

# Treatment preferences in Crohn's disease perianal fistula: patient perspectives

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## Background

- Perianal fistulas (PF) are a common complication associated with Crohn's disease (CD).<sup>1,2</sup>
- Patients with Crohn's perianal fistulas (CPF) have a high treatment burden and typically undergo repeated cycles of treatments and interventions with limited success, which can negatively impact their quality of life.<sup>3</sup>
- This study assessed patient treatment experience, patient satisfaction with current CPF treatments and preferences for future treatment attributes in order to identify patient-centric attributes for consideration when assessing treatment effectiveness.

## Methods

- An observational study using a web-enabled questionnaire was conducted in US adults with CPF.
- Eligible patients were aged 21–89 years at the time of consent, with self-reported physician-diagnosed and treated CPF in the past 12 months.
- Patients diagnosed with ulcerative colitis were excluded.
- Patients were recruited via an online panel into two cohorts.
  - Cohort 1: patients with CPF who received pharmacotherapy and/or seton placement (but no PF-related surgery in the past 12 months).
  - Cohort 2: patients with CPF who had received PF-related surgery (with or without pharmacotherapy) in the past 12 months.
- The study was approved by Advarra Institutional Review Board and ethics body.

## Treatment attribute importance, patient satisfaction, treatment goals and attitudes toward current CPF treatments

- Patients rated treatment attribute importance using a 1–9 scale (1 = not at all important, 9 = extremely important).
- Patients rated their satisfaction with current CPF treatments using a 1–9 scale (1 = not at all satisfied, 9 = extremely satisfied).
- CPF intervention/treatment options included medication, short-term and long-term seton placement, endorectal/anal advancement flap, fibrin glue, anal fistula plug, fistulectomy/fistulotomy and ligation of the intersphincteric fistula tract.
- Patients were asked to rate their top three CPF treatment goals from a list.
- Patients rated their attitudes toward statements about current CPF treatments using a 1–9 scale (1 = strongly disagree, 9 = strongly agree).

## Treatment preferences

- Patient preferences for future treatment attributes were assessed using a discrete choice experiment (DCE) (Table 1).
- Treatment attributes were derived from evidence in currently available literature.<sup>4–8</sup>
- Combinations of these attributes were used to generate 14 sets of two hypothetical treatment profiles for each patient.
- Patients evaluated two treatment profiles at a time and identified their most preferred treatment of the two or selected neither.

**Table 1. Treatment attribute examples used to generate hypothetical treatment options for the discrete choice experiment to determine patient preferences.**

Attributes	Level 1	Level 2	Level 3	Level 4
Invasiveness of procedure (cutting or puncturing the skin or seton placement)	Involves cutting or puncturing and insertion of surgical instruments into the anal area	Involves minimal cutting or puncturing and an injection of the treatment into the anal area	Involves minimal puncturing and insertion of a thin silicone string into the anal area for greater than 6 months	NA
Benefits of therapy (symptom control and/or fistula closure)	39% symptom control without fistula closure	55% fistula closure	60% fistula closure	90% fistula closure
Level of discomfort experienced after procedure	Low/none	Medium	High	NA
Time required for recovery	≤ 1 week	> 1 week	NA	NA
Proportion of patients with a return of symptoms related to anal fistulas (discharge, pain, odor) after treatment	19%	21%	26%	NA
Proportion of patients who experienced fecal incontinence after treatment (beyond what they currently experience with CD)	NONE	16%	21%	NA

CD, Crohn's disease; NA, not applicable.

## Statistical analysis

- Data were summarized using descriptive statistics: Pearson's chi-squared test of independence (for proportions) and independent samples t-test (for means). Statistically significant comparisons were assessed at a significance level of 95%.
- Data collected from the DCE were analyzed using a hierarchical Bayesian model using the attribute levels as predictor variables and choice as the outcome variable. The model generated relative mean preference weights for each attribute and utility scores for each level within the attributes tested.

## Results

**Table 2. Patient demographics and clinical characteristics were broadly similar across the cohorts with and without PF-related surgery, except a greater proportion of those who had experienced surgery had severe CPF.**

Clinical characteristic	Cohort 1 (seton only ± medication) (n = 50)	Cohort 2 (PF-related surgery ± medication) (n = 50)	All CPF (n = 100)
Age, years, mean (SD)	41.1 (12.3)	38.9 (12.2)	40.0 (12.2)
Sex, female, n (%)	28 (56)	28 (56)	56 (56)
Number of unique CPF, mean (SD)	2.6 (2.3)	2.9 (2.6)	2.7 (2.4)
Disease duration since diagnosis, years, mean (SD)	8.8 (10.1)	9.5 (9.7)	9.1 (9.9)
Severe CPF (classified by a physician), n (%)	10 (20)	18 (36)	28 (28)
Complex CPF, n (%)	26 (52)	27 (54)	53 (53)
Recurrent fistula, n (%)	25 (50)	27 (54)	52 (52)

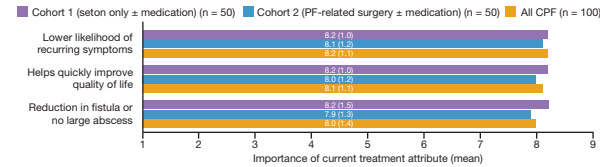
CPF, Crohn's perianal fistulas; PF, perianal fistula; SD, standard deviation.

**Table 3. Treatment experience: the majority of patients in this study had received CPF-related pharmacotherapies and procedures/surgeries or seton placement in the past 12 months.**

	Cohort 1 (seton only ± medication) (n = 50)	Cohort 2 (PF-related surgery ± medication) (n = 50)	All CPF (n = 100)
<b>PF-related procedures/surgeries in the past 12 months, n (%)</b>			
Short-term seton placement	18 (36)	12 (24)	30 (30)
Long-term seton placement	14 (28)	10 (20)	24 (24)
Endorectal/anal advancement flap	–	26 (52)	26 (52)*
Fibrin glue	–	14 (28)	14 (28)*
Anal fistula plug	–	16 (32)	16 (32)*
Fistulectomy/fistulotomy	–	29 (58)	29 (58)*
Ligation of the intersphincteric fistula tract	–	13 (26)	13 (26)*
<b>Patients who experienced PF-related procedure/surgery/seton placement in the past 12 months, n (%)</b>			
One procedure/surgery	6 (12)	18 (36)	24 (24)
Two or more procedures/surgeries	14 (28)	32 (64)	46 (46)
<b>Patients who experienced complications after PF-related procedure/surgery/seton placement, n (%)</b>			
Number of complications after PF-related procedure/surgery, mean (SD)	3.2 (2.5)	2.6 (2.0)	2.8 (2.1)
<b>Most common complications after procedure surgery, n (%)</b>			
Worsening pain/difficulty with bowel movements	10 (50)	13 (26)	23 (33)
Worsening of pain and swelling around anus	8 (40)	13 (26)	21 (30)
Fever/infection	7 (35)	13 (26)	20 (29)
<b>Any pharmacotherapy use for CPF in the past 12 months, n (%)</b>			
Any biologic use <sup>b</sup>	48 (96)	39 (78)	87 (87)
	(n = 48)	(n = 39)	(n = 87)
	43 (90)	35 (90)	78 (90)

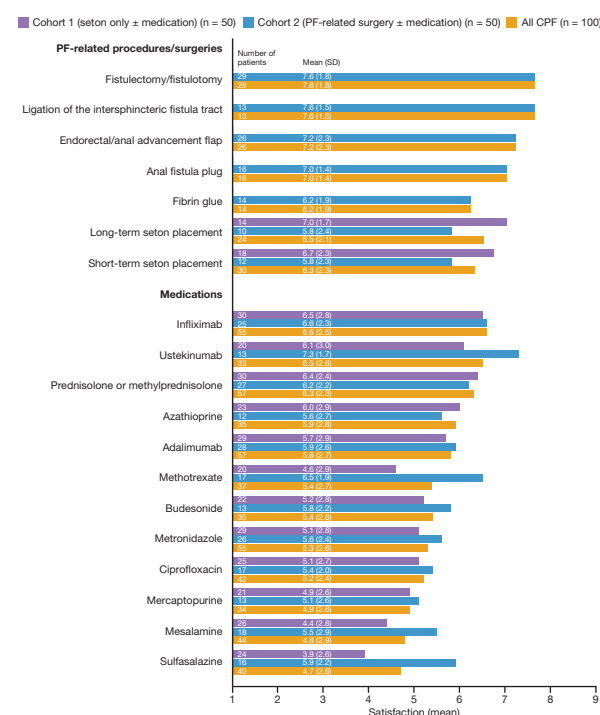
\*For surgeries, percentages are based on the total number of patients in cohort 2 (n = 50). <sup>b</sup>Biologics included: adalimumab, certolizumab, infliximab, ustekinumab and vedolizumab. CPF, Crohn's perianal fistulas; PF, perianal fistula; SD, standard deviation.

**Figure 1. The top 3 most important CPF treatment attributes were rated between 8.0 and 8.2 by all patients with CPF (on a 1–9 scale: 1 = not at all important, 9 = extremely important).**



Data in bars represent mean (standard deviation). CPF, Crohn's perianal fistulas; PF, perianal fistula.

**Figure 2. Patient satisfaction with current CPF treatments was moderate and ranged from 3.9 to 7.6 (on a 1–9 scale; 1 = not at all satisfied; 9 = extremely satisfied).**

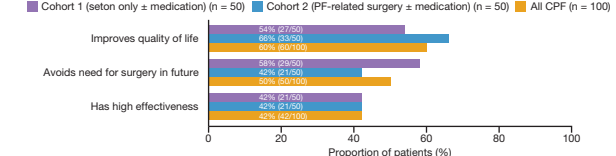


CPF, Crohn's perianal fistulas; PF, perianal fistula; SD, standard deviation.

## References

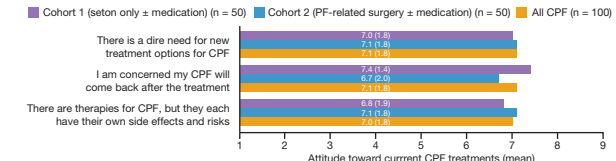
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**Figure 3. Improvement in quality of life and avoidance of future surgery were in the top three treatment goals of ≥ 50% of patients with CPF.**



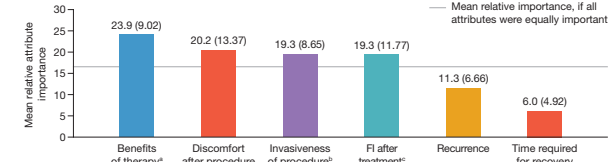
Data in bars represent proportion of patients (n/N). CPF, Crohn's perianal fistulas; PF, perianal fistula.

**Figure 4. Attitudes toward current CPF treatments indicate an unmet need for new therapies that treat CPF among the top three concerns (rated on a 1–9 scale: 1 = strongly disagree, 9 = strongly agree).**



Data in bars represent mean (standard deviation). CPF, Crohn's perianal fistulas; PF, perianal fistula.

**Figure 5. Patients with CPF considered symptom control/fistula closure rate the most important treatment attribute for future CPF treatments, followed by discomfort after procedure.**



Mean relative attribute importance is a measure of how important an attribute is when selecting a procedure for CPF, in the context of all attributes tested in the DCE design. It is presented as a normalized score summing to 100 across all attributes tested. A higher value for an attribute indicates higher importance when selecting a procedure for CPF, and a lower value indicates lower importance. Data above columns represent mean relative attribute importance (standard deviation). <sup>a</sup>Symptom control and/or fistula closure. <sup>b</sup>Cutting or puncturing the skin or seton placement. <sup>c</sup>Beyond what they currently experience with CD. <sup>d</sup>CD, Crohn's disease; CPF, Crohn's perianal fistulas; FI, fecal incontinence.

## Conclusions

- Satisfaction with current medical and surgical treatments for CPF among patients in the USA is only moderate, which highlights a need for new treatments that address the treatment attributes considered most important to patients.
- Patients most value CPF treatments that deliver symptom control, a high rate of fistula closure, low levels of discomfort and FI after treatment, and minimal invasiveness.
- Clinical development of CPF treatments should consider patient-centric attributes for clinical trial endpoints and when assessing treatment effectiveness.

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## Disclosures

Amod Athavale, Josiah Edelblut and Nandini Hadker are employees of Trinity Partners, LLC, Waltham, MA, USA. Lily Chen, Susan Cazzetta, Pradeep Nazarey, Tao Fan and Jeanne Jiang are employees of Takeda Pharmaceuticals USA, Inc., Lexington, MA, USA.