Validation of a health-related quality of life questionnaire in patients with recurrent *Clostridioides difficile* infection in ECOSPOR III, a Phase 3 randomized trial

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Background

- *Clostridioides difficile* infection (CDI) is the leading cause of healthcare-associated diarrhea in the US
- Debilitating symptoms of CDI often lead to long-term effects on health-related quality-of-life (HRQOL)
- Garey et al developed a CDI-specific questionnaire, the *Clostridium difficile* Quality of Life Survey, Cdiff32, to measure physical, mental, and social health domains of HRQOL

Objective

To establish the validity and responsiveness of Cdiff32 for patients with history of recurrent CDI enrolled in ECOSPOR III, regardless of treatment arm

Methods

- Exploratory analysis of data from ECOSPOR III
- Patients with 3 or more CDI episodes within 12 months were screened; 182 patients with symptom resolution were randomized and completed Cdiff32 at baseline, week 1, and week 8
- Reliability and validity were evaluated based on COSMIN guidelines
  - Structural validity was assessed with confirmatory factor analysis
  - Convergent validity compared Cdiff32 to EQ-5D
  - Known groups validity compared responses across age and recurrence status at week 1
- Responsiveness was assessed in 134 patients without CDI recurrence by week 8

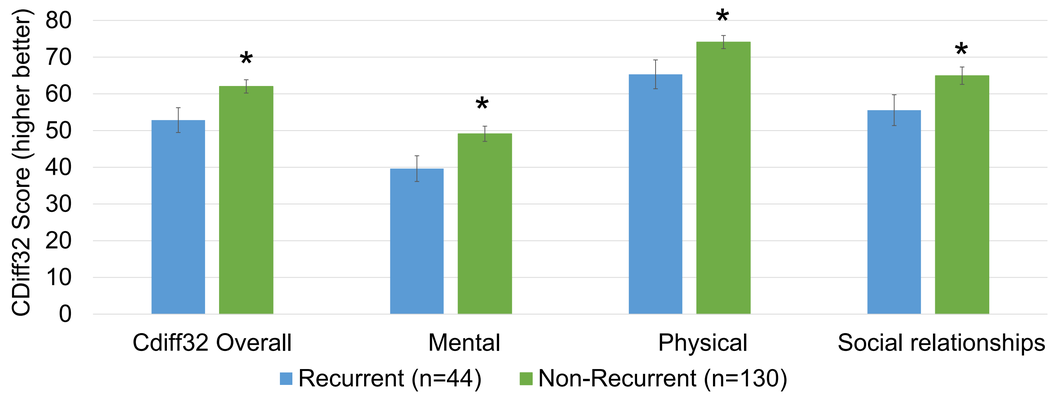
Results

Table 1. Characteristics of Study Sample, n=182

Characteristics	Statistic
Age, mean ± sd	65.5 ± 16.5
Female Sex, %	59.9%
Body Mass Index (kg/m^2), mean ± sd	26.9 ± 6.7
Non-White, %	6.6%
Patient-Reported Outcomes, mean ± sd	
Baseline Cdiff32 Total Score	52.4 ± 18.4
Baseline EQ-5D Index	0.767 ± 0.175

- Structural validity was established with a 3-factor model fitting the data well (domains of mental, physical, and social relationships)
- High internal reliability with overall Cronbach's alpha = 0.94
- Convergent validity evidenced by significant correlations between similar Cdiff32 and EQ-5D domains (Pearson correlation coefficient ranged from 0.27-0.44, p<0.05 for all)

Figure 1. Known Groups Validity: Cdiff32 scores by week 1 recurrence status



*p<0.05; n=8 patients did not complete Cdiff32 at 1 week. Vertical lines represent standard errors.

- Cdiff32 overall score and domain scores able to distinguish between age groups and recurrence status at week 1 (Figure 1)
- Internal responsiveness established for 134 patients without episodes of recurrent CDI from baseline to week 8: significant improvement across all domains (p<0.001 for all)

Conclusions

- In our exploratory analysis, Cdiff32 questionnaire demonstrated validity, reliability and responsiveness to measure and compare HRQOL for patients with recurrent CDI
- Cdiff32 differentiated recurrent from non-recurrent patients and identified significant improvements after 8 weeks in patients without recurrence
- Minimal important differences in Cdiff32 can be approximated as 10 points
- Our findings highlight the negative impact of CDI on HRQOL, particularly mental health, and support the use of Cdiff32 in trials of patients with recurrent CDI

Summary

- In a secondary analysis of 182 outpatients included in a Phase 3 clinical trial, reliability, validity, and responsiveness of a 32-item disease-specific questionnaire (Cdiff32) was established for patients with recurrent *Clostridioides difficile* infection

Funding

This work was supported by Seres Therapeutics.

References

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