Table 2: Polyp characteristics by intervention (with cold snare vs with cold forceps)

	Cold snare (N=138)	Cold forceps (N=141)	*p*-value
Mean polyp size, mm (SD)	2.5 (0.5)	2.6 (0.5)	0.161
Location of polyp			0.119
Cecum, N(%)	33 (23.9)	27 (19.1)	
Ascending, N(%)	46 (33.3)	37 (26.2)	
Transverse, N(%)	37 (26.8)	35 (24.8)	
Descending, N(%)	10 (7.2)	22 (15.6)	
Sigmoid, N(%)	10 (7.2)	14 (9.9)	
Rectum, N(%)	2 (1.4)	6 (4.3)	
Pathology			0.009
Tubular adenoma	110 (79.7)	93 (66.0)	
Sessile serrated polyp	0 (0.0)	4 (2.8)	
Hyperplastic polyp	7 (5.1)	20 (14.2)	
Other non-neoplastic tissue	1 (0.7)	4 (2.8)	
Normal colonic mucosa	20 (14.5)	20 (14.2)	
Polyp morphology			0.962
Is	129 (93.5)	132 (93.6)	
IIa	9 (6.5)	9 (6.4)	
Positive margin biopsy pathology, N(%)	2 (1.4)	2 (1.4)	0.983
Polyp removed in more than one piece, N(%)	5 (3.6)	22 (15.6)	<0.001
Polypectomy by fellow, N(%)	23 (16.7)	25 (17.7)	0.814
Hemostatic clip used, N(%)	0 (0.0)	1 (0.7)	0.322
Mean Polypectomy time, s (SD)	42.3 (55.5)*	23.2 (23.4)**	<0.001

SD = Standard deviation
*Available for 130 polyps
**Available for 136 polyps

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CP101, AN INVESTIGATIONAL ORALLY ADMINISTERED MICROBIOME THERAPEUTIC, WAS EFFECTIVE FOR PREVENTION OF RECURRENT *C. DIFFICILE* INFECTION: RESULTS FROM OPEN-LABEL PRISM-EXT TRIAL

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Background Disruption of the microbiome is key to the pathogenesis of recurrent *C. difficile* infection (CDI); however, there is a paucity of safety and efficacy data from rigorously conducted trials of microbiome therapies. Few trials have evaluated the effect of a second dose with an orally administered microbiome therapeutic following a recurrence after initial dosing. CP101 is an investigational orally administered microbiome therapeutic designed to restore microbiome diversity and enable early intervention in recurrent CDI. The PRISM-EXT trial evaluated the safety and efficacy of open-label treatment with CP101 in adults with recurrent CDI and participants that experienced a CDI recurrence in the PRISM3 trial. **Methods** PRISM-EXT enrolled participants with one or more CDI recurrences at 51 sites in the U.S. and Canada. The qualifying CDI episode was diagnosed prior to trial entry by guideline-recommended testing (PCR-based or toxin EIA-based). Following standard-of-care (SOC) antibiotics, eligible participants received a one-time oral administration of CP101 without bowel preparation. PRISM-EXT comprised: 1) participants who rolled over from PRISM3, a Phase 2 randomized double-blind placebo-controlled trial, following an on-study CDI recurrence and 2) direct entry participants with recurrent CDI who were not previously enrolled in PRISM3. The primary efficacy endpoint was sustained clinical cure, defined as an absence of CDI recurrence, through Week 8 following dosing. Secondary endpoints of efficacy and safety were evaluated through Week 24. **Results** A total of 132 participants were analyzed comprising two cohorts 1) PRISM3 rollover participants (n=50) and 2) direct entry participants (n=82). The PRISM3 rollover cohort included CP101 rollover participants (participants that received CP101 in PRISM3, had an on-study recurrence and enrolled in PRISM-EXT) (n=20) and placebo rollover participants (n=30). Median age was 69 years (18-95). In the direct entry group, 52% of participants entered the trial after a first CDI recurrence (Table 1). Overall, the proportion of participants with sustained clinical cure through Week 8 was 80.3%. Efficacy was maintained with a sustained clinical cure rate of 78.8% through Week 24 (Figure 1). Among the PRISM3 CP101 rollover participants, 70% (14/20) had a sustained clinical cure through Week 8, following a second dose of CP101 in PRISM-EXT. There were no treatment-related serious adverse events. **Conclusion** In PRISM-EXT, CP101 prevented recurrence of CDI through Week 8 which was sustained through Week 24 with no treatment-related serious adverse events, consistent with previously reported data from the randomized, placebo-controlled PRISM3 trial. The PRISM-EXT results also suggest that a second dose of CP101 successfully rescued a significant proportion of participants who did not respond to an initial dose of CP101.

Table 1: Clinical and demographic characteristics

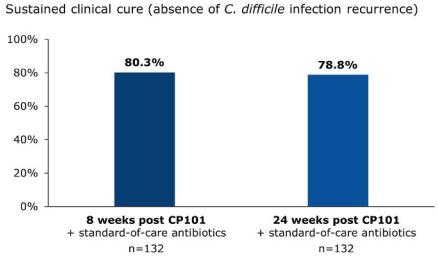
	PRISM-EXT			
	PRISM3 Rollover		Direct Entry N=82	Total N=132
	CP101 in PRISM3 N=20	Placebo in PRISM3 N=30		
Age in years - median (range)	76.5 (63-94)	71.0 (30-94)	67.0 (18-95)	69.5 (18-95)
Female sex - n (%)	17 (85%)	22 (73%)	60 (73%)	99 (75%)
Charlson comorbidity index - mean (SD)	5.3 (2.5)	3.6 (2.6)	3.0 (2.2)	3.5 (2.5)
Number of CDI episodes within the previous 6 months - n (%)				
≤ 2	1 (5%)	2 (7%)	43 (52%)	46 (35%)
≥ 3	19 (95%)	28 (93%)	39 (48%)	86 (65%)
Positive CDI laboratory test at study entry - n (%)				
PCR-based testing (alone or in combination)[1]	1 (5%)	0	46 (56%)	47 (36%)
Toxin EIA-based testing (alone or in combination)[2]	19 (95%)	30 (100%)	32 (39%)	81 (61%)
Not reported	0	0	4 (5%)	4 (3%)
Standard-of-care CDI antibiotic at study entry - n (%)				
Oral vancomycin (alone or in combination)	19 (95%)	25 (83%)	73 (89%)	117 (89%)
Oral fidaxomicin (alone or in combination)	2 (10%)	6 (20%)	16 (20%)	24 (18%)
Oral metronidazole (alone or in combination)	0	0	1 (1%)	1 (0.8%)

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

1. PCR based testing includes: PCR positive alone or in combination (e.g. GDH+/PCR+; GDH+/toxin EIA-/PCR+; PCR+/Toxin EIA-/without toxigenic culture)

2. 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+)

Figure 1: Sustained clinical cure through Week 8 and Week 24 in PRISM-EXT



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VEDOLIZUMAB INTRAVENOUS IS EFFECTIVE ACROSS MULTIPLE TREATMENT TARGETS IN CHRONIC POUCHITIS: RESULTS OF THE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED EARNEST TRIAL

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Background: Pouchitis is a common complication of ileal pouch-anal anastomosis (IPAA) after proctocolectomy in ulcerative colitis (UC). There are currently no approved therapies for chronic pouchitis. Here, we report a multicenter trial of intravenous (IV) vedolizumab (VDZ) for chronic pouchitis after IPAA in patients with UC. **Methods:** EARNEST was a randomized, double-blind, placebo (PBO)-controlled, phase 4 study of VDZ in patients aged 18-80 years with chronic pouchitis after proctocolectomy with IPAA for UC (NCT02790138). Male and female patients with a history of IPAA for UC and chronic pouchitis were eligible. Patients were randomized (1:1) to receive VDZ IV (300 mg) or PBO on Day 1 and at Weeks (W) 2, 6, 14, 22, and 30, as well as ciprofloxacin for the first 4 weeks. The primary endpoint was modified Pouchitis Disease Activity Index (mPDAI) remission at W14; efficacy was also assessed through other mPDAI/PDAI secondary endpoints and endoscopic exploratory endpoints (assessed by a central reviewer) at W14 and W34. Safety (adverse events [AEs]) was monitored throughout the study. **Results:** In total, 102 patients were treated (51 per group). Patients had a mean age of 40.8 years (VDZ) and 42.9 years (PBO). mPDAI remission rates (comprising clinical symptoms and endoscopy domains) were 31.4% (n=16/51) for VDZ vs 9.8% (n=5/51) for PBO at W14 (p=0.013; **Figure 1**). Significant differences in favor of VDZ over PBO were also seen in mPDAI remission at W34, mPDAI response at W14 and W34, and PDAI remission (comprising clinical symptoms, endoscopy, and histology domains) at W14 and W34 (**Figure 1**). The rate of sustained remission (defined as remission at both W14 and W34) was higher for VDZ vs PBO on both the mPDAI (VDZ 27.5% [n= 14/51] vs PBO 5.9% [n=3/51]; difference 21.6 percentage points [95% confidence interval (CI), 6.5-37.0]) and the PDAI (VDZ 31.4% [n=16/51] vs PBO 7.8% [4/51]; difference 23.5 percentage points [95% CI, 8.0-38.8]). Endoscopic ulceration analysis showed greater reductions in number of ulcers from baseline for VDZ over PBO at W14 and W34 (**Figure 2**). A higher proportion of patients in the VDZ vs PBO group had an improved SES-CD score and achieved SES-CD remission of pouchitis (**Figure 2**). Overall, AE rates were similar between groups and no new safety signals were identified. Treatment-related AEs were reported in 12 (23.5%) patients treated with VDZ and 11 (21.6%) patients treated with PBO. One treatment-related serious AE was reported (PBO group). **Conclusion:** This is the first and largest randomized, double-blind PBO-controlled trial of biologic therapy to show significant benefits across multiple treatment outcomes in patients with chronic pouchitis after IPAA for UC. VDZ showed consistent treatment benefits over PBO across clinical, endoscopic, and histologic endpoints, together with safety consistent with its established profile.