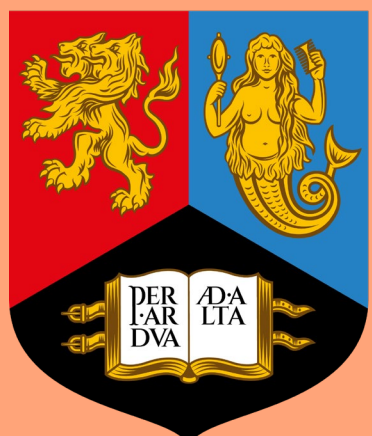


A CLINICAL GLOBAL IMPRESSION (CGI) SCALE FOR PBC: Validation of a clinical trials outcome tool



Contact information

Dr Nasir Hussain

nxh100@student.bham.ac.uk

N Hussain¹, R Smith², S Barnum³, N Abbas¹, S Al-Shakshir¹, G Carroll⁴, L Jopson⁴, J Leighton⁴, G Mells², M Christie⁵, R Mitchell-Thain⁵, A Wetton⁴, J Dyson⁶, J Neuberger¹, M Doverskog⁷, P Trivedi¹, J Jaeger³, D Jones⁶

¹ University of Birmingham, Birmingham, UK; ²Cambridge University Hospital NHS Trust, Cambridge, UK; ³CognitionMetrics LLC, Connecticut, USA; ⁴Newcastle upon Tyne NHS Foundation Trust, Newcastle, UK; ⁵PBC Foundation, Fife, UK; ⁶Newcastle University, Newcastle, UK; ⁷Umeocrine Cognition AB, Solna, Sweden

Introduction

- Primary biliary cholangitis (PBC) is a cholestatic liver disease resulting in significant symptom burden
- Regulatory drug development require clinical outcome assessments that measure clinically meaningful change, that can be used as trial endpoints
- Clinical Global Impression (CGI) scales are a clinician rated outcome measure of patients’ symptoms, used as reliable efficacy endpoints in interventional clinical trials of psycho-pharmological therapies
- The CGI-Severity (CGI-S) scale measures the clinicians impression of the severity of patients symptoms (**Table 1**) and the CGI-Change (CGI-C) scale measures any change in symptoms following an intervention (**Table 2**)

Aim

- Our aim was to develop and validate the first specific CGI-Severity scale for PBC (and indeed any liver disease)

Method

Derivation Phase

- The CGI-S scale was based on the six symptom domains of the patient-derived PBC-40
- A clinical expert panel of 13 hepatologists reviewed and developed a finalised CGI-S PBC scale following the rating of 6 patient interviews with expert discussion and review in consensus meetings

Validation Phase

- The clinical expert panel used the developed CGI-S PBC scale to rate 13 video recorded patient interviews
- Inter-rater agreement was measured, and the ratings were correlated with patients PBC-40 scores

Table 1: Clinical Global Impression-Severity (CGI-S) scale

1	2	3	4	5	6	7
Normal/ Not at all impaired	Borderline, slightly distressing/impaired	Mildly distressing/impaired	Moderately distressing/impaired	Markedly distressing/impaired	Severely impaired	Among the most extremely impaired

Table 2: Clinical Global Impression-Change (CGI-C) scale

1	2	3	4	5	6	7
Very much improved	Much improved	Minimally, but definitely and meaningfully improved	NO CHANGE or minimal but not clinically meaningful	Minimally but definitely and meaningfully worse	Much worse	Very much worse

Results

Table 3: Inter rater agreement amongst the clinical expert panel

Symptom domain	Degree of agreement (Krippendorff’s alpha)	95% confidence interval
Itch	0.93	0.92-0.95
Fatigue	0.82	0.80-0.84
Subjective cognition	0.80	0.77-0.82
Psychosocial impact	0.79	0.76-0.82
Emotional distress	0.90	0.89-0.92
Somatic symptoms	0.65	0.61-0.69
Overall rating	0.81	0.78-0.84

Table demonstrating the inter-rater agreement amongst the clinical expert panel for the CGI-S PBC ratings of 13 PBC-patient video recorded interviews. Agreement measured using the Krippendorff’s alpha: >0.80 represent a strong/high level of agreement, 0.67-0.79 is moderate agreement, and <0.69 represent weak/poor level of agreement.

Conclusions

- CGI scales are in line with regulatory guidance as efficacy endpoints for patient focussed drug development
- The CGI-S PBC is a valid and reliable rating instrument for PBC symptoms
- The CGI-S PBC can be used as a robust outcome measure for use in clinical trials of symptom directed therapies
- The CGI-S PBC and CGI-C PBC scales are currently being utilised in an interventional phase 2 trial

Figure 1: Construct validity: CGI-Severity ratings correlate with PBC-40 scores

