

# THE IMPACT OF INVESTIGATIONAL PURIFIED MICROBIOME THERAPEUTIC SER-109 ON HEALTH-RELATED QUALITY OF LIFE (HRQoL) OF PATIENTS WITH RECURRENT CLOSTRIDIODES DIFFICILE INFECTION (rCDI) in ECOSPOR-III, A PLACEBO-CONTROLLED CLINICAL TRIAL

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## Disclosures

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- Dr. Garey has received research grants from Seres Therapeutics paid to the University of Houston

# Background

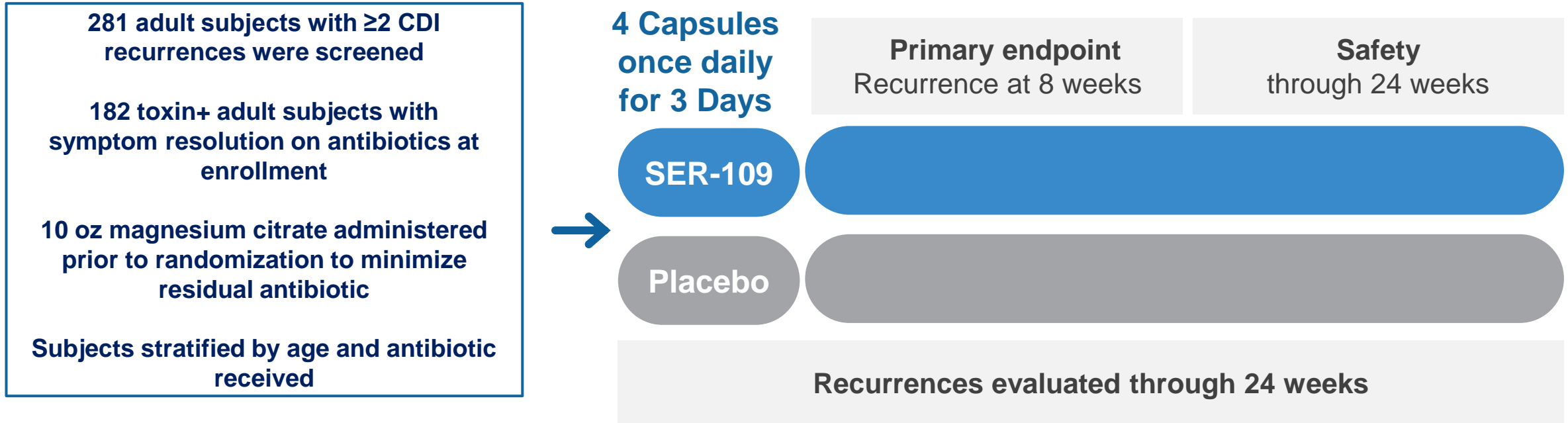
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- *Clostridioides difficile* infection (CDI) and especially recurrent CDI has been shown to have a significant impact on patient's physical, psychological, social, professional and financial status.<sup>1</sup>
- SER-109, an investigational oral microbiome therapeutic of purified bacterial spores, was designed to reduce CDI recurrence.
  - ECOSPOR-III, a Phase 3, double-blind, randomized trial, demonstrated the superiority of SER-109 compared to placebo in the reduction of rates of CDI recurrence at Week 8, the primary endpoint.<sup>2</sup> The observed safety profile of SER-109 was comparable to placebo.<sup>3</sup>
  - However, whether SER-109 also improves health-related quality of life (HRQoL) is unknown.
- HRQoL was an exploratory endpoint in the ECOSPOR-III trial.
- Herein, we present a preliminary analysis of these data.

<sup>1</sup>Lurienne L et al. J Pat Rep Outcomes 2020;4:14. <sup>2</sup>Berenson et al. SHM Annual Meeting 2021. Abstract #974338. <sup>3</sup>Korman L et al. Gastroenterology 2021;6:S-368.

# ECOSPOR-III

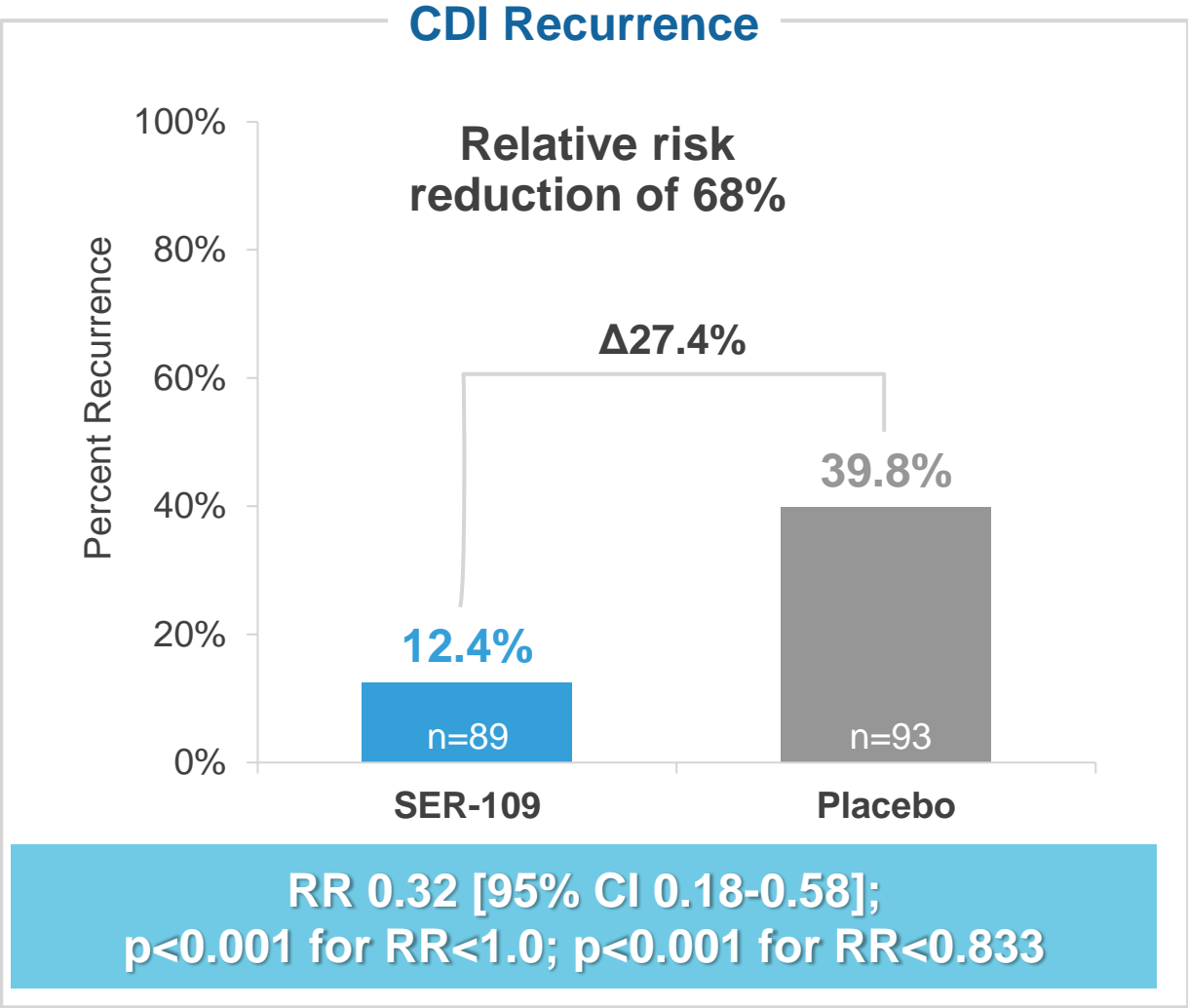
## Phase 3 Double-blind, Placebo-Controlled Trial of SER-109 for Multiply rCDI



### Adult Study Participants $\geq 18$ Years

- Toxin testing required at study entry and at suspected recurrence to ensure enrollment of patients with active disease and accurate assessment of endpoint
- All subjects had acute infection
- No chronic suppressive antibiotics allowed

# SER-109 was Superior to Placebo in Reducing CDI Recurrence at Week 8



- SER-109 met the primary endpoint of superiority compared to placebo
- The number needed to treat (NNT) for SER-109 is 3.6

## Objective

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- To evaluate the impact of SER-109 versus placebo on HRQoL using a disease-specific measure, Cdiff32.<sup>4</sup>

<sup>4</sup>Garey KW et al. J Clin Gastroenterol 2016;50:631–37.

# EQ-5D-5L and CDiff32 HRQoL Measures

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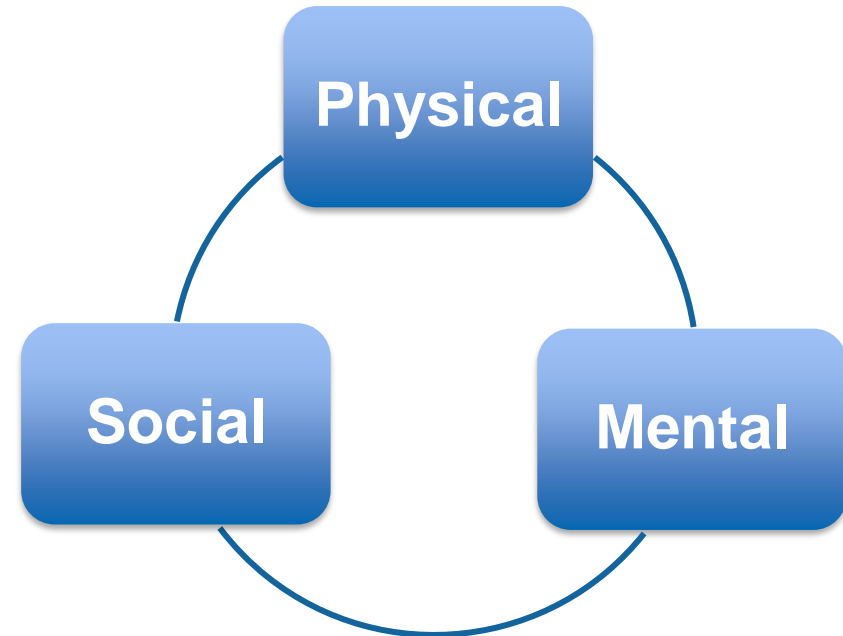
**EQ-5D-5L is a general measure used across a wide population of respondents**

- Measures 5 health domains
- Used for Baseline Evaluation



**CDiff32 is a disease-specific measure which includes content applicable to CDI patients**

- Measures 3 health domains
- Primary Outcome Measure



# EQ-5D-5L and CDiff32 HRQoL Measures

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## EQ-5D-5L Anxiety/Depression Questions

- I am not anxious or depressed
- I am slightly anxious or depressed
- I am moderately anxious or depressed
- I am severely anxious or depressed
- I am extremely anxious or depressed

## CDiff32 Mental Questions

### Anxiety – Current

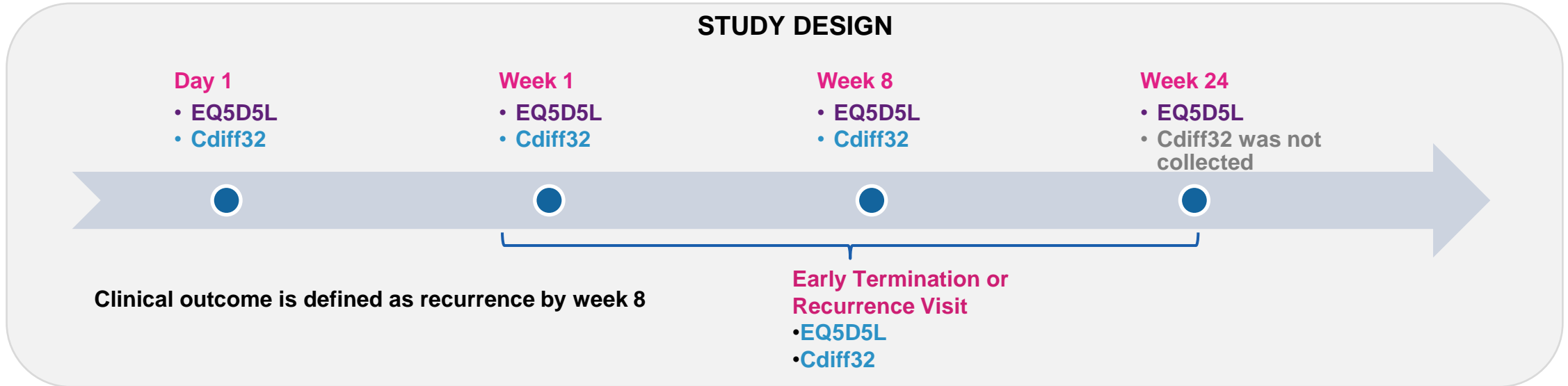
- I feel that my health is more delicate than other people's
- Despite my C Diff infection, I can live a normal life
- I feel that I am not in control of my C diff infection

### Anxiety – Future

- Are you afraid that the next time you'll need antibiotics, your C diff infection will appear again?
- Have you been worried about not knowing when the next diarrhea would arise?



# HRQoL Exploratory Endpoint: By Treatment Group and Clinical Outcome



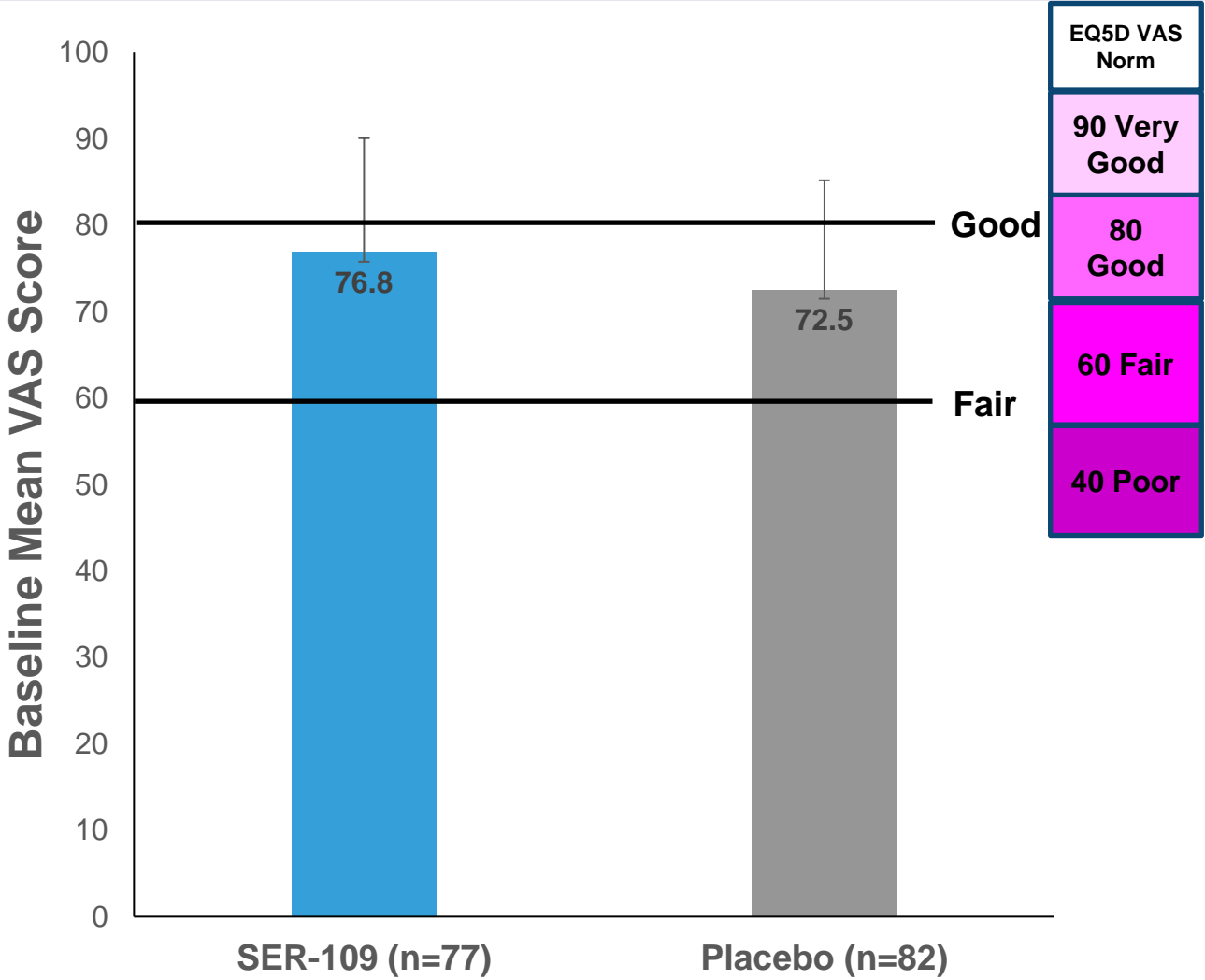
- Changes from baseline were assessed between SER-109 and placebo and by clinical outcome (recurrence vs. nonrecurrence) in the ITT population and within each treatment arm
- The between treatment group comparison analysis controlled for age, gender, prior antibiotics, and number of prior CDI episodes

## Baseline Demographics (ITT Population)

Characteristic	SER-109 (N = 89)	Placebo (N = 93)
<b>Age (yrs), mean (SD)</b>	65.6 (16.5)	65.5 (16.7)
< 65 years, n (%)	41 (46.1)	38 (40.9)
≥ 65 years, n (%)	48 (53.9)	55 (59.1)
<b>Sex, n (%)</b>		
Female*	60 (67.4)	49 (52.7)
<b>Prior antibiotic, n (%)</b>		
Vancomycin	64 (71.9)	69 (74.2)
<b># prior CDI episodes, n (%)</b>		
2	49 (55.1)	61 (65.6)
≥3	39 (43.8)	32 (34.4)
Missing	1 (1.1)	0 (0.0)
<b>N = Population size; n = Number of Subjects.</b>		

\*More females were in the SER-109 than the placebo arm (p=0.0427)

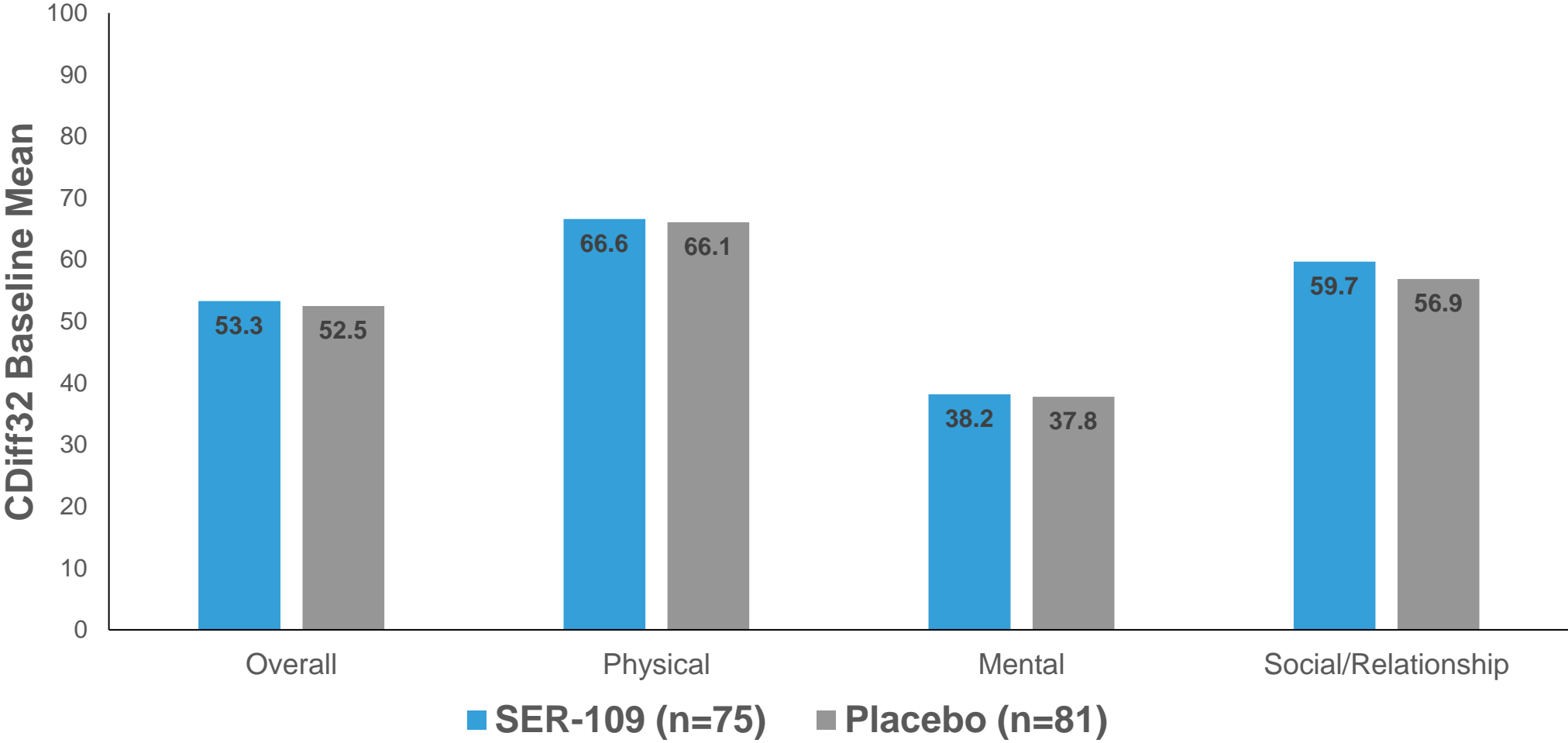
# At Baseline, ECOSPOR-III Patients' General Health Status is Between Good and Fair Compared to the EQ-5D-5L VAS Norm



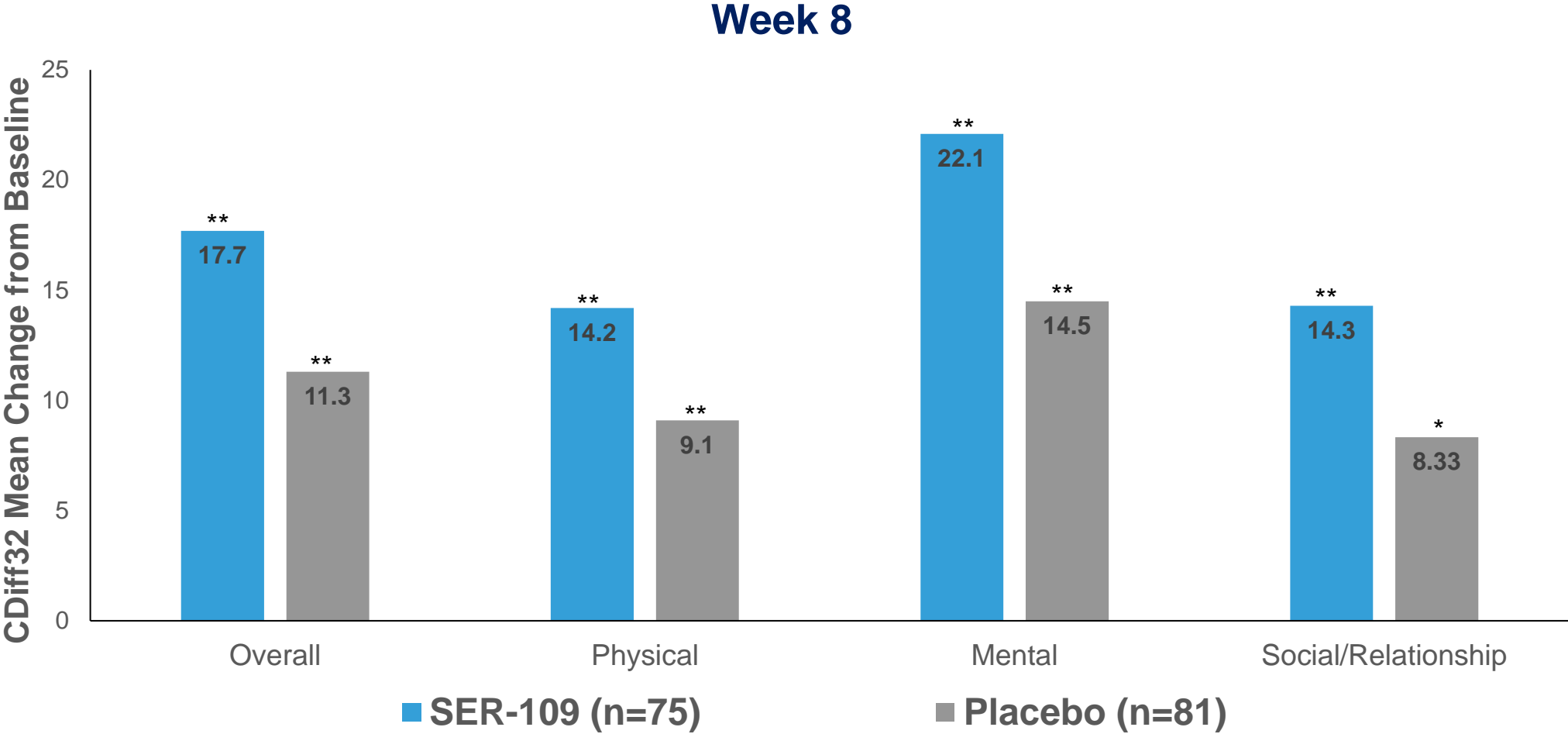
- We analyzed 159 HRQoL surveys in this preliminary analysis
- EQ-5D-5L VAS Norm is defined by the health of the general population and allows for benchmarking of HRQoL status of patients in ECOSPOR-III vs. the general healthy population<sup>5</sup>
- As expected, no differences were observed between groups at follow-up due to the lack of sensitivity of a general HRQoL measure

<sup>5</sup>Jiang R et al. Qual Life Res 2021;30:803-816.

# HRQoL Measured at Baseline With CDiff32 Was Comparable in Patients Treated with SER-109 or Placebo

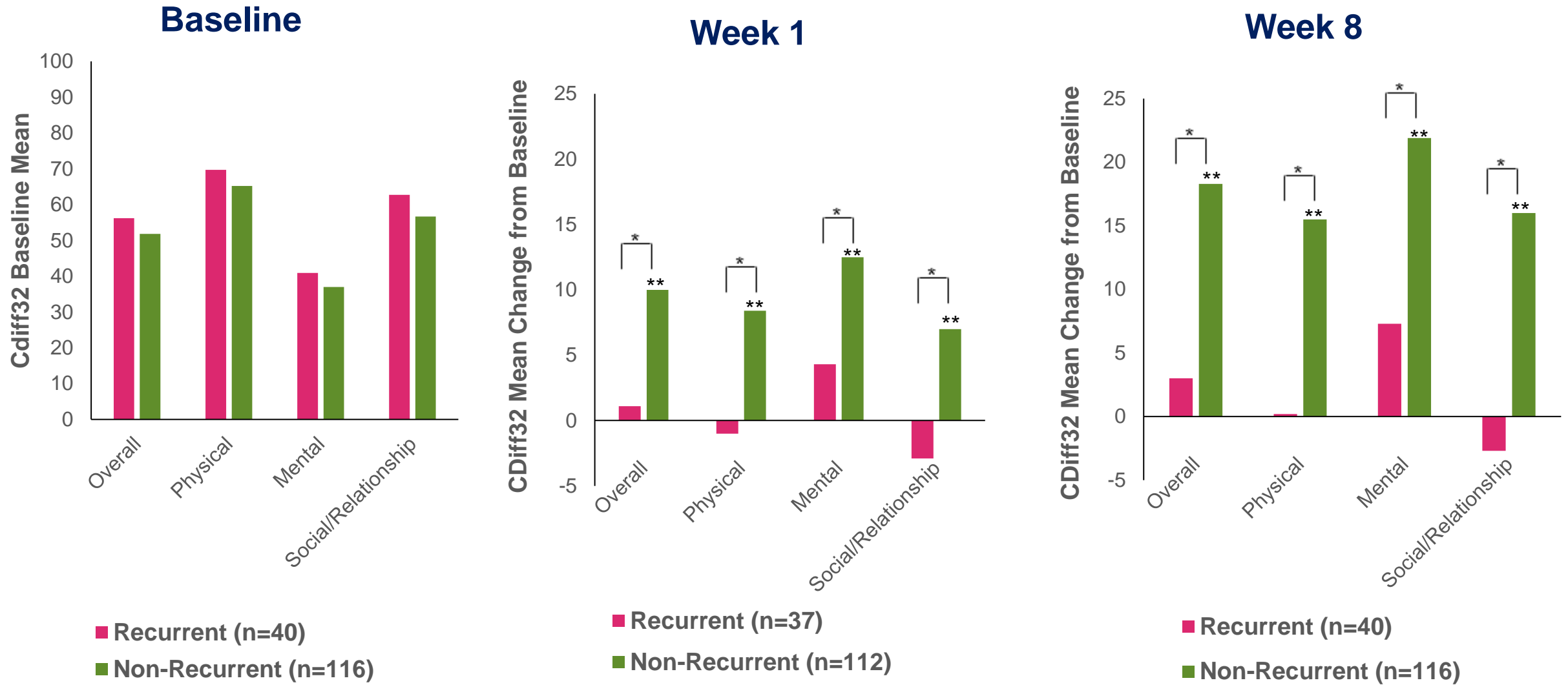


# Regardless of Treatment Group, All Patients Achieved Significant Improvement from Baseline on All CDiff32 Domains by Week 8 With a Greater Magnitude of Change Observed in the SER-109 Group



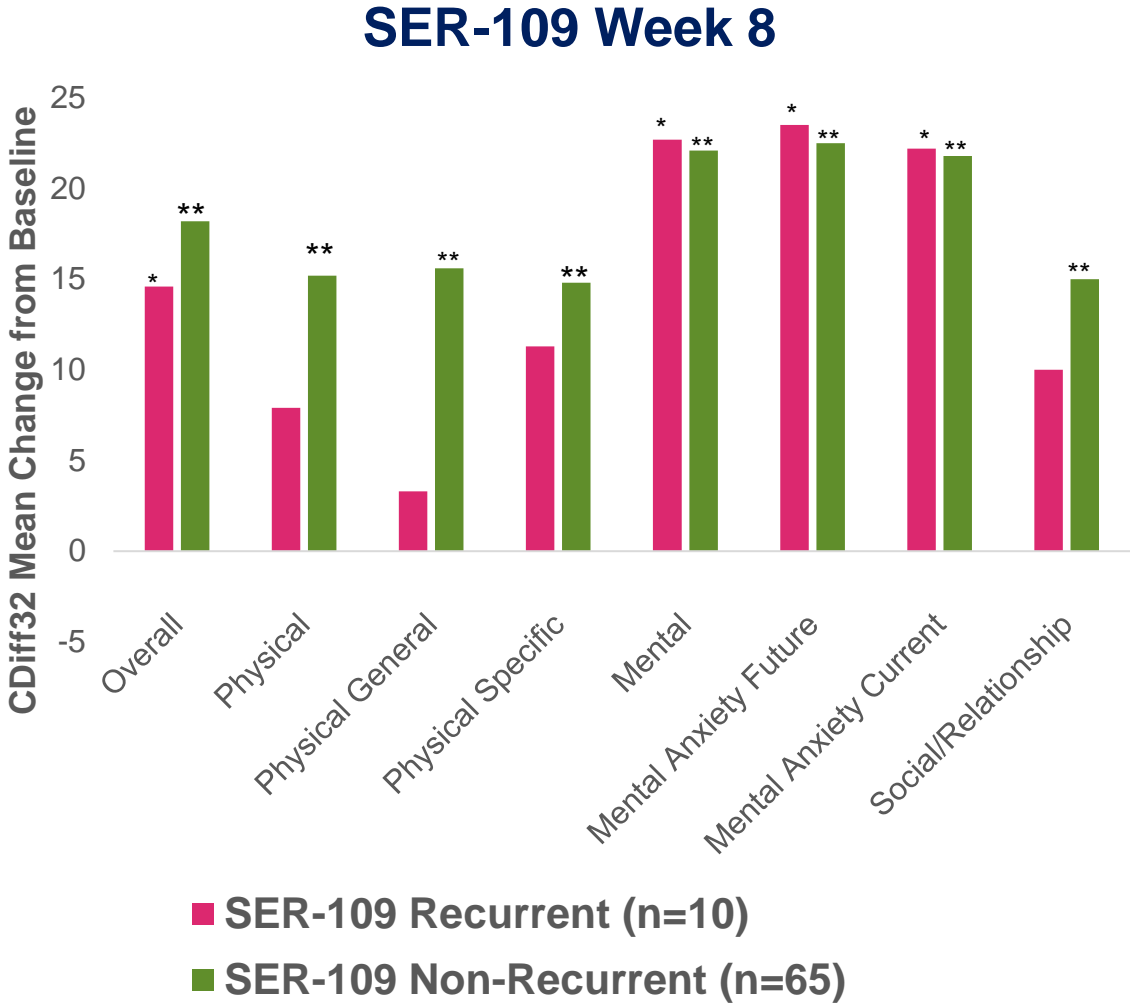
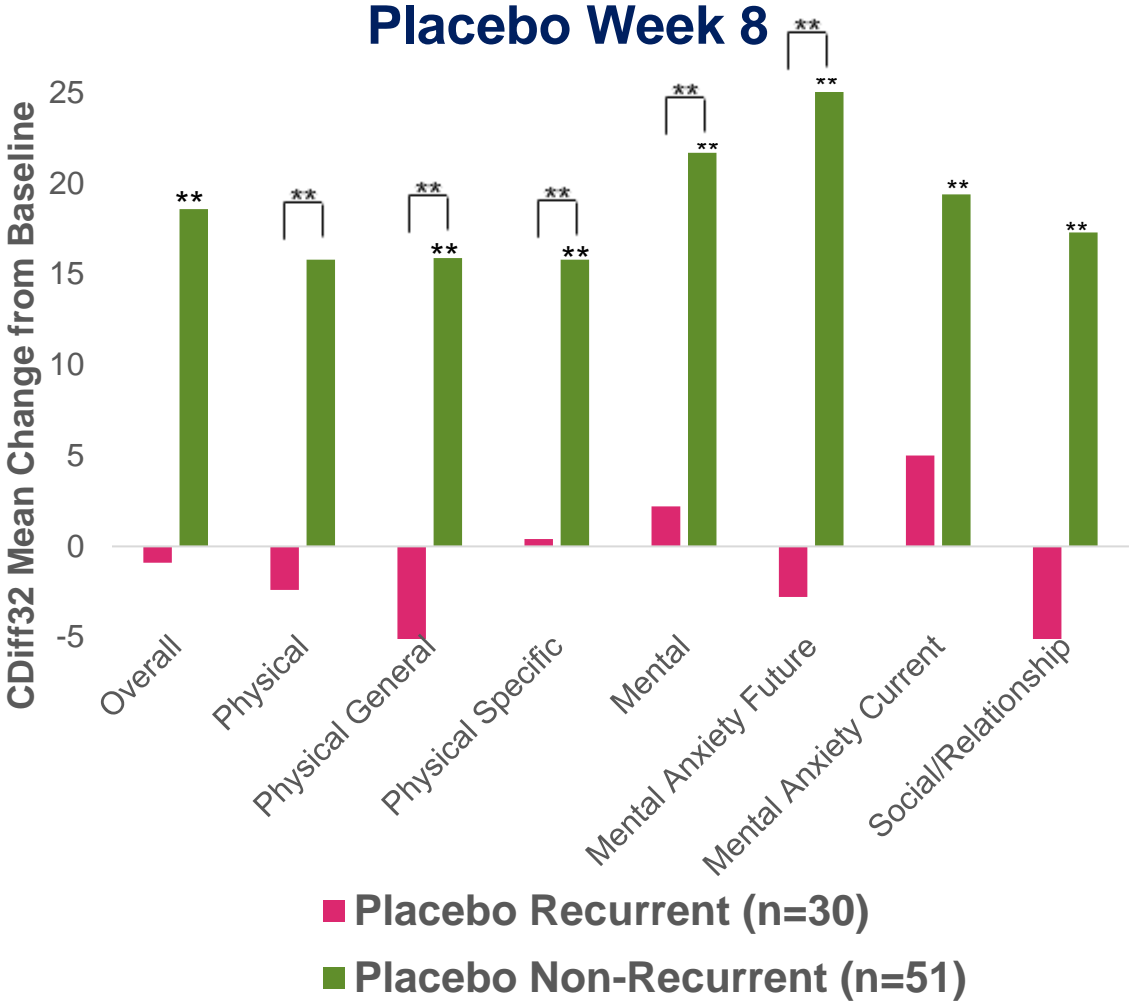
\*p<0.05    \*\*p<0.001

# Regardless of Treatment Group, Non-Recurrent Patients Had Significant Improvements in All CDiff32 Domains Compared with Recurrent Patients



\*p<0.05    \*\*p<0.001    [ ] between group comparison

# HRQoL in SER-109 and Placebo Patients By Clinical Outcome at Week 8



\* p<0.05    \*\* p<0.001      between group comparison

Caution due to small number of patients with recurrence

## Conclusions

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- Significant disease-specific HRQoL improvements were associated with CDI nonrecurrence, which highlights the negative impact of rCDI.
- SER-109 was associated with improved overall and mental health scores compared to baseline regardless of clinical outcome as measured by CDiff32.
- In light of emerging data on the potential impact of the gut microbiome on neurologic diseases, future studies should evaluate whether SER-109 may provide mood and anxiety enhancing properties through modulation of the gut-brain axis.



# References

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1. Lurienne L, Bandinelli PA, Galvain T, et al. Perception of Quality of Life in People Experiencing or Having Experienced a *Clostridioides difficile* infection: a US Population Survey. *J Pat Rep Outcomes* 2020;4:14.
2. Berenson C, Korman L, Kraft C, et al. ECOSPOR-III: A Phase 3 double-blind, placebo-controlled randomized trial of SER-109 an investigational microbiome therapeutic for treatment of recurrent *Clostridioides difficile* infection. Presented at Society of Hospital Medicine; May 3-7, 2021. Plenary session.
3. Korman L, Lashner B, Kraft C, et al. 24-week efficacy and safety data from ECOSPOR-III, a phase 3 double-blind, placebo-controlled randomized trial of ser-109, an investigational microbiome therapeutic for treatment of recurrent *Clostridioides difficile* infection. *Gastroenterology* 2021;6:S-368.
4. Garey KW, Aitken SL, Gschwind L, et al. Development and validation of a *Clostridium difficile* health-related quality-of-life questionnaire. *J Clin Gastroenterol* 2016;50:631–37.
5. Jiang R, Janssen MFB, Pickard AS. US population norms for the EQ-5D-5L and comparison of norms from face-to-face and online samples. *Qual Life Res* 2021;30:803-816.

## Acknowledgements

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