

CORRELATION BETWEEN PHYSICIAN AND PATIENT DISEASE ASSESSMENTS IN ULCERATIVE COLITIS: BASELINE DATA FROM THE ICONIC STUDY OF 1816 PATIENTS IN 33 COUNTRIES

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BACKGROUND

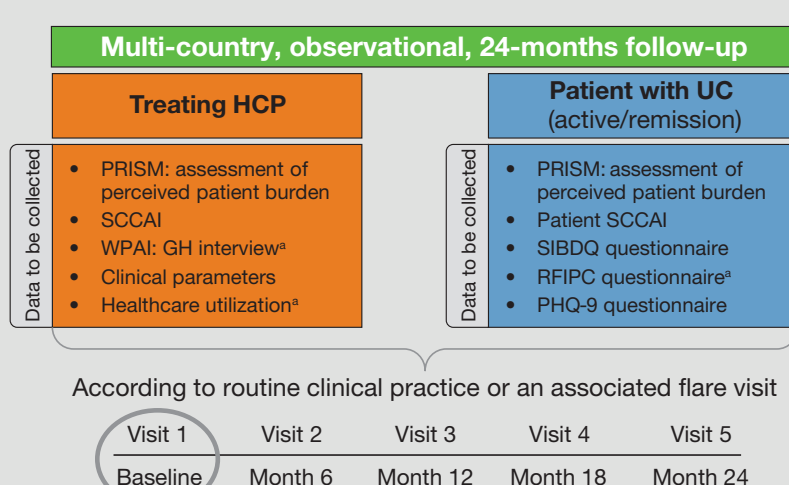
- ICONIC is the largest, ongoing, prospective, observational study aimed at assessing cumulative disease-associated burden in adult patients with ulcerative colitis (UC) under routine care
- The objective of ICONIC is to evaluate the many forms of UC-associated burden, utilizing both traditional and novel patient reported outcome measures
- In this analysis we evaluate demographics, clinical characteristics, and the extent of agreement between patients and physicians in measures of disease activity at baseline

METHODS

ICONIC STUDY DESIGN

- ICONIC is the prospective, observational study evaluating cumulative disease burden in adult patients with early UC (diagnosed ≤ 36 months) under routine care in 33 countries, irrespective of disease severity or treatment
- Both patient and physician assessments of disease activity and life impact were captured at baseline and will be captured at 6 month intervals through 2 years, as shown in **Figure 1**
 - PRISM (Pictorial Representation of Illness and Self Measure[®]) is a novel, non-verbal, graphical tool, which demonstrates current perception of disease-associated suffering and is used in ICONIC for the first time in IBD research

Figure 1. ICONIC Study Design

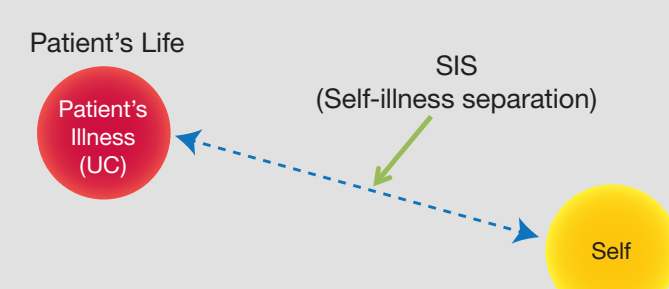


DATA ANALYSES

- The following assessments are included in this analysis:
 - Patients and physicians ratings of patients' general disease severity, PRISM, Patient Health Questionnaire-9 (PHQ-9), Short Inflammatory Bowel Disease Questionnaire (SIBDQ), Patient-modified Simple Clinical Colitis Activity Index (P-SCCAI) and physician's SCCAI

- Baseline characteristics were obtained from observed data by calculating means
- Agreement between physician assessment and patient perception of disease severity was performed by kappa statistics
- Correlation between PRISM, SIBDQ, PHQ-9, P-SCCAI and SCCAI was evaluated by Pearson correlation coefficient
 - The scale qualifies the extent of agreement as no correlation ($r/\kappa < 0.0$), slight ($r/\kappa = 0.0-0.2$), fair ($r/\kappa = 0.21-0.4$), moderate ($r/\kappa = 0.41-0.6$), high ($r/\kappa = 0.61-0.8$), and almost perfect ($r/\kappa = 0.81-1.00$)²
- Mean differences between patient and physician measures were calculated using a one-sample t-test
- PRISM assessments were performed independently by both patients and physicians, without conferring. Each placed a red disk (representing the patient's illness - UC) anywhere in the rectangle (representing the patient's life), in relation to the yellow disk, which represents the patient's self, **Figure 2**
 - The distance between red and yellow disks is measured and represents the "self-illness separation" (SIS). Smaller distances indicate worse perceived suffering

Figure 2. Pictorial Presentation of PRISM Which Illustrates the Place UC Occupies in Patient's Life at a Given Moment



RESULTS

BL CHARACTERISTICS

- Of 1816 patients enrolled, 28.3% of patients (n = 514) had symptoms for ≥ 1 year before receiving a diagnosis of UC (**Table 1**)
- Although 70.4% of patients (n = 1278) indicated their disease had improved since diagnosis, nearly half of the patients still had moderate to severe disease activity (41.8% of patients by endoscopy and 49.7% by physician assessment) (**Table 1**)
- While 94.9% of patients (n = 1724) had received treatment for their UC, 43% had partial or no response to current therapy
- The most common co-morbidities diagnosed in > 20% of patients were fatigue (27.9%), anxiety/depression (25.3%), cardiac abnormalities/cardiac disease (20.8%), and sleep disorder (20.8%)
 - Of patients clinically diagnosed with anxiety/depression (n = 459), approximately 22% were considered to have moderate to severe disease (by physician assessments)
- Of patients self-assessing depression by PHQ-9, alignment existed between this and clinical diagnosis, with 22.9% of patients reporting PHQ-9 depression severity of moderate to severe in nature (**Table 1**)
- Of note, ICONIC has a greater proportion of patients with < 1 year of disease duration (n = 1296; 71.4%) vs. 1-3 years (n = 380, 20.9%), **Table 1**. This imbalance is a result of modified inclusion criteria: originally patients with UC < 1 year were allowed to enroll, but a protocol amendment allowed enrolment of patients with disease duration of 1-3 years

Table 1. Baseline Clinical and Demographic Characteristics of Patients with UC in ICONIC

Characteristic	All Patients N = 1816
Sex (N = 1807), n (%)	
Female	833 (45.9)
Age (N = 1810), years	
Mean \pm SD	38.5 \pm 14.6
Current smoker (N = 1807), n (%)	212 (11.7)
Time since UC diagnosis, days	
Median (25% Q, 75% Q)	171 (59, 317)
Disease duration since UC diagnosis, n (%)	
0 - 6 months	873 (48.1)
6 months - 1 year	584 (32.2)
1 - 3 years	278 (15.3)
> 3 years	6 (0.3)
Missing	75 (4.1)
Duration of symptoms prior to UC diagnosis, n (%)	
< 1 year	1296 (71.4)
1 - 3 years	380 (20.9)
> 3 years	134 (7.4)
Missing	6 (0.3)
Disease severity since UC diagnosis, n (%)	
Improved	1278 (70.4)
Worsened (flare)	157 (8.6)
Remains similar	330 (18.2)
Missing	51 (2.8)
Endoscopic finding, n (%)	
Normal/Inactive	93 (5.1)
Mild	390 (21.5)
Moderate	550 (30.3)
Severe	209 (11.5)
Not available/Missing	574 (31.6)
Physician assessment of UC severity, n (%)	
Mild	672 (37.0)
Moderate	668 (36.8)
Severe	234 (12.9)
In remission	230 (12.7)
Missing	12 (0.7)
SIBDQ	
Mean \pm SD	48.4 \pm 13.2
PHQ-9	
Mean \pm SD	6.3 \pm 5.4
PHQ-9 depression severity, n (%)	
None-minimal	822 (45.3)
Mild	556 (30.6)
Moderate	256 (14.1)
Moderately severe	109 (6.0)
Severe	51 (2.8)
Missing	22 (1.2)
ELMs, n (%)	186 (10.2)
Any treatment since UC diagnosis, n (%)	1724 (94.9)
Response to current UC treatment, n (%)	
Not applicable/no current treatment	63 (3.5)
Too early to assess	187 (10.3)
Complete response	757 (41.7)
Partial response	712 (39.2)
No response	70 (3.9)
Missing	27 (1.5)

PERCEPTION OF DISEASE SEVERITY AND SUFFERING

- Both physician assessment and patient perception of disease severity were available for 1796 patients, **Table 2**
- Simple κ coefficient of 0.43 (95% CI 0.40 - 0.47), $P < 0.001$, suggested moderate agreement between physicians' assessment and patient's perception of disease severity
- Overall, patients and physicians were in agreement in 60.3% (1083/1796) of instances (green cells of **Table 2**)
 - Physicians and patients were more likely to agree on the middle range of disease severity (i.e., 22.5% concordance for both mild or moderate disease), but less likely to agree on the extremes, (i.e., 8.0% concordance for remission and 7.3% concordance for severe disease)
- Conversely, 39.7% (713/1796) of disease severity evaluations were discordant (orange cells in **Table 2**)
 - For example, when treating physicians assessed their patients were in remission, patients rated their disease as mild (n = 58), moderate (n = 22) or severe (n = 4) (**Table 2**; column Remission)

Table 2. Agreement Between Physicians' Assessment and Patients' Perception of Disease Severity in 1796 Patients at Baseline

		Disease Severity Assessed by Physician				Total, n
		Remission n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	
Disease Severity Perceived by Patients	Remission	143 (8.0)	87 (4.8)	47 (2.6)	9 (0.5)	286
	Mild	58 (3.2)	404 (22.5)	137 (7.6)	15 (0.8)	614
	Moderate	22 (1.2)	158 (8.8)	404 (22.5)	76 (4.2)	660
	Severe	4 (0.2)	21 (1.2)	79 (4.4)	132 (7.3)	236
Total, n		227	670	667	232	1796

Green - concordant pairs, orange - discordant pairs.

- Using PRISM, physicians rated the UC-associated suffering of their patients higher than patients rated themselves, **Figure 3A**
 - Mean difference \pm SD of patient-PRISM - physician PRISM = -0.4 ± 2.2 , $P < 0.0001$
- For SCCAI, patients reported higher mean scores when compared with physician assessment, **Figure 3B**
 - Mean difference \pm SD of P-SCCAI - SCCAI = 1.26 ± 2.42 , $P < 0.0001$

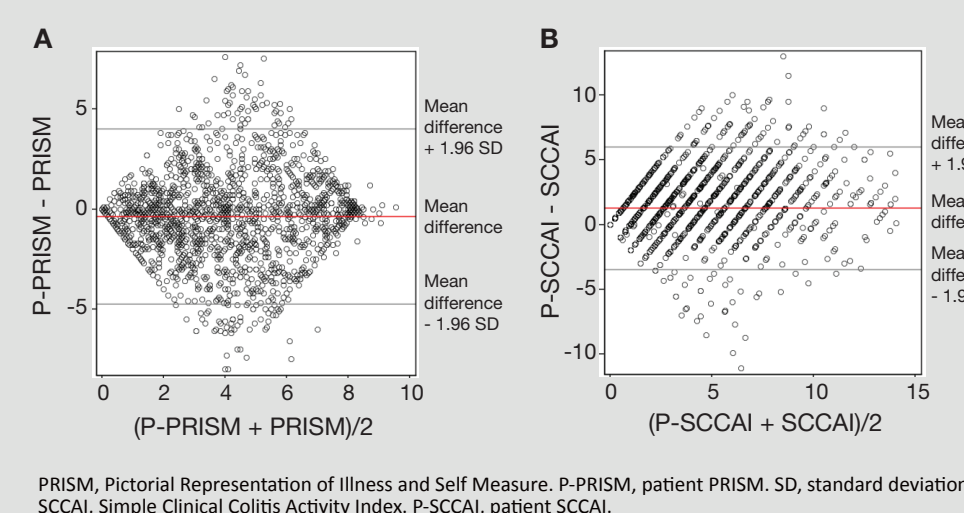
Figure 3. Bland-Altman Plots of Mean Differences Between Patient PRISM and Physician PRISM (A) and P-SCCAI and SCCAI (B)

	SIBDQ	PHQ-9 ^a	PRISM (Physician)	P-SCCAI ^a
PRISM (Patient), r (P-value)	0.5 (< 0.0001)	-0.4 (< 0.0001)	0.59 (< 0.0001)	-0.4 (< 0.0001)
SCCAI (Physician), r (P-value)	ND ^b	ND ^b	-0.44 (< 0.0001)	0.75 (< 0.0001)

^aNegative coefficients result from instruments with opposite direction of scales.
^bNot determined.

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- For SCCAI, patients reported higher mean scores when compared with physician assessment, **Figure 3B**
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Figure 3. Bland-Altman Plots of Mean Differences Between Patient PRISM and Physician PRISM (A) and P-SCCAI and SCCAI (B)



PRISM, Pictorial Representation of Illness and Self Measure. P-PRISM, patient PRISM. SD, standard deviation. SCCAI, Simple Clinical Colitis Activity Index. P-SCCAI, patient SCCAI.

CONCLUSIONS

- In this analysis of patient data in ICONIC study at baseline, the majority of patients received therapy and reported improved disease activity since diagnosis, however nearly half still have moderate-to-severely active disease
- Approximately 40% patients and physicians disagreed on the severity of their current UC disease state, indicating a communication disconnect and potential unaddressed burden linked to patient perception of their disease
- PRISM, used for the first time for patients with UC, was moderately correlated with disease-specific measures (SIBDQ and SCCAI) and a general depression assessment (PHQ-9); alignment between patients and physicians on UC-associated burden assessment may depend on the instrument used and the disease component being evaluated
- As an adjunct to standard measures of disease assessment, PRISM may serve as a valuable tool for improving patient/physician communication regarding the disease-associated suffering of patients with UC

TRANSPARENCY

AUTHOR DISCLOSURES

S Ghosh: is a steering committee member for Pfizer, Janssen, AbbVie, BMS, Celgene and receives speaker honorarium from AbbVie, Janssen, Takeda, Shield, and Falk Pharma.

L Peyrin-Biroulet: receives consulting fees from Merck, AbbVie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Therakos, Pharmacosmos, Pilege, BMS, UCB-pharma, Hospira, Celtrion, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, Pfizer, HAC-Pharma, Index Pharmaceuticals, Amgen, Sandoz, Forward Pharma GmbH, Celgene, Biogen, Lycera, Samsung Bioepis and lecture fees from Merck, AbbVie, Takeda, Janssen, Takeda, Ferring, Norgine, Tillots, Vifor, Therakos, Mitsubishi, HAC-pharma.

T Sensky: is a shareholder in Prismium, a small organization aiming at fostering the development and application of PRISM.

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C O'Shea, B Pappalardo, J Petersson are AbbVie employees and may own AbbVie stock and/or

options.

ROLE OF AUTHORS AND SPONSOR

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