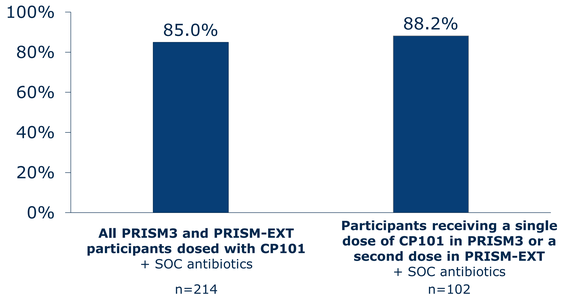
PRISM-EXT efficacy through Week 8 and Week 24

Proportion without CDI recurrence



PRISM3 and PRISM-EXT cumulative efficacy through Week 8

Proportion without CDI recurrence through Week 8



No drug-related SAEs were reported in PRISM3 and PRISM-EXT

- This post-hoc safety analysis combined data from PRISM3 and PRISM-EXT
- No drug-related serious adverse events (SAEs) were reported in any participants that received CP101 in PRISM3 and/or PRISM-EXT, including no drug-related SAEs in the 20 participants who received a second dose of CP101.
- Among participants that received CP101 in either PRISM3 or PRISM-EXT, drug-related treatment emergent adverse events were mild (Grade 1) or moderate (Grade 2), and primarily gastrointestinal in nature.

Discussion

- This is the largest reported dataset of an investigational orally administered microbiome therapeutic for the prevention of recurrent CDI.
- CP101 is the first orally-administered investigational microbiome therapeutic studied in a large RCT and open-label trial which included participants with first CDI recurrence and multiply recurrent CDI.
- In this post-hoc analysis, the cumulative proportion of participants without CDI recurrence following SOC antibiotics and CP101 was 85.0% across both studies through Week 8.
- Among participants that received CP101 in PRISM3, inclusive of those that rolled over to PRISM-EXT and received a second dose, 88.2% of participants were without CDI recurrence through 8 weeks in this post-hoc analysis.

Conclusions

The findings from this post-hoc combined analysis support the hypothesis that CP101 may be efficacious for the prevention of recurrent CDI.

Repeat dosing with CP101 may be beneficial in patients not responding to an initial dose of CP101.

Disclosures:
Allegretti - Scientific Advisory Board: Finch Therapeutics, Iterative Scopes; Consulting: Pandion, Pfizer, Servatus, Abbvie, Takeda, Janssen; Artugen, Morphic, Baccain, Bristol Meyers Squibb; Research Support: Merck, Pfizer; Advisory Board (unpaid): OpenBiome; Clinical Trial Research: Finch Therapeutics
Kelly - Clinical Trial Research: Finch Therapeutics; Clinical Advisory Board: OpenBiome
Fisher - Clinical Trial Research: Finch Therapeutics; Advisory Board (unpaid): OpenBiome; DSMB: Rebiotix/Ferring; Consulting: Bristol-Myers Squibb
Cohen – Employee: Finch Therapeutics
Budree - Employee & Shareholder: Finch Therapeutics.
Khanna - Research: Rebiotix (Ferring), Seres, Vedanta; Consulting: Shire, Takeda, Finch, GSK, Probiotech, Facile, Jetson, Niche, Immuron

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